



Omni Amelia
Island Plantation
Resort



Amelia Island, FL



March 7-12, 2020

North American Neuro-Ophthalmology Society

1975-2020





North American Neuro-Ophthalmology Society

46th Annual Meeting

March 7 – March 12, 2020

Omni Amelia Island Plantation Resort • Amelia Island, FL

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North American Neuro-Ophthalmology Society

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MISSION STATEMENT

The North American Neuro-Ophthalmology Society (NANOS) is dedicated to the achievement of excellence in patient care through the support and promotion of education, communication, research, and the practice of neuro-ophthalmology.

TARGET AUDIENCE

Neurologists, Ophthalmologists, Neuro-Ophthalmologists, physicians and other health care professionals who have a special interest in Neuro-Ophthalmology, or have fellowship training in Neuro-Ophthalmology and are members of the North American Neuro-Ophthalmology Society.

POLICY ON COMMERCIAL SUPPORT AND FACULTY DISCLOSURE

The North American Neuro-Ophthalmology Society maintains a policy on the use of commercial support which ensures that all educational activities sponsored by NANOS provide in-depth presentations that are fair, independent, and scientifically rigorous. To this end, all speakers and planners are required to complete a “Disclosure Form.” This information is included in this syllabus and/or may be supplemented by announcements by moderators.

DISCLOSURE OF UNLABELED/UNAPPROVED USES

This educational program may include references to the use of products for indications not approved by the FDA. Areas of unapproved uses will be disclosed at each presentation. Opinions expressed with regard to unapproved uses of products are solely those of the faculty and are not endorsed by the North American Neuro-Ophthalmology Society or any other manufacturers of pharmaceuticals.

ACCREDITATION

The North American Neuro-Ophthalmology Society is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

CREDIT DESIGNATION

NANOS designates this live activity for a maximum of 32.75 AMA PR Category 1 Credits. Physicians should claim only the credit commensurate with the extent of their participation.



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NANOS CME MISSION STATEMENT

The North American Neuro-Ophthalmology Society (NANOS) is dedicated to achieving excellence in care of patients with neuro-ophthalmic diseases by the support and promotion of education, research, and the practice of neuro-ophthalmology.

The Society's main CME activity is its annual scientific meeting. The educational meeting includes seminars, workshops, hands-on training, platform presentations, and discussion of cases and best practices in neuro-ophthalmic research, basic science, and patient care.

The CME goal of the meeting is to improve the attendees' knowledge of neuro-ophthalmology basic science and practice. More specifically, the goals of the meeting are:

1) To achieve competence in neuro-ophthalmic diagnosis, treatment, and teaching; 2) To improve performance as physicians, teachers, and researchers by using information presented at the meeting to change clinical practice and instruction; and 3) To review research projects to investigate questions raised by the meeting's scientific sessions.

The expected results of our CME program, and of our annual meeting as its main CME activity, is that our members will increase their knowledge of neuro-ophthalmology and improve their skill in its practice, so that they can apply that knowledge and skill to enhance their performance and competence as clinical neuro-ophthalmologists, research neuro-ophthalmologists, and teachers of neuro-ophthalmology.

NANOS uses multiple data sources to measure the impact of its educational activities on learners and on the discipline of neuro-ophthalmology. These sources translate professionals' need into current practices to improve competence in knowledge, diagnosis, performance, and treatment of neuro-ophthalmic diseases.

Approved by the NANOS CME Subcommittee and NANOS Board of Directors as of 2017

NANOS would like to thank the following individuals for their generous donations:
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- Kimberly Winges
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- John Charley, MD (*In honor of Preston Calvert, MD*)
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It is the policy of the North American Neuro-Ophthalmology Society (NANOS) in accordance with the Accreditation Council for Continuing Medical Education (ACCME) to ensure independence, balanced view of therapeutic options, objectivity, scientific rigor, and integrity in all of its continuing education activities.

Anyone engaged in content development, planning, or presenting must disclose any relevant financial relationships. The ACCME defines relevant financial relationships as those in which an individual (including the individual's spouse/partner) in the last 12 months: 1) has had a personal financial relationship in any amount with a commercial interest. A commercial interest is any entity producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients; and who 2) also has the opportunity to affect the content of CME activity about the products or services of that commercial interest.

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The next three pages list the relevant financial disclosures for the faculty and planners.

Please note that platform presenter disclosure information is listed in the syllabus at the end of each abstract.

First Name	Last Name	Designations	Commercial Interest	What was received	For what Role
Valerie	Biousse	MD (P)	GenSight Biologics	Consulting fee	Consultant
			NeuroPhoenix	Consulting fee	Consultant
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			Alcon Laboratories	Honoraria	Advisory Committee
			Allergan NZ	Honoraria	Advisory Committee
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			Travase Lloyd Erickson Saalfeld, Shad P.A. Law Firm	Consultation Fee	Medical Legal Consultation
			Ekblom & Partners, LLP	Consultation Fee	Medical Legal Consultation
Larry	Frohman	MD (P)	Quark grant	Grant contract	Site PI
Steven	Galetta	MD (F)	Biogen	Honorarium	Consultant
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			Argenx	Consulting Fee	Consulting
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			Synaptive Medical	Consulting fees/travel expense	Consultant
			Medtronic	Medical Advisory Board	Travel Expense
			KLS Martin	Royalties	Consultant
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			Airmed Precision Instruments, LLC	Ownership interest	Management position
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			Springer	Royalties	Author
			Uptodate	Royalties	Author
			Vindico	Honorarium	Panel, author
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Key: P = Planner; F = Faculty

All other faculty and planners have declared that they have no relevant financial disclosures.

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Susan	Mollan	MBChB, FRCOphth (F)	Allergan	Honorarium	Speaker
			Roche	Honorarium	Advisory board and speaker
			Chugai Pharma UK Limited	Honorarium	Advisory board and speaker
			Heidelberg Engineering	Honorarium	Speaker
			Neurodiem	Honorarium	Consulting fees
			Santhera	Honorarium	Advisory board and speaker
			Santen	Honorarium	Speaker
			Janssen	Honorarium	Advisory board
			Novartis	Honorarium	Speaker
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			Springer	Personal payment	Educational article
			Legal firms	Personal payment	Record review
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			Regenera	Research Support	Site Principal Investigator
			Sanofi Genzyme	Honorarium	Speaker
Nancy J.	Newman	MD (F, P)	GenSight	Consulting fees, research support	Consultant, PI
			Santhera	Consultant fees research support	Consultant, PI
			Stealth	Consultant fees	Consultant
Joseph	Rizzo	MD (F)	Bionic Eye Technologies	Equity; shared patents	Founder; researcher
Janet	Rucker	MD (P)	Sun Pharma in India	Honorarium and travel expenses for CME Neuro-ophthalmology course in India. Course funded by unrestricted educational grants	Speaker
Aseem	Sharma	MD (F)	Correlative Enhancement LLC	Equity	Founder

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			Allergan	Consulting fees	Advisory committees
			Invex Therapeutics	Salary and stock options	Director of company
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Kimberly	Winges	MD (F)	Horizon Therapeutics	Honorarium	Advisory Board
Patrick	Yu-Wai-Man	MD, PHD (F)	GenSight Biologics	Honorarium	Consultant
			Santhera Pharmaceuticals	Honorarium	Speaker

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Saturday, March 7

8:00 am – 12:00 pm

NANOS Board Meeting

Talbot

2:00 pm – 7:30 pm

Registration/Help Desk

Amelia Foyer

3:00 pm – 4:30 pm

Neuro-Radiology Symposium [1.5 CME]

Amelia Ballroom

Manu S. Goyal, MD, MSc, Laurie A. Loevner, MD, and Aseem Sharma, MD

This neuroradiology session is designed to provide participants with education and information regarding (1) the imaging appearance and evaluation of cranial nerve anatomy and pathology, (2) identification and selection of imaging modalities and sequences within those modalities and (3) the imaging appearance and evaluation of intracranial venous diseases including those involving the cavernous sinuses.

Upon completion of this session, participants should be able to: (1) review imaging anatomy of the oculomotor cranial nerves (CN III, IV, and VI) from their brainstem origin through the cavernous sinuses and parasellar spaces, and into the orbits, (2) discuss the imaging appearance and evaluation of certain cranial nerve involving pathologies, (3) review common, uncommon, and novel CT and MRI based sequences used in neuro-ophthalmology, (4) discuss the imaging modalities and sequences used to evaluate for intracranial venous diseases, in particular thrombosis and arteriovenous fistulae and (5) discuss the imaging appearance of intracranial venous thrombosis and arteriovenous fistulae.

6:00 pm – 7:30 pm

Opening Reception

Magnolia Garden

All are welcome! Light hors d'oeuvres provided.

Sunday, March 8

6:30 am – 7:30 am

Breakfast

Magnolia Ballroom

6:30 am – 5:30 pm

Registration/Help Desk

Amelia Foyer

7:30 am – 9:30 am

Frank B. Walsh (I) [1.75 CME]

Amelia Ballroom

Moderators: Sophia Chung, MD and Leanne Stunkel, MD

This session is designed to present a wide variety of neuro-ophthalmic cases to an audience of physicians with varying neuroscience backgrounds who have a common intellectual interest in the broad range of conditions that impact the human visual pathways and ocular motor systems.

The format is a clinicopathologic conference. Clinical cases will be presented by neuro-ophthalmologists with comments by a neuroradiologist, neuropathologist and other selected experts. Neuroimaging, laboratory and surgical pathology data will help illustrate clinical point. Cases will be discussed from

clinical, anatomic, radiologic and pathologic aspects with emphasis on diagnosis, pathophysiology and management. Audience participation is encouraged.

Upon completion of this session, participants should be able to: 1) recognize the varied presentations of neuro-ophthalmic disease, 2) correlate the anatomic localization and histopathologic appearance with the clinical presentations, 3) use radiologic procedures in diagnosis effectively, 4) recognize both the value and limitations of neuropathology, and 5) discuss newly described diseases and their connection to neuro-ophthalmology.

7:30 am – 7:45 am	Welcome/Introduction	
7:45 am – 8:05 am	A Myel-In, a Long Way to Go <i>Aishwarya V. Pareek, MD</i>	
8:05 am – 8:25 am	From Brainstem to Stern <i>Neena R. Cherayil, MD</i>	
8:25 am – 8:45 am	Are We "Tilting at Windmills"? <i>Michael Vaphiades, DO</i>	
8:45 am – 9:05 am	Objects Jumping, Body Bumping, Hearing Slumping.... Quick, He is Crumping <i>Jorge C. Kattah, MD</i>	
9:05 am – 9:25 am	Look in The Back <i>Tatiana K. Deveney, MD</i>	
9:25 am – 9:30 am	Wrap-Up	
9:30 am – 10:00 am	Coffee Break	Magnolia Ballroom
10:00 am – 12:00 pm	Frank B. Walsh (II) [1.75 CME]	Amelia Ballroom
	<i>Moderators: Nathan Kung, MD and Gregory Van Stavern, MD</i>	
10:00 am – 10:20 am	Not All Men with Thick Skulls Have High Testosterone	
	<i>Yosbelkys Martin Paez, MD</i>	
10:20 am – 10:40 am	You're Too Young for That! <i>Sravanthi Vegunta, MD</i>	
10:40 am – 11:00 am	Tumefactive MS <i>Anthony J. Brune III, DO</i>	
11:00 am – 11:20 am	Tissue Is the Issue <i>Christine Greer, MD, MS</i>	
11:20 am – 11:40 am	Well Here Is Another Uveo-Meningeal Syndrome You Might Muck Up <i>David DeLeon</i>	
11:40 am – 11:45 am	Morning Wrap-Up	
12:00 pm – 12:20 pm	Lunch	Magnolia Ballroom
12:00 pm – 12:30 pm	International Relations Committee Meeting	Ossabaw A
12:00 pm – 1:30 pm	Fellowship Directors Committee Meeting	Talbot
12:20 pm – 2:20 pm	Poster Session I: Clinical Highlights	Magnolia Ballroom
12:20 pm – 1:20 pm	Odd Numbered Posters	
1:20 pm – 2:20 pm	Even Numbered Posters	
2:20 pm – 3:00 pm	Business Meeting	Amelia Ballroom
	NANOS's Strategic Plan will be presented. All NANOS members are encouraged to attend.	
3:00 pm – 5:15 pm	Frank B. Walsh (III) [2.25 CME]	Amelia Ballroom
	<i>Moderators: Sangeeta Khanna, MD and Collin McClelland, MD</i>	
3:00 pm – 3:20 pm	A Par 3 Macular Hole? <i>Archana Srinivasan, MBBS, MD</i>	
3:20 pm – 3:40 pm	Smoke Gets In Your Eyes <i>Tatiana Bakaeva, MD, PhD</i>	
3:40 pm – 4:00 pm	Undiscovered Islands - So Close, Yet So Far <i>Magdalena Wirth, MD</i>	

4:00 pm – 4:20 pm	Bones of the Past <i>Bart K. Chwalisz, MD</i>	
4:20 pm – 4:40 pm	Close Encounters of The Third Kind <i>Trishal Jeeval-Patel, MD</i>	
4:40 pm – 5:00 pm	Oh Oh Oh It's Magic, You Know...Never Believe It's Not So! <i>Zeeshan Haq, MD</i>	
5:00 pm – 5:15 pm	Closing Remarks	
5:30 pm – 6:00 pm	Walsh Committee Meeting	Ossabaw B
5:45 pm – 6:45 pm	Members-in-Training Reception (This reception is for Students, Residents, Fellows-in-Training, NANOS Board of Directors members, Fellowship Directors, Student Clerkship, and Neurology and Ophthalmology Residency Directors.)	Magnolia Foyer

New this year! All fellowship directors with availability and applicants or potential applicants looking for a fellowship are invited to participate in fellowship “speed dating.” If you have a vacancy during these fellowship periods, please stop by.

6:00 pm – 6:15 pm	2020 - 2021 Fellowship Period	
6:15 pm – 6:35 pm	2021 – 2022 Fellowship Period	
6:35 pm – 6:45 pm	2022 – 2023 Fellowship Period	
6:45 pm – 7:45 pm	YONO Social Hour (This event is not financially supported by NANOS.)	Magnolia Foyer



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Frank B. Walsh: Session I

Moderators: Sophia Chung, MD and Leanne Stunkel, MD

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North American Neuro-Ophthalmology Society

46th Annual Meeting

March 7 – March 12, 2020

Omni Amelia Island Plantation Resort • Amelia Island, FL

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“A Myel-In, a Long Way to Go”

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History & Exam

A 9-year-old previously healthy female with two recent admissions for presumed diagnosis of ADEM re-presented with persistent headache and ataxic gait. During her initial admissions, she presented with fever, acute onset of ataxia, facial asymmetry and abnormal eye movements. Inpatient ocular exam showed normal vision and fundus in both eyes, but her motility exam revealed right 6th and 7th nerve palsy. MRI showed dorsal brainstem and right cerebellar lesions concerning for ADEM, and additional lesions extending to the 4th ventricle with associated mass effect. After extensive negative infectious disease/rheumatology work ups, she was treated with a course of IVIG and steroids during each admission, and both times demonstrated considerable clinical response with near total resolution of her ataxia and cranial nerve deficits. Four days after 2nd discharge, she presented with symptoms of slurred speech, diplopia, ataxia and severe occipital headache. On examination, she had 20/20 vision and full visual fields bilaterally. She was noted to have new horizontal nystagmus, and right 4th, 6th and 7th nerve palsy. MRI demonstrated worsening of brainstem/cerebellar lesions, new diffusion restriction in the pons concerning for ischemic infarction, and an acute communicating hydrocephalus requiring emergent EVD placement. These new findings shifted the diagnostic focus to potential etiologies of stroke including CLIPPERS, CNS vasculitis, infection, and rheumatologic disease, though extensive work up was unrevealing, including cerebral and conventional angiogram which were normal. Given the uncertainty of diagnosis, a novel plasma detection test for microbial cell-free DNA (cfDNA) identified free DNA from *Cladophialophora bantiana* fungi. A brain biopsy was performed with gross visualization of intraventricular pus and black, web-like material. Histopathology confirmed branching hyphae, and fungal PCR testing was positive for *Cladophialophora bantiana*, which validated the cfDNA test. Anti-fungal treatment was initiated systemically, and locally with novel intraventricular approach to directly target the ventricular fungal burden.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“A Myel-In, a Long Way to Go”

Answer

Final Diagnosis

Multifocal CNS phaeohyphomycoses with ventriculitis due to *Cladophialophora bantiana*.

Summary of Case

A 9-year-old girl presented with morning headaches associated with vomiting, gait ataxia, and facial and ocular nerve palsies. Her initial imaging was concerning for possible demyelinating disease. After extensive infectious and rheumatologic work up returned negative, she was treated twice with IVIG and IV steroids with near complete resolution each time. She re-presented, however, with worsening neurologic deficits and imaging revealing focal ischemic infarction in the brainstem as well as new-onset hydrocephalus. A multi-specialty work up was initiated with the aid of consultants in rheumatology, neuroimmunology, and infectious disease without conclusive diagnosis. Brain biopsy revealed gross evidence of infection as well as microscopic evidence of fungus, and non-invasive pathogen testing of plasma established a diagnosis of *C. bantiana*. Treatment was initiated with systemic voriconazole and intraventricular Amphotericin B. This patient's hospital course spanned nearly 6 months and was complicated by tracheostomy and G-tube placement, multiple EVD and VP shunt revisions, and cardiac arrest requiring prolonged resuscitation. Additionally, fungal cultures continued to grow positive after three months of aggressive treatment, prompting craniotomy and wash out of the 4th ventricle. Today, the patient is continuing her long path to recovery at home with her family. She is bed-ridden with daytime trach collar and is receiving G-tube feeds. Her strength is slowly improving with physical therapy and her personality is returning.

Struggle/Dilemma of the Clinical Presentation Description

This case illustrates the difficulty in diagnosis of *C. bantiana* due to its indolent course and mimicry of neurologic etiologies. Masquerading as a demyelinating disorder, IV steroids resulted in short-term improvement but fostered disseminated fungal infection. Finally, the clinical course and optimal management of *C. bantiana* CNS infection is not defined in pediatric cases.

Keywords: Demyelinating disease, Infectious, Ischemia, 4th nerve palsy

References

1. Ahmad M, Jacobs D, Wu H, et al. : A rare intracerebral fungal Abscess—Case series and review of literature. . 2017;03(02):e62-e68. doi: 10.1055/s-0037-1598248.
2. Shrivastava A, Tadepalli K, Goel G, Gupta K, Kumar Gupta P. Melanized fungus as an epidural abscess: A diagnostic and therapeutic challenge. *Medical Mycology Case Reports*; *Medical Mycology Case Reports*. 2017;16:20-24. doi: 10.1016/j.mmcr.2017.04.001.
3. Walsh TJ, Groll A, Hiemenz J, Fleming R, Roilides E, Anaissie E. Infections due to emerging and uncommon medically important fungal pathogens. *Clinical Microbiology and Infection*. 2004;10:48-66. doi: 10.1111/j.1470-9465.2004.00839.
4. Garzoni C, Markham L, Bijlenga P, Garbino J. *Cladophialophora bantiana*: a rare cause of fungal brain abscess. Clinical aspects and new therapeutic options. *Med Mycol* 2008;46(05):481–486

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“From Brainstem to Stern”

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History & Exam

A previously healthy 32-year-old man complained of diplopia and one month of worsening positional headaches. He then acutely developed confusion and chills, prompting ER referral. Further history was limited by altered mental status. On presentation, he was afebrile and encephalopathic. Serum WBC was 16.9/mL. Lactate was 6.2 mmol/L. Head CT was read as normal (Figure 1). Lumbar puncture revealed WBC 48/mL (80% monocytes, 19% lymphocytes, 1% neutrophils), RBC 234/mL, protein >600 mg/dL, and glucose 75 mg/dL. Vancomycin, ceftriaxone, acyclovir, ampicillin, and dexamethasone were started for infectious meningoencephalitis. The following day, he developed progressive obtundation with left mydriasis and ptosis. Head CT revealed evolving hydrocephalus (Figure 2). An external ventricular drain (EVD) was placed emergently. Head MRI showed diffuse leptomeningeal enhancement with expansile pontomedullary T2 hyperintensity (Figure 3). Mental status improved with EVD. Patient reported five months of binocular horizontal diplopia worse in right gaze. Neuro-ophthalmologic examination revealed normal afferent visual function and pupil reactivity. There was a right eye abduction deficit. Fundus examination was normal. Chronicity of diplopia suggested long-standing peripheral or fascicular 6th nerve lesion. Extensive testing for insidious infectious and inflammatory causes of rhombencephalitis was unrevealing. Repeat EVD sampling showed WBC count of 14/mL (89% neutrophils, 10% lymphocytes) and protein 60 mg/dL. Cytology and flow cytometry were normal. EVD was internalized. *Listeria* rhombencephalitis was presumptively diagnosed given acute decompensation, MRI findings, and inflammatory CSF, all of which stabilized on antibiotics. He was discharged on 6-week course of ampicillin and gentamicin. A month later, persistent abduction deficit and new hyperreflexia were noted. Repeat MRI brain, cervical, and thoracic spine revealed diffuse subarachnoid space enhancement displacing the spinal cord (Figure 4a,b). Given thickened, infiltrative intra- and extra-axial lesions in a young patient, neurosarcoidosis was suspected. Patient deferred testing given clinical stability. Two months later, he developed painful bilateral leg weakness.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“From Brainstem to Stern”

Answer

Final Diagnosis

Diffuse midline glioma (DMG) is a midline CNS tumor which presents almost exclusively in childhood with cranial neuropathies and long tract signs. Obstructive hydrocephalus is typically a later finding of DMG (4). Radiographic appearance of DMG is variable, ranging from expansile, infiltrative lesion as in our patient to rim-enhancing mass with central necrosis mimicking astrocytomas found in adults (5)(6). Biopsy proves challenging given DMG's deep location and brainstem involvement. Traditional chemotherapy regimens have proven ineffective, and craniospinal radiation is the mainstay of treatment (7). Imipridone, a molecular therapy promoting tumor apoptosis, is currently being studied in adults with recurrent H3-K27M mutant gliomas (8) though disseminated gliomas are excluded. Median survival in pediatric DMG is 10 months but may be slightly longer in adults. (7)(9)(10)

Summary of Case

Repeat MRI revealed extensive intradural subarachnoid enhancement displacing the spinal cord (Figure 5a,b). After an unsuccessful trial of corticosteroids, biopsy of spinal dura via L5 laminectomy revealed H3-K27M mutant diffuse midline glioma (Figure 6a-h), previously known as diffuse intrinsic pontine glioma (DIPG) (1). Craniospinal radiation and temozolamide were initiated. Bevacizumab was added for rapid progression and functional decline but caused severe anasarca. Patient passed away in hospice 9 months from diagnosis. The initial diagnosis of *Listeria rhombencephalitis* was predicated on the presentation of peripheral leukocytosis, hydrocephalus, radiographic rhombencephalitis with leptomeningeal enhancement, and CSF pleocytosis. Hydrocephalus is a rare complication of untreated *Listeria* (2)(3). Despite clinical improvement following EVD placement, his 6th nerve palsy persisted implicating a brainstem or subarachnoid space cranial neuropathy rather than a falsely-localizing sign of increased ICP. Moreover, CSF profile improvement after antibiotics was more likely a result of EVD sampling rostral to the level of obstructive hydrocephalus with the initial elevated protein and pleocytosis on lumbar puncture reflecting CSF stagnation, not infection. Neuroanatomically disseminated symptoms and prominent leptomeningeal thickening on MRI in a young otherwise healthy patient suggested alternative diagnosis of neurosarcoidosis. However, his symptoms and imaging did not improve with steroids prompting biopsy, which lead to the correct diagnosis of disseminated diffuse midline glioma with leptomeningeal seeding.

Struggle/Dilemma of the Clinical Presentation Description

This patient's course highlights the particular diagnostic challenge of diffuse midline glioma in adults. His initial presentation of acute confusion with hydrocephalus, leptomeningeal enhancement, and pontine lesion suggested an infectious rhombencephalitis. The subsequent evolution of leptomeningeal thickening in an otherwise healthy patient his age was suggestive of an inflammatory disorder such as neurosarcoidosis. Radiographic progression without response to steroids prompted biopsy which ultimately led to the correct diagnosis and treatment.

Keywords: 6th nerve palsy, Brain stem syndromes, Increased intracranial pressure, Intracranial tumors

References

1. Louis, DN et al, "2016 WHO Classifications of CNS Tumors", *Acta Neuropathol*, 131:803-20, 2016.
2. Liang, JJ et al, "Rhombencephalitis Caused by *Listeria* with Hydrocephalus and ICH", *World J Clin Cases*, 7:538-47, 2019.
3. Nachmias, B et al, "Early Hydrocephalus in *Listeria* Meningitis", *ID Cases*, 14:1-4, 2018
4. Guida, L et al, "Safety and Efficacy of ETV in DIPG Related Hydrocephalus" *World Neurosurg*, 124:29-35, 2019
5. Aboian, MS et al, "Imaging Characteristics of Pediatric Diffuse Midline Gliomas with H3K27M Mutation" *Am J Neuroradiol*, 38:795-800, 2017
6. Solomon, DA et al, "Diffuse Midline Gliomas with H3K27M Mutation", *Brain Pathol*, 6:569-80, 2016
7. Vitanza, NA, Monje, M. "DIPG: From Diagnosis to Next-Generation Clinical Trials", *Curr Treat Opt N*, 21:37, 2016
8. Arrillaga-Romany, I et al. "A Phase 2 Study of the First Imipridone ONC201" *Oncotarget*. 8:79298-304, 2017
9. Daoud, EV et al. "Adult Brainstem Gliomas With H3K27M mutation: Radiology, Pathology, and Prognosis" *J Neuropath Exp Neur*, 77:302-11, 2018
10. Schreck, KC et al, "Incidence and Clinicopathologic Features of H3K27M Mutations in Adults with Midline Gliomas" *J Neuro-Onc*. 143:87-93, 2019

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"Are we 'tilting at windmills'?"

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History & Exam

A 52-year-old African American woman presented to her primary care physician with a 4 week history of headaches, nausea, vomiting, fever and ataxia. Her medical history includes rheumatoid arthritis, hypertension and a recent diagnosis of pulmonary sarcoidosis for which she was taking 20 mg of prednisone daily. Her general medical and neurologic examination was normal. A chest x-ray was normal and an MRI Brain without contrast showed numerous small abnormal foci with surrounding FLAIR hyperintensity, some of which were ring shaped. The patient was admitted to the hospital, broad spectrum antibiotics were initiated, she became confused and developed respiratory compromise requiring intubation. Her confusion soon gave way to seizures, stupor and coma. A contrasted head CT showed that the lesions were enhancing and some in a ring like fashion. The superior ophthalmic veins now appear enlarged concerning for cavernous sinus thrombosis. Bedside examination showed an intubated patient non-responsive to external stimuli. The patient's eyes were directed in primary position and lids were closed. She had marked proptosis with inferior conjunctival chemosis and facial swelling. No corneal reflexes present. Exophthalmometry measured 33 mm OU with base of 115 mm. Intraocular pressures measured 36 mm Hg OD, 35 mm Hg OS and latanoprost was prescribed. Labs show an elevated WBC of 16.7 with 95% neutrophils, normal H/H and platelets. BMP normal. ESR 46, CRP 115.30 mg/L, RPR NR, blood cultures negative. PPD skin test was nonreactive. HIV negative. Lumbar puncture showed 25 WBC, 78 RBC, glucose 83 mg/dL (40-75), protein 57 mg/dL (18-53), no AFB, cryptococcal antigen negative, PCR for herpes virus negative. Flow cytometry analysis shows that 70% of total cells are lymphocytes. Contrasted CT chest and abdomen showed necrotic adenopathy in the right axilla along with multiple indeterminate subcentimeter hypodensities within the liver parenchyma. A diagnostic procedure was performed.

Financial Disclosures: The authors had no disclosures.

Grant Support: This work was supported in part by an unrestricted grant from the Research to Prevent Blindness, Inc. N.Y., N.Y.

“Are we “tilting at windmills”?”

Answer

Final Diagnosis

Neurotuberculosis. *Mycobacterium tuberculosis* stains weakly positive with Gram’s stain but is characterized by a bright red (acid-fast) appearance when treated with Ziehl-Neelsen stain.

Summary of Case

A 52-year-old woman presented with headache, fever, nausea, vomiting, ataxia, confusion and coma requiring intubation. Neuroimaging showed numerous ring-enhancing lesions with surrounding edema. CSF and serum studies were negative for an etiology including tuberculosis. The chest x-ray and PPD skin test was also negative. HIV was negative. A biopsy of the right axillary lymph node showed caseating granulomatous lymphadenitis with giant cells, necrosis and acid fast bacilli in keeping with tuberculosis. Once tuberculosis therapy was initiated with rifampin, pyrazinamide, ethambutol, isoniazid and dexamethasone, the patient made a dramatic clinical improvement with resolution of her proptosis and normalization of her neuro-ophthalmologic examination.

Struggle/Dilemma of the Clinical Presentation Description

Given the negative chest x-ray, PPD, CSF for AFB and HIV, TB was not our main differential diagnosis. Clinically she was worsening until a diagnosis of TB was made from an axillary lymph node biopsy. Once treated for TB, she improved dramatically. The diagnosis of neurotuberculosis can be difficult and the clinical outcome depends greatly upon early diagnosis and treatment.

Keywords: Tuberculosis, Meningitis

References

1. Leonard JM. Central nervous system tuberculosis. UpToDate. Mar 16, 2015.
2. Rodrigues MG, da Rocha AJ, Masruha MR, Minett TS. Neurotuberculosis: an overview. *Cent Nerv Syst Agents Med Chem*. 2011;11:246-60.
3. Venkatesh P, Garg SP, Verma L, et al. Combined optic neuropathy and central retinal artery occlusion in military tuberculosis. *Retina* 2001;21:375-377.
4. Barnes PF, Bloch AB, Davidson PT, et al. Tuberculosis in patients with human immunodeficiency virus infection. *N Engl J Med* 1991;324:1644-1650.
5. Iraci IG, Giordano R, Gerosa M, et al. Tuberculoma of the anterior visual pathways. *J Neurosurg* 1980;52:129-133.

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“Objects Jumping, Body Bumping, Hearing Slumping.... Quick, He is Crumping”

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History & Exam

A 45 y/o man developed insidious unsteadiness and bilateral hearing impairment. A neurosurgeon diagnosed possible myelopathy, and despite an anterior cervical discectomy, he noted progressive gait difficulty, poor handwriting, and inability to play the guitar. Additionally, dysarthria, oscillopsia and dizziness with rapid head movement developed. He had ~ 40% sensorineural hearing loss in his left ear, and eventually hearing loss in his right ear. When we first saw him, he used a walker at home, but had frequent falls. Finally, he had disabling episodes of vertigo, nausea and vomiting about twice per month, lasting several hours at a time. His PMH was significant for testicular seminoma, s/p resection in 2007, (left orchiectomy), and had normal oncologic monitoring in July 2017. Family history of ataxia or hearing loss was negative. He did not drink alcohol. The exam showed limb and truncal ataxia, dysarthria, primary gaze downbeat nystagmus, saccadic pursuit and bilateral decreased hearing with normal VOR. A head MRI (pre and post-contrast was normal). He had a chest/abdomen and pelvis CT scan that showed two enlarged lymph nodes, one periaortic (2 x 2.2 cm), and one near the left renal artery (3 x 1, 8 cm). A biopsy showed small lymphocytes and a focus of non-necrotizing granulomatous inflammation, without evidence of carcinoma on H&E or pancytokeratin immunostains. CD68 identified histiocytes (non-necrotizing granulomatous inflammation). Staining of the tissue after the pathologist became aware of the seminoma history showed rare seminoma cells and immunostaining with OCT4 was positive, leading to final diagnosis of “metastatic seminoma” CSF examination showed 13 white cells (all lymphocytes), protein: 28.56 mg/dL, and glucose: 50 mg /dL; there was no local IGG synthesis and no oligoclonal bands. The anti-Ma antibody was negative, 14-3-3 protein level was 2 ng/mL (normal). A paraneoplastic panel performed at the Mayo Clinic was negative.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“Objects Jumping, Body Bumping, Hearing Slumping.... Quick, He is Crumping”

Answer

Final Diagnosis

"Recurrent metastatic testicular Seminoma-related Paraneoplastic ataxia and sensorineural hearing loss due to anti kelch-11 protein antibodies" The clinical manifestations of this syndrome involve eye movement abnormalities, nystagmus, ataxia, sensorineural hearing loss and episodic vertigo. Brainstem eye movement abnormalities may also be present. In some cases immunosuppression may lead to rapid improvement.

Summary of Case

A young man with a history of testicular seminoma (2007) developed progressive gait ataxia, impaired fine motor coordination of the upper extremities and bilateral sensorineural hearing loss. His 2017 Oncology monitoring was normal. On exam, he was wheelchair bound for long distance and used a walker at home. He had a wide base standing and displayed F to N and H to K dysmetria; he could not walk without support due to truncal ataxia. He had a downbeat nystagmus in straight-ahead fixation and in lateral and down gaze, saccadic pursuit and a normal VOR. Eye movement recording showed a bilateral sub clinical INO. MRI pre and post-contrast was normal CSF showed a lymphocytic inflammatory process and the biopsy showed: The pathologist studying the initial biopsy, was not aware of seminoma history; re-examination after the new information, showed positive "Seminoma cells," What is the Next Step Now? 1. Ordered seminoma serum markers Date beta HCG 04-29-2018 Pre-treatment 2.02 mIU/mL (normal) 05-30-2018 Pre-Treatment 91.42 mIU/mL 06-20-2018 Post -i.v.IG < than 2.0 mIU/mL 09-11-2018 Post - acute sepsis < than 2.0 mIU/mL Normal :

Struggle/Dilemma of the Clinical Presentation Description

Case Dilemma 1. Neurological syndrome in a patient with a history of neoplasm suggests "paraneoplastic etiology." A Radiology report error stated previous diagnosis of "carcinoma of the prostate," therefore the initial lymph node study diagnosed non-specific granulomatous inflammation. Additional stains corrected to metastatic seminoma. 2. In support, CSF showed lymphocytic inflammation and serum HCG was elevated, thus, without confirmation of an antibody, we began high-dose steroids and PLEX. 3. Anti- Ma antibody negative. Now what?

Keywords: Eye movements, Autoimmune diseases, Neurologic disorders, Nystagmus, Vestibular ocular system

References

1. Madel-Brehm C, et al. Kelch –like protein antibodies in Seminoma Associated Paraneoplastic Encephalitis. N Eng J of Med. 2019; 381: 47-54.
2. Voltz R, et al. A serologic marker of limbic and brainstem encephalitis in patients with testicular cancer. N Eng J of Med. 1999; 340: 1788-1795

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“Look In The Back”

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History & Exam

A 59-year old man with Graves disease developed increasing proptosis and diplopia. Attributing these abnormalities to worsening of the Graves disease, an ophthalmologist treated him with high-dose oral and intravenous corticosteroids. When improvement did not occur, he underwent orbital x-irradiation (unknown dose). He developed new bilateral hearing loss, bilateral lower extremity weakness, and urinary retention eliciting catheter placement. Visual acuity declined, so he was referred to our institution for urgent orbital decompression. When we first encountered him, he was confused and drowsy. Best-corrected visual acuity was 20/80 in the right eye and 20/200 in the left eye. There was no afferent pupillary defect. External examination revealed marked proptosis. Extraocular motility was reduced in all directions. There was marked superficial punctate keratopathy bilaterally. Ophthalmoscopy through dilated pupils revealed multifocal white/yellow subretinal lesions without vitreous cells in both eyes. He had bilateral sensorineural hearing loss and bilateral lower extremity weakness with diminished lower extremity deep tendon reflexes. Orbital CT revealed bilaterally enlarged extraocular muscles with fullness at the orbital apex but no clear compression of the optic nerves. Brain MRI revealed diffuse intracranial leptomeningeal enhancement and enhancement of both auditory canals. Additionally, there was restricted diffusion in the left fornix and right putamen. Spine MRI revealed enhancement of the cauda equina roots. Lumbar puncture showed a normal opening pressure with a white blood cell count of 578 (78% lymphocytes), a protein of 348 mg/dL, and negative cytology. The leading diagnosis was non-Hodgkin lymphoma (NHL). The putaminal and fornix abnormalities, believed to be consistent with ischemic stroke, led to more detailed review of the brain MRI, which disclosed vessel wall enhancement of the right internal carotid artery. A procedure was performed.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“Look In The Back”

Answer

Final Diagnosis

Multiple neurologic manifestations of VZV (ischemic brain parenchymal stroke, inflammation of the meninges, cranial nerves, nerve roots, and retina) in the setting of advanced Graves disease treated with high dose steroids.

Summary of Case

The procedure was a repeat dilated ophthalmoscopy, which now demonstrated bilateral chorioretinal whitening and retinal necrosis. A vitreous tap disclosed 6,900,000 copies/mL of varicella zoster (VZV) PCR (upper limit of normal 3,160 copies/mL). The following day, cerebrospinal PCR returned an elevated VZV PCR titer (22,000 copies/mL). He was treated with IV acyclovir and intravitreal foscarnet, but died 8 weeks later. Autopsy was not performed. Transaxonal spread of VZV to the meninges and arterial vessel walls accounts for the abnormalities in our patient, except for the retinal necrosis, whose pathogenesis remains unexplained. (1-4) High-definition MRI has recently been reported to disclose intracranial vascular wall enhancement in VZV, (1) which was evident even on traditional MRI in our patient, and which led to the correct diagnosis. The initial retinal examination had suggested NHL retinopathy. However, VZV retinal necrosis can share features with other causes of retinal whitening. Retinal findings can become more classically necrotic over time, highlighting the need for repeat fundus examination. (5)

Struggle/Dilemma of the Clinical Presentation Description

Misstep #1 was inadequate attention to the altered mental status, hearing loss, and cauda equina syndrome. Misstep #2 was attribution of the abnormalities to NHL, partly based on misinterpretation of the retinal abnormalities. Misstep #3 was not realizing that the strokes were a key feature. Finding vasculitis on brain MRI helped move VZV into the spotlight, prompting retinal re-examination that now showed necrosis, and leading to vitreous and cerebrospinal sampling, demonstrating PCR positivity for VZV.

Keywords: Herpes zoster (zoster ophthalmicus), Vasculitides, Magnetic resonance imaging, Thyroid eye disease

References

- 1) Song JW, Ojeda S, Romero JM. High resolution vessel wall MRI and vasculopathy related to herpes zoster ophthalmicus. Clin Imaging. 2018; 50:336-339.
- 2) Savoldi F, Kaufmann TJ, Flanagan EP, Toledano M, Weinshenker BG. Elsberg syndrome: A rarely recognized cause of cauda equina syndrome and lower thoracic myelitis. Neurol Neuroimmunol Neuroinflamm. 2017; 4: e355.
- 3) Lynch K, Agarwal P, Paranandi A, Hadley S, Vullaganti M. Extensive VZV Encephalomyelitis without Rash in an Elderly Man. Case Rep in Neurol Med. 2014;2014: 694750.
- 4) Nagel MA, Gilden D. Neurological Complications of Varicella Zoster Virus Reactivation. Cur Opin Neurol. 2014; 27:356-360.
- 5) Karma A, von Willebrand EO, Tommila PV, Paetau AE, Oskala PS, Immonen IJ. Primary Intraocular Lymphoma: Improving the Diagnostic Procedure. Ophthalmology. 2007; 114: 1372-1377.

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“Not all Men with Thick Skulls Have High Testosterone”

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History & Exam

A 54-year-old retired USAF fighter pilot was referred in Aug 2016 for evaluation of possible bilateral optic disc swelling noted on routine optometric examination. His past medical history included low testosterone discovered 2 years prior in the context of fatigue and exercise intolerance. MRI brain at that time as well as serologic investigations for other hormonal abnormalities were normal by report, and he was using topical testosterone gel for replacement. Initial ophthalmologic exam showed normal visual acuity, color vision, and Humphrey visual fields. On fundus exam, both optic nerves were elevated without obvious swelling, fluorescein angiography showed no leakage, and OCT of the RNFL was normal in both eyes. The patient returned for surveillance in 3 months, at which time visual function remained normal but peripapillary hemorrhage was noted in the right eye. FA now had disc leakage OD. CT orbits (Fig 1) showed an ill-defined bilateral orbital process as well as diffuse bony thickening consistent with a prior diagnosis of osteopetrosis. MRI brain and orbits (Fig 2) confirmed an infiltrative process of the sella, cavernous sinuses, and orbits. Prolactin was mildly elevated (45.3 ng/ml); CBC, C-ANCA, and P-ANCA were normal. A diagnostic procedure was performed.

Financial Disclosures: The authors had no disclosures.

Grant Support: Supported in part by a Challenge Grant to the Department of Ophthalmology, University of Colorado School of Medicine, by Research to Prevent Blindness, USA.

“Not all Men with Thick Skulls Have High Testosterone”

Answer

Final Diagnosis

Erdheim Chester disease with BRAF V600E mutation positivity.

Summary of Case

A right anterior orbital biopsy was performed in December 2016 (Fig. 3) demonstrating “dense fibrous tissue with perivascular inflammation consistent with sclerosing orbital pseudotumor.” No plasma cells were seen. He was treated with prednisone 50 mg daily with a slow taper and transitioned to methotrexate. Despite compliance with therapy, his orbital and intracranial lesions increased in size by April 2018, albeit subtly (Fig. 4). He remained systemically well; screening labs for MTX showed only low serum protein and albumin (stable). A bone scan 2 months later showed changes consistent with osteopetrosis. All neuroimaging was re-reviewed, and the MRI brain from 2014 was obtained from his first institution after a long delay. It showed an infiltrative process at the skull base and cavernous sinuses that was less extensive than noted on subsequent scans. Because the current imaging showed soft tissue and bony lesions in the sphenoid sinus, an endoscopic endonasal biopsy of this tissue was performed (Fig. 5). A greater population of inflammatory cells was seen as were foamy histiocytes infiltrating bone. A mutation in the BRAF gene (V600E) was identified. The patient had his methotrexate discontinued and was prescribed vemurafenib (a BRAF-inhibitor that was FDA approved for Erdheim Chester disease in Nov 2017) 960 mg BID starting in mid-October 2018. Because of elevated creatinine levels, dosing was reduced to 240 mg BID. Repeat neuroimaging performed after 8 months of treatment showed marked remission of the orbitocranial process (Fig. 6). During treatment, the original biopsy specimen was re-evaluated and was found to have a small population of CD68+ cells that were initially thought to be fibroblasts. Furthermore, the BRAF V600E mutation was identified in the specimen as well.

Struggle/Dilemma of the Clinical Presentation Description

The patient presented with asymptomatic optic disc swelling and hemorrhage. He had extensive bony changes in his facial more than appendicular skeleton; such changes can be seen with Erdheim Chester disease but are uncommon. Bone scan also was thought to be consistent with osteopetrosis. His initial biopsy specimen was technically adequate and showed no histiocytic cells. Once Initial imaging was obtained, we were more convinced of slow lesion growth and the need for repeat biopsy.

Keywords: Orbital inflammation, Optic disc edema

References

Blombery, Wong, Lade, Prince, Erdheim-Chester Disease Harboring the BRAF V600E Mutation, J Clin Oncol, 30, e331-e332, 2012.

Diamond, Subbiah, Lockhart, Blay, Puzanov, Vemurafenib for BRAF V600–Mutant Erdheim-Chester Disease and Langerhans Cell Histiocytosis: Analysis of Data From the Histology-Independent, Phase 2, Open-label VE-BASKET Study, JAMA Oncol, 4, 384-388, 2018.

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“You're Too Young for That!”

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History & Exam

An 11-year old boy presented with right orbital pain for two months with recent double vision. He had no recent viral illnesses or sick contacts. He had no past medical history. His brother had Kawasaki disease; his paternal grandmother had rheumatoid arthritis; and his father died of a myocardial infarction at age 48. Our patient's exam showed only inability to abduct OD. Brain MRI showed dural thickening and enhancement along the right lateral cavernous sinus, right orbital apex, and tentorium. His lumbar puncture showed 6 white blood cells, 1 red blood cell, normal protein, glucose, and CSF ACE, and negative oligoclonal bands, gram stain, and cultures. The working diagnosis was Tolosa Hunt. He was started on high dose oral steroids with taper. Five months after initial presentation, he developed new right V2 numbness, complete right ophthalmoplegia, and weakness and numbness of his right hand and leg. These symptoms were again responsive to steroids. He had further workup that showed elevated ESR (44mm/hr), CRP (4.7mg/dL), and C4 (37mg/dL) while on oral steroids. He was hepatitis immune. Serum ACE, IgG4, B12, RF, ANA, quantiferon gold, VZV IgM, and cytometry were normal or negative. Repeat MRI brain showed decreased dural thickening. His symptoms resolved, and his disease was stable for 15 months. He returned with two weeks of left-sided headaches and acute diplopia, and on exam had a left sixth nerve palsy. He also reported pain in his knees and ankles with mild swelling on exam. MRI Brain showed new hypertrophic pachymeningitis isolated to the right middle cranial fossa with slight extension superiorly overlying the lateral sulcus and frontal parietal junction. Extensive work up was negative: CSF Lyme, coccidioides, and aspergillus antibodies, meningitis/encephalitis PCR panel, CSF gram stain, culture, cytology, and cytometry, serum electrophoresis, dsDNA, RF, and lysozyme. A diagnostic procedure was performed.

Financial Disclosures: The authors had no disclosures.

Grant Support: Research to Prevent Blindness

“You’re Too Young for That!”

Answer

Final Diagnosis

Our patient was diagnosed with sporadic Blau syndrome (SBS), also known as early onset sarcoidosis (EOS), with a mutation in NOD2 on chromosome 16. Classically, Blau syndrome was a familial disease with an autosomal dominant mutation in NOD2. EOS was considered distinct from Blau syndrome, since EOS occurred sporadically in children. However, with widespread genetic testing, it has become apparent that EOS and SBS are the same disease. SBS/EOS is an auto-inflammatory disease caused by gain-of-function mutations in the NOD domain. NOD2 is primarily expressed in peripheral leukocytes as an intracellular sensor of bacterial lipopolysaccharides. It activates nuclear factor- κ B protein, which activates hundreds of other genes involved in immune response. Blau syndrome was simultaneously described in 1985 by both Blau and Jabs. Blau described a triad of granulomatous boggy polyarthritis, uveitis, and papuloerythematous rash; whereas, Jabs described polyarthritis with uveitis and cranial neuropathy without rash. Uveitis occurs in 80% to 85% of patients and is typically a chronic bilateral granulomatous iridocyclitis with posterior uveitis. Patients can eventually develop severe panuveitis with multifocal choroiditis. In the largest case series of Blau syndrome (N=45) Rose et al. reported that patients with NOD2 mutations are more likely to have the triad of findings (75.5%). The phenotype has expanded over the last 30 years to include vasculitis, neuropathy, and liver, kidney, spleen, salivary gland, and other organ involvement. The prevalence and incidence of CNS findings in SBS/EOS is not reported due to the rarity of this disease. Sarcoidosis, and therefore neurosarcoidosis, is a distinct disease from SBS/EOS.

Summary of Case

Differential at that time included neurosarcoidosis, lymphoma, histiocytosis, granulomatosis with polyangiitis, polyarteritis nodosa, IgG4 disease, rheumatoid arthritis-related meningitis, and recurrent Tolosa Hunt syndrome. Chest X-ray was unremarkable but suspicion for neurosarcoidosis was still high. PET scan was performed to evaluate for a multisystem disease and possibly identify extra-cranial sites of disease for biopsy. The PET scan just showed small calcifications in the left hilum, likely related to prior granulomatous disease. Thus, dural biopsy was performed with IgG4 staining, AFB cultures, gram stain, and culture. The biopsy had nonspecific mononuclear inflammation without granulomatous changes. He was again started on steroids, which treated his headache, and rituximab was scheduled. As the diagnosis was still unclear, our patient had genetic testing with a commercially available primary immunodeficiency panel of 207 genes. The testing resulted in an increased risk allele variant in NOD2 c.3019dup (p.Leu1007Profs*2), which is associated with increased risk for Crohn's disease. However, our patient did not have symptoms of Crohn's disease. Mutations in NOD2 (nucleotide-binding oligomerization domain 2) are also associated with autosomal dominant Blau syndrome. Our patient's specific variant has not been previously reported in association with Blau syndrome. Genetic testing made the diagnosis of Blau syndrome possible. He was switched to methotrexate and infliximab, as infliximab has good efficacy in treating CNS sarcoidosis. Prednisone was tapered off. His left sixth nerve palsy slowly resolved.

Struggle/Dilemma of the Clinical Presentation Description

Blau syndrome was classically the triad of arthritis, dermatitis, and uveitis in a child with negative RF, ANA, and HLA-B27. In ophthalmology clinic, the panuveitis, iridocyclitis and multifocal choroiditis are clues to the diagnosis. Our patient did not have uveitis, and he only had arthritis on one admission. Even in “atypical Blau” syndrome, the CNS is rarely affected. Our patient's dural biopsy was negative for granulomatous disease. The final diagnosis was revealed with genetic testing.

Keywords: Autoimmune diseases, 6th nerve palsy, Steroids, Sarcoidosis

References

1. Blau. Familial granulomatous arthritis, iritis, and rash, *J Pediatr*, 107, 689, 1985.
2. Gelfand, Bradshaw, Stern, Clifford, Wang, et al. Infliximab for the treatment of CNS sarcoidosis: A multi-institutional series, *Neurology*, 14, 2092, 2003.
3. Jabs, Houk, Bias, Arnett. Familial granulomatous synovitis, uveitis, and cranial neuropathies, *Am J Med*, 78, 801, 1985.
4. Kanazawa. [Clinical features of Blau syndrome and early-onset sarcoidosis and associating CARD15/NOD2 gene mutations], *Nihon Rinsho Meneki Gakkai Kaishi*, 30, 123, 2007.
5. Rosé, Aróstegui, Martín, Espada, Scalzi, et al. NOD2-associated pediatric granulomatous arthritis, an expanding phenotype: study of an international registry and a national cohort in Spain, *Arthritis Rheum*, 60, 1797, 2009.
6. Rosé, Pans, Casteels, Anton, Bader-Meunier, et al. Blau syndrome: cross-sectional data from a multicentre study of clinical, radiological and functional outcomes, *Rheumatology (Oxford)*, 54, 1008, 2015.

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“Tumefactive MS”

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History & Exam

A 26-year-old woman with history of diabetes insipidus and hypothyroidism presented for evaluation of painless vision loss in her right eye. She was evaluated by a local neurologist and multiple sclerosis (MS) specialist who diagnosed acute optic neuritis. MRI brain showed an enhancing T2 hyperintense lesion of the body of the corpus callosum on the right. The pituitary and infundibulum were not enlarged or abnormally enhancing. A lumbar puncture demonstrated 8 WBC, 1 RBC, protein 29 mg/dL, glucose 84 mg/dL, IgG index 0.99 (normal < 0.70), and 5 CSF specific oligoclonal bands. CSF bacterial and fungal cultures, cytology, Lyme and VDRL were negative. She was diagnosed with tumefactive multiple sclerosis (MS) and was treated with 5 days of high dose oral corticosteroids and glatiramer acetate was initiated. She never recovered vision. She discontinued glatiramer acetate 6 months later because of site reactions. Fingolimod was recommended, but never initiated. Fourteen months after her initial presentation, she noted declining visual acuity OS. A neurologist diagnosed acute optic neuritis OS and started 5 days of high dose oral corticosteroids. She was referred to our clinic for further evaluation. Best-corrected visual acuity was 20/100 OD and 20/80 OS. There was a right APD and both optic discs were pale. The differential diagnosis included neoplasm and atypical inflammatory processes. Anti-aquaporin 4 and anti-myelin oligodendrocyte glycoprotein antibodies were negative. Repeat MRI brain/orbits demonstrated a heterogeneously enhancing T2 hyperintense lesion of the subcortical right frontal lobe, involving the corpus callosum, hypothalamus, pituitary stalk and optic chiasm. CT of the chest, abdomen, and pelvis were negative. A diagnostic procedure was performed.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“Tumefactive MS”

Answer

Final Diagnosis

Germinoma.

Summary of Case

Right frontal brain biopsy revealed markedly atypical cells arranged in discohesive sheets with large central nuclei and prominent nucleoli on a background of lymphocytic infiltrate. Immunohistochemical stains were diagnostic of germinoma. Repeat lumbar puncture demonstrated a lymphocytic pleocytosis (16 cells/mm³) with negative B-HCG and AFP supporting a diagnosis of germinoma. Systemic chemotherapy with carboplatin and etoposide was initiated. Craniospinal radiation is planned. Germinomas are the most common type of germ cell tumor and 90% arise in patients under the age of 20. Typical locations include pineal and suprasellar regions (including the infundibulum). While the imaging features of our case are consistent with germinoma, tumefactive demyelinating lesions, gliomas, glioneuronal tumors and inflammatory lesions (eg. neurosarcoidosis) can appear similarly. There are fewer than 10 reported cases radiologically similar to ours of germinoma involving the corpus callosum without extension from a more typical location or additional CNS lesions. Not only was the site of the initial lesion highly unusual for germinoma, but the CSF studies were also supportive of an inflammatory process, leading the neurologist to make an incorrect diagnosis of MS. However, these CSF characteristics are not specific for MS and can also be seen in response to malignancy, including germinoma. The clinical course, including lack of painful vision loss and lack of visual recovery, were also inconsistent with a diagnosis of MS. In retrospect, the development of diabetes insipidus (DI), 3 years prior to our patient's vision loss, was the first symptom of germinoma despite negative imaging at the time of her DI diagnosis. Although a normal pituitary infundibulum reduces the risk of malignancy, endocrine abnormalities may precede infundibulum abnormalities by years and diagnosis of germinoma by years more. This underscores the importance of surveillance imaging in patients with presumed idiopathic DI.

Struggle/Dilemma of the Clinical Presentation Description

DI was the first symptom of germinoma. When she lost vision in the right eye, the lack of an infundibular lesion, the location of her sentinel lesion in the right corpus callosum, and inflammatory CSF, all led to a misdiagnosis of MS. The lack of visual improvement after the diagnosis of optic neuritis should also have led to reconsideration of alternative etiologies. MRI surveillance may have resulted in earlier diagnosis and prevented second eye involvement.

Keywords: Optic neuropathy, Tumor, Vision loss

References

None.

Contact Information: None provided.

“Tissue is the Issue”

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History & Exam

A 34-year-old man with a past medical history of bilateral corneoscleral lesions and brainstem, thalamic, and temporal lobe lesions presented with progressive vision loss over seven months. He described graying out of vision with light sensitivity. Bilateral, retrobulbar, deep ocular pain started 2 months ago but otherwise he denied headache. He endorsed baseline foreign body sensation. His ophthalmologic exam was notable for bilateral count fingers vision, normal IOP, pupils were round and reactive with no RAPD. His extraocular motility was significant for a bilateral gaze palsy. His slit lamp exam was notable for a gelatinous infiltrate circumferentially around the corneal limbus nasally on the right eye and 360 degrees around the left, but the visual axis remained clear. He had grade two posterior subcapsular cataracts and his dilated fundus exam was notable for diffusely pale optic nerves with a normal cup-to-disc ratio of 0.3. Cranial nerves III-XII were otherwise intact. On neurologic exam, he was oriented to person, place, time. His recent and remote memory was intact. He exhibited a normal fund of knowledge and awareness of current events. His speech fluency difficult to assess because of profound dysarthria. Sensation was normal to light touch. Motor exam was significant for L arm 3/5 in deltoid 4/5 triceps and 1 in wrist and fingers. Coordination was poor, patient could not perform finger to nose. Reflexes were 3+ throughout, with the exception of 4+ with clonus in the left patella. The left toe was upgoing. MR orbits showed enhancement of bilateral optic nerves with edema and enhancing lesions were present within the pons and the left mesial temporal lobe. He was admitted for workup and intravenous steroids.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“Tissue is the Issue”

Answer

Final Diagnosis

The pathologic specimen demonstrated atypical histiocytic proliferation and infiltration with abundant cytoplasm, CD68+, S100+, consistent with Rosai Dorfman (RDD). The patient had been treated with steroids with a partial response and disease stabilization with radiation therapy with subsequent progression. He was treated with cobimetinib as a part of the clinical trial #15-216 with a partial response. He progressed off treatment and was treated with cladribine with a complete response of his parenchymal disease in early 2019. He was readmitted with vision loss while off treatment. In light of this history, we presumed that the optic nerve and chiasm disease in this case was infiltration by RDD. He was treated with steroids and re-initiated of MEK inhibitor therapy.

Summary of Case

We describe a 34-year-old gentleman with a multifocal central nervous system and ocular disease, with chronic lesions of the corneosclera, pons, thalami, pituitary with chronic left sided weakness and dysarthria, now presenting with progressive vision loss associated with involvement of the optic nerves and chiasm. Further history revealed that the patient had suffered progressive clinical impairments for several years including gait instability, pseudobulbar affect, difficulty sleeping, and dysphagia. He also had chronic corneal scleral lesions leading to an excision with pathology showing conjunctiva with goblet cell loss, squamous metaplasia, subepithelial fibrosis and scattered lymphocytes. There was no distinct neoplasm. Some basal epithelial pigmentation were present, but no atypical melanocytes. MR imaging for the neurological symptoms in 2015 was notable for FLAIR hyperintense and enhancing lesions in the brainstem having spread further throughout brainstem, diencephalon, and bilateral temporal lobes. Serologic and spinal fluid workup were negative for an acute inflammatory or infectious etiology as well as malignancy. A left temporal lobe biopsy in 2015 was therefore undertaken given severe, refractory disease. Repeat lumbar puncture in the context of presumed optic neuritis demonstrated normal cell counts. Cytological analysis and flow cytometry was normal.

Struggle/Dilemma of the Clinical Presentation Description

Severe vision loss with optic nerve and chiasmal enhancing disease has a long differential. Though cases of orbital RDD have been reported, to our knowledge, cases radiologically mimicking optic neuritis are extremely rare.

Keywords: Optic neuritis, MRI, Horizontal gaze palsy

References

1. AlWadani, S, Robinson, S, Myers, R, Akpek, EK, Eberhart, CG. No increase in IgG4-positive plasma cells in limbal Rosai-Dorfman disease. *Cornea*. 33:844-847, 2014.
2. Cavouto K, Galor A, Dubovy SR, Gregori N, McCarthy M. Subconjunctival masses associated with central nervous system rosai-dorfman disease. *Cornea*. 30(2), 237-240, 2011.
3. Dalia S, Sagatys E, Sokol L, Kubal T. Rosai-dorfman disease: Tumor biology, clinical features, pathology, and treatment. *Cancer control : journal of the Moffitt Cancer Center*. 21(4), 322-327, 2014.
4. Diamond, E.L., Durham, B.H., Ulaner, G.A. et al. Efficacy of MEK inhibition in patients with histiocytic neoplasms. *Nature* **567**, 521–524, 2019.
5. Foucar E, Rosai J, Dorfman RF. The ophthalmologic manifestations of sinus histiocytosis with massive lymphadenopathy. *American Journal of Ophthalmology*, 87(3), 354-367, 1979.
6. Sandoval-Sus JD, Sandoval-Leon AC, Chapman JR, et al. Rosai-dorfman disease of the central nervous system: Report of 6 cases and review of the literature. *Medicine*. 93(3), 165-175, 2014.

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“Well here is another Uveo-meningeal syndrome you might muck up.”

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History & Exam

A 16 y/o Caucasian female with a BMI of 24, went for an eye exam for blurry vision which corrected with refraction, however bilateral disc edema was found. There was a 4-year history of headaches that were intermittent and escalating in nature around 5 days a week, about 1 hour after awakening, and 50% became severe (9/10) lasting about 2 hours. Only during headaches did she note pulsatile tinnitus, and when severe headaches, light sensitivity and nausea. TVO's occurred when standing up quickly. Family believed allergies resulted in her headaches, as she had longstanding intermittent rashes which at times were pruritic and red eyes without photophobia or pruritus. Fatigue, recently developed, such that the patient slept all day/night following school and had to be awakened to eat. Despite this she was an honor student, but had to discontinue PE classes and cheerleading and felt winded with walking, despite a normal chest X-ray. Furthermore, patient noted puffiness and aching in hands, knees and ankles. A school screening test uncovered a bilateral hearing loss, and no obvious change over years. On exam patient had a 20/20 OU vision, normal IOP, pupils were equal, no APD, with slight light near dissociation. Her slit lamp exam showed diffuse conjunctival injection, subtle subepithelial/anterior stromal corneal opacities inferiorly. Anterior chamber had rare cell and 1+ flare OU, anterior vitreous had 1-2+ cell OU. Bilateral chronic appearing disc edema (Frisen 3-4) was present, with no obvious retinal, choroid or vascular process after examination with ICG and FA, the later showing disc leakage. VF minor nasal depression. OCT showed bilateral thickening NFL. MRI, MRA/MRV were normal. LP demonstrated an OP of 44cm H2O, WBC 60 (mostly PMN). Patient's work-up was negative for infectious/autoimmune serology despite very elevated inflammatory markers. Diagnosis and management with disappearance of symptoms ensued.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“Well here is another Uveo-meningeal syndrome you might muck up.”

Answer

Final Diagnosis

Uveomeningeal Syndrome with Raised Intracranial Pressure due to Muckle Wells Syndrome, the later also explaining rashes, red eyes, hearing loss, fatigue.

Summary of Case

A 16 year old female presented with worsening headaches associated with significant papilledema and an intermediate uveitis. All neuroimaging was negative however, her CSF confirmed very elevated ICP and showed cells mostly polys, yet an infectious etiology was not uncovered. Her history of polyarticular aching with swelling, progressive fatigue and elevated inflammatory markers resulted in an extensive pediatric rheumatologic evaluation. Neuro-Behets was top on the differential amongst other diseases, yet no diagnosis was made after significant diagnostic investigation. When her history of intermittent rashes, dating to childhood, red eyes and hearing loss were added to the equation of her more recent symptoms and signs, cryopyrin-associated periodic syndromes (CAPS) came into the differential. Of these syndromes, Muckle Wells syndrome seemed to be most aligned to the patients presentation. However, the lack of progressive hearing loss and the absence of a genetic history made such a diagnosis perhaps a possible but unlikely contender. Once laboratory confirmation of the NLRP3 gene was made, she had rapid treatment with an IL1 inhibitor which resulted in all of her symptoms to disappear, even from childhood, except for her hearing loss. After 2-3 weeks on the IL1 inhibitor, she no longer had rashes, red eyes, fatigue, polyarticular aching and puffiness and her headaches resolved.

Struggle/Dilemma of the Clinical Presentation Description

Initially the patient appeared to have a uveomeningeal syndrome, yet an infectious or rheumatic etiology was not found. Before submitting the patient to further rheumatic and spinal fluid investigations which were already negative (although some studies had not been obtained), we chose to look for the unusual diagnosis, genetic in nature (CAPS), Autosomal Dominant, in a patient with NO family history. A Muckle Wells diagnosis, would unify her newer developments with her lifelong medical issues.

Keywords: Increased intracranial pressure, Meningo-uveitis, Neurologic disorders, Hearing Loss, monoclonal antibody therapy

References

i Terreri MTR, Bernardo WM, Len CA, Silva CAAD, Magalhães CMRD, Sacchetti SB, et al. Guidelines for the management and treatment of periodic fever syndromes. *Revista Brasileira de Reumatologia (English Edition)*. 2016;56(1):44–51.

ii Kitley JL, Lachmann HJ, Pinto A, Ginsberg L. Neurologic manifestations of the cryopyrin-associated periodic syndrome. *Neurology*. 2010;74(16):1267–70.

iii Oberg TJ, Vitale AT, Hoffman RO, Bohnsack JF, Warner JE. Cryopyrin-associated Periodic Syndromes and the Eye. *Ocular Immunology and Inflammation*. 2013Oct;21(4):306–9.

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“A Par 3 Macular Hole?”

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History & Exam

A 78-year old woman with 3-week history of sudden onset “visual blur” OU and difficulty reading was evaluated by her ophthalmologist and suspected to have macular hole secondary to posterior vitreous detachment and vitreomacular traction (VMT). Her past medical history was significant for hypertension, hyperlipidemia, depression and carcinoid tumor of the appendix. She consulted a retina specialist who confirmed bilateral VMT and advised follow up with regular ophthalmologist. Her visual acuity at presentation was 20/60 OD and 20/50 OS. She returned 2 weeks later with worsening vision loss and no change in retinal findings, at which point she was referred for neuro-ophthalmic consultation. At her first neuro-ophthalmology visit, vision was count fingers close to face OD and hand motion OS. Pupils were sluggish with no afferent pupillary defect. Dilated fundus exam revealed normal optic discs, epiretinal membrane and VMT OU. On further questioning, she reported being treated with prednisone for the past year by rheumatology for a "presumed vasculitis" after she had symptoms of fever, weight loss, rash, lower extremity edema, lack of energy and skin nodules. She denied headache, jaw claudication and scalp tenderness.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“A Par 3 Macular Hole?”

Answer

Final Diagnosis

Progressive Multifocal Leukoencephalopathy with underlying angioimmunoblastic T-Cell lymphoma.

Summary of Case

The initial evaluation of rapidly progressive visual loss with mildly sluggish pupils raised concern for bilateral occipital disease. The recent "vasculitis" history with systemic symptoms also put GCA high on the list of differentials. Lab abnormalities included elevated ESR (86), CRP (.90) and platelet count (442). MRI revealed an extensive area of increased signal on FLAIR images bilaterally involving the occipitoparietal regions, cerebellar peduncles and splenium of the corpus callosum. CSF exam revealed 3 WBCs and a protein of 45. 14-3-3 protein test was ambiguous, but tau test was negative. There were no oligoclonal bands but myelin basic protein (28.5) and IgG index (0.71) were elevated. The JC virus PCR was elevated at 343,124 copies in CSF and 3623 copies in serum (nl <500). A diagnosis of progressive multifocal leukoencephalopathy (PML) was made, but the underlying immune predisposition wasn't obvious with negative HIV testing, CD4/CD8 ratio normal and lymphoma/leukemia phenotyping negative. The only risk noted was her steroid use. Over the following 3 weeks of hospitalization vision deteriorated to NLP OU. She was discharged home but readmitted 3 weeks later with progressive lethargy and difficulty breathing. Evaluation for possible pulmonary embolus led to a CT chest revealing extensive bilateral hilar, mediastinal and axillary adenopathy. Prior portable CXR had shown prominence of the superior mediastinum likely related to the portable technique. Axillary lymph node biopsy revealed expansion of the paracortical T zone by pleomorphic lymphocytic population with scattered immunoblasts and increased vascularity throughout. Immunohistochemistry showed positivity for CD3, CD5, CD7 and pan T cell markers consistent with a diagnosis of angioimmunoblastic T cell lymphoma. PCR identified clonal rearrangement of the T-cell receptor genes. Repeat MRI showed progression of her PML lesions. She was discharged to hospice and died a few months later. Post-mortem examination was not obtained.

Struggle/Dilemma of the Clinical Presentation Description

The first issue was that her initial visual symptoms were attributed to findings of vitreomacular traction, so a neurologic cause wasn't pursued and this delayed diagnosis. Secondly, although steroid use and an underlying vasculitis may be enough of a substrate to reactivate JC virus and cause PML, it likely was the lymphoma that was the predisposing factor. Additionally, the lymphoma likely caused many of the symptoms that were diagnosed as vasculitis.

Keywords: Progressive multifocal leukoencephalopathy, Vision loss binocular, Immunodeficiency, Vasculitides, JC virus

References

None.

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“Smoke gets in your eyes”

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History & Exam

A 61-year-old woman, active smoker with history of COPD, presented with bilateral progressive vision loss and ataxia. Four months prior to her presentation she developed “black spot” in her right eye (OD) and was found to have “OD disc edema and right hypertropia” by an outside ophthalmologist. She was admitted to the hospital where she had a brain MRI that was interpreted as normal. Lumbar puncture showed elevated CSF white cells and protein. CSF cultures were negative. She was diagnosed with viral meningitis and treated supportively with subjective improvement of vision. Over the next three months she developed progressive bilateral vision loss and severe ataxia to the point that she was not able to ambulate without a walker. On presentation to our neuro-ophthalmology clinic, her best corrected visual acuities were 20/60-2 OD and 3/200 OS, she missed 6.5 Richmond color plates OD and was unable to see the control plate OS. She had a left relative afferent pupillary defect. Her extraocular motility was full, and she had downbeat nystagmus. The external and anterior segment exams were normal. On funduscopic exam, she had bilateral moderate optic disc edema. Automated perimetry showed an inferonasal defect OD and generalized depression OS. The rest of her neurological exam was notable for dysmetria with left heel-to-shin probe and severe swaying in all directions when standing. She was unable to take any steps due to imbalance.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“Smoke gets in your eyes”

Answer

Final Diagnosis

CRMP-5 paraneoplastic syndrome with bilateral optic neuropathy and cerebellar syndrome.

Summary of Case

This patient, who is an active smoker, developed bilateral progressive vision loss and ataxia. Her examination demonstrated bilateral optic neuropathy with optic disc edema and downbeat nystagmus. A repeat MRI revealed multifocal contrast-enhancing lesions throughout the brain suggestive of intracranial metastatic disease. FDG PET scan demonstrated intensely FDG avid left hilar lymphadenopathy. Biopsy of the hilar lymph node yielded pathology consistent with small cell carcinoma. Because the cerebral lesions found on MRI did not explain the degree of her vision loss, we pursued further work up that revealed normal ESR, CRP, ANCA, ACE level and blood flow cytometry, negative syphilis and Lyme serology, and no serum NMO and MOG antibodies. A lumbar puncture revealed normal opening pressure and glucose, mildly elevated CSF white cells (8 mononuclear cells suspicious for blasts), and moderately elevated protein (134 mg/dL). CSF culture, VDRL, NMO antibodies, cytology and flow cytometry were negative. CSF IgG index and IgG synthesis rate were both elevated. Serum paraneoplastic panel revealed extremely high collapsin response-mediator protein-5 (CRMP-5-IgG) antibody titers (1:30,720). She was diagnosed with CRMP-5 paraneoplastic syndrome with bilateral optic neuropathy and cerebellar syndrome and treated with systemic steroids along with chemotherapy for her cancer and whole brain radiation therapy for cerebral metastatic disease. The combination of bilateral progressive optic neuropathy with disc edema and cerebellar syndrome without clear causative lesion on MRI raised our concern for a more diffuse process. CRMP-5-associated paraneoplastic syndrome was first described in 1993 in a patient with cerebellar ataxia, peripheral neuropathy, uveitis, and axillary lymph node metastasis of an undifferentiated carcinoma [1]. The clinical features include cognitive dysfunction, cerebellar ataxia, chorea, parkinsonism, sensorimotor polyneuropathy and cranial neuropathies. CRMP-5-associated optic neuropathy is characterized by subacute bilateral vision loss and optic disc edema and may be accompanied by uveitis, vitritis and retinal vasculitis [2].

Struggle/Dilemma of the Clinical Presentation Description

The metastatic lesions found on this patient's brain MRI helped to identify the underlying cancer; however, they did not explain the profound vision loss and debilitating ataxia. Even though a single negative CSF cytology did not fully rule out leptomeningeal spread of her cancer, it made it less likely, which in addition to inflammatory CSF profile led us to further investigation of immune-mediated etiologies and establishing the final diagnosis of CRMP-5 paraneoplastic syndrome.

Keywords: Optic neuropathy, Disc edema, Paraneoplastic syndromes

References

1. Antoine JC et al. J Neurol Sci: Jul 1993, Vol. 117(1-2): 215-23
2. Cross SA et al. Ann Neurol. 2003 Jul; 54(1): 38-50

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“Undiscovered islands - so close, yet so far.”

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History & Exam

A 30-year old female, visiting Canada from India, presented to ophthalmology with a 2-day history of right periorbital swelling, painful proptosis, fevers and chills. Initial examination suggested a clinical diagnosis of post-septal cellulitis with mild motility restriction, without optic nerve compromise, and patient was admitted and started on IV broad-spectrum antibiotics. Serologic analysis revealed mildly elevated CRP and white blood cell count. CT orbits revealed two ovoid-shaped ring-enhancing lesions in the right lateral and superior rectus muscles (Fig.1) and clear sinuses, atypical for infectious post-septal cellulitis, raising other considerations of the differential diagnosis. ACE, ANA, ANCA, HIV, and TB testing were negative. The patient received a course of oral steroids. As an inpatient, she was noted to have bradycardic episodes. Holter-monitor was unremarkable. Antibiotic and steroid treatment resulted in clinical improvement. MRI orbits was performed for further characterization, confirming the presence of the lesions in the right lateral and superior rectus muscles and an additional lesion in the left superior rectus muscle (Fig. 2). The largest ring-enhancing lesion in the right lateral rectus muscle did not show restricted diffusion, arguing against an abscess. Orbital biopsy was discussed, but deferred due to non-compliance. Given the bilaterality of these findings, a parasitic process, i.e. orbital cysticercosis was suspected, despite low eosinophil count and negative taenia solium serology. A course of albendazole, along with steroids was initiated, which led to the resolution of her symptoms. 8 weeks after her initial presentation, she presented to the ER with a 3-day history of nausea, vomiting, diarrhea, fevers and weakness. Abdominal sonography and CT ordered for iron deficiency and elevated liver enzymes showed a 3cm mass, likely arising from the neck of the pancreas, along with numerous lesions in kidneys, liver, T12 vertebral body, and periaortic/retroperitoneal lymphadenopathy (Fig. 3). A diagnostic test was performed.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“Undiscovered islands - so close, yet so far.”

Answer

Final Diagnosis

Orbital involvement of metastatic pancreatic neuroendocrine tumor, grade 2.

Summary of Case

The hepatic lesions were easily amenable to ultrasound-guided biopsy and three 18-gauge core biopsies of one of the lateral right lobe hepatic masses were obtained. The histopathological sections revealed a metastatic tumor composed of monomorphic cell proliferation, with insular growth pattern (Fig. 4). Based on these features, the tumor was diagnosed as a metastatic neuroendocrine tumor, grade 2. Given the positivity for CDX2 and the upper endoscopic findings of extrinsic compression of antrum/pylorus, the patient was diagnosed with a neuroendocrine carcinoma, with primary origin being pancreatic and widely metastatic (Fig. 5). Sadly, her visitor health insurance did not cover medical expenses for chemotherapy. Thus, she was transferred back to India for further care. Orbital metastases secondary to neuroendocrine carcinoma are exceedingly rare, with only 22 cases reported so far. Average age at diagnosis is reported to be 67.5 (range 42-79). Hence, this is an extremely unusual presentation for a 30-year old patient (1-8). Das et al. found that surgical biopsy of the orbital lesion is not necessary for diagnosis in the setting of a previously established diagnosis, systemic metastases and classic radiologic findings (2). In strong contrast to other primary malignancies with orbital metastases, patients with orbital involvement from neuroendocrine tumours carry an excellent prognosis with 10-year survival rates of close to 40% (9).

Struggle/Dilemma of the Clinical Presentation Description

This woman presented with acute orbital inflammation, with atypical features. Differential diagnoses included inflammatory and infectious processes; serology and chest-X-ray were non-contributory. Orbital biopsy was not performed. She then presented with non-specific, presumably unrelated gastrointestinal symptoms. Finally, imaging and pathology led to the diagnosis of metastatic neuroendocrine carcinoma. Diagnostic challenge and delay were driven by the unusual demographic presentation of an exceedingly rare malignancy and a deferral of orbital biopsy due to health insurance limitations.

Keywords: Metastatic carcinoma, Orbital tumors, Proptosis, Tumor

References

1. Borota et al. Carcinoid tumour metastatic to the orbit with infiltration to the extraocular orbital muscle, *APMIS*, 113(2):135-9, 2005.
2. Das et al. The eye of the beholder: orbital metastases from midgut neuroendocrine tumors, a two institution experience, *Cancer Imaging*, 18(1):47, 2018.
3. Matsuo et al. Neuroendocrine tumor metastatic to orbital extraocular muscle: case report and literature review. *Strabismus*, 18(4):123-8, 2010.
4. Peixoto et al. Neuroendocrine tumor metastatic to the orbit treated with radiotherapy. *World J Gastrointest Oncol*, 5(8):177-80, 2013.
5. Riddle et al. Carcinoid tumors of the eye and orbit: a clinicopathologic study of 15 cases, with histochemical and electron microscopic observations. *Hum Pathol*, 13(5):459-69, 1982.
6. Turaka et al. A case series of neuroendocrine tumor metastasis to the orbit. *Oman J Ophthalmol*, 4(3):125-8, 2011.
7. Kozubowska et al. Neuroendocrine tumour metastasis to the orbit. *Endokrynol Pol*, 2019.
8. Halliday et al. Pseudocystic appearance of an orbital carcinoid metastasis. *Orbit*, 1-4, 2019.
9. Mehta et al. Orbital carcinoid metastases. *Ophthalmology*, 113(3):466-72, 2006.

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“Bones of the Past”

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History & Exam

A 44-year-old woman presented with two episodes of binocular horizontal diplopia within one year. She had a history of Cushing's syndrome status post transsphenoidal resection and bilateral adrenalectomy 4 years prior, hypertension, and secondary diabetes mellitus. Nine months prior she developed severe right-sided headache and a right abducens nerve palsy, which improved over several weeks. At presentation, she described left-sided headache and neck pain, followed by development of horizontal diplopia worst on left gaze. She had normal visual acuity, color vision, visual fields, pupillary function, and fundi. There was an isolated left abduction deficit with incomitant esotropia. MRI of the brain with contrast showed stable residual postoperative findings in the sella, with unchanged residual contrast-enhancing pituitary tissue, and some contact of the left AICA with the left abducens nerve but no enhancement or other abnormality of the abducens nerves or extraocular muscles. A second radiologic opinion noted previously missed confluent but heterogeneous T1-hypointense marrow in the clivus with diffusion restriction, which in retrospect was progressively worsening over serial scans from preceding years. Lumbar puncture yielded normal cerebrospinal fluid. A CT PET of the skull base showed abnormal enhancing soft tissue within the sella and extending along the epidural surface of the clivus, and progression of bony sclerosis within the clivus compared to prior scans; there was hypermetabolism of the clivus. Follow-up MRI demonstrated progression of the changes in the sella and clivus compared to her postoperative imaging. Serum adrenocorticotrophic hormone (ACTH) levels were significantly higher than prior. A transsphenoidal biopsy revealed tumor with surrounding fibrotic reaction in the sella, sphenoid sinus and superior clivus. Pathology was consistent with corticotroph adenoma with elevated proliferation index and scattered mitoses. A diagnosis of Nelson's syndrome was made. The patient underwent radiation therapy, with full resolution of her diplopia and headache.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“Bones of the Past”

Answer

Final Diagnosis

Sequential abducens palsies secondary to Nelson's syndrome (regrowth of corticotroph pituitary adenoma into the clivus).

Summary of Case

A 44-year-old woman presented two sequential episodes of painful 6th nerve palsy unilateral that alternated sides. Although MRI was initially considered unrevealing, a second radiologic opinion drew attention to gradually progressing changes in the clivus that in retrospect had been present on surveillance scans but not noted for several years. CT-PET showed clivus fibrosis and abnormal adjacent soft tissue, and the clivus was hypermetabolic. A diagnosis of Nelson syndrome was suspected based on the imaging findings and elevated ACTH, and this was confirmed with transsphenoidal biopsy. Nelson's syndrome was previously seen in about 8-47% of people that undergo bilateral adrenalectomy for Cushing's disease, but has become a rare disease with newer treatment protocols.¹ Neuro-ophthalmic presentations of Nelson syndrome are extremely rare. A patient with bilateral oculomotor palsy has been reported, and another case of painful diplopia and sixth nerve palsies in a patient who presented with pituitary adenoma apoplexy and subarachnoid hemorrhage.^{2,3} We are not aware of a single report of Nelson syndrome presenting with abducens palsy because of tumor growth within the clivus for several years, with no concurrent growth in the sella or cavernous sinus.

Struggle/Dilemma of the Clinical Presentation Description

To our knowledge Nelson syndrome presenting with abducens palsy due to clival regrowth is not previously described. The subtle imaging changes in the clivus were only noted on careful re-review of previous imaging. This case also demonstrates the added utility of CT-PET scanning of the skull base in patients with unrevealing or subtle MRI changes. Patients with Cushing syndrome status post bilateral adrenalectomy require careful clinical and radiologic follow up.

Keywords: 6th nerve palsy, Skull base, Pituitary surgery (transphenoidal adenectomy), PET

References

1. Patel J, Eloy JA, Liu JK. Nelson's syndrome: A review of the clinical manifestations, pathophysiology, and treatment strategies. *Neurosurg Focus*. 2015;38(20):E14. doi:10.3171/2014.10.FOCUS14681
2. Garg M, Brar K, Bharwaj R, et al. Nelson's syndrome presenting as bilateral oculomotor palsy. *Indian J Endocrinol Metab*. 2013;17(6):114-6. doi:10.4103/2230-8210.122643
3. Gazioglu N, Kadioglu P, Ocal E, et al. An unusual presentation of Nelson's syndrome with apoplexy and subarachnoid hemorrhage. *Pituitary*. 2002;5(4):267-74.

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“Close Encounters of The Third Kind”

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History & Exam

A 65-year old woman started experiencing headaches which increased in severity over two weeks. She eventually sought care in the emergency department. Neurological examination was reported as normal. Unenhanced CT of the brain was performed and reported as normal. Headaches continued and she was prescribed oral morphine by her family physician to control the pain without a definite diagnosis. 1 week later she developed oblique binocular diplopia and left upper lid ptosis. She saw her family physician again who referred her for neuro-ophthalmological consultation. On exam, central acuities were normal in each eye, there was obvious left upper lid ptosis, left pupil was 2 mm larger than the right, there was no relative afferent pupillary defect, there were obvious supra-, infra- and adduction motility deficits in the left eye. A diagnosis of partial pupillary involving left third cranial nerve palsy was made. Urgent admission for CT angiogram (CTA) was arranged. After arrival to the hospital the patient collapsed in the cafeteria but regained consciousness in less than a minute which was felt to be a vaso-vagal episode. CT demonstrated smooth, homogeneously hyperdense abnormal thickening along the dura of the falx, tentorium cerebellum, clivus, and floor of the posterior fossa (Figure 1). The distribution was felt to be unusual for subdural hemorrhage and the possibility of inflammatory (IgG-4 disease) or neoplastic infiltrate was raised. Long-standing dural venous thrombosis was also entertained. No aneurysm was identified on CTA. CT of the chest, abdomen and pelvis was performed and was interpreted as unremarkable. A diagnostic procedure was performed.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“Close Encounters of The Third Kind”

Answer

Final Diagnosis

It is taught that recognizing PCOM aneurysms on non-invasive modern neuro-imaging by experienced neuro-radiologist should be possible when aneurysmal size is at least 2-3mm. This case emphasizes that PCOM aneurysms can be very difficult to diagnose despite high quality imaging interpreted by experienced neuro-radiologists. The skullbase with its many bony structures can obscure small aneurysms near big vessels and bones and very thin axial slices are required for its visualization which are not generated in all centres. It also teaches us that aneurysms can rarely rupture into subdural rather than subarachnoid space. Resulting subdural hematoma can be difficult to recognize on imaging as the spacial distribution of blood can be very unusual: instead of localizing along convexity, blood can pool around the entire tentorium/falx/posterior fossa. This in turn can lead to the incorrect focus of differential diagnosis on inflammatory and neoplastic entities. PCOM aneurysms big enough to produce a compressive third nerve palsy can also be occasionally very difficult to see on CTA and in our case it was missed by a very experienced interventional neuro-radiologist. Intracranial aneurysms rupturing into subdural space are very rare and only a few reports describing it were published. No cases of third nerve palsies were described in PCOM aneurysms rupturing into subdural space. Several theories were proposed to explain it: successive small bleeding can cause adhesion of aneurysm to adjacent arachnoid membrane thus when rupturing, aneurysm will bleed into subdural space; stream of blood could also rupture through subarachnoid membrane at its weak point producing blood in the subdural space; lastly, decompression of intracerebral hematoma into subdural space following disruption of the arachnoid covering of cerebral cortex may occur.

Summary of Case

MRI and MRV of the brain and orbits was performed. It showed that the hyperdense thickening along the dura on CT was subdural rather than thickening of the dura itself. This subdural material was non-enhancing, intermediate signal intensity on T1-weighted images, and it bloomed on susceptibility-weighted imaging (SWI). This was interpreted as subacute subdural blood (Figure 2). When MR venogram was closely re-examined in the context of subdural blood, a small rounded vascular structure along the lateral aspect of the left cavernous sinus was noticed, and correlation with the previous CTA suggested that this was a posterior communicating artery (PCOM) aneurysm. (Figure 3). Urgent diagnostic angiography of the brain was performed and demonstrated a boot-shaped aneurysm of the left posterior communicating artery which was wide-necked with the maximal diameter of the "round" portion of only 5 mm (Figure 4). Aneurysm was then treated with endovascular coil embolization. We presumed that the rupture of PCOM aneurysm into subdural space occurred either shortly after patient's visit to ED with the thunderclap headache, or during her collapse in the hospital cafeteria, as the blood was still hyper-dense on CT scan which usually lasts for less than a week.

Struggle/Dilemma of the Clinical Presentation Description

Presence of pupillary involving third nerve palsy accompanied by severe pain localizing behind left eye led to initial suspicion of idiopathic cavernous inflammatory syndrome. Brain CT and CTA demonstrated a very unusual pattern of diffuse thickening along dura which was initially felt to be inflammatory or neoplastic in nature. Only when MR with SWI was performed, dural thickening was re-interpreted as subdural blood and PCOM aneurysm rupturing into subdural rather than subarachnoid space was diagnosed.

Keywords: 3rd nerve palsy, Subarachnoid hemorrhage

References

1. Oh SY, Kwon JT, Park YS, Nam TK, Park SW, Hwang SN. Clinical features of acute subdural hematomas caused by ruptured intracranial aneurysms. J Korean Neurosurg Soc. 2011 Jul;50(1):6-10.
2. Tsao JW, Waldman JL, Manley GT. Ruptured posterior communicating artery aneurysm presenting as acute subdural hematoma. Am J Emerg Med. 2003 Mar;21(2):162-4.
3. Mrfka M, Pistracher K, Augustin M, Kurschel-Lackner S, Mokry M. Acute subdural hematoma without subarachnoid hemorrhage or intraparenchymal hematoma caused by rupture of a posterior communicating artery aneurysm: case report and review of the literature. J Emerg Med. 2013 Jun;44(6):e369-73.
4. Verhey LH, Wang W, Adel JG. True Cortical Saccular Aneurysm Presenting as an Acute Subdural Hematoma. World Neurosurg. 2018 May;113:58-61.

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“Oh Oh Oh It’s Magic, You Know...Never Believe It’s Not So!”

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History & Exam

A 72-year-old man with chronic sinusitis, obstructive sleep apnea, and recent extensive travel presented with right-sided headaches, vision changes, and allergy symptoms. A head CT demonstrated a sinus infection and he was treated with amoxicillin-clavulanate and prednisone. His headache persisted and he presented to an ophthalmologist. Visual acuity was 20/30 OD and 20/25 OS, Ishihara color plates testing was 1 (test plate)/15 OU, there was no RAPD, extraocular motility was full. Anterior segment and fundus exams were unremarkable. Visual fields demonstrated a dense left homonymous hemianopia. Brain MRI revealed multifocal infarctions in the right parieto-occipital region. Further work-up was recommended; however, he left against medical advice. He followed up with his otolaryngologist who re-started him on corticosteroids. The patient developed confusion and agitation and returned to the ER. He was arousable to voice but required constant stimulation to maintain alertness. He had difficulty with repetition. His strength, reflexes and sensation were grossly intact. A CT demonstrated progression of his infarction and a left-sided parotid mass. His bloodwork was normal. He was started on empiric intravenous antibiotic and antiviral treatment, later broadened to systemic antifungals. An MRI with contrast demonstrated new leptomeningeal enhancement and new cerebral and cerebellar infarcts. Lumbar puncture demonstrated an opening pressure of 46 cm H₂O with straw colored fluid. Constituents: WBC 14 (65% lymphocytes, 16% monocytes, 19% eosinophils) RBC 38, protein 225 (N<50), glucose 63, IgG index 1.0 (N<0.6), and 2 unique oligoclonal bands. An extensive infectious, neoplastic, and autoimmune work-up was negative. An echocardiogram was normal. CT scan of the chest, abdomen, and pelvis demonstrated a few small pulmonary nodules. His neurologic exam continued to worsen. He developed bilateral optic disc swelling. Repeat neuroimaging and lumbar puncture demonstrated new areas of infarction and persistently elevated opening pressure and a similar CSF profile. A diagnostic procedure was performed.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“Oh Oh Oh It’s Magic, You Know...Never Believe It’s Not So!”

Answer

Final Diagnosis

Amyloid beta-related angiitis (ABRA) complicated by secondary cerebral and cerebellar infarcts and elevated intracranial pressure.

Summary of Case

A biopsy of the right temporal lobe showed chronic inflammation with no granulomas or organisms present. A PET scan demonstrated focal hypermetabolism in the region of the left parotid gland. A fine needle aspirate revealed the parotid gland lesion to be a Warthin tumor. Anti-fungal therapy was broadened and albendazole was initiated along with dexamethasone. The CSF profile improved with a decrease in protein, opening pressure and eosinophilia - however, the neurologic exam remained unchanged. The bilateral optic disc swelling worsened and new peripapillary splinter hemorrhages developed every two to three days. Repeat MRI revealed yet more areas of new infarction and leptomeningeal enhancement. A biopsy of the right occipital lobe was performed. The pathology demonstrated markedly thickened vessel walls due to accumulation of homogenous eosinophilic material, perivascular granulomatous and transmural lymphoplasmacytic inflammation with several foci of vessel wall destruction, diagnostic of vasculitis. In addition, there were areas of ischemic damage with collections of foamy macrophages, reactive gliosis, and tissue rarefaction consistent with subacute infarcts. Congo red stain highlighted abundant amyloid within the majority of blood vessel walls. Immunohistochemistry for beta amyloid was extensively positive in blood vessels. The features were consistent with amyloid beta-related angiitis (ABRA) associated with secondary subacute cerebral infarcts. All anti-pathogen treatments were discontinued and intravenous high-dose methylprednisolone and cyclophosphamide were initiated. The optic nerve head findings resolved and the opening pressure normalized. Unfortunately, the patient remained severely encephalopathic with significant left-sided focal neurologic deficits at his last evaluation.

Struggle/Dilemma of the Clinical Presentation Description

The patient’s travel history, and CSF eosinophilia directed investigations to favor an infectious etiology but no pathogen was found. The optic disc swelling with progressive peripapillary hemorrhages further complicated the picture - an extremely rare and unique feature of ABRA. The parotid gland mass and pulmonary nodules raised concern for a neoplastic process. The non-diagnostic results from the initial brain biopsy further confused the clinical picture, necessitating a second larger biopsy from the occipital lobe.

Keywords: Amyloid-beta related angiitis, homonymous hemianopsia, Optic disc edema, Increased intracranial pressure, Subarachnoid hemorrhage

References

1. Scolding NJ, Joseph F, Kirby PA, Mazanti I, Gray F, et al. A β -related angiitis: primary angiitis of the central nervous system associated with cerebral amyloid angiopathy. *Brain* 128, 500-515, 2005.
2. Danve A, Grafge M, and Deodhar A. Amyloid beta-related angiitis—a case report and comprehensive review of literature of 94 cases. *Seminars in arthritis and rheumatism* 44, 86-92, 2014.
3. Dumitrascu OM, Okazaki EM, Cobb SH, Zarka MA, De Souza SA, et al. Amyloid-beta-related angiitis with distinctive neuro-ophthalmologic features. *Neuro-ophthalmology* 42, 237-241, 2018.
4. Child ND, Braksick SA, Flanagan EP, Keegan BM, Giannini C, et al. Amyloid-beta-related angiitis presenting as a uveomeningeal syndrome. *Neurology* 81, 1796-1798, 2013.

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North American Neuro-Ophthalmology Society

46th Annual Meeting

March 7 – March 12, 2020

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Poster Session I: Clinical Highlights in Neuro-Ophthalmology

Sunday, March 8th- 12:20 pm – 2:20 pm

Authors will be standing by their posters during the following hours:

Odd Numbered Posters: 12:20 pm – 1:20 pm

Even Numbered Posters: 1:20 pm – 2:20 pm

Poster #	Abstract Title	Presenting Author
Category: Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)		
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2	Primary Progressive Multiple Sclerosis Presenting with Isolated Optic Atrophy	Michael A. Jordan
3	Acute painless vision loss caused by optic nerve cavernoma – a rare suprasellar vascular malformation	Maja Kostic
4	Acute Macular Neuroretinopathy	Priyanka Kukkar
5	Glaucomatous-like Optic Neuropathy due to Compression of the Optic Nerve by the Internal Carotid Artery	Jonathan A. Micieli
6	Optic Disc Drusen with Optic Nerve Head Edema and Normal ICP Treated with Acetazolamide	John M. Pyun
7	Optic Disc Edema and Peripapillary Choroidal Neovascularization in Acute Posterior Multifocal Placoid Pigment Epitheliopathy (APMPPE)	Meghan J. Smith
8	Three Presentations of Female Relatives Affected by 11778 Mutation of Leber's Hereditary Optic Neuropathy (LHON)	Sudip D. Thakar
9	A Unique Case of Transient Vision Loss Caused by Forceful Eye Rubbing During Sleep	Michael W. Thorne
10	Early Visual Changes Portend Visual Loss in a Case of Fludarabine Toxicity	Judd M. Cahoon
11	Leber's Hereditary Optic Neuropathy Phenotype in a Male Adolescent with Paternally Transmitted Autosomal NSUN3 Mutation.	Berthold Pemp
12	Papilledema as the Presenting Sign of Lymphocytic Hypophysitis	Nita Bhat
13	Preretinal Hemorrhages In Intracranial Hypertension: A Case Series	Megan E. Bill
14	An unusual cause of inflammatory optic neuropathy	Maira R. Altszul
15	Binocular Visual Field Defects Caused by Temporal Posterior Subcapsular Cataracts	Kelsey M. Mileski
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22	A Case of Bartonella Neuroretinitis Secondary to a Horse Bite	Chantal J. Boisvert
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Poster 1

Two Perplexing Cases of Craniopharyngioma

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Introduction:

Craniopharyngioma are solid or mixed solid-cystic tumors arising from remnants of Rathke's pouch. We encountered two perplexing cases of craniopharyngioma that presented within weeks of each other.

Description of Case(s):

Case 1: A 19 yo man presented with sinus pressure, headaches, and neck stiffness not relieved by a course of antibiotics. He subsequently noticed bilateral loss of peripheral vision and binocular horizontal diplopia. Exam revealed a VA of 20/30 OD and 20/40 OS without relative afferent pupillary defect and with alternating esophoria on alternate cover test. Fundus exam showed bilateral disc edema. CT head revealed a suprasellar mass with calcified, solid enhancing, and cystic components. MRI head showed a suprasellar large cystic mass with peripheral enhancement resulting in obstructive hydrocephalus with transependymal CSF flow. He received intravenous dexamethasone and subsequent right frontal intracranial intraventricular endoscopy with cyst wall fenestration and aspiration. Pathology confirmed craniopharyngioma with acellular calcific or keratinous material. Case 2: A 9 yo girl presented with one month of severe vision loss, longstanding frontal HA and dizziness. Exam revealed a VA of 20/200 OU with no relative afferent pupillary defect and grade V optic disc edema OU on fundus exam. MRI revealed a large heterogeneously enhancing suprasellar mass with T1 hyperintense proteinaceous components on pre-contrast images with obstructive hydrocephalus. She received intravenous dexamethasone and an external ventricular drain followed by decompressive resection of the mass. Pathology showed an adamantinomatous craniopharyngioma. After discharge, she developed a large right subdural fluid collection with a midline shift and required subdural peritoneal shunt. Unfortunately, the patient had LP vision OU at follow up.

Conclusions, including unique features of the case(s):

Craniopharyngiomas occur in a bimodal distribution and represent 5-10% of all brain tumors in children. Malignant transformation is rare. Risk factors for visual decline include younger age at diagnosis, optic nerve edema at presentation, and tumor recurrence.

References: 1. Bunin GR, Surawicz TS, Witman PA, et al. The descriptive epidemiology of craniopharyngioma. J Neurosurg 1998; 89:547. 2. Jane JA Jr, Laws ER. Craniopharyngioma. Pituitary 2006; 9:323. 3. Karavitaki N, Brufani C, Warner JT, et al. Craniopharyngiomas in children and adults: systematic analysis of 121 cases with long-term follow-up. Clin Endocrinol (Oxf) 2005; 62:397. 4. Lo AC, Howard AF, Nichol A, et al. Long-term outcomes and complications in patients with craniopharyngioma: the British Columbia Cancer Agency experience. Int J Radiat Oncol Biol Phys 2014; 88:1011. 5. Olsson DS, Andersson E, Bryngelsson IL, et al. Excess mortality and morbidity in patients with craniopharyngioma, especially in patients with childhood onset: a population-based study in Sweden. J Clin Endocrinol Metab 2015; 100:467.

Keywords: Tumors, Neuroimaging, High intracranial pressure/headache, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 2

Primary Progressive Multiple Sclerosis Presenting with Isolated Optic Atrophy

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Introduction:

Primary progressive multiple sclerosis (PPMS) is a devastating condition that affects 10-15 percent of patients with MS. PPMS typically presents with progressive spastic paresis in 80% of patients, or with progressive cerebellar dysfunction in 15 percent of patients. The literature is sparse regarding optic atrophy as the initial manifestation of PPMS.

Description of Case(s):

We present a 49-year-old Caucasian woman with progressive blurred vision in both eyes for 2 years. She denied any focal neurological deficits. Past medical history included breast cancer diagnosed 4 years prior status post lumpectomy and tamoxifen for 3 years. It also included alcohol abuse for which she takes disulfiram weekly since 2008. Visual acuity was 20/40 OU with an afferent pupillary defect OS. She identified 11/11 color plates OD, and 7/11 OS. Anterior segment exam was unremarkable. Dilated fundus exam showed temporal pallor OU. Visual field testing showed an inferonasal defect OD and a cecocentral scotoma OS. OCT rNFL showed temporal thinning in both eyes. The rest of her entire neurological examination was normal. Brain and orbit MRI showed more than 20 supra-and infratentorial white matter lesions including three enhancing lesions. Cervical spine imaging showed three intramedullary lesions. Lumbar puncture showed 4 oligoclonal bands and there were an undetermined amount of oligoclonal bands on serum testing. She was diagnosed with PPMS by a neurologist and started on ocrelizumab.

Conclusions, including unique features of the case(s):

We present a case of PPMS with the initial presentation of isolated bilateral optic atrophy. Future studies into isolated optic atrophy as the initial presentation of PPMS are warranted to further characterize and describe this unique finding.

References: None.

Keywords: Demyelinating disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 3

Acute painless vision loss caused by optic nerve cavernoma – a rare suprasellar vascular malformation

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Introduction:

A 49-year-old healthy woman was evaluated in the eye emergency room for acute progressive painless vision loss in the right eye over 2 days. Six weeks prior to the visual loss, she had a routine normal ocular examination elsewhere. She had tingling sensation in the neck and arms for years. She reported intermittent hearing problem in the right ear and a few episodes of lightheadedness.

Description of Case(s):

Best-corrected visual acuity was 20/300 right eye and 20/20 left eye with a right afferent pupillary defect. Confrontation visual field showed depression and dense defect inferiorly. Eye movements were full. Slit-lamp exam showed that the right optic nerve had a diffuse pallor without edema; the left was normal. Orbit and brain MRI with GAD showed a 17x12x10 mm suprasellar mass with heterogeneity in signal encompassing the right prechiasmatic optic nerve, separate from the pituitary gland and stalk. The abnormality was predominantly T1 isointense with areas of high signal and T2 heterogeneous signal. Minimal T2/FLAIR hyperintense foci in the periventricular white matter was noted. Given the heterogeneity of the mass with acute progressive vision loss, the patient was referred for surgical resection, and a diagnostic procedure was performed. Resection was performed five days after onset. Elastic van Gieson (EVG) immunohistochemistry staining showed absence of elastic layer, confirming the venous nature of the vessels. The patient's vision improved significantly from 20/300 to 20/30 at month two post-surgery.

Conclusions, including unique features of the case(s):

Optic nerve cavernomas (ONC) are rare and often difficult to diagnose on neuroimaging. Our case highlights the importance of including ONC in the differential diagnosis of heterogeneous lesions given treatment is challenging owing to operating in a difficult surgical field with risk of hemorrhage in an eloquent area of the brain, as well as the risk of not intervening and losing vision.

References: 1. Deshmukh V, Albuquerque F, Zabramski J, Spetzler RF. Surgical management of cavernous malformations involving the cranial nerves. *Neurosurgery*. 53(2): 352-357; 2003. 2. Itshayek E, Perez-Sanchez X, Cohen JE, Umansky F, Spektor S. Cavernous hemangioma of the third cranial nerve: case report. *Neurosurgery*. 61(3): E653; 2007. 3. Matias-Guiu X, Alejo M, Sole T, Ferrer I, Noboa R, Bartumeus F. Cavernous angiomas of the cranial nerves. *J Neurosurg*. 73(4):620-622; 1990. 4. Ogilvy C, Pakzaban P, Lee J. Oculomotor nerve cavernous angioma in a patient with Roberts syndrome. *Surg Neurol*. 40(1):39-42; 1993.

Keywords: Tumors, Magnetic resonance imaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 4

Acute Macular Neuroretinopathy

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Introduction:

We report a case of paracentral scotomata of acute macular neuroretinopathy.

Description of Case(s):

A 44 year old woman reports visualizing five omnipresent irregularly shaped spots with each eye, with a triangular shape flashing like a strobe light inside each spot for 6 months, waning over time, following flu symptoms. Medical history reveals a long history of typical complex migraine headaches with aura with visual symptoms, and a TIA, 5 years prior to presentation. She sustained a small right cerebellar stroke thought to be related to chiropractic high velocity neck manipulation with resultant vertebral artery injury, 1 year prior to presentation. Family history reveals deep venous thrombosis and hypercoagulable state. On Examination patient has visual acuity of 20/20 in each eye, normal color perception bilaterally and abnormal Amsler grid. Dilated ophthalmoscopy reveals healthy appearing optic disks, multiple paracentral petalloid lesions in the macula bilaterally, and scattered hypopigmented lesions in the nasal periphery of the right eye. Visual field testing with HVF 30-2 reveals small paracentral scotomata bilaterally. OCT scanning reveals multiple paracentral hyperreflective band-like lesions in the outer retina of each eye at the level of the outer plexiform layer and/or outer nuclear layer. There are multiple parafoveal petalloid hyporefective areas in the enface infrared image bilaterally. ICG angiography reveals some focal hypofluorescent areas corresponding to the lesions seen in infrared imaging bilaterally. These lesions are pronounced during the early and arteriovenous phases with no areas of hyperfluorescence. MRA of head and neck reveals fibromuscular dysplasia and lab work high homocysteine levels.

Conclusions, including unique features of the case(s):

Patients with AMNR present with unilateral or bilateral central or paracentral scotomas for which they are referred to neuro ophthalmologist as these mimic symptoms of optic neuritis but careful examination of pupils, macula and OCT helps in differentiation.

References: 1. Bos PJ, Deutman AF. Acute macular neuroretinopathy. *Am J Ophthalmol.* 1975;80(4): 573-84 2. Bhavsar KV, Lin S, Rahimy E, Joseph A, Freund KB, Sarraf D, Cunningham ET Jr. Acute macular neuroretinopathy: A comprehensive review of the literature. *Surv Ophthalmol.* 2016;61(5):538-6 3. Schofield JR, Palestine AG, Pelak V, Mathias MT. Deep capillary retinal ischemia and high-titer prothrombin-associated antiphospholipid antibodies: A case series of three patients. *Am J Ophthalmol Case Rep.* 2019 Apr 2;14:105-109

Keywords: Pupils Retina, Visual fields, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 5

Glaucomatous-like Optic Neuropathy due to Compression of the Optic Nerve by the Internal Carotid Artery

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Introduction:

Compression of the optic nerve by the supraclinoid internal carotid artery (ICA) has long been recognized as a potential cause of an optic neuropathy. Visual field defects and optic nerve cupping resembling glaucoma were surprisingly found in a previous case series.[1] We describe 3 patients with radiological ICA compression of the optic nerve without elevated intraocular pressure (IOP) and a phenotype that resembled glaucoma. All patients had preserved visual acuity (VA), color vision, glaucomatous visual field defects, cupping without pallor, open angles, unilateral disease and a normal IOP. They were referred to neuro-ophthalmology due to low IOP or progression despite low IOP.

Description of Case(s):

Patient 1 was 58-years-old and referred due to unilateral cupping and an inferior arcuate defect (MD -18.73dB) despite an IOP of 12. He had a VA of 20/30, cup-to-disc ratio of 0.95 and an optical coherence tomography (OCT) retinal nerve fiber layer-(RNFL) thickness of 43mm. Patient 2 was 29-year-old man who was referred due a visual field defect despite the low IOP of 9 on latanoprost. He had a VA of 20/20, superior/inferior arcuate defect (MD -12.82dB) and a cup-to-disc ratio of 0.95 with an OCT-RNFL thickness of 58mm. Patient 3 was an 82-year-old woman with a maximum IOP of 14 that had visual field progression despite an IOP of 10. She had a VA of 20/20, superior and inferior arcuate defect (-14.33dB) and an OCT-RNFL thickness of 77mm. All patients had radiological evidence of optic nerve compression by the ICA on coronal T2-MRI images.

Conclusions, including unique features of the case(s):

Compression of the optic nerve by the ICA can cause an optic neuropathy that resembles glaucoma and should be included in the differential diagnosis of normal-tension glaucoma. MRI should be considered in patients with significant visual field defects and consistently normal IOP or progression despite low IOP.

References: 1. Jacobson DM. Symptomatic compression of the optic nerve by the carotid artery. *Ophthalmology* 1999;106:1994-2004.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 6

Optic Disc Drusen with Optic Nerve Head Edema and Normal ICP Treated with Acetazolamide

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Introduction:

Optic disc drusen (ODD) is a well known cause of optic nerve elevation and pseudopapilledema. Although acetazolamide has been shown to be an effective therapy for disc edema associated with increased intracranial pressure (ICP), prior studies have not reported the use of acetazolamide to address concurrent optic disc head elevation (ODHE) in ODD in the setting of normal ICP. We present a series of three patients of such condition treated successfully with acetazolamide.

Description of Case(s):

A retrospective review of all patients found to have ODD with ODHE with normal ICP who presented between April 2016 and June 2018 at our tertiary medical center was performed. Three pediatric patients (ages 7-13) who presented to our facility with concerns for ONHE were evaluated and found to have ODD (6/6 eyes) confirmed with fundus autofluorescence (FAF), enhanced depth optical coherence tomography (ED-OCT), and B-scan ultrasound. ODHE was found by ED-OCT in 4/6 eyes [mean retinal nerve fiber layer thickness 221.75 μm \pm 50.42 vs 113.5 μm \pm 3.5 in the unaffected eyes (p-value >0.05)]. All patients had normal findings on magnetic brain imaging and magnetic brain venography, normal opening pressures with lumbar puncture (mean 18.83 mmH₂O \pm 3.52) with normal cerebrospinal fluid analysis. All patients were initiated on oral acetazolamide therapy (250-2,810 mg daily) with improvement in ODHE on OCT (mean change -96.25 μm \pm 63.37).

Conclusions, including unique features of the case(s):

ODD may represent a spectrum of disease with an association with ONHE. Patients with ODD found to have ODHE and normal ICP may be successfully treated with acetazolamide therapy.

References: None.

Keywords: Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 7

Optic Disc Edema and Peripapillary Choroidal Neovascularization in Acute Posterior Multifocal Placoid Pigment Epitheliopathy (APMPPE)

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Introduction:

APMPPE is a rare, bilateral ocular inflammatory disease of unknown etiology characterized by creamy white placoid lesions at the level of the retinal pigment epithelium or choroid (1). We describe a rare case of presumed APMPPE presenting with bilateral optic disc edema and peripapillary choroidal neovascularization (PPCNV).

Description of Case(s):

A 21-year-old healthy lady presented with a five-day history of blurred vision and a black scotoma in her right eye. She had a headache but denied neurological or systemic symptoms or a preceding flu-like illness. Visual acuity was 20/40 OD and 20/20 OS, she had normal colour vision and there was no relative afferent pupillary defect. Visual fields demonstrated enlarged blind spots, worse on the right. Slit lamp examination revealed quiet anterior segments and there was no vitritis. Fundus examination revealed bilateral optic disc edema and peripapillary subretinal hemorrhages with subretinal fluid extending toward the macula. There were multiple discrete creamy white placoid lesions in the posterior poles. Fluorescein angiography demonstrated early hypofluorescence of the lesions followed by late staining and optic disc leakage. An extensive investigation for infectious and inflammatory conditions was unrevealing; there was no evidence of cerebral vasculitis on MRI and she underwent a lumbar puncture with normal opening pressure and CSF constituents. Following two weeks of steroid therapy the placoid lesions resolved. She was subsequently treated with intravitreal anti-VEGF for PPCNV in the right eye.

Conclusions, including unique features of the case(s):

Optic disc swelling has rarely been described in association with APMPPE in the setting of papillitis, serous neurosensory detachments, and central retinal vein occlusion (2-4). Macular CNV is a rare feature of APMPPE, but to our knowledge, PPCNV in APMPPE has never been described (5-7). We describe a rare case of presumed APMPPE presenting with bilateral optic disc edema, subretinal fluid, and subsequent PPCNV.

References: (1) Gass. Acute posterior multifocal placoid pigment epitheliopathy. Arch Ophthalmol 80:177–85, 1968. (2) Abu El-Asrar et al. Acute Posterior multifocal placoid pigment epitheliopathy with retinal vasculitis and papillitis. Eye (Lond) 16(5):642-4, 2002. (3) Allee et al. Acute posterior multifocal placoid pigment epitheliopathy with bilateral central retinal vein occlusion. Am J Ophthalmol 126(2):309-12, 1998. (4) Vedantham et al. Atypical manifestations of acute posterior multifocal placoid pigment epitheliopathy. Indian J Ophthalmol 54(1):49-52, 2006. (5) Bowie et al. Acute posterior multifocal placoid pigment epitheliopathy and choroidal neovascularization. Retina 25:362–364, 2005. (6) Mavranakas et al. Intravitreal ranibizumab for choroidal neovascularization secondary to acute multifocal posterior placoid pigment epitheliopathy. Acta Ophthalmol 88(2):54-5, 2010. (7) Pagliarini et al. Foveal involvement and lack of visual recovery in APMPPE associated with uncommon features. Eye 9:42-47, 1995.

Keywords: Visual fields, Pupils retina

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 8

Three Presentations of Female Relatives Affected by 11778 Mutation of Leber's Hereditary Optic Neuropathy (LHON)

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Introduction:

Three female cousins presented with unexplained vision loss. The first (19-year-old) developed acutely blurred vision OD; she kept missing the ball during soccer practices. The second (34-year-old in her second pregnancy) reported a history of optic neuritis OS after painless vision loss during her first pregnancy. She had periventricular plaques characteristic of multiple sclerosis (MS). The third (37-year-old) described debilitating headaches and decreased vision OD; she had previously been diagnosed as malingering.

Description of Case(s):

All three cousins separately reported having four male relatives with severely decreased vision from LHON; they all tested positive for the 11778 mutation. 19-year-old presented with best corrected visual acuity (BCVA) of 20/20 OU and mildly hyperemic discs. Neuroimaging was normal. She started idebenone and her latest BCVA was 20/50 OD, 20/30 OS. 34-year-old presented with BCVA of 20/20 OD, CF 6' OS with segmental pallor OS. Patient had presumed Harding's syndrome (MS-LHON). Idebenone was deferred during pregnancy, and she delivered her second child (26 months after first episode) with stable vision. 37-year-old presented with BCVA of 20/60 OD, 20/20 OS. Neuroimaging was normal. She was enrolled in the GenSIGHT/REFLECT study. Her most recent BCVA is CF 3' OD, 20/200 OS.

Conclusions, including unique features of the case(s):

LHON is an inherited mitochondrial disorder classically presenting (80-90% of cases) in males during their second-third decade with acute, painless visual deterioration. It remains unclear how and with what severity this affects females. To our knowledge, this is one of only a few reported case-series of three female relatives with LHON with the 11778 mutation in the US. It is prudent that we continue to publicly report these cases to understand common trends and more rapidly detect this disease. Ideally this will help us collaboratively identify therapeutic options for these challenging cases.

References: Harding AE, Sweeney MG, Govan GG, Riordan-eva P. Pedigree analysis in Leber hereditary optic neuropathy families with a pathogenic mtDNA mutation. *Am J Hum Genet.* 1995;57(1):77-86. Newman NJ. Hereditary optic neuropathies: from the mitochondria to the optic nerve. *Am J Ophthalmol.* 2005;140:517-523. Newman NJ, Lott MT, Wallace DC. The clinical characteristics of pedigrees of Leber's hereditary optic neuropathy with the 11778 mutation. *Am J Ophthalmol.* 1991;111(6):750-62. Ortiz RG, Newman NJ, Manoukian SV, Diesenhouse MC, Lott MT, et al. Optic disk cupping and electrocardiographic abnormalities in an American pedigree with Leber's hereditary optic neuropathy. *Am J Ophthalmol.* 1992;113(5):561-6. Qu J, Wang Y, Tong Y, Zhou X, Zhao F, et al. Leber's hereditary optic neuropathy affects only female matrilineal relatives in two Chinese families. *Invest Ophthalmol Vis Sci.* 2010;51(10):4906-12. Thieme H, Wissinger B, Jandek C, Christ-Adler M, Kraus H, et al. A pedigree of Leber's hereditary optic neuropathy with visual loss in childhood, primarily in girls. *Graefes Arch Clin Exp Ophthalmol.* 1999;237(9):714-9.

Keywords: Optic neuropathy, Genetic disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 9

A Unique Case of Transient Vision Loss Caused by Forceful Eye Rubbing During Sleep

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Introduction:

Transient monocular vision loss upon awakening is thought to represent a benign phenomenon. We present a case that provides exception to this rule.

Description of Case(s):

A 23 year old woman was referred to neuro-ophthalmology for evaluation of recurrent episodes of complete monocular visual loss strictly occurring upon awakening at night. Family had witnessed extremely forceful eye rubbing during her sleep, to the point that she was burying her knuckles deep in her globes, with twisting movements that were audible across the room. She had tried various measures such as wearing mittens and goggles at night, with no effect. Her vision during the day remained normal. Past medical history included episodic migraine, restless legs syndrome, and somnambulism as a child. Best corrected visual acuity was 20/20 OU. Ophthalmological and neurological examination was normal. Humphrey automated perimetry was normal. Investigations that were completed and normal included a CT head, MRI head, routine EEG, and OCT. Overnight polysomnography was normal and did not reveal any abnormal movements. Corneal topography studies were negative for secondary keratoconus.

Conclusions, including unique features of the case(s):

The patient underwent three admissions to the epilepsy monitoring unit (EMU) for continuous (including nocturnal) video-electroencephalogram (EEG) recording. During her third EMU admission several examples of her stereotyped eye rubbing were finally captured on video-EEG, occurring on different sides, and all definitively originating out of stage-2 non-REM sleep. The diagnosis of non-REM parasomnia was made. In the two months since starting prescription oral cannabidiol (CBD) oil 30mg three times daily, however, she has not had any further episodes, and she has woken up in the morning with makeup on her knuckles only twice, instead of nearly every day.

References: Ifran M, Schenck CH, Howell MJ. (2017) Non-Rapid Eye Movement Sleep and Overlap Parasomnias. *Continuum* 23(4):1035-50. Turner DC, Girkin GA, Downs JC. (2019). The magnitude of intraocular pressure elevation associated with eye rubbing. Ben-Eli H, Erdinest N, Solomon A. (2019) Pathogenesis and complications of chronic eye rubbing in ocular allergy. *Curr. Opin. Allergy Clin. Immunology* Oct;19(5):526-534. Bouffard MA, Cornblath WT, et.al. (2017). Transient Monocular Vision Loss on Awakening: A Benign Amaurotic Phenomenon. *J Neuropthal.* 37:122-5. Savastano A, Savastano MC, Carlomusto L, Savastano S. (2015) Bilateral Glaucomatous Optic Neuropathy Caused by Eye Rubbing. *Case Rep Ophthalmol.* 2015 Sep 2;6(3):279-83. Pecora L, Carrasco MA. (2002) Eye-rubbing Optic Neuropathy. *American Journal of Ophthalmology* 134 (3):460-2. Ioannidis AS, Speedwell L, Nischal KK. (2005) Unilateral keratoconus in a child with chronic and persistent eye rubbing. *American Journal of Ophthalmology* 139(2):356-7. Jafri B, Lichter H, Stulting RD. (2004) Asymmetric keratoconus attributed to eye rubbing. *Cornea* 23(6):560-4.

Keywords: Optic neuropathy, Orbit/ocular pathology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 10**Early Visual Changes Portend Visual Loss in a Case of Fludarabine Toxicity**

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Introduction:

Visual loss after fludarabine is a rare side effect. Here, we report a case of early visual changes associated with initiation of fludarabine treatment followed by rapid vision loss four weeks later.

Description of Case(s):

A 55-year-old male with aplastic anemia presented with deteriorating vision. He received fludarabine 30mg/m² for four consecutive days prior to total body irradiation in preparation for bone marrow transplant. Starting the day after the first infusion of fludarabine, the patient noted contrast alteration and light sensitivity. Day two post-infusion he noted shiny and flickering lights in both eyes. On day three of infusion he endorsed palinopsia with images in his field of vision appearing tilted or smaller than normal. One month after fludarabine treatment the patient experienced profound, sudden, painless vision loss in both eyes over the course of four days. On presentation visual acuity was 20/800 and CF. His pupils were sluggish without a relative afferent pupillary defect. He was unable to complete the control plate on Ishihara color testing. There was no obvious pallor of his optic nerves. Humphrey visual field reveal global suppression. Optical coherence tomography (OCT) demonstrated thinning of the inner nuclear layer. Electroretinography showed a preserved a-wave but an absent b-wave. Review of the MRI demonstrated symmetric increased signal intensity of the optic nerves bilaterally and periventricular hyperintensity on T2 FLAIR images of the brain.

Conclusions, including unique features of the case(s):

We present a case of a 55-year-old male who experienced early visual changes after initiation of fludarabine treatment followed by severe vision loss. The visual changes noted the first day after fludarabine treatment may serve as a harbinger of complications to come and should be taken into consideration of continuing treatment. Despite the use of lower doses of fludarabine, visual loss is still a devastating, albeit rare, consequence without any evidence of remedy.

References: None.

Keywords: Chemotherapy and radiation injury, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 11**Leber's Hereditary Optic Neuropathy Phenotype in a Male Adolescent with Paternally Transmitted Autosomal NSUN3 Mutation.**

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Introduction:

Leber's hereditary optic neuropathy (LHON) is clinically characterized by subacute progressive vision impairment and optic nerve atrophy in both eyes without other symptoms. After the initial visual decline, some patients show a recovery of visual function either spontaneously, or more often treatment-induced. The disease is usually caused by maternally inherited point mutations in mitochondrial genes encoding for subunits of complex I of the mitochondrial respiratory chain, leading to an imbalance in mitochondrial energy generation and increased oxidative stress in retinal ganglion cells. Visual recovery in LHON is attributed to a reactivated signal transduction in dysfunctional ganglion cells and nerve fibers that survived the energetic and oxidative crisis of the acute phase.

Description of Case(s):

An eleven-year-old boy experienced a painless decrease of vision in both eyes. During six months his visual acuity reduced to 20/400 and both optic nerves developed temporal atrophy. Laboratory tests, MRI and neurologic examinations were unremarkable and analysis of the mitochondrial DNA was negative for LHON-mutations and polymorphisms. Ten months after onset, visual acuity slowly began to increase and recovered to 20/50 after fourteen months. Whole exome sequencing detected a pathogenic homozygous frameshift mutation in the NSUN3 gene, which encodes for a mitochondrial tRNA-methyltransferase. This enzyme is required for efficient mitochondrial translation in humans and if defective, causes reduced mitochondrial protein synthesis, predominantly of complex I proteins. Examination results from the patient's family indicated an autosomal recessive inheritance, whereupon interestingly only the father had the same homozygous mutation (indicating paternal uniparental isodisomy in the index patient) and a similar clinical picture with atrophy of both optic nerves and unequally reduced visual acuity.

Conclusions, including unique features of the case(s):

This case demonstrates for the first time a LHON-like disease caused by a nuclear mutation that affects mitochondrial function. The interaction of nuclear and mitochondrial translation factors adds further pathogenic concepts to this mitochondrial disease.

References: Carelli, Carbonelli, de Coo, Kawasaki, Klopstock et al. International Consensus Statement on the Clinical and Therapeutic Management of Leber Hereditary Optic Neuropathy. *Journal of Neuro-Ophthalmology*. 37: 371-381. 2017 Van Haute, Dietmann, Kremer, Hussain, Pearce et al. Deficient Methylation and Formylation of mt-tRNA(Met) Wobble Cytosine in a Patient Carrying Mutations in NSUN3. *Nature Communications*. 7: 12039. 2016 Van Haute, Powell, Minczuk. Dealing with an Unconventional Genetic Code in Mitochondria: The Biogenesis and Pathogenic Defects of the 5-Formylcytosine Modification in Mitochondrial tRNA(Met). *Biomolecules*. 7: 24. 2017

Keywords: Genetic disease, Optic neuropathy

Financial Disclosures: Chiesi Pharmaceuticals: travel support, consultancy fee

Grant Support: None.

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Poster 12

Papilledema as the Presenting Sign of Lymphocytic Hypophysitis

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Introduction:

In a young female presenting with headache, sixth cranial nerve palsy, papilledema and visual field defects, pseudotumor cerebri is the most common cause. We report a patient with a normal BMI, panhypopituitarism and prolactinemia who presented with papilledema. Recognition and treatment of the pituitary lesion with steroids resulted in complete resolution of her visual as well as systemic symptoms.

Description of Case(s):

A 33-year-old female with a body mass index (BMI) of 27.5 presented with headache, blurred vision, nausea, and vomiting. She then developed galactorrhea. Neuro-ophthalmic exam revealed visual acuity of 20/25 in both eyes (OU) and a relative afferent pupillary defect in the left eye (OS). There was a mild restriction of abduction OS and Frisén grade 4 optic disc edema OU. Automated perimetry showed a superior altitudinal defect and inferior arcuate defects OD and an enlarged blind spot as well as superior and inferior arcuate defects OS. Non-contrast CT of the head revealed a suprasellar mass and MRI showed a rim enhancing sellar cystic lesion with suprasellar extension and a thickened and enhancing pituitary stalk. Acetazolamide (Diamox) 1500 mg orally was started. Lumbar puncture showed an elevated opening pressure of 27, mildly elevated CSF protein and 6 WBCs. The remainder of the CSF analysis was normal. Endoscopic endonasal hypophysectomy and biopsy showed heavy lymphocytic infiltration with only a few nests of normal pituitary cells. Immunohistochemistry was consistent with lymphocytic hypophysitis without Langerhans cells. The patient was treated empirically with steroids and after surgery the headache and diplopia resolved completely and the disc edema and visual field testing improved OU.

Conclusions, including unique features of the case(s):

Papilledema is a very uncommon finding in pituitary adenomas and usually occurs from obstructive hydrocephalus. In our patient inflammatory mechanisms from the lymphocytic infiltration including the pituitary stalk likely accounted for the optic disc edema and the increased intracranial pressure.

References:

None.

Keywords: Tumors, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Visual fields, Neuroimaging, High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 13**Preretinal Hemorrhages In Intracranial Hypertension: A Case Series**

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Introduction:

Preretinal hemorrhage with papilledema is associated with Terson's syndrome and intracranial hemorrhage but may also occur without intracranial hemorrhage. Data is limited regarding preretinal hemorrhage in the setting of intracranial hypertension (IH) without intracranial hemorrhage. We present three cases with varied causes of IH and preretinal hemorrhage.

Description of Case(s):

1. 22 year-old woman with cerebral venous sinus thrombosis, right > left papilledema, and right eye sub-ILM hemorrhage. LP opening pressure was 25 cm of water. She had no history of excessive vomiting, coughing, or Valsalva. She was treated with rivaroxaban, acetazolamide, and right ONSF, and over the next year her visual acuity, papilledema, and sub-ILM hemorrhage improved. 2. 25 year-old man with idiopathic IH and right > left papilledema with right eye vitreous and optic disc hemorrhages. LP opening pressure was 28 cm of water. He was treated with topiramate with improvement of his papilledema and intraocular hemorrhages. 3. 53 year-old woman with new headaches and vision changes, bilateral mild papilledema with bilateral peripapillary hemorrhages and a subtle, linear preretinal hemorrhage in the right eye. Brain MRI revealed a large planum sphenoidale meningioma with edema of the frontal lobes, prechiasmatic optic nerves, optic chiasm and optic tracts. Her papilledema, retinal and preretinal hemorrhages improved following tumor resection.

Conclusions, including unique features of the case(s):

Despite papilledema with preretinal hemorrhage, with appropriate treatment no patient in the series suffered significant permanent visual loss. The variety of causes of IH with preretinal hemorrhage in this series without intracranial hemorrhage supports a proposed mechanism of increased intracranial pressure transmitted to the optic nerve sheath and retinal veins, causing potential venous stasis and capillary rupture. Preretinal hemorrhage was present in the eye with more severe papilledema when asymmetry was present. Further research is needed to determine the prognostic value of preretinal hemorrhage in the setting of IH.

References: None.

Keywords: High intracranial pressure/headache, Pupils retina, Tumors, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 14

An unusual cause of inflammatory optic neuropathy

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Introduction:

Inflammatory optic neuropathies can be caused by different etiologies. Optic neuritis due to infectious sinusitis is a rare cause (1). It is associated to a greater extent with inflammation of ethmoid and sphenoid rather than other paranasal sinuses. (2) This condition occurs acutely and is caused by bacterial infections (3).

Description of Case(s):

A 59-year-old female, with no relevant systemic or ophthalmologic history, presented with acute blurred vision in her right eye associated with headache two days before onset. Best corrected visual acuity in the right eye was 9/10 with RAPD and a lower visual field scotoma. Extraocular muscle movements were full in both eyes but painful in the right eye. Color desaturation was absent. At fundus, the patient presented a unilateral swollen optic disc in the right eye. Complete blood work, including sedimentation rate was performed. All results were normal. Multiple sclerosis, rheumatological and sexually transmitted diseases were ruled out. Neuroimaging showed right optic neuritis and perineuritis associated with ipsilateral sphenoid sinusitis. The case was interpreted as optic neuritis due to sinusitis. Empiric antibiotic treatment was established. Within 24 hours, the patient denied blurred vision and eye pain. At fundus, improvement of optic disc edema was observed. RAPD disappeared three days later. VEP returned to normal few days after.

Conclusions, including unique features of the case(s):

Inflammatory optic neuropathy due to sinusitis is a true diagnostic challenge, since paranasal sinus disease can mimic demyelinating optic neuritis (1). Neuroimaging, mostly MRI, is mandatory when the history or examination show atypical optic neuritis. In such cases, additional appropriate tests should be performed so that timely and adequate treatment can be established, and to avoid the use of corticosteroids in etiologies that may not respond or even worsen the condition including life-threatening complications.

References: 1. Del Noce C, Marchi F, Sollini G, Iester M. Swollen Optic Disc and Sinusitis. Case Rep Ophthalmol 2017;8;421–424. 2. Kim YH. et al. Optic nerve changes in chronic sinusitis patients: Correlation with disease severity and relevant sinus location. PLoS One 2018;13(7):e0199875. 3. Chen L, Jiang L, Yang B, Subramanian PS. Clinical features of visual disturbances secondary to isolated sphenoid sinus inflammatory diseases. BMC Ophthalmology 2017;17(1):237.

Keywords: Optic neuropathy, Magnetic resonance imaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 15**Binasal Visual Field Defects Caused by Temporal Posterior Subcapsular Cataracts**

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Introduction:

The first structures of the eye that light passes through are the refracting components; the cornea and lens. Therefore, it is possible, although not common, to have a visual field defect secondary to a corneal or lens opacity. Understanding where visual information reverses is crucial to attributing the defect to an anterior structure. Since the nodal point of the eye is at the posterior lens/anterior vitreous, an opacity anterior to this will cause an ipsilateral defect whereas it will be reversed at the nodal point. Although cataracts do not typically cause a visual field defect, there have been several case reports of defects secondary to posterior subcapsular cataracts (PSC) that resolve after surgery. We report a case supporting this finding.

Description of Case(s):

A 55-year old woman developed blurry vision nasally OU. Best corrected visual acuity was 20/30 OD and 20/40 OS with normal color vision and no RAPD. Slit lamp examination was remarkable for bilateral temporal PSC respecting the vertical meridian. Dilated fundus examination was unremarkable as was optic nerve OCT and ganglion cell analysis. 24-2 HVF demonstrated a general reduction in sensitivity with nasal depression OU. Following cataract surgery, her visual field defect resolved OU.

Conclusions, including unique features of the case(s):

A cataract often has a negligible effect on visual field, typically only affecting the total deviation. However, our patient and few other case reports support that a PSC can cause a visual field defect that resolves after cataract surgery. Such visual fields from PSC are classically opposite to the lesion location, similar to what we see in the optic nerve and retina, whereas lesions affecting the anterior portion of the lens, or the cornea will give a visual field defect ipsilateral to the lesion. This is explained by optics and the anatomic location of the nodal point in the eye.

References: Karp CL, Fazio JR. Traumatic cataract presenting with unilateral nasal hemianopsia. J Cataract Refract Surg 1999; 25(9):1302-3 Harris WF. Nodes and nodal points and lines in eyes and other optical systems. Ophthalmic and Physiol Opt; 2010; 30(1):24-42 Rahman I, Nambiar A, Spencer AF. Unilateral nasal hemianopsia secondary to posterior sub capsular cataract. Br J of Ophthalmol 2003; 87(8):1045-1046

Keywords: Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 16**Acute vision loss post cataract surgery associated with bilateral panretinal dysfunction secondary to autoimmune retinopathy?**

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Introduction:

Autoimmune retinopathies can be paraneoplastic or non-paraneoplastic and are associated with antibodies that may cause loss of visual acuity, dyschromatopsia, visual field deficits and pan-retinal photoreceptor dysfunction (rods and cones). We report a series of patients who present with acute vision loss post cataract surgery with evidence of non-paraneoplastic autoimmune retinopathy.

Description of Case(s):

Series of five patients (3 males and 2 females, ages 70 - 81, x=74) who present with acute, painless unilateral vision loss post cataract surgery. Visual acuity ranged from 20/200 to CF at presentation. Fundus exams, OCT and fluorescein angiography was unremarkable. There was bilateral (worse in the symptomatic, post-operative eye) visual field loss (central > peripheral) as well bilateral impairments on Ganzfeld and multifocal electroretinograms. There were positive retinal autoantibodies in all cases and positive retinal immunohistochemistry in three out of five cases. Full workups did not reveal any neoplastic or significant autoimmune disorders. Three out of five cases were treated with immune-based therapy.

Conclusions, including unique features of the case(s):

Patients with laboratory evidence of non-paraneoplastic autoimmune retinopathy may first present clinically with acute vision loss post cataract surgery. Such retinas may decompensate in response to surgery-related factors such as phototoxic injury or inflammation. This association has not been previously described and is important to recognize as it may be amenable to immune-based therapies once paraneoplastic causes have been ruled out.

References: Rahimy E., Sarraf, D. Paraneoplastic and non-paraneoplastic retinopathy and optic neuropathy: Evaluation and management. Survey of Ophthalmology, Vol.58(5), pp.430-58, 2013. Sen HN., Grange L., Akanda M., Fox A. Autoimmune Retinopathy: Current Concepts and Practices (An American Ophthalmological Society Thesis). Transactions of the American Ophthalmological Society, Vol.115, pp.T8, 2018.

Keywords: Pupils retina, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 18

Retrolaminar and Intraventricular Migration of Intraocular Silicon Oil, Masquerading a Chiasmal Syndrome

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Introduction:

Present a case report of a rare post-vitreectomy complication, secondary to Silicon Oil migration through the visual pathway, to the Central Nervous System (CNS).

Description of Case(s):

A 75-year-old woman who had undergone vitreoretinal surgery with silicon oil (SO) in her right eye (OD) followed by ocular hypertension (40 mm Hg) developed contralateral – left eye (OS) - visual acuity (VA) and visual field (VF) deterioration 14 months later. Brain MRI showed findings compatible with SO in right optic nerve and chiasm, and later migration to subarachnoid space. So SO was surgically extracted and intramuscular corticosteroids applied. Her OS VA and VF improved to basal. (Funduscopy, VF tests and Brain MRI images will be presented).

Conclusions, including unique features of the case(s):

How long should the silicon oil remain in the operated eye is still unclear, specially in patients with high postoperative IOP as well as pre-existing glaucoma, and with optic disk risk factors such as: megalopapillae, optic pit, morning glory. These should be considered for the management of these patients after vitrectomy. Nevertheless, there's much more to be studied to understand the pathophysiology of our patient. In conclusion, silicone oil optic neuropathy may be more frequent than diagnosed. It is therefore advisable to perform neuroimaging studies in patients with otherwise unexplained visual field loss after successful vitrectomy.

References: 1. Cibis PA, Becker B, Okun E, Canaan S. The use of liquid silicone in retinal detachment surgery. Arch Ophthalmol 1962;68:590–599. 2. Boren RA, Cloy CD, Gupta AS, Dewan VN, Hogan RN. Retrolaminar Migration of Intraocular Silicone Oil. J Neuroophthalmol. 2016;36(4):439-447. 3. Bobba S, Fox OJK, Lee MB, Parker R, Jain NS, Semmonds AK, Agar A, Francis IC. Contiguous Silicone Oil Migration From the Vitreous Cavity to the Optic Tract. J Neuroophthalmol. 2017;37(4):464-465. 4. Eckle D, Kampik A, Hintschich C, Haritoglou C, Tonn JC, Uhl E, Lienemann A. Visual field defect in association with chiasmal migration of intraocular silicone oil. Br J Ophthalmol. 2005 Jul;89(7):918-20. 5. Shields CL, Eagle RC Jr. Pseudo-Schnabel's cavernous degeneration of the optic nerve secondary to intraocular silicone oil. Arch Ophthalmol. 1989 May;107(5):714-7.

Keywords: Optic neuropathy, Neuroimaging, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 19**Reversible Unilateral Visual Field Defect as the Presentation of a Pituitary Adenoma and Cerebral Aneurysm**

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Introduction:

Bitemporal hemianopsia is a well known sequelae of compression of the optic chiasm, oftentimes by a pituitary tumor. Here we present a case of a patient with unilateral visual symptoms as the presenting sign of a pituitary adenoma and a large cerebral aneurysm.

Description of Case(s):

Our patient was a 47 year-old male without prior medical history presenting with decreased vision and photopsias in the right eye for 9 months. He was referred to neuro-ophthalmology for his unexplained decreased vision. Examination revealed decreased color vision, and a rAPD in the right eye; no deficits were identified in the left eye. On Humphrey Visual Field testing, the patient was found to have an inferotemporal deficit in the right eye that respected the vertical meridian; no corresponding deficits were found in testing of the left eye. MRI of the brain was recommended and revealed a large compressive pituitary macroadenoma and an anterior communicating aneurysm. The patient subsequently underwent urgent aneurysm coiling and tumor resection. At his post operative follow-up, the patient had improvement of his vision with full color vision and resolved rAPD. Repeat Humphrey Visual Field testing demonstrated resolution of the patient's prior inferotemporal deficit.

Conclusions, including unique features of the case(s):

Chiasmal compression typically presents with bitemporal visual field defects. We present a case of chiasmal compression from a pituitary macroadenoma and a large aneurysm presenting with subtle unilateral symptoms and a unilateral visual field defect. This case highlights the importance of considering a chiasmal etiology whenever a temporal visual field defect is seen, even when unilateral. We also demonstrate that early treatment can result in improvement or resolution of the visual field defect.

References: Anik, I., et al. "Evaluation of Early Visual Recovery in Pituitary Macroadenomas after Endoscopic Endonasal Transsphenoidal Surgery: Quantitative Assessment with Diffusion Tensor Imaging (Dti)." *Acta Neurochir (Wien)* 153.4 (2011): 831-42. Print. Cohen, A. R., et al. "Visual Recovery after Transsphenoidal Removal of Pituitary Adenomas." *Neurosurgery* 17.3 (1985): 446-52. Print. Poon, A., et al. "Patterns of Visual Loss Associated with Pituitary Macroadenomas." *Aust N Z J Ophthalmol* 23.2 (1995): 107-15. Print.

Keywords: Neuroimaging, Visual fields, Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 20

Three Uncommon Tumors Mimicking More Common Tumors Affecting Vision

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Introduction:

The practice of neuro-ophthalmology overlaps frequently with neuro-oncology. Meningioma, pituitary macroadenomas, and other primary and common metastatic tumors are often in our differential. We present three cases where the initial impression of a more common tumor, was ultimately determined to be a rare mimic with additional implications for the care of the patient.

Description of Case(s):

Case 1: A 25-year-old woman was referred due to gradual vision loss in the left eye. The history and examination were concerning for a compressive optic neuropathy. MRI and CT, were consistent with a meningioma at the left anterior clinoid. At surgery, the impression before and after, was meningioma. Case 2: A 70 year-old man was seen due to new field deficits of two months' duration. The history and examination were suggestive of a compressive lesion at the chiasm. Neuro-imaging demonstrated a large suprasellar consistent with a pituitary macroadenoma. At surgery, only subtotal resection was possible due to extensive bleeding. Case 3: An 81 year-old woman was admitted following an abnormal brain MRI ordered due to painless, progressive vision loss in both eyes. The history and examination were suggestive of a bilateral optic neuropathy; worse on the right. MRI of the brain showed multiple enhancing foci with notable diffusion restriction, concerning for central nervous system lymphoma. Lumbar puncture was not diagnostic. Body CT found equivocal thickening of the ureters and bladder. Brain biopsy was consistent with metastatic carcinoma.

Conclusions, including unique features of the case(s):

Case 1: Tenosynovial giant cell tumor; a rare, benign, but locally aggressive tumor potentially mimicking meningioma. Case 2: Spindle cell oncocytoma, an exceedingly rare tumor with imaging characteristics mimicking pituitary macroadenomas. Highly vascular, these tumors pose surgical difficulties distinct from other sellar tumors. Case 3: Brain metastasis from urothelial carcinoma is exceedingly uncommon. Diffusion restriction occurs with highly cellular lesions; and is more common to lymphoma than metastases.

References: Tenosynovial giant cell tumors of the temporomandibular joint and lateral skull base: Review of 11 cases. Laryngoscope. 2017 Oct;127(10):2340-2346. Chondroblastoma of the clivus: Case report and review. J Neurol Surg Rep. 2015 Nov;76(2):e258-64. Giantini Larsen AM, et al. Spindle cell oncocytoma of the pituitary gland, J Neurosurg. 2018 Oct 19:1-9 Billeci D, et. al. Spindle cell oncocytoma: Report of two cases with massive bleeding and review of the literature, J Clin Neurosci. 2017 May;39:39-44. Boyle HJ, et. al. Brain metastases in patients with urothelial carcinoma, Journal of Clinical Oncology 2012 30:15_suppl, e15009-e15009 Duygulu G, et. al. Intracerebral metastases showing restriction diffusion: Correlation with histopathologic findings, Eur J Radiol. 2010 Apr;74(1):117-20.

Keywords: Neuroimaging, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Optic neuropathy, Tumors, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 21**Idiopathic Orbital Inflammatory Syndrome Mimicking Optic Nerve Sheath Meningioma on Orbital Imaging**

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Introduction:

Idiopathic orbital inflammatory syndrome (IOIS), or orbital pseudotumor, is a non-specific inflammatory disease of unknown origin. The diagnosis of IOIS is one of exclusion and can mimic many infectious, neoplastic, and autoimmune disorders. We report patient with MRI findings concerning for optic nerve sheath meningioma who was diagnosed to have orbital pseudotumor.

Description of Case(s):

A 64-year-old woman presented to ophthalmology clinic with worsening pain and progressive loss of vision in left eye of 10 days duration. Ophthalmology examination revealed VA of CF, APD, mild abduction deficit, ptosis, and proptosis in left eye. Fundus examination showed normal optic discs and retina in both eyes. MRI orbit revealed enhancing mass surrounding the optic nerve with narrowing of left optic nerve due to mass effect. There was extension of enhancement into the intracranial components of the optic nerve sheath up to level of optic chiasm. Right orbit appeared unremarkable. Inflammatory workup detected antinuclear antibodies with normal DNA antibody titers. CSF studies revealed 19 WBCs with negative infectious work up. CT chest negative for hilar lymphadenopathy. The case was discussed in tumor board and optic nerve sheath meningioma was favored, with recommendation for biopsy. Patient was seen in Neuro-ophthalmology clinic with conclusion of clinical suspicion for IOIS. Patient given high dose IV pulse steroids for 5 days, followed by oral taper. On 10 day follow up, there was significant improvement in VA to 20/25 with resolution of abduction deficit in left eye.

Conclusions, including unique features of the case(s):

1. Radiological findings should always be correlated with clinical presentation to reach final diagnosis. 2. Rarely, IOIS can mimic optic nerve sheath meningioma. Radiological or clinical suspicion of other common etiologies of optic nerve sheath enhancement should not veer the clinician away from considering IOIS. 3. Often described as “benign”, without proper identification and management, permanent visual loss can occur.

References: None.

Keywords: Optic neuropathy, Neuroimaging, Optic nerve trauma and treatment, Tumors, Higher visual functions

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 22

A Case of Bartonella Neuroretinitis Secondary to a Horse Bite

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Introduction:

Neuroretinitis is characterized by optic disc edema with fluid or lipid exudates in the papillomacular bundle and around the fovea. Most infectious cases are due to cat-scratch disease, caused by Bartonella species. Bartonella is one of the most common types of bacteria in the world, and cats are considered the natural reservoir of this pathogen.

Description of Case(s):

A 56 year-old Hispanic male presented with progressive vision loss in both eyes for 10 days (OS first, now OD) associated with a ~3-week history of fatigue, malaise, and headaches. His symptoms started after being bit by a race horse. On exam, his BCVA was OD: 20/100 and OS: 20/500, Ishihara plates: OD: 4/11 and OS: 2/11, pupils were reactive without APD. He had 0.5+ cells in the AC and trace cells in the anterior vitreous OU. Fundus examination showed bilateral optic nerve edema with subretinal fluid extending into the macular area OS>OD, these findings were confirmed by OCT testing. Neuro-imaging was normal. His LP showed an opening pressure of 26 cm H₂O with a normal CSF analysis. ESR and CRP were both elevated, and his B henselae serum antibody titers were highly positive. Other infectious causes were excluded. The patient was treated with oral doxycycline x 14 days with significant improvement in his symptoms over time.

Conclusions, including unique features of the case(s):

Data about Bartonella in equids are very scant. Two cases of equine bartonellosis were reported in 2008. A study from Central Italy showed a seroprevalence of the antigen of 58% in asymptomatic horses. In addition to cats, numerous domestic and wild animals, including bovine, equine, canine, and rodent species can serve as reservoir hosts for various Bartonella species. Teaching point: Not only cats can transmit cat-scratch disease!

References: Suhler EB, Lauer AK, Rosenbaum JT. Prevalence of serologic evidence of cat scratch disease in patients with neuroretinitis. Ophthalmology. 2000;107:871-876. Jones et al. Detection of Bartonella henselae in the Blood of 2 Adult Horses. J Vet Intern Med 2008;22:495-498. Ebani et al. Bartonella infection in asymptomatic horses and donkeys from Tuscany, Central Italy. Asian Pacific J Trop Med 2017;10(11):1077-1079.

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 23

Gazing into the Crystal Ball: Calciphylaxis Causing Orbital Ischemia and Crystalline Retinopathy

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Introduction:

A patient presents with progressive vision loss after cataract surgery secondary to calciphylaxis.

Description of Case(s):

A 72-year-old female with diabetic nephropathy and failed renal transplant on peritoneal dialysis presented with bilateral vision loss. She reported months of diminishing right eye vision which worsened following cataract extraction. Visual acuity was hand motion in the right and 20/100 in the left eye with right afferent pupillary defect. Color vision was 2/11 plates in the left eye. Visual fields to confrontation were constricted bilaterally. Intraocular pressures were 23 and 16 mm of Hg in the right and left eye. There was diffuse right eye central corneal opacity with iris neovascularization. Fundus examination revealed bilateral pale optic nerves with cotton wool spot inferior to right optic disc. Retinal examination showed diffuse arteriolar whitening with crystalline deposits in the left eye macula. On further inquiry, patient reported development of gluteal skin nodules a month prior. Biopsy revealed calcinosis cutis, a dermatopathologic finding on the spectrum of calcific vasculitides. Her vision worsened to light perception in the right and 20/400 in the left eye with increasing visual field constriction. Hemodialysis with intravenous sodium thiosulfate was started with improvement of left eye vision to 20/125.

Conclusions, including unique features of the case(s):

Pathogenesis of systemic calciphylaxis is poorly understood but believed to result from upregulation of osteogenesis and decreased inhibition of vascular calcification in parathyroid-axis dyscrasias and chronic inflammatory states such as end-stage renal disease. Excess serum calcium-phosphate deposits in blood vessels causing tissue infarction, most commonly in the skin (1). Prior case reports have described ischemic optic neuropathy mimicking giant cell arteritis (2)(3)(4) and crystalline retinopathy with ocular ischemic syndrome (5) separately. Treatment with empiric intravenous sodium thiosulfate and calcium chelation may preserve vision in some patients.

References: Nigwekar, SU et al, "Calciphylaxis: Risk Factors, Diagnosis, and Treatment", Am J Kidney Dis., 66(1): 133–146, 2015 Al-Absi, Al et al, "Medial arterial calcification mimicking temporal arteritis", AJKD, 44(4): 73-78, 2004 Roverano, S et al, "Calciphylaxis of the temporal artery masquerading as temporal arteritis: case presentation and review of literature", Clin Rheum, 344(11):1985-88, 2015 Sivertsen MS, Strøm EH, Endre KMA, Jørstad ØK. "Anterior Ischemic Optic Neuropathy Due to Calciphylaxis", J Neuroophthalmol, 38(1), 54–6, 2018 Naysan, J et al "Crystalline Retinopathy and Retinal Vasculopathy in Calciphylaxis" Retinal Cases & Brief Reports, 12:331-335, 2018

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Orbit, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 24

Extra orbital manifestations of MOGAD

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Introduction:

MOGAD(myelin oligodendrocyte associated disorder) is an inflammatory demyelinating condition of the CNS characterized by a monophasic or relapsing course of neurological dysfunction. The most common presentation of anti MOG positive disorder is optic neuritis (70-88%) followed by myelitis (30%) and brain stem (7%) involvement. Multiple cranial nerve involvement is a rare presentation although a few cases have been reported.

Description of Case(s):

We present here a 70-year female with history of migraines without aura, left eye herpes zoster ophthalmicus, rheumatoid arthritis, presenting with acute onset left eye blurry vision. This was preceded two weeks earlier by a left facial dysesthesia, left ear and left eye pain with ocular motility along with tingling down her left face. An emergent MRI stroke protocol ruled out a stroke. A few days later she developed burning and tearing of the left eye. She then developed left eye blurry vision the same day, with progressive worsening in all fields. She also had associated headaches with left eye retro-orbital pain. On exam she had pain on eye movements and V1/V2 distribution paresthesia. Exam was significant for decreased left eye visual acuity (20/125 left eye improving to 20/60 with correction) along with an afferent pupillary defect. Left eye showed limitation in abduction and supraduction. There was subtle diffuse swelling of the left optic nerve with obliteration of the cup.

Conclusions, including unique features of the case(s):

MRI showed T2 hyperintensity and enhancement of the intra-orbital optic nerve and surrounding tissues. There were no intracranial abnormalities. Serum studies showed elevated MOG IgG. Additional serum studies and CSF analysis were unrevealing. She was treated with IV methylprednisolone 1000mg daily for 3 days and was discharged on prolonged prednisone taper with significant improvement in a week. Our case highlights the involvement of trigeminal and other cranial nerves in MOG antibody disorder masquerading as orbital inflammatory process.

References: 1. Lana-Peixoto MA, Talim N. Neuromyelitis Optica Spectrum Disorder and Anti-MOG Syndromes. *Biomedicines*. 2019 Jun 12;7(2) 2. Cobo-Calvo A, Vukusic S, Marignier R. Clinical spectrum of central nervous system myelin oligodendrocyte glycoprotein autoimmunity in adults. *Curr Opin Neurol*. 2019 Jun;32(3):459-466 3. Chen JJ et al. Myelin oligodendrocyte glycoprotein antibody-positive optic neuritis: clinical characteristics, radiologic clues, and outcome. *Am J Ophthalmol* 2018; 195:8 – 15. 4. Cobo-Calvo A et al. Clinical spectrum and prognostic value & of CNS MOG autoimmunity in adults: the MOGADOR study. *Neurology* 2018; 90: e1858–e1869. 5. Cobo-Calvo A et al. Cranial nerve involvement in & patients with MOG antibody – associated disease. *Neurol Neuroimmunol-Neuroinflamm* 2019; 6: e543. 6. Salama S, Pardo S, Levy M. Clinical characteristics of myelin oligodendrocyte glycoprotein antibody neuromyelitis optica spectrum disorder clinical characteristics of myelin oligodendrocyte glycoprotein antibody neuromyelitis optica spectrum disorder *Mult Scler Relat Disord*. 2019 May; 30:231-235

Keywords: Demyelinating disease, Optic neuropathy, Orbit/ocular pathology

Financial Disclosures: The authors had no disclosures.

Grant Support: Unrestricted Grant from Research to Prevent Blindness.

Contact Information: None provided.

Poster 25

Junctional Scotoma as the Initial Presentation of Neurocysticercosis

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Introduction:

Neurocysticercosis (NCC) is a parasitic infection involving the infiltration of *Taenia solium* in the intestine and hematogenous spread to the central nervous system. NCC commonly presents with seizure-like activity, but may manifest with headaches and intracranial hypertension. 1 Historically junctional scotomas have been associated with aneurysms or pituitary neoplasms. 2 3 We present a rare case of NCC presenting as a junctional scotoma.

Description of Case(s):

A 32-year-old Peruvian male presented with a 6-week history of progressive blurred vision predominantly in his right eye that began one month after returning from a trip to Peru. The patients' history was positive for occipital headaches two years prior that subsided, leptomeningeal enhancement of unclear etiology on brain magnetic resonance imaging (MRI) two years prior at an outside facility, and annual visits to Peru from the United States for 16 years. Examination revealed visual acuity of 20/80 OD and 20/50 OS, right-sided relative afferent pupillary defect and bilateral optic disc edema. Automated perimetry revealed a junctional scotoma, concerning for a lesion at the junction of the right optic nerve and optic chiasm. Brain MRI revealed mild ventriculomegaly, a suprasellar cystic lesion with mild mass effect upon the optic chiasm, and an area of calcification in the left parietal lobe. CSF was positive for anticysticercal antibody IgG. The patient was treated with albendazole, praziquantel, corticosteroids, acetazolamide, and required a ventriculoperitoneal shunt. His vision improved over the subsequent months.

Conclusions, including unique features of the case(s):

This case demonstrates an alternative presentation of NCC and exemplifies the importance of a detailed history and prompt assessment of patients with junctional scotomas. To the author's knowledge there is no known documented case of NCC presenting with a junctional scotoma.

References: 1. Garcia, H. H. (2018). Neurocysticercosis. *Neurologic Clinics*, 36 (4), pp. 851-864. doi: 10.1016/j.ncl.2018.07.003. 2. Traquair, H.M. *An Introduction to Clinical Perimetry*. St. Louis: The C.V. Mosby Company, 1946, pp. 93-115, 207-211. 3. Bird, A. (1972). Field Loss due Lesions at the Anterior Angle of the Chiasm. *Proc roy Soc Med*, 65, pp 519-520.

Keywords: Visual fields, High intracranial pressure/headache, Neuroimaging, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Perimetry

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 26**Dramatic Visual Recovery in Central Retinal Artery Occlusion Treated with Local Intra-Arterial Tissue Plasminogen Activator**

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Introduction:

Central retinal artery occlusion (CRAO) is a rare, but devastating disease that results in profound visual loss in a majority of cases. It has no proven treatment and a variety of management options used clinically all have dismal rates of success.

Description of Case(s):

A 72-year-old male had undergone uncomplicated cataract surgery in his left eye. Post-operative check at 2.5 hours documented uncorrected vision of 20/60, intraocular pressure of 18 mmHg, trace corneal edema and a well-positioned intraocular lens. He returned an hour later, and his left eye vision had reduced to light perception. He had a brisk relative afferent pupillary defect (RAPD), but the retina and optic nerve appeared normal. Intravenous fluorescein angiography confirmed vascular attenuation and reduced flow. The patient underwent local intra-arterial thrombolysis (LIT) of his left ophthalmic artery 2.75 hours after the onset of his vision loss. Within one minute of injection, the patient noted improvement in his vision. By the next day, his vision had improved to 20/40 and by one week, his vision was 20/20 with no RAPD. CT angiography of his chest, neck and brain revealed a large plaque in the left subclavian artery that was the presumed source of his embolic CRAO.

Conclusions, including unique features of the case(s):

There are various potential treatment options for CRAO, however they lack strong evidence for their efficacy. While the EAGLE study concluded that there was no difference in visual outcome between observation and LIT, the mean interval between symptom onset and therapy was 13 hours. This case demonstrates that in cases of CRAO, the retina may initially appear normal – even in the presence of an RAPD. Also, early administration of LIT can have profound effect on the final visual outcome. Working closely with experienced interventional neuro-radiologists can provide excellent outcomes for this rare, but visually significant condition.

References: None.

Keywords: Stroke trauma, Interventional neuroradiology, Vascular disorders, Pupils retina

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 27**RETINAL HEMORRHAGE IN MYELIN-OLIGODENDROCYTE GLYCOPROTEIN-ANTIBODY ASSOCIATED OPTIC NEURITIS – A CASE REPORT**

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Introduction:

Myelin oligodendrocyte glycoprotein-immunoglobulin G (MOG-IgG) associated optic neuritis is currently recognized as a particular entity of which the knowledge has been evolved quickly in this decade. However, the retinal hemorrhage has yet been reported in patients with this disease.

Description of Case(s):

We report an interesting case of a 59-year-old healthy Thai man, presenting with bilateral sequential optic neuritis. On initial examination, visual acuity was counting finger and 20/100 in the right and left eyes, respectively. Relative afferent pupillary defect (RAPD) was present in the right eye. Fundoscopy showed diffuse optic disc swelling and also multifocal retinal hemorrhages in the posterior pole of both eyes. Optical coherence tomography (OCT) of the macula confirmed all layered retinal hemorrhages in the right eye, while only retinal nerve fiber layer hemorrhage was observed in the left eye. Fundus fluorescein angiography demonstrated only leakage from bilateral optic discs without neither delay in arteriovenous transit time nor retinal vasculature abnormality. Magnetic resonance imaging (MRI) of the brain and orbit was significant for enhancement of bilateral anterior optic nerves and their nerve sheath complexes. Blood test was positive for MOG-IgG, and thrombophilia testings were all negative. Other alternative causes of diffuse multi-layered retinal hemorrhage were investigated and ruled out. Following intravenous methylprednisolone for 3 days, his vision returned to normal. Oral prednisolone was given and gradually tapered. The findings of retinal hemorrhage resolved within three months.

Conclusions, including unique features of the case(s):

To the best of our knowledge, this is the first report of multifocal retinal hemorrhages in the MOG-IgG associated optic neuritis.

References: None.

Keywords: Optic neuropathy, Demyelinating disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 28**VARIOUS CLINICAL ENTITIES OF OPTIC NEUROPATHY IN LEUKEMIA**

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Introduction:

Optic neuropathy in leukemic patients has various etiologies, including infiltration, increase intracranial pressure from central nervous system (CNS) involvement or medication, infection and compression. Moreover, leukemic infiltrative optic neuropathies have diverse presentations ranging from normal to obvious optic disc abnormalities with or without orbital involvement.

Description of Case(s):

#Case 1: A 19-year-old woman with history of resolved acute lymphocytic leukemia, presented with painless progressive visual loss in the left eye for 2 weeks. Ophthalmic examination of the left eye showed visual acuity of counting finger, presence of afferent pupillary defect and mild blurred optic disc margin. Magnetic resonance imaging (MRI) revealed enhancement with restricted diffusion of bilateral entire optic nerves, compatible with leukemic infiltration. Leukemic infiltrative optic neuropathy was confirmed by cerebrospinal fluid (CSF) cytology. Intrathecal chemotherapy was initiated. Her vision regained 20/20 bilaterally. At 3-month follow up, she developed binocular horizontal diplopia. Visual acuity was 20/20 bilaterally. Fundus examination showed bilateral generalized swollen optic discs with hemorrhages. Ocular motility demonstrated mild abduction deficit bilaterally. Visual field showed bilateral blind spot enlargement. CSF analysis was normal except for high opening pressure. After thorough medication review, a diagnosis of acute papilledema due to norethisterone was made. Acetazolamide was initiated and norethisterone was discontinued. #Case 2: A 43-year-old man, previously diagnosed of end-stage chronic myeloblastic leukemia, noticed painful progressive visual deterioration in the right eye for 3 days. Ophthalmic examination showed visual acuity of no light perception in the right eye and 20/200 in the left eye, bilateral generalized swollen discs with hemorrhages and orbital inflammation in the right eye. MRI revealed infiltrative enhancing lesions involve bilateral orbits and optic nerves. Chemotherapy was refrained due to dilapidated condition of the patient.

Conclusions, including unique features of the case(s):

Optic neuropathy in leukemic patients has multitudinous etiologies. Recognition of various clinical entities should lead to appropriate treatment and excellent visual outcome.

References: None.

Keywords: Optic neuropathy, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 29**Long Term Follow-Up Of Two Cases Of Optic Nerve Head Angioma; A Photo Essay.**

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Introduction:

Optic nerve head angiomas (ONHA) are uncommon, as such there is little regarding the natural history and management of these lesions. This poster aims to share our follow-up of two patients (11 and 8 years) with these rare tumors.

Description of Case(s):

Case 1: Thirty-six-year-old female with Von Hippel Lindau Syndrome (VHLS) presented to us in 2014 with an incidental finding of a left optic nerve head (ONH) lesion. She had photographic documentation of the lesion since 2008. Visual acuity remained 6/6 till April 2019 when it dropped to 6/24, despite macular edema documented by ocular coherence tomography since 2012. Her acuity decreased as she developed a full thickness macular hole. She underwent trans pars plana vitrectomy with membrane peel in May 2019. Post operatively her vision improved to 6/15 with anatomic closure of the macular hole, albeit with persistent macular edema. Case 2: Seventy-eight-year-old female with diabetes, hypertension, ischemic heart disease and renal failure (on dialysis) was on follow-up for normal tension glaucoma and diabetic retinopathy. A drance hemorrhage was noted on her right ONH in 2012, this however increased in size and fluorescein angiography in 2014 was consistent with ONHA. She had no evidence of VHLS. Vision was 6/9 in 2013 due to epiretinal membrane from vitreomacular traction, slow deterioration to 6/15 in 2015 and presently 6/30 is secondary to macular edema. She had small amounts of vitreous hemorrhage in 2015 as again in 2019. She was offered photodynamic therapy but declined due to her myriad of other medical problems.

Conclusions, including unique features of the case(s):

Although ONHA are benign tumors, they result in slow deterioration of vision due to edema of the surrounding retina or vitreous hemorrhage. There is presently no good treatment for this condition.

References: None.

Keywords: Tumors, Neuro-opth & systemic disease (eg. MS, MG, thyroid), Vascular disorders, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 30**Timely reversal of profound acute vision loss in a case of dural carotid-cavernous fistula**

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Introduction:

Dural carotid cavernous fistulae are abnormal connections between the carotid system and the cavernous sinus via small shunt vessels. Anterior drainage of blood shunted through the cavernous sinus into the orbital venous system accounts for the typical features of presentation. Vision loss has been reported by a variety of proposed mechanisms including elevated IOP, hypoxic venous stasis, retinal vessel occlusion, ischemic optic neuropathy, mechanical compression, and others. Many cases can be observed and spontaneous resolution is common, often preceded by partial thrombosis with transient worsening of symptoms. It is not clear whom it is safe to observe through this process. Treatment often restores vision unless the vision loss has occurred via glaucoma or an ischemic insult.

Description of Case(s):

A 59 year old woman followed by the ophthalmology and neurosurgery services at our institution for a dural CCF presented to the emergency department with 3 days of worsening proptosis, redness, diplopia, and a mildly blurred vision. Exam disclosed normal central acuity, a relative afferent pupil defect, and signs of retinal venous congestion. She was admitted for observation and imaging. Her vision deteriorated overnight to bare light perception and she underwent emergent catheter angiography demonstrating a patent indirect CCF without thrombosis, which was coiled successfully. Her orbital signs and symptoms and retinal vascular changes quickly resolved and she recovered excellent visual acuity.

Conclusions, including unique features of the case(s):

This was a rare case of rapidly progressive vision loss in a patient with an indirect CCF and signs of retinal venous congestion which was felt to be an appropriate indication for emergent angiography and embolization. Though pre-resolution thrombosis was considered, her profound vision loss precluded observation. Ischemic vision loss due to ION, ischemic CRVO etc. are feared irreversible complications of the oft benign dural CCF, however in this case profound vision loss was averted with timely intervention.

References: Das S et al. Return of vision after transarterial coiling of a carotid cavernous sinus fistula: case report. *Surgical Neurology*. 2006 Jul;66(1):82-5; discussion 85. Gonzalez Castro et al. Carotid-Cavernous Fistula: A Rare but Treatable Cause of Rapidly Progressive Vision Loss. *Stroke*. 2016 Aug;47(8):e207-9. Halbach et al. Carotid cavernous fistulae: indications for urgent treatment. *AJR Am J Roentgenol*. 1987 Sep;149(3):587-93. Hedges et al. Reversible optic neuropathy due to carotid-cavernous fistula. *J Clin Neuroophthalmol*. 1985 Mar;5(1):37-40. Miller NR. Diagnosis and management of dural carotid-cavernous sinus fistulas. *Neurosurg Focus*. 2007;23(5):E13. Razeghinejad et al. Sudden onset and blinding spontaneous direct carotid-cavernous fistula. *J Ophthalmic Vis Res*. 2011 Jan;6(1):50-3. Sergott et al. The Syndrome of Paradoxical Worsening of Dural-Cavernous Sinus Arteriovenous Malformations. *Ophthalmology* 1987 Sanders et al. Hypoxic ocular sequelae of carotid-cavernous fistulae. *Br J Ophthalmol*. 1969 Feb;53(2):82-97. Witmer, Matthew MD. Understanding the CCF/Vein occlusion connection. *Review of Ophthalmology* Apr 22, 2010

Keywords: Vascular disorders, Interventional neuroradiology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 31

A Case of Acute Macular Neuroretinopathy Associated with Acute Optic Neuritis

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Introduction:

Acute optic neuritis (AON) is a common inflammatory optic neuropathy. Demyelinating AON is the most common type. AON is associated with inner nuclear layer thickening and microcystic macular edema on optical coherence tomography (OCT), independently of demyelination. Conversely, acute macular neuroretinopathy (AMN) type 2 is a rare outer retinal disorder, with suspected vascular etiology mainly affecting the deep capillary plexus, resulted with thinning of the outer nuclear layer. Both entities most commonly affect young Caucasian women. We present a case of AMN associated with AON.

Description of Case(s):

A 37-year-old Caucasian woman presented with acute blurred vision and small scotomata in her right visual field. Past medical history was significant only for clinically isolated left AON, for which no etiology was found. Best corrected visual acuity was 20/40 in the right eye and 20/20 in the left eye. Color vision was normal, but there was a positive right relative afferent pupillary defect and mild right disc edema. Visual field showed right ceco-central scotoma, and on Amsler grid the patient drew a few rounded patches. Infrared imaging (IR) showed several right parafoveal hyper-reflective lesions characteristic of AMN, corresponding with the rounded patches on Amsler grid. Spectral-domain OCT (SD-OCT) showed a right focal hyper-reflective lesion of the outer plexiform layer. Brain magnetic resonance imaging was normal. The patient's visual complaints and imaging findings gradually improved with oral corticosteroids treatment. On follow up, visual field improved and there was thinning of the inner segment/outer segment junction with no hyper-reflective lesion on SD-OCT.

Conclusions, including unique features of the case(s):

Our case suggests a new and intriguing association between AMN and AON. The association of these entities is unclear. Clinicians should be aware of this possible new association, and appropriate evaluation using multimodal imaging may facilitate the diagnosis of AMN in patients with AON.

References: 1. Kaufhold F, Zimmermann H, Schneider E, Ruprecht K, Paul F. Optic neuritis is associated with inner nuclear layer thickening and microcystic macular edema independently of multiple sclerosis. *PLoS One*. 6 ; 8(8):e71145, 2013 2. Deschamps R, Vasseur V, Shor N, Vignal C, Salomon L. A new association: acute macular neuroretinopathy in acute optic neuritis. *Acta Ophthalmol*. ;97(5):e753-e756, 2019 3. Bhavsar KV, Lin S, Rahimy E, Joseph A, Freund KB. Acute macular neuroretinopathy: A comprehensive review of the literature. *Surv Ophthalmol*. ;61(5):538-65, 2016 4. Saurabh K, Roy R, Shah D, Goel S, Mishra S. Multimodal imaging characteristics of acute macular neuroretinopathy. *Indian J Ophthalmol*. ;67(3):403-404, 2019 5. Azar G, Wolff B, Cornut PL, Sahel JA, Mauget-Faÿsse M. Spectral domain optical coherence tomography evolutive features in acute macular neuroretinopathy. *Eur J Ophthalmol*. ;22(5):850-2, 2012

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy, Visual fields, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 33

Inferior Branch Retinal Artery Occlusion Due to a Calcific Plaque in a Patient with Calciphylaxis

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Introduction:

Branch Retinal Artery Occlusion (BRAO) presents as acute painless loss in a distribution concordant with visual field of the occluded artery. BRAO most frequently occurs secondary to emboli, which are most commonly cholesterol emboli from proximal aortic or carotid disease. Other identified sources of emboli are platelet-fibrin and calcific, which most commonly occur as a result of valvular heart disease or peri-procedurally. (1,2) Calcific emboli tend to lodge in the first or second order arteries and may overlap the optic disc, making its detection difficult due to similarities in background color.

Description of Case(s):

A 29-year-old female developed right eye superior visual field loss one day after transient vertigo, diplopia and oscillopsia. Head CT was unrevealing. Her optometrist observed right optic nerve pallor and referred to Neuro-Ophthalmology. Past medical history included ESRD with calciphylaxis and prior embolic disease from cardiac calcified masses. Neuro-ophthalmic exam 19 days after the event confirmed right eye superior visual field loss and bilateral optic nerve pallor, without rAPD. Fundus Photography with red free imaging demonstrated a calcific plaque of the inferior temporal branch retinal artery on the optic nerve without vascular occlusion. Optical Coherence Tomography demonstrated inferior retinal thinning compared with the left eye. MRI/MRA brain did not show acute infarct, patent proximal ophthalmic arteries, and lack of flow limiting stenosis.

Conclusions, including unique features of the case(s):

This case demonstrates acute right eye superior visual field loss attributable to inferior branch retinal artery occlusion with calcific plaque masked by similarly hued optic nerve tissue, but easily appreciated on red-free imaging. This was attributed to her known calciphylaxis, an arteriopathy leading to calcification, fibrosis, and thrombus formation commonly involving the medial layer of arteries, and arterioles. BRAO as a result of calcific emboli is a well-described phenomena but this case report demonstrates a rare and minimally described etiology of calcific BRAO related to calciphylaxis.

References: 1. Samardzic, Embolism in retinal circulation after invasive cardiovascular procedures, Medical Archives, 66, p.66, 2012.
2. Younge, The significance of retinal emboli, Journal of clinical neuro-ophthalmology, 9.3, 190-194, 1989

Keywords: Vascular disorders, Visual fields, Stroke trauma, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: Research to Prevent Blindness, NIH P30 026877

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Poster 34**Nonarteritic Anterior Ischemic Optic Neuropathy: Exceptions to the Rules**

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Introduction:

Two unusual aspects of nonarteritic anterior ischemic optic neuropathy (NAION) include: 1) incipient NAION, and 2) prolonged resolution of optic disc edema. We present a patient who had an unusual course where it took 15 months (65 weeks) for her to note a change in vision with associated visual field loss. Of additional concern was the fact that for our patient's right optic disc edema was present for 19 months (82.5 weeks). This, too, is highly unusual for NAION as optic disc edema typically resolves within 5 to 18 weeks.

Description of Case(s):

A 61 year-old woman was noted to have asymptomatic right optic disc edema on routine eye examination. She was ultimately referred for neuro-ophthalmic evaluation 9 months later. She denied jaw claudication, scalp tenderness, weight loss, fever, chills or headache. Visual acuity was 20/30, right eye and 20/20, left eye. Color vision was normal bilaterally and pupillary reactions were intact without a relative afferent pupillary defect. The anterior segments were normal in appearance while funduscopy revealed right optic disc edema. Automated visual fields (Humphrey 30-2) showed slight central depression of the right eye. Extensive work-up was negative. Six months later, the patient reported a 5 day history of a "dark gray band" in her right visual field. At that time, acuity in her right eye was 20/25 with a superior field defect and persistent right optic disc edema. Nineteen months following the onset of right optic disc edema, visual acuity in the patient's right eye was 20/20, the right visual field defect had improved and the disc edema had resolved. The patient has remained stable over the ensuing 7 months.

Conclusions, including unique features of the case(s):

Our report serves as a reminder that, at times, NAION may follow a protracted time course, and this may prompt concern for other causes of optic nerve edema.

References: 1. Hayreh SS. Anterior ischemic optic neuropathy. V. Optic disc edema an early sign. Arch Ophthalmol 1981; 99: 1030 – 1040. 2. Hayreh SS. Acute ischemic disorders of the optic nerve: pathogenesis, clinical manifestations and management. Ophthalmol Clin North Am 1996; 3: 407 – 442. 3. Hayreh SS, Zimmerman MB. Incipient nonarteritic anterior ischemic optic neuropathy. Ophthalmology 2007; 114: 1763 – 1772. 4. Chua D, Cullen JF. Incipient non-arteritic anterior ischemic optic neuropathy: a distinct clinical entity, the Singapore Scene 3. Singapore Med 2014; 55: 473 – 475. 5. Arnold AC. Ischemic optic neuropathy. In Miller NR, Newman NJ (eds). Walsh & Hoyt's Clinical Neuro-Ophthalmology. 6th edition. Philadelphia: Lippincott Williams & Wilkins, 2005, p. 366.

Keywords: Optic neuropathy, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: This work was supported in part by an unrestricted grant from the Research to Prevent Blindness, Inc. N.Y., N.Y.

Contact Information: None provided.

Poster 35**Bilateral Ischemic Optic Neuropathy Following Buttock Augmentation In An IIH Suspect.**

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Introduction:

Perioperative vision loss (POVL) is a complicated process associated with multiple factors including prone positioning, anemia, and vascular anatomy (1). Idiopathic Intracranial Hypertension (IIH) typically affects obese women of childbearing age and is characterized by increased intracranial pressure of unknown origin (2). We present a case of an IIH-suspect who developed rapidly progressive bilateral painless vision loss after undergoing fat transfer surgery to her buttocks.

Description of Case(s):

A 51-year-old woman was transferred from an outside facility 5 days after buttock augmentation surgery in the prone position. On examination, there was no light perception in the right eye and hand motion vision in the left eye. The nerves were pale and edematous in both eyes. Exam was otherwise unremarkable. Outside MRI/MRA showed distension of the optic nerve sheaths and empty sella. The hemoglobin was 6.5 g/dL at the outside facility and she had received 1 unit of blood. Hemoglobin was rechecked and found to be 7.5 g/dL with normal MCV suggesting acute blood loss anemia. The provisional diagnosis was perioperative vision loss due to ischemic optic neuropathy. However, given the patient's risk factors, papilledema, and neuroimaging findings, suspicion remained for underlying IIH. She underwent spinal tap with an opening pressure of 31 mmHg and was started on oral acetazolamide. At post-operative week 7 her vision remained NLP in the right eye but recovered to 20/20 in the left eye with resolution of nerve edema.

Conclusions, including unique features of the case(s):

We present the case of POVL due to ischemic optic neuropathy with a possible component of underlying IIH. There is a relative lack of research on POVL due to its rarity and restricted access to POVL registries. This case highlights the need for developing evidence-based prevention and management guidelines for POVL and to always consider other contributory diagnoses.

References: 1. Ho VT, Newman N, Song S, et al. Ischemic Optic Neuropathy Following Spine Surgery. J Neurosurg Anesthesiol. 17(1):38-44, 2005. 2. Friedman DI, Jacobson DM. Diagnostic criteria for idiopathic intracranial hypertension. Neurology. 59(10), 2002.

Keywords: Optic neuropathy, High intracranial pressure/headache, Neuroimaging, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 36**Pseudotumor Cerebri Secondary to Use of All-Trans Retinoic Acid for Treatment of Acute Promyelocytic Leukemia**

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Introduction:

Multiple randomized trials have demonstrated that all-trans retinoic acid (ATRA) improves the outcome of patients with acute promyelocytic leukemia (APL). Secondary pseudotumor cerebri has been estimated to occur in 1.7% of overall APL patients treated with ATRA and is more common in children. We present a case of an adult with pseudotumor cerebri secondary to ATRA therapy.

Description of Case(s):

A 30-year-old woman with a history of APL treated with ATRA and arsenic trioxide presented with transient visual obscurations and daily headaches, which had been worsening while on APL treatment. Neuro-ophthalmic examination showed bilateral grade 1 optic nerve swelling with surrounding peripapillary watermarks and Paton's lines. Magnetic resonance imaging showed no evidence of mass effect or abnormal enhancement. Lumbar puncture revealed an opening pressure of 28cm H₂O with normal cerebrospinal fluid studies, including protein, glucose, cell count, and flow cytometry. She was diagnosed with pseudotumor cerebri, likely secondary to ATRA therapy.

Conclusions, including unique features of the case(s):

Patients with APL rarely may present with pseudotumor cerebri induced from ATRA treatment. Due to the major component of tretinoin in ATRA, pathophysiology likely is associated with vitamin A toxicity. Thus, the pseudotumor course is expected to improve after cessation of the ATRA treatment. While discovery of papilledema in a patient with known leukemia should invoke a work up to rule out central nervous system leukemic involvement, pseudotumor cerebri secondary to ATRA should be recognized as a potential cause for papilledema in this group when the work up is unrevealing.

References: None.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 37**Presentation of Giant Cell Arteritis With Normal Inflammatory Markers**

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Introduction:

Giant cell arteritis (GCA) can be challenging to diagnose when patients have mild symptoms, normal inflammatory markers, or subtle pathological abnormalities.

Description of Case(s):

All four patients with atypical GCA were male, Caucasian, and between 75 to 81-years-old. Each had multiple cardiovascular risk factors including hypertension, diabetes, transient ischemic attack, or coronary artery disease. None had history of inflammatory disease or used non-steroidal anti-inflammatory drugs. One patient had myositis of unclear etiology treated with steroids within the last year. Two patients had slowly progressive vision loss over several weeks. One was diagnosed with re-perfused central retinal artery occlusion while the other had no ischemic ocular injury. They recovered near-baseline visual acuity. The other two patients presented with acute vision loss over days and were diagnosed with ischemic optic neuropathy with subsequent severe vision loss. All four patients reported either jaw claudication or headaches, but no fever or scalp tenderness. One had weight loss; another had myalgia several months before. They all had normal erythrocyte sedimentation rate, C-reactive protein, hemoglobin, and platelet levels. One temporal artery biopsy was initially read as negative, but on reevaluation, the pathologist noted sectoral inflammatory cells, intimal hyperplasia, and disruption of internal elastic lamina. Another had retrobulbar perineural optic nerve enhancement on MRI. Three patients were treated with intravenous corticosteroids, all four received prednisone taper, and one required methotrexate.

Conclusions, including unique features of the case(s):

GCA classically presents with rapid vision loss, a constellation of systemic symptoms, and elevated inflammatory markers. However, some patients present with milder symptoms, normal inflammatory markers, and subtle pathological findings. Fluorescein angiography, perineural enhancement on MRI, and review of biopsy results with a pathologist are helpful in these cases. Despite what appears to be a slower disease process, treatment with intravenous corticosteroids followed by prednisone taper is still important in preventing vision loss.

References: None.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 38

Asymptomatic Unilateral Optic Disc Oedema preceding Ischaemic Strokes secondary to Giant Cell Arteritis-related Intracranial Vasculitis

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Introduction:

Ischaemic stroke secondary to giant cell arteritis (GCA)-related intracranial vasculitis is rare. Asymptomatic unilateral optic nerve head oedema is not typically associated with GCA. We present a case of a 72-year-old man with persistent asymptomatic unilateral optic nerve head oedema for 11 months prior to diagnosis of GCA-related intracranial vasculitis.

Description of Case(s):

A 72-year-old man presented with two days of slurred speech, dizziness and unsteady gait with new onset of headaches and unintentional weight loss of 22 kilograms in the preceding year. Eleven months prior to this presentation he was noted to have asymptomatic right optic disc oedema which persisted on ophthalmology follow-up several months later. CT brain and orbits with contrast was normal. Past history included ischaemic heart disease, hypertension, hypercholesterolaemia and macular edema OS. Pertinent findings on presentation were visual acuities of 6/9 OD and 6/12 OS, Frisén grade-2 optic disc edema OD with normal peripapillary retina without cotton wool spots or haemorrhages, normal optic nerve OS, dense right inferior homonymous quadrantanopia, gaze evoked nystagmus, dysarthria and ataxia. ESR was 123mm/H (normal <40mm/H), CT head showed acute left anterior inferior cerebellar artery infarction and old left posterior cerebral artery infarction. CT angiogram showed beading of vertebral arteries with distal occlusion. Temporal artery biopsy confirmed GCA. MRI could not be obtained due to defibrillator. Alternative aetiologies for optic disc oedema were explored, none identified. Following treatment with prednisolone, headaches, general functional state and optic disc oedema improved.

Conclusions, including unique features of the case(s):

It is important to consider GCA in older patients presenting with cerebral infarction, particularly in the vertebro-basilar territory, even with co-existing cardiovascular risk factors and especially when associated with headache and weight loss. The exact mechanism of the unilateral optic disc oedema in this patient remains elusive. Given temporal improvement after steroids raises the possibility of a link between intracranial vasculitis and the optic disc oedema.

References: Paiente, Guedon, Dellal, Mekinian, Ischemic stroke in giant cell arteritis: French retrospective study, J Autoimm, 99, 48-51, 2019. de Boysson, Liozon, Parienti, Bienvenu, Giant cell related stroke: a retrospective multi-centre case-control study, J Rheumol, 43(3), 648-56, 2016. Kargiotis, Safouris, Tsivgoulis, Giant cell arteritis with acute ischaemic strokes due to diffuse intracranial stenoses, Neurology 89(15):e190-e191, 2017. Najem, Margolin, Unilateral optic nerve edema with preserved visual function, JAMA Ophthalmol, 135(2), 157-158, 2017. Bidot, Bruce, Newman, Biousse, Asymmetric papilledema in idiopathic intracranial hypertension, J Neuroophthalmol 35(1), 31-36, 2015.

Keywords: Vascular disorders, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), High intracranial pressure/headache, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 39**Case report:Occult GCA presented with episodes of transient visual loss and subsequently developed CRAO.**

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Introduction:

AION is the most common cause of vision loss in GCA. Other signs and symptoms of GCA include transient visual loss, PION, CRAO, BRAO, choroidal infarction and diplopia which can also caused by carotid atherosclerosis.

Description of Case(s):

A 65 year-old-man, U/D Type2 DM, HT, ischemic heart disease, chronic kidney disease. A month before, he had sudden visual loss in left eye and went to another hospital, VA was OD 20/20 OS hand motion, he was diagnosed CRAO in left eye. He came to the hospital with multiple episodes of transient visual loss in right eye for 1 day. He denied systemic symptoms. Eye exam found VA OD 6/7.5, OS counting fingers, normal disc with multiple cotton wool spot in right eye, pale disc with sclerotic vessels in left eye. Laboratory tests found mild elevated of ESR(39mm/hr) and CRP(11.30), no choroidal ischemia on FFA ICG. Rheumatologist suggested thromboembolic cause rather than GCA.He was admitted to the hospital. In the admission, the duration of each episode extended to hours and VA get worse to 6/60 with increased cotton wool spot and retinal whitening, hyperreflection of inner retina on OCT consistent with CRAO. FFA ICG found patchy choroidal ischemia. We discussed to neurologist and rheumatologist and started treatment with intravenous methylprednisolone. MRA brain vessel wall protocol shows multifocal circumferential enhancement and thicken wall at both STAs. Left temporal artery found granulomatous vasculitis. After initiated treatment his vision was improved and never had episode of visual loss again, At 3 weeks, VA was 6/12 in right eye with just few faint cotton wool spots.

Conclusions, including unique features of the case(s):

Patient with multiple episodes of transient visual loss, persist more than few minutes, cotton wool spot in fundus, although with mild elevated of ESR CRP should be considered as GCA. Immediate treatment can improve vision.

References: None.

Keywords: Neuro-opth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 40

Small-Vessel Vasculitis in Giant Cell Arteritis

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Introduction:

We present a rare case of biopsy-proven giant cell arteritis (GCA) causing small-vessel vasculitis on fluorescein angiography (FA).

Description of Case(s):

A 76-year-old African American female with a past medical history of hypertension, diabetes, stroke, and recent cranial nerve IV palsy presented to the Emergency Department with 10 days of progressively decreasing vision in her left eye. Review of systems was positive for jaw claudication. Visual acuity was count fingers at 2 feet in the left eye with a relative afferent pupillary defect. Dilated fundus exam revealed diffuse optic nerve pallor without retinal findings in either eye. ESR, CRP, and platelets were elevated to 67, 2.2, and 601, respectively. A provisional diagnosis of posterior ischemic optic neuropathy (PION) secondary to GCA was made, and treatment with high dose intravenous steroids was promptly initiated. The diagnosis was confirmed on temporal artery biopsy and she was continued on a slow oral prednisone taper. The patient re-presented one month later with worsening vision in the right eye to 20/70. Dilated fundus examination revealed a new cotton wool spot along the inferior arcade in this eye. FA was performed, which showed patchy choroidal non-perfusion in both eyes; the right eye was transited and showed slowed arteriolar filling which was not complete until 80 seconds after initial arteriolar flush with late staining of small peripheral arteries, consistent with small vessel arteritis. She was transitioned to tocilizumab, and vision in this eye stabilized.

Conclusions, including unique features of the case(s):

GCA typically affects large to medium vessels with AION and central retinal artery occlusion being the most common ophthalmic presentations. Small caliber retinal vasculitis is a rare presentation of GCA, with only one case previously described. [1] GCA should be kept on the differential diagnosis for patients with unexplained arteriolar leakage on FA.

References: 1. Papakostas TD, et al. Small-Caliber Retinal Vasculitis Associated With Giant Cell Arteritis: A New Finding. Ophthalmic Surgery, Lasers and Imaging Retina 2016; 47(11): 1054-1056.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Neuro-opth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 41

Neurosarcoidosis presenting as isolated optic perineuritis

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Introduction:

Optic perineuritis can occur as a manifestation of sarcoidosis, Behcet's, granulomatosis with polyangiitis, idiopathic orbital inflammation, IgG4 disease, anti-myelin oligodendrocyte protein spectrum disorders, giant cell arteritis and infections such as TB and syphilis. We present a case of neurosarcoidosis presenting as isolated optic perineuritis.

Description of Case(s):

A 41 year-old female presented to Ophthalmology with decreased vision in the left eye for 3 months and left optic disc edema. Initial MRI showed prominence of the left optic nerve head with no enhancement, no evidence of demyelinating disease. She was referred to Neuro-ophthalmology for query optic neuritis. On our assessment, visual acuity was 20/20 and 20/60-2, 20/40 with pinhole. No RAPD. Anterior segment examination was normal. The left optic nerve showed edema 360 degrees and choroidal folds were present. Infectious serology and markers of systemic inflammatory disease including ESR, CRP, ACE levels, ANA, ANCA and protein electrophoresis were all normal. Repeat MRI of the orbits showed subtle enhancement of the left optic nerve sheath. CT chest, abdomen and pelvis did not reveal any pulmonary disease or underlying malignancy. Though vision in the left eye continued to gradually worsen, she declined steroid treatment as there was no definitive diagnosis. MRI of the brain one year later showed multiple focal enhancing nodules. Left temporal lobe lesions were biopsied and revealed foci of non-caseating granulomas, negative for fungal and acid-fast staining. She was diagnosed with neurosarcoidosis and started on prednisone and methotrexate.

Conclusions, including unique features of the case(s):

While ocular involvement occurs in approximately 25% of patients with sarcoidosis, neuro-ophthalmic disease is uncommon (2-3% of all cases) and rarely occurs in isolation, unaccompanied by other neurologic manifestations or features such as pulmonary involvement (Zajcek et al., 1999; Koczman et al., 2008). This case highlights the challenge of diagnosing neurosarcoidosis in the absence of systemic disease.

References: Zajicek JP, Scolding NJ, Foster O, et al. Central nervous system sarcoidosis – diagnosis and management. *QJM*, 92(2):103–117, 1999. Koczman JJ, Rouleau J, Gaunt M, Kardon RH, Wall M et al. Neuro-ophthalmic sarcoidosis: the University of Iowa experience. *Semin Ophthalmol*, 23(3):157-68, 2008.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 42**MOG antibody disease with hearing loss**

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Introduction:

MOG antibody disease is an autoimmune disease of the central nervous system associated with antibodies against myelin outer membrane oligodendrocyte glycoprotein. MOG antibody disease commonly presents with episodes of optic neuritis, transverse myelitis and/or encephalitis.

Description of Case(s):

A 53 year old woman with long standing blindness from MOG antibody disease presented with tinnitus and hearing loss in her right ear, confirmed by audiology. MRI scan showed inflammation of the inner ear. Workup was negative for lupus and other etiologies. She had good recovery, although not complete, after 10 days of treatment with prednisone taper. Two years later, she had a second episode of hearing loss in the right ear, again partially responsive to steroids.

Conclusions, including unique features of the case(s):

The spectrum of MOG antibody disease is expanding beyond optic neuritis and transverse myelitis. Our MOG patient suffered bilateral blindness from recurrent optic neuritis and then two episodes of sensorineural hearing loss with a permanent deficit in her right ear. To our knowledge, this is the first case of MOG antibody disease associated with hearing loss reported in the literature.

References: None.

Keywords: Optic neuritis

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 44**Atypical MOG Optic Neuritis Presentations**

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¹*University of Calgary, Calgary, Canada*

Introduction:

Recurrent optic neuritis is a known presentation of MOG antibody disease (MOGAD). Patients are typically younger than their AQP4 antibody positive counterparts, with a more balanced ratio of females to males and Caucasians to non-Caucasians. One of the hallmarks of MOGAD is the excellent response to high-dose corticosteroids. However, as we learn more about MOGAD, a wider spectrum of presentations and therapeutic responses are coming to light. At our institution, we have noted such heterogeneity in our MOG optic neuritis cohort. The aim of this study was to review the spectrum of MOG optic neuritis presentations, characteristics and treatment responses with a focus on atypical cases.

Description of Case(s):

The authors have collected MOG optic neuritis cases since the cell-based assay became available at our institution. Initial case review has revealed several patients that would be deemed "atypical" by current MOG definitions, including several patients presenting with bilateral, severe and treatment-refractory optic neuritis. A full review of identified MOG optic neuritis patients will be presented, with a specific focus on atypical cases, including two Asian men, both in their 40's, with bilateral and severe optic neuritis that required multiple rescue therapies on top of high-dose corticosteroids including repeated plasmapheresis and rituximab.

Conclusions, including unique features of the case(s):

Our understanding of the phenotypes, characteristics, and treatment responses in MOGAD, and MOG optic neuritis specifically, are continually evolving. With a better appreciation of the range of disease manifestations, we will be able to improve and tailor treatment regimens more efficiently with better patient outcomes.

References: None.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Demyelinating disease, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 45

Clinical overlap between neuromyelitis optica and GFAP astrocytopathy

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Introduction:

Neuromyelitis optica (NMO) and glial fibrillary acidic protein (GFAP) astrocytopathy both result from an inflammatory reaction to astrocyte antigens. NMO is characterized by severe optic neuropathy, myelitis and area postrema syndrome, while GFAP astrocytopathy more commonly presents with meningitis, encephalopathy, disc edema, myelitis, tremor and ataxia (1-3). We report a patient with both GFAP and aquaporin 4 (AQP4) antibodies.

Description of Case(s):

This is a 32-year-old African American female with a history of systemic lupus erythematosus, end stage renal disease and a prior episode of vision loss OS of unknown etiology one year prior to presentation (baseline visual acuity (VA) 20/20 OD, CF OS). She presented with two weeks of worsening encephalopathy, fever, weakness, blurry vision and ptosis. Exam showed VA 20/400 OD and HM OS, APD OS, anisocoria with smaller right pupil, mild right ptosis, healthy appearing optic nerve OD and pale, cupped optic nerve OS without edema. Anisocoria and ptosis reversed with apraclonidine. CT head was unrevealing. CT myelogram showed diffuse enlargement of her cervical spinal cord (MRI contraindicated due to pacemaker). An extensive infectious and malignancy workup was negative. Pertinent laboratory abnormalities included elevated CSF protein, eosinophils, and positive AQP4 and GFAP serologies (1:>100,000 and 1:32, respectively). She was managed with high dose IV steroids and PLEX, with mild improvement in her mental status and vision.

Conclusions, including unique features of the case(s):

As our patient exhibited extensive encephalopathy, we suspected GFAP astrocytopathy. In her case, an initial episode of NMO may have caused the release of astrocyte antigens, leading to the development of GFAP antibodies and subsequent encephalopathy (4). MRI is typically helpful in distinguishing between these two etiologies, as they exhibit distinct patterns of enhancement, but was not an option in our patient due to her pacemaker. Clinicians should consider co-existence of these antibodies when the presentation has features of both NMO and GFAP astrocytopathy.

References: 1. Wingerchuck et al, International consensus diagnostic criteria for neuromyelitis optica spectrum disorders, *Neurology*, 85(2): 177–189, 2015. 2. Fang et al, Autoimmune Glial Fibrillary Acidic Protein Astrocytopathy: A Novel Meningoencephalomyelitis, *JAMA Neurol*, 73(11):1297-1307, 2016. 3. Flanagan et al, Glial fibrillary acidic protein immunoglobulin G as biomarker of autoimmune astrocytopathy: Analysis of 102 patients, *Ann Neurol*, 81(2):298-309, 2017. 4. Uzawa et al, Cerebrospinal fluid interleukin-6 and glial fibrillary acidic protein levels are increased during initial neuromyelitis optica attacks, *Clin Chim Acta*, 421:181-3, 2013.

Keywords: Demyelinating disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Pupils retina

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 46**Neuromyelitis Optica Spectrum Disorders-like Relapses In HIV-Infected Person Correlated With Infectious Activities: A Case Report**

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Introduction:

Inflammatory optic neuropathy in HIV-infected persons can be dramatic and very little is known about the physiopathology or management of this condition as it has been scarcely described in medical literature.

Description of Case(s):

A 44-year-old untreated HIV-infected female developed a severe visual loss within 48 hours and movement-linked pain on the left eye. Light was detected only in the nasal quadrant with a deep afferent pupillary deficit but a normal fundus. Brain MRI showed an optic nerve enhancement all along the intraorbital optic nerve at T1-contrast sequence. Spinal MRI was normal. Lumbar puncture revealed lymphocytary meningitis with specific oligoclonal bands and high viral load (VL). Anti-Aquaporin 4 and anti-MOG antibodies were negative. Based on the clinical picture the diagnosis of neuromyelitis optica spectrum disorders-like (NMOSD-like) secondary to HIV infection was promoted. After retroviral treatment associated to high dose of corticosteroids, she recovered 10/10 visual acuity on the left eye. She relapsed few months later with similar clinical presentation on the right eye, as she spontaneously stopped retroviral therapy.

Conclusions, including unique features of the case(s):

We observed that the disease's activity, including relapses, were correlated to the cerebrospinal fluid's VL. Following this observation, we advanced the hypothesis that these auto-immune optic nerve dysfunctions are correlated with the VL rather than the hyperactivation of the immune system during the lymphocytes recovery phase in the course of the treatment (IRISyndrom). Although we present a single case to describe the correlation between the activity of the auto-immune disease and VL, the determination of this condition's physiopathology should support our observations. We present a case of optic neuritis in an HIV-infected person with a well-documented relationship between viral activities and optic neuritis relapses which support the hypothesis of an immunologic dysfunction induced by HIV virus.

References: None.

Keywords: Demyelinating disease, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 47**A new homoplasmic mtDNA mutation described in mother and son with clinical LHON**

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Introduction:

A 48 year old woman presented with acute painless sequential visual loss that progressed over two months. The patient had no previous ophthalmologic history. She was a chronic smoker with intermittent alcohol abuse and an amphetamine addiction 15 years prior.

Description of Case(s):

Visual acuity was 20/200 in her right eye and 20/400 in her left eye. Automated visual fields demonstrated bilateral central scotomas. On examination both optic discs showed temporal pallor and OCT showed temporal reduction of the peripapillary RNFL as well as the GCL. MRI of the orbits and brain showed enhancement in the chiasm and optic tracts and centrally in the optic nerves. Further testing for anti-MOG, anti-AQ-4, ANA and nutritional factors was unrevealing and full-field ERG was normal. Whole genome sequencing of DNA isolated from muscle revealed a unique, previously unreported homoplasmic mitochondrial DNA (mtDNA) mutation, m.13345G>A, p.(Ala337Thr) in NADH:ubiquinone oxidoreductase core subunit 5 (MT-ND5) of complex I of the respiratory chain. The amino acid affected by the mutation is evolutionary very well conserved and the mutation is predicted to be pathogenic according to several prediction tools. Measurement of the mitochondrial respiratory chain enzymes in muscle revealed a slightly reduced activity of complex I. The patient did not present with other clinical signs of mitochondrial disease. Formal audiometry, ECG and peripheral limb EMG were all normal. In addition, the patient had a 20 year old son who approximately at the same time presented with bilateral subacute visual loss (20/500 and 20/1000), temporal disc pallor and central scotomas. Analysis of DNA isolated from muscle identified the same mutation in homoplasmy and enzyme function was also lower in complex I.

Conclusions, including unique features of the case(s):

We herein report a novel mtDNA mutation in MT-ND5 with a phenotypic presentation resembling an isolated Leber Hereditary Optic Neuropathy.

References: None.

Keywords: Optic neuropathy, Genetic disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 48**Nuclear mitochondrial DNA mutation causing a Leber hereditary optic neuropathy phenotypic expression**

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Introduction:

Leber hereditary optic neuropathy (LHON) is associated with mutations of the mitochondrial (mt) DNA. The most common point mutations are positions 11778, 3460, and 14484 of subunit ND4, ND1 and ND6, respectively resulting in mitochondrial complex 1 deficiency. We report the first known case of a LHON “plus” phenotypic expression associated with pathogenic mutations of a nuclear (n) DNA gene that encodes NDUFAF5, a mitochondrial complex I assembly factor.

Description of Case(s):

An 8-year-old girl presented with two years of progressive bilateral dystonia in her lower extremities. Brain magnetic resonance imaging (MRI) revealed bilateral basal ganglia abnormalities. Brain MR spectroscopy was normal. Testing for organic acids, cerebrospinal (CSF) neurotransmitters, targeted mitochondrial DNA mutations, DYT1 mutation, PANK2 mutation, lysosomal enzymes, heavy metals, paraneoplastic panel, and blood lactate were all normal. A detailed autoimmune workup was normal. Electromyography was normal. Skin, muscle, and brain biopsies were unremarkable. Eye examination was normal. A mitochondrial disorder was suspected as the cause of her dystonia and bilateral basal ganglia abnormalities but could not be proven at that time. Fifteen years later, she developed bilateral, sequential, painless, vision loss over a period of three months. Ophthalmologic examination revealed bilateral optic disc pallor with MRI showing mild chiasmal enlargement. Whole mtDNA genome sequencing was unrevealing. However, nDNA sequencing revealed heterozygous mutations in NDUFAF5, which has previously been associated with autosomal recessive mitochondrial respiratory complex 1 deficiency syndromes (i.e. Leigh syndrome).

Conclusions, including unique features of the case(s):

To our knowledge only 14 cases have been associated with mutations in NDUFAF5 and none with acute visual loss reminiscent of LHON. This case illustrates a novel presentation of acute visual loss due to a nDNA mutation. A patient presenting with acute visual loss suggestive of LHON, with negative testing for the 3 primary point mutations and whole mtDNA sequencing, should undergo nDNA testing.

References: None.

Keywords: Genetic disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 49**There is more to mitochondria than Leber's**

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Introduction:

It is not surprising that the mitochondria play a pivotal role in oxidative phosphorylation, but other abnormalities in the mitochondrial genome can affect physiologic and in particular, optic nerve function. Enoyl-coA-Hydratase in codes for a second step in the mitochondrial fatty acid betaoxidative passer ray categorizing the hydration of 2-trans-enoil-coenzyme A intermediates to L-3-hydroxyacyl-coA's. Abnormalities in this gene lead to an abnormal protein, and may cause optic neuropathy.

Description of Case(s):

A single case of a 4 year old gentleman referred for optic atrophy found to have ECHS 1 deficiency. Evaluation of this 4 year old shows visual acuity of 20/400 OD and 20/200 OS. Near vision was 20/400 equivalent. Pupils were 2.5mm OD and 2.8mm OS, reactive without definite afferent pupillary defect. Automated retinoscopy showed minimal refractive error at -0.25 +1.00 x 25 OD and -1.00 +0.50 x 150 OS. Funduscopy revealed significant bilateral optic atrophy. Fundus photos confirmed marked atrophy of the right disc. We were unable to get OCT because of difficulty with fixation.

Conclusions, including unique features of the case(s):

As the mitochondrial encoded genome is responsible for oxidative phosphorylation, it is not surprising that anything that affects the metabolic pathways can result (as, in this case) bilateral optic atrophy, decreased central acuity, and secondary nystagmus. We can now add patients with ECHS1 gene abnormalities to the differential of optic atrophy in children.

References: None.

Keywords: Genetic disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 50**Novel OPA3 Mutation in an Afghani Family with 3-Methylglutaconic Aciduria Type III and Optic Atrophy**

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Introduction:

To describe and distinguish clinical phenotypes with the overlapping feature of optic atrophy caused by distinct mutations in the same gene, OPA3. We report 3 affected siblings in a consanguineous family harboring a novel OPA3 mutation causing 3-methylglutaconic aciduria type III with optic atrophy.

Description of Case(s):

Three siblings (2 male, 1 female) among 6 children in a consanguineous Afghani family developed decreased vision from early childhood. Both parents and all extended family members were unaffected. All 3 affected siblings suffered from severe visual impairment ranging from visual acuities of 20/150 to counting fingers. All had spastic lower extremity weakness and ataxia. Two of the three affected siblings also had a history of seizures, and the female sibling had limited cognition with diffuse atrophic changes on brain MRI. Two of the three individuals also had migraine-like headaches. Urine organic acid analysis revealed mildly elevated 3-methylglutaconic acid for the male siblings. Whole exome sequencing and subsequent PCR confirmation revealed a novel variant in OPA3 (intron1, c.142+2_142+3dupTG), affecting the consensus sequence of the splice site, for which all 3 clinically affected siblings were homozygous.

Conclusions, including unique features of the case(s):

Mutations in OPA3 can cause optic atrophy in a dominant pattern of inheritance associated with cataract or in a recessive pattern associated with spastic paresis and ataxia. The novel recessive mutation and clinical presentations described herein further support how different mutation types affecting OPA3 can produce distinct clinical phenotypes and underscore the critical and susceptible role of mitochondrial health in optic nerve function.

References: None.

Keywords: Optic neuropathy, Genetic disease

Financial Disclosures: The authors had no disclosures.

Grant Support: EDG: NIH K08 EY030164

Contact Information: None provided.

Poster 51**JAK2 Mutation Associated Pseudotumor Cerebri Without Cerebral Venous Thrombosis**

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Introduction:

Myeloproliferative disorders complicated by cerebral venous thrombosis (CVT) can rarely cause intracranial hypertension. We present a case of pseudotumor cerebri syndrome (PTCS) associated with the Janus kinase 2 (JAK2 V617F) mutation induced polycythemia vera (PCV) without evidence of CVT.

Description of Case(s):

A 48 year-old woman presented with a five-month history of headaches, pulsatile tinnitus and diplopia. Exam revealed bilateral cranial nerve 6 palsies and moderate optic disc edema (ODE) OU. Lumbar puncture (LP) opening pressure was 39 cmH₂O with normal constituents. MRI of the brain and orbits was consistent with intracranial hypertension. MR venography did not show thrombosis. Despite two months of acetazolamide treatment, symptoms remained stable and ODE worsened. Repeat brain MRI and MRV showed only nonspecific findings of intracranial hypertension without CVT. Repeat LP showed elevated opening pressure with normal cytology. Laboratory evaluation showed leukocytosis, thrombocytosis and polycythemia. Hematology evaluation revealed positive JAK2 V617F mutation leading to the diagnosis of PCV. ODE in the left eye resolved one month after optic nerve sheath fenestration (ONSF). The right eye did not undergo ONSF and ODE increased despite maximal acetazolamide therapy. ODE in the right eye resolved after initiation of PCV treatment, namely hydroxyurea and phlebotomy. Acetazolamide was weaned completely. The patient did have one episode of papilledema recurrence when the hydroxyurea dose was decreased but has since been stable off acetazolamide with resolution of papilledema and symptoms of intracranial hypertension.

Conclusions, including unique features of the case(s):

Most of the limited published reports of PCV presenting with PTCS occurred in the setting of CVT. MR imaging, including venography, was obtained twice, without evidence of CVT in our patient. The etiology for increased intracranial pressure may have been hyperviscosity induced functional impairment in venous drainage rather than CVT. Clinicians should be aware that PCV can present with PTCS in the setting of a negative MRV for CVT.

References: None.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 52**Complete paternal uniparental isodisomy of chromosome 4 in a patient with isolated optic neuropathy**

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Introduction:

Wolfram syndrome (WS) is a rare progressive neurodegenerative disease with optic atrophy being one of the defining clinical features. This syndrome is also known by its historical acronym of DIDMOAD (Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness). The majority of cases are due to biallelic variants in WFS1 (4p16.3), encoding an endoplasmic reticulum membrane protein. Complete uniparental isodisomy (iUPD) is a rare genetic phenomenon resulting in two identical chromosomes originating from a single parental allele. If the latter carries a pathogenic variant in a recessive gene, it can lead to a recessive disorder manifesting itself as a non-Mendelian trait. Here, we report a case of paternal iUPD of chromosome 4 resulting in WS.

Description of Case(s):

A 15-year-old female from a non-consanguineous family was seen in the genetics clinic with a longstanding subnormal vision since the age of 7-8 years old. Her visual acuity was 6/48 (right eye) and 6/38 (left eye), with reduced color vision bilaterally. Fundus examination showed bilateral optic atrophy with significant thinning of the peripapillary retinal nerve fiber layer on optical coherence tomography. Electrophysiological testing was consistent with primary retinal ganglion cell and optic nerve dysfunction. As there was no relevant family history, an autosomal recessive inherited optic neuropathy was suspected. Genetic analysis revealed a homozygous candidate pathogenic variant in WFS1, heterozygous in the proband's father but absent from the mother's DNA sample. In light of this, we excluded the presence of a large deletion affecting WFS1 on the maternal allele, and investigated the possibility of iUPD. We examined homozygous regions in the proband's genome and confirmed the entire chromosome 4 was homozygous, indicating an absence of parental heterodisomy.

Conclusions, including unique features of the case(s):

Complete paternal iUPD of chromosome 4 with a homozygous deletion in WFS1 can result in isolated optic neuropathy, expanding the phenotypic spectrum of WFS1-related disease.

References: None.

Keywords: Genetic disease, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 53**GBA and ATP13A Mutation in Parkinson's Disease: Ocular Motor Abnormalities and Pathogenic Implications**

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Introduction:

Mutations of GBA (Glucocerebrosidase) and ATP13A2 (P5-ATPase) genes are risk factors for Parkinson's disease (PD). Homozygous mutations of these genes cause rare, early onset diseases: Gaucher and Kufor-Rakeb, respectively. Given that supranuclear gaze palsy (SGP) is characteristic in Gaucher (horizontal SGP) and Kufor-Rakeb (vertical SGP), detailed eye movement analysis was performed in a patient with young-onset parkinsonism and heterozygous mutations of both genes.

Description of Case(s):

A 28 year-old woman of Ashkenazi Jewish ancestry was diagnosed with levodopa-responsive PD at age 23. DaTscan was positive. Early age of onset, despite negative family history, prompted genetic testing. Metabolic/neurological genetic panel showed heterozygous pathogenic mutations of the GBA gene (N370S) and the ATP13A2 gene (3057delC). Clinical exam revealed convergence insufficiency, motor impersistence with difficulty maintaining fixation, and subtle vertical (downward) saccade slowing (though with intact optokinetic downward quick phases). VOG confirmed motor impersistence, abnormal smooth pursuit, antisaccade and self-paced saccade deficits, impaired generation of large vertical saccades, and low-normal large vertical and horizontal saccadic velocities. Definitive SGP was not evident.

Conclusions, including unique features of the case(s):

A growing number of pathogenic genetic mutations have been identified in familial and sporadic PD, some of which only represent risk factors, such as GBA and ATP13A2. Both of these genes are important for membrane trafficking and for the endo-lysosomal compartment. We suspect the 'double hit' to the same metabolic pathway is responsible for the phenotype of our patient. Screening for multiple genetic mutations should be considered, especially in the context of early onset PD or unexplained ocular motor abnormalities to improve understanding of genetic background and pathogenic mechanisms. The lack of classic SGP in our patient may be due to milder phenotypic manifestations of heterozygous mutations, though eye movements were abnormal and monitoring for future SGP evolution is warranted.

References: None.

Keywords: Ocular motility, Genetic disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 54**Optic Tract Syndrome due to Aneurysmal Compression**

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Introduction:

Optic tract lesions as a site of homonymous visual field defects are not common.

Description of Case(s):

A 66 year old male was referred to our neurologic department because of visual field defect which was found incidentally through routine ophthalmologic evaluation a month ago. He had no systemic disease, and no history of smoking and excessive alcohol consumption. In the neurologic examination, right upper homonymous quadrantanopia and relative afferent pupillary defect in the right eye were observed. Extraocular movement, ocular alignment, and other cranial nerves function were normal. Corrected visual acuity was 0.4 (right eye) and 0.9 (left eye). Color discrimination of each eye on Hardy-Rand-Rittler-Ishihara test was normal. Goldman perimetry showed homonymous and congruent quadrant hemianopia on the right side. And on the optical coherent test, retinal nerve fiber layer was thinning at the inferior quadrant part in both eyes with predominance on the left eye which was corresponding to the ophthalmoscopy findings of optic atrophy. Magnetic resonance imaging and angiography revealed 2 cm sized aneurysm at the left posterior communicating artery, compressing left optic tract and optic chiasm. He was treated successfully with coil embolization of the aneurysm.

Conclusions, including unique features of the case(s):

Although visual field defects caused by optic tract lesions are often incomplete and incongruent, it was congruent in this case. And RAPD in the contralesional side resulting from simultaneous involvement of optic chiasm was seen in our patient. Our case infers that although homonymous and congruent hemianopia may be a rare symptom of an intracranial aneurysm, further diagnostic evaluation is important, which is not caused by occipital lobe lesions.

References: None.

Keywords: Vascular disorders, Pupils retina, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 55**Cerebral Blindness Resulting from Bilateral Optic Radiation Infarction; A Case Report**

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Introduction:

Cerebral blindness is characterized by absence of blink to threat and optokinetic responses with normal fundi and preserved pupillary light reflexes (Liu 310). It results from bilateral retrogeniculate dysfunction (310). Anton's syndrome refers to visual loss that is characterized by denial of blindness. While it classically presents in the form of cortical blindness, which is defined by bilateral occipital cortex involvement, to our knowledge, bilateral optic radiation involvement has not been previously described.

Description of Case(s):

A 28 year old right handed man with a history of type one diabetes mellitus, hypertension, hyperlipidemia, and alcohol use, initially presented with diabetic ketoacidosis. He developed cardiac arrest for eight minutes, with hypoxemic and hypercarbic respiratory failure. He later had pulseless electrical activity arrest for three minutes. His hospital course was complicated by septic shock requiring pressors and acute renal failure requiring dialysis. A CT scan of head was obtained showing acute supratentorial and infratentorial infarcts. Neurologic exam was notable for preserved pupillary light reflexes, no blink to threat bilaterally, preserved voluntary eye movements, denial of blindness, and quadriparesis with greater weakness on the left. When asked to identify objects, the patient made incorrect guesses. MRI brain showed bilateral supratentorial and infratentorial border zone infarcts affecting the optic radiations bilaterally. The patient did not recover vision during the hospitalization.

Conclusions, including unique features of the case(s):

This patient's presentation is unusual as, to our knowledge, there have been no previously described cases of Anton's syndrome resulting from bilateral optic radiation infarcts. While Anton's syndrome may result from different pathological lesions in multiple locations along the visual pathways, this expands the spectrum of Anton's syndrome resulting from cerebral infarction.

References: Liu, Grant T., et al. Liu, Volpe, and Galettas *Neuro-Ophthalmology: Diagnosis and Management*. Elsevier Inc, Third edition, page 310, 2019.

Keywords: Higher visual cortical functions, Neuroimaging, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 56**Posterior Reversible Encephalopathy Syndrome After Transsphenoidal Surgery For Pituitary Adenoma**

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Introduction:

Bilateral, simultaneous, painless vision loss after pituitary adenoma surgery is rare. While iatrogenic causes are most common, failure of cerebral autoregulation may lead to breakdown in blood brain barrier leading to vasogenic edema affecting the occipital lobes, a clinical entity named posterior reversible encephalopathy syndrome(PRES). We report a rare case of PRES, five days after an uneventful transsphenoidal surgery for pituitary adenoma.

Description of Case(s):

A 51 year old white female presented with bilateral blurred vision and dense bitemporal hemianopsia and was found to have a pituitary macroadenoma compressing the optic chiasm. She underwent an uncomplicated transsphenoidal resection of the pituitary adenoma and was monitored for recovery. Five days into the post-operative period, the patient developed acute onset, bilateral, simultaneous, painless loss of vision to hand movements. Her blood pressure was 180/97 mm Hg. On exam, pupils were briskly reacting and fundus exam showed mild temporal pallor of discs. Non contrast CT scan of the brain showed post-operative changes, subdural hygromas and hypodensities in bilateral occipital lobes. MRI brain without contrast revealed vasogenic edema in bilateral occipital lobes. Blood pressure was controlled with intravenous titratable agents, the lumbar drain was clamped to help improve intracranial pressure along with treatment with intravenous steroids to help improve cerebral perfusion. Vision continued to improve to 20/70 OU over the next few days. At two months post-operative visit, patient's vision returned improved to her baseline pre-operative acuity.

Conclusions, including unique features of the case(s):

Posterior reversible encephalopathy syndrome (PRES) is an important cause of cortical vision loss in the setting of elevated systemic blood pressure and failed autoregulation due to endothelial dysfunction. The typical MRI features include symmetrical posterior subcortical vasogenic edema. Good control of blood pressure and intracranial pressure, can lead to reversal of vision loss, as was seen in our patient.

References: Sudulagunta SR, Sodalagunta MB, Kumbhat M, Settikere Nataraju A. Posterior reversible encephalopathy syndrome(PRES). Oxf Med Case Reports. 2017;2017(4):omx011. Published 2017 Apr 3.

Keywords: Higher visual cortical functions, Neuroimaging, Pupils retina, Visual fields, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 57**Homonymous Hemianopsia in Normal Pressure Hydrocephalus**

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Introduction:

Homonymous hemianopsia (HH) without structural correlate on neuroimaging has a limited differential diagnosis (occipital seizure, subclinical ischemia, nonketotic hyperosmolar hyperglycemia, Heidenhein variant prion disease, or posterior cortical atrophy (PCA)). In elderly patients with progressive neurocognitive deficits over months to years and a HH with normal or near normal structural brain imaging, the cause is usually thought to be PCA. We report a case of reversible neurologic and visual symptoms and signs in normal pressure hydrocephalus (NPH) in an elderly patient treated with a ventriculo-peritoneal shunt. To our knowledge this is the first case to be described in English-language ophthalmic literature.

Description of Case(s):

An 86-year-old male presented with a five-year history of recurrent falls, neurocognitive deficit, incontinence, and bilateral visual loss. He had been on memantine without improvement. Color vision measured with Ishihara plates was 0/14 in both eyes. His pupils reacted well to light and there was no relative afferent pupillary defect (RAPD). Formal visual field testing (Humphrey 24-2) revealed a right-sided incomplete congruous macular splitting HH. On reviewing serial neuroimaging, progressive increase in the Evans index to 0.38 was noted, consistent with ventriculomegaly, compatible with NPH. Striking improvement in gait and cognition in response to a high volume lumbar puncture confirmed the diagnosis. Post ventriculo-peritoneal shunt placement, he had a marked improvement in memory and cognition, gait instability and complete resolution of incontinence. The right sided HH improved compared with his pre-operative field.

Conclusions, including unique features of the case(s):

While obstructive and communicating high pressure hydrocephalus is known to cause neuro-ophthalmic findings (papilledema, sixth nerve palsy), to our knowledge this is the first case of NPH with reversible visual loss in English-language literature. The mechanisms for NPH related reversible neurologic deficits are presumed to be pressure related mass effect but remain controversial and the precise reason for lack of visual loss in cases of NPH is unknown.

References: None.

Keywords: Visual fields, Perimetry, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 58

Migraine with Photophobia - Is the Pupil at Fault ?

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Introduction:

Migraine attack has core features of light sensitivity (photophobia). Pupillary size and function influencing light sensitivity and triggering migraine attacks has not been studied extensively. Although chance association of Adie's pupil with migraine is reported, Adie's pupil as a cause of migraine with photophobia is not well known. 0.125% pilocarpine in Adie's pupil is an effective diagnostic tool and treatment option for Adie's pupil but in this case helped in reducing migraine attacks as well.

Description of Case(s):

A 32 year old female suffered a concussion injury 4 years back. Following this she started developing migraine attacks on the right side of her head triggered by bright lights with extreme light sensitivity before and during attacks. At presentation her MIDAS score was 23. Her CNS Examination, MRI, MRA, MRV were all reported to be normal. Her visual acuity was 6/6 in both eyes with normal fundus evaluation. Anterior segment was all normal except for anisocoria with pupil size in right eye being larger than left. The right pupil did not react to light or near and had segmental vermiform movements on slit lamp examination. 0.125% pilocarpine caused pupillary constriction confirming right Adie's pupil. Patient was started on pilocarpine 0.125% drops 2 times a day and reported significant reduction in migraine attacks and improvement in daily life. 6 months follow up revealed MIDAS score of 6.

Conclusions, including unique features of the case(s):

This case highlights the importance of pupillary examination in cases of migraine. This case also illustrates Adie's pupil as a cause of migraine with photophobia and successful response to topical therapy. Studies involving a larger group of patients having migraine with photophobia need to have detailed pupillary examination to establish whether pupillary abnormalities could be a trigger factor for migraine attacks and if these patients could improve with topical therapy.

References: Tafakhori A, Aghamollaii V, Modabbernia A, Pourmahmoodian H, Adie's pupil during migraine attack: case report and review of literature, *Acta Neurol Belg*, 111, 66–8, 2011. Cortez MM, Rea AN, Hunter AL, Digre BK, Brennan CK, Altered pupillary light response scales with disease severity in migrainous photophobia, *Cephalalgia*, 37, 801–11, 2013. Skeik N, Jabr IF, Migraine with benign episodic unilateral mydriasis, *Int J Gen Med*, 4, 501–3, 2011.

Keywords: Pupils retina, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 59**Cogan lid-twitch and lid-hopping signs in a patient initially diagnosed as ocular myasthenia gravis.**

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Introduction:

We often seek Cogan lid-twitch sign in a patient suspected to have myasthenia gravis.

Description of Case(s):

A 44-year old man presented with a few-day history of ptosis, and diplopia from diffuse weakness of all extraocular muscles. He had prominent fatigability of the lids, Cogan lid-twitch and lid-hopping signs. The initial diagnosis was ocular myasthenia gravis. However, on further interrogation the patient reported tingling in the median nerve innervated fingers, contemporaneous to development of ocular symptoms. He had no limb weakness, objective sensory loss or ataxia. All deep tendon reflexes were normal. Nevertheless, we considered acute ophthalmoparesis variant of Miller-Fisher syndrome as a differential diagnosis. Spinal fluid was normal. Nerve conduction study on day 6 of illness was normal; but careful scrutiny revealed a hint of the distinctive sural nerve-sparing reduction of sensory nerve action potentials. There was no prolongation of median distal motor or sensory latencies, which would have suggested pre-existent carpal tunnel syndrome, to explain his acral symptoms. This, and the absence of significant decremental response on 3Hz repetitive stimulation of proximal nerves, prompted us to test serum anti-GQ1b Ig G. It was significantly raised. Anti-acetylcholine receptor antibody was absent. A repeat nerve conduction study 1 week later showed a more definite sural-sparing pattern. Patient made an uneventful recovery over the next few weeks from his illness, acute ophthalmoparesis variant of Miller-Fisher syndrome.

Conclusions, including unique features of the case(s):

The possible physiological basis of Cogan lid-twitch is discussed. Hence the necessary caution against over-ascribing this sign to pathology at the neuromuscular junction. Dr Cogan expressed it too in the original paper describing the sign.

References: Myasthenia gravis: a review of the disease and a description of lid twitch as a characteristic sign. Cogan DG. Arch Ophthalmol 1965;74:217–22. The hopping lid twitch in myasthenia gravis. Andrea C. Quiroga, Joseph J. Sabatino, David S. Zee, Daniel R. Gold. Neurology Aug 2016, 87 (5) e55

Keywords: Myasthenia

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 60**BILATERAL SIXTH NERVE NUCLEAR LESIONS IN WERNICKE'S ENCEPHALOPATHY (WE). RECOVERY WITH THIAMINE**

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Introduction:

Ophthalmoplegia is an integral part of the classic WE triad. Horizontal gaze palsy (h-GP) in previous WE series was present in 102 of 232 cases. We examined a patient with vertical and bilateral h-GP and video-monitored the daily evolution of the ophthalmoplegia while on high-dose intravenous thiamine.

Description of Case(s):

A 64- year old woman status post vertical band sleeve gastropasty ~ 25 years earlier presented with generalized weakness. Two months prior to admission, she developed persistent nausea and vomiting, and underwent gastric dilatation, without improvement. The day of admission, she was awake, though verbally unresponsive to her husband. Initial examination showed encephalopathy, unstable station and complete horizontal and vertical gaze palsy, sparing lids and pupils. She had paralysis of saccades and pursuit, but was not alert enough to test the slow vestibulo-ocular reflex (VOR). In attempted right gaze, she had a few degrees of adduction of the left eye, suggesting greater involvement of motoneurons over interneurons in the left sixth nerve nucleus. Baseline thiamine level was 28 mg/DL. Intravenous thiamine induced rapid, albeit asymmetric gaze recovery. The next day, she had left gaze paretic nystagmus and only partial right gaze. Vertical gaze became normal. Two days later, she had bilateral h-gaze holding failure but ophthalmoplegia resolved; the h-head impulse test became bilaterally positive with reduced gain, the vertical VOR was normal.

Conclusions, including unique features of the case(s):

Absence of pupillary or eyelid involvement is characteristic for WE associated ophthalmoplegia. In this case, motoneurons in the left sixth nerve nucleus (cholinergic) had greater involvement than the (glutamatergic) interneurons. Vertical gaze improved rapidly. Recovery was initially asymmetric, but once h-GP recovered, she had gaze holding failure (Medial vestibular (MVN) and prepositus hypoglossi nucleus), without abducens paresis. At this point, she showed bilaterally impaired h-VOR (MVN compromise) . Vertical gaze palsy resolved, the vertical neural integrator function and VOR were normal.

References: 1. Horn A K E, et al Identification of functional cell groups in the abductees nucleus of monkey and humans by perineural nets and Choline Acetyltransferase Immunolabelling. *Frontiers of Neurology* 2018;12:75 2. Victor M, Adams R, Collins G. *The Wernicke's Korsakoff's Syndrome* F.A Davis Co , Philadelphia , 1978.pp 25-26 3. Kattah J C. The Spectrum of Ocular Motor and Vestibular abnormalities in Thiamine Deficiency. *Curr Neurol Neuroscience Rep.* 2017 May; 17(5):40

Keywords: Ocular motility, Ocular manifestations of vestibular disorders, Nystagmus, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 61**The HINTS exam in acute vestibular neuritis – don't look too hard for the skew...**

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Introduction:

An ocular tilt reaction (OTR) is a triad of a skew deviation, head tilt, and an ocular-counterroll, that can be partial or complete. OTR can occur anywhere along the utriculo-ocular motor pathways from the labyrinth to brainstem with more cases related to central localizations. The true incidence in vestibular neuritis (VN) is unknown.

Description of Case(s):

1. 48-year-old man with vascular risk factors reports symptoms of AVS. HINTS plus suggested a right vestibular neuritis and neuroimaging was normal. Six canal vHIT showed only evidence of superior vestibular nerve damage (horizontal canal only). An ipsiversive OTR was discovered upon follow-up that resolved in a few weeks. 2. 60 year-old man with hypothyroidism reports symptoms of AVS. HINTS plus and normal neuroimaging suggested a left vestibular neuritis. Six canal vHIT showed only evidence of superior vestibular nerve damage (horizontal + anterior canal). An ipsiversive OTR was discovered upon follow-up that resolved over a month. 3. 57-year-old man with vascular risk factors reports symptoms of AVS and vertical diplopia. HINTS plus suggested possible central vestibulopathy given skew with normal initial (within 48 hours) and follow-up (2 weeks later) neuroimaging was normal. Six canal vHIT showed only evidence of superior vestibular nerve damage (horizontal + anterior canal). A right vestibular neuritis and accompanying ipsiversive OTR was diagnosed which resolved over months.

Conclusions, including unique features of the case(s):

Features of the OTR in acute vestibular neuritis, aided by tools including the Maddox rod, fundus photography), and the bucket test. A partial or complete OTR can be appreciated in most (if not all) patients with superior division involvement.

References: None.

Keywords: Vestibular, Ocular motility, Nystagmus, Ocular manifestations of vestibular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 62**SANDO Syndrome associated with new POLG heterozygous gene mutation: Case Report**

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Introduction:

The nuclear-encoded POLG gene encodes gamma subunit of the mitochondrial DNA polymerase that is responsible for the replication of the mitochondrial DNA (mtDNA). Mutations of the POLG gene can have multiple phenotypic presentations including sensory ataxic neuropathy with dysarthria and ophthalmoplegia or SANDO syndrome, first described in 1997. At the molecular level, A467T and W748S POLG mutations have been described in SANDO. We describe a novel mutation of the DNA polymerase subunit gamma (POLG) gene with a phenotypic presentation of Sensory Ataxic Neuropathy, Dysarthria and Ophthalmoparesis Syndrome (SANDO).

Description of Case(s):

A 69-year-old female presented with two years of progressive ophthalmoplegia, ataxia, falls, hoarseness and dysphagia. Her mother also suffered from ataxia and falls. Neurological exam showed multifocal dystonia, significant truncal ataxia with postural instability, minimal appendicular ataxia, diffuse hyperreflexia, abnormal Hoffman and Babinski reflexes and frontal release signs. She had minimal rigidity and bradykinesia without tremors. Neuro-ophthalmological exam showed near-total absence of both vertical and horizontal eye movements bilaterally, esotropia and right hypertropia and weak orbicularis oculi and oris weakness bilaterally. She had abnormalities of alternate trail marking, figure copying, and clock drawing indicating visuospatial and executive dysfunction. Extensive workup including CSF, blood work and MRI Brain were unremarkable. Growth differentiation factor 15 levels were elevated suggesting a mitochondrial cytopathy. Genetic evaluation revealed single nucleotide heterozygous gene mutation of the POLG gene (c.3614G>C p.Gly1205Ala). This mutation has previously not been associated with pathology and hence felt to be of uncertain significance.

Conclusions, including unique features of the case(s):

We report the phenotypic presentation of SANDO syndrome with a gene mutation previously classified as uncertain significance. Due to the clinical heterogeneity, overlapping phenotypes, diagnosis of mitochondrial diseases relies on the molecular detection of genetic mutations.

References: None.

Keywords: Genetic disease, Ocular motility

Financial Disclosures: Licensed technology with EON Reality

Grant Support: None.

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Poster 63**“Can’t see well when I am moving” A case of brain stem tumor**

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Introduction:

There are several typical initial signs and symptoms of patients with brain tumors including headache, papilledema. In early stage, patients may present minor/atypical visual symptoms in particular condition. Here, we present a young men who complaints visual discomfort only when he is moving, with gaze-evoked nystagmus, skew deviation, mild papilledema, good central vision.

Description of Case(s):

A previously healthy 18 year old male visited clinic with blurring and discomforts to focus on some target, only when he is moving by car or walking. It started 2 months ago. His best visual acuity was 20/20 in both eyes, intraocular pressure were also normal. He was preparing for college entrance exam, performed excessive near work over ten hours a day. The doctor who first examined him prescribed a new glasses, with reassurance. After 1 week, he visited neuro-ophthalmologic clinic with same complaints. He has 2 prism diopter right hypertropia in primary position, it slightly aggravated (upto 4 PD) in right head tilt position, without abnormal head posture. However, when he attempt to see right side, there was tiny jerky movement to right side, it resolved in primary position and when sighting other side. At the fundus examination, there was intorsion in right eye and extorsion in left eye, mild papilledema without blurring of disc margin was presented.

Conclusions, including unique features of the case(s):

Possible explanation of his initial symptom is gaze-evoked nystagmus on right gaze, visual dimness with positional change due to papilledema, and abnormal ocular tilt reaction with skew deviation. The nystagmus might be a gaze-evoked nystagmus, or a type of Bruns nystagmus. Clinicians should be consider immediate brain imaging with neurologic tests with the patients who have newly presented nystagmus, vertical strabismus with fundus torsion.

References: None.

Keywords: Nystagmus, Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 64**Severe Delay in Saccadic Eye Movement in Parkinsonism Associated with Vascular Risk Factors**

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Introduction:

The hallmark of Parkinson's disease (PD) is motor difficulties due to loss of dopaminergic neurons in the substantia nigra pars compacta. Patients with PD exhibit a variety of eye movement abnormalities, and eye movement abnormality can be particularly prominent in progressive supranuclear palsy and other causes of parkinsonism. We described a patient with atypical parkinsonism with marked volitional saccadic eye movement abnormality.

Description of Case(s):

We describe a 68 year-old Caucasian woman with parkinsonism and multiple vascular risk factors who presented for evaluation due to symptomatic blurry vision and difficulty reading because of difficulty looking down. She has had right hand tremor for 5 years, progressive festinating gait, and poor balance. Brain magnetic resonance imaging revealed moderate deep white matter ischemic changes. On neuro-ophthalmic examination, patient had visual acuity with pinhole of 20/25 OD and 20/40 OS and normal optic nerves. Patient was consented for videography of her eye movement abnormality. She had horizontal and vertical ophthalmoparesis and convergence insufficiency. Her alignment was orthophoric at distance in primary gaze and exotropic at near. On levodopa/carbidopa, her reflexive saccades were hypometric and highly variable delay in latency of onset. Sometimes her horizontal saccades were more affected than her vertical saccades, and sometimes they were both severely affected. At times, she exhibited approximately 20 seconds delay in the latency of saccades in horizontal and vertical directions. She was more able to pursue her own thumb than a target from the examiner. Her speech and motor behavior were similarly affected during these episodes. Her pursuit was saccadic in all directions.

Conclusions, including unique features of the case(s):

Atypical parkinsonism can manifest as nonspecific blurry vision and difficulty reading due to eye movement disorder. We show videography of a patient with vascular risk factors and atypical parkinsonism with severe and variable delay in the latency of saccades, saccadic smooth pursuit, and convergence insufficiency.

References: None.

Keywords: Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 65**Alternating Involvement of Bilateral Oculomotor Nerves in Recurrent Ophthalmoplegic Cranial Neuropathy**

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Introduction:

Recurrent ophthalmoplegic cranial neuropathy (ROCN), formerly ophthalmoplegic migraine, is a rare disorder of episodic unilateral headache with reversible paresis of ipsilateral cranial nerves III, IV, and/or VI. Almost exclusively, laterality is consistent between recurrences(1). We report a case of alternating laterality of headache and oculomotor paresis between ROCN episodes.

Description of Case(s):

A 59 year-old male presented with acute diplopia and right-sided ptosis following 13 days of severe throbbing right-sided headache with nausea and photophobia. An isolated right-sided pupil-sparing third nerve paresis was diagnosed. There was no history of diabetes, hypertension, or smoking. Workup including CTA, MR head with gadolinium, extensive laboratory investigations including CSF analysis, and CT chest was normal. The headache resolved 3 weeks after onset. The diplopia gradually improved until six weeks later when the patient re-presented with acute worsening of diplopia following 1 week of similar left-sided headache. The examination was notable for a new left-sided pupil sparing third nerve paresis and improved function of the right third nerve. Laboratory and imaging studies were again negative. Based on International Classification of Headache Disorders criteria, ROCN was diagnosed(2). The headache resolved with corticosteroid treatment. Four months later, ocular motility was normal and there has been no recurrent headache. Repeat neuroimaging, obtained eight months after initial presentation, is completely normal.

Conclusions, including unique features of the case(s):

To our knowledge, this is the second report of alternating laterality between episodes of ROCN, and the only reported case with normal imaging. Choi et al reported a case with alternating laterality of internal ophthalmoplegia with headache and gadolinium enhancement of bilateral oculomotor nerves(3). In this case all three neuroimaging studies were normal as is frequently the case with ROCN(4). There remains debate whether ROCN is a primary headache disorder or a neuropathy. The quality of headache and normal imaging in the present case support a migrainous etiology.

References: 1. Smith, Schuster, Relapsing Painful Ophthalmoplegic Neuropathy: No longer a "Migraine," but Still a Headache, Curr Pain Headache Rep, 22, 50, 2018. 2. Headache Classification Committee of the International Headache Society (IHS), The International Classification of Headache Disorders, 3rd edition. Cephalalgia, 38, 1, 2018. 3. Choi, Jang, Park, Kim, Lee, Ophthalmoplegic migraine with alternating unilateral and bilateral internal ophthalmoplegia, Headache, 47, 726, 2007. 4. Lal, Sahota, Singh, Gupta, Prabhakar. Ophthalmoplegia with migraine in adults: Is it ophthalmoplegic migraine?, Headache, 49, 838, 2009.

Keywords: Ocular motility, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 66**Ipsilateral Abducens Nerve Palsy and Contralateral Hemiparesis from Pontomedullary Infarction (Raymond syndrome without facial involvement)**

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Introduction:

The combination of abducens nerve palsy and contralateral hemiparesis is termed Raymond's syndrome. The French neurologist Fulgence Raymond described the clinical picture that bears his name in 1895. In Classic Raymond's patient, the hemiparesis included central facial palsy. The lesion lies in the medial ventral caudal pons. Here, we report a case of pontomedullary infarction that caused ipsilateral abducens nerve palsy and contralateral hemiparesis sparing the face.

Description of Case(s):

A 78-year-old man with past medical history of hypertension and type 2 diabetes visited the emergency room complaining of acute dizziness, horizontal diplopia, worsened by directing gaze to the left and right hemiparesis that had started suddenly from 1 day ago. Neurological examination showed left abducens nerve paresis and right hemiparesis (MRC grade Rt. IV/IV). Both spontaneous and voluntary facial movements were normal. DWI and ADC showed acute small infarction in left anteromedial aspect of pontomedullary junction. Intracranial MRA showed mild focal stenosis of basilar artery.

Conclusions, including unique features of the case(s):

A patient with abducens nerve paresis and contralateral hemiparesis sparing the face, caused by a lesion in the pontomedullary junction, was recently diagnosed with Raymond's syndrome. Others suggested using the eponym only when central facial palsy is present. This controversy likely reflects uncertainty about the anatomical course of corticofacial fibers in the brainstem. Regardless of the presence or absence of central facial palsy, the combination of abducens nerve palsy and contralateral hemiparesis should direct the clinician's attention towards the medial ventral caudal pons.

References: None.

Keywords: Vascular disorders, Ocular motility, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 67**Cranial Nerve Three Palsy – The Wider Differential Based on MRI Findings**

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Introduction:

The etiology of cranial nerve (CN) 3 palsy includes aneurysmal or dolichoectatic vessel compression, microischemic injury, cavernous sinus lesions, infiltration by infectious, granulomatous or neoplastic entities, pathology affecting the third nerve nucleus and fascicle in the midbrain, ophthalmoplegic migraine and radiation-induced neuropathy.^{1,2,3,4} Vascular neuroimaging is commonly performed in most cases of CN 3 palsy to exclude aneurysm. Advances in high resolution MRI allow for the entire course of CN 3 to be visualised which refines the anatomical location and possible etiology of CN 3 palsies. MRI enhancement of CN 3 may indicate underlying infiltrative or inflammatory disease.^{1,3}

Description of Case(s):

A 72-year old woman presented with complete right pupil-involving CN 3 palsy. She had a history of metastatic breast cancer to the lungs, pleura, lymph nodes and bone for which she was currently undergoing chemotherapy. She also had a history of pituitary macroadenoma for which she underwent surgery with partial resection and radiation therapy 23 years ago. She had 2 mm of anisocoria, right ptosis and absence of right supraduction, adduction and infraduction.. Her remaining neuro-ophthalmic examination was unremarkable. MRV Head with time-of-flight MRA/MRV demonstrated no evidence for cerebral aneurysm or venous sinus thrombosis. MRI Brain with GAD revealed avid enhancement and mild smooth thickening of the pre-cisternal third cranial nerves bilaterally. No other areas of leptomeningeal or intraparenchymal enhancement was seen. Three separate lumbar punctures, one week apart, with 15 cc of spinal fluid analyzed were acellular with normal cytology.

Conclusions, including unique features of the case(s):

We concluded that the most likely etiology of this patient's CN 3 palsy was either infiltrative secondary to metastatic disease or alternatively, through a process of exclusion, due to radiation-induced cranial neuropathy as the extensive work up for carcinomatous meningitis was negative. This would then make this case the longest reported interval between administration of radiation therapy and subsequent radiation-induced cranial neuropathy.

References: 1. Blake PY, Mark AS, Kattah J, Kolsky M. MR of Oculomotor Nerve Palsy. Am J Neuroradiol. 16: 1665-1672, 1995 2. Yassin A, Hashwani A, Shanina E. Oculomotor Nerve Enhancement in a Patient with Headache. Neurological Cases. 2(3): 11-13, 2015 3. Mark AS, Blake P, Scott WA, Ross M, Brown D, Kolsky M. Gd-DTPA Enhancement of the Cisternal Portion of the Oculomotor Nerve on MR Imaging. AJNR 13: 1463-1470, 1992 4. Vaphiades MS, Spencer SA, Riley K, Francis C, Deitz L, Kline LB. Radiation-Induced Ocular Motor Cranial Nerve Palsies in Patients With Pituitary Tumor. Jnl of NeuroOphthalmol. 31: 210-213, 2011

Keywords: Chemotherapy and radiation injury, Tumors, Neuroimaging, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 68**Artery of Percheron infarction: the two extremes of clinical manifestations**

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Introduction:

This report demonstrates neuro-ophthalmological disturbances caused by the rare but well-described artery of Percheron (AOP) infarction (1), presented in approximately 0.1% - 2% of ischemic strokes (2).

Description of Case(s):

Case 1: A 51-year-old man was referred for ophthalmic evaluation because of a one year history of double vision associated to vertical gaze paralysis soon after recovering from a stroke. On ophthalmic examination, his best-corrected visual acuity was 20/30 on both eyes (OU). Slit lamp examination, tonometry and fundoscopy were unremarkable. Ocular motility showed supraversion and infraversion deficit motility (OU) (Image 1). Pupils showed reduced direct light reaction (+2 OU). Laboratory investigation and cerebrospinal fluid did not reveal any abnormalities. Magnetic resonance imaging (MRI) showed bilateral hyperintense lesion in the thalamus (Image 2), corresponding to an AOP infarction. Case 2: A 84-year-old female patient was admitted to the emergency department with dizziness, diplopia, dysarthria and sudden reduction of the level of consciousness. Past medical history was significant for hypertension. Neurological examination confirmed coma, and marked anisocoria, with the right pupil larger than the left, both fixed to light. Corneopalpebral, cough, gag reflexes, and ventilatory pattern were normal. Motor responses were bilaterally abnormal, with extensor posturing to pain. MRI showed bilateral infarction of the upper midbrain and paramedian portion of the thalamus (suggestive of AOP), and chronic small vessel disease (Fazekas 2). Transthoracic echocardiogram, carotid-vertebral duplex scan were unremarkable. The patient remained bedridden for two years, mRS 5 (modified Rankin scale) and died after pulmonary infection.

Conclusions, including unique features of the case(s):

It is a rare anatomic variant of the paramedian arteries, in which a single thalamoperforating artery arises from the P1 segment of one of two posterior cerebral arteries and supplies the paramedian thalamus bilaterally. Symptoms include vertical gaze palsy, altered mental status and memory impairments, oculomotor disturbances, cerebellar ataxia, hemiplegia and movement disorders, depending if the midbrain is affected 2,3.

References: 1 - Puri PR, Sijapati A. Bilateral internuclear and internal ophthalmoplegia due to artery of Percheron infarction. Clin Case Rep. 2017; 5(3):280-284 2 - Aryan S, Thakar S, Hegde AS. Artery of percheron infarction after endoscopic pituitary surgery. Acta Neurochir 2016;158:1973–5. 3 - Lamot U, Ribaric I, Popovic KS. Artery of percheron infarction: review of literature with a case report. Radiol Oncol 2015;49:141–6.

Keywords: Ocular motility, Neuroimaging, Stroke trauma, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 69

Trochlear Nerve Palsy due to Quadrigeminal Plate Cistern Lipoma

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Introduction:

Intracranial lipomas are rare, accounting for <0.1% of primary brain lesions. The majority are interhemispheric (45%) followed by a quarter that are quadrigeminal or superior cerebellar (25%). Intracranial lipomas are most often asymptomatic incidental imaging findings. 55% of patients have associated brain malformations as the primary source of neurologic symptoms. Prior case reports and literature reviews have shown that isolated symptomatic quadrigeminal plate cistern lipomas can result in obstructive hydrocephalus, elevated intracranial pressure, and seizures. In this case report, we present a rare clinical presentation for a classically asymptomatic brain lesion.

Description of Case(s):

A 71 year old male with past medical history of hypertension, ocular migraines, Sjogren's syndrome, and stage 3 chronic kidney disease, presented for consultation of worsening binocular oblique diplopia since onset 3 years prior, without preceding head trauma. Extraocular muscle examination revealed right hypertropia of 18 prism diopters in primary gaze, worse in left gaze, down gaze, and right head tilt. Magnetic resonance imaging of the brain without contrast revealed a left-sided quadrigeminal plate cistern lipoma, without mass effect or hydrocephalus, in close proximity to cranial nerve IV at its exit from the left dorsal midbrain at the level of the inferior colliculi.

Conclusions, including unique features of the case(s):

In a patient with progressive trochlear nerve palsy without preceding head trauma, imaging revealed lipomatous cranial nerve IV impingement. This is the first reported case of a trochlear nerve palsy secondary to a quadrigeminal plate cistern lipoma. There are only 3 reported cases to date of quadrigeminal lipomas resulting in strabismus: one unspecified, one with upgaze restriction, and one with abducens palsy. This case demonstrates that, while the vast majority of cranial nerve IV palsies are secondary to trauma the nerve is also susceptible to impingement by space occupying lesions as we demonstrate in this unusual patient scenario.

References: Truwit, Barkovich. Pathogenesis of intracranial lipoma: An MR study in 42 patients. American Journal of Neuroradiology, 11(4), 665-674, 1990. Ono, Ikeda, Imai, Mano, Matsuoka, Nagai, Okada. Intracranial lipoma of the quadrigeminal region associated with complex partial seizures. Pediatric radiology, 28(9), 729-731, 1998. Ambrosetto, Martinelli, Bacci, Daidone. Lipoma of the quadrigeminal plate cistern. The Italian Journal of Neurological Sciences, 6(3), 347-349, 1985. Yilmaz, Egemen, Tekiner. Lipoma of the quadrigeminal cistern: report of 12 cases with clinical and radiological features. Turkish neurosurgery, 25(1), 16-20, 2015. Nikaido, Imanishi, Monobe. Lipoma in the quadrigeminal cistern. Neurologia medico-chirurgica, 35(3), 175-178, 1995.

Keywords: Tumors, Neuroimaging, Ocular motility, Adult strabismus with a focus on diplopia

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 70**Prison Attack Resulting in Ophthalmoplegia: Case of Cavernous Sinus Thrombosis and Superior Orbital Fissure Syndrome**

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Introduction:

Pathology in the cavernous sinus may produce a syndrome identical to superior orbital fissure syndrome (SOFS). Lesion localization may be challenging since cranial nerves III, IV, VI, and V1 traverse both the cavernous sinus and superior orbital fissure (SOF). Deficits of the V2 nerve, if present with palsies of the former nerves, localize the lesion to the cavernous sinus since V2 does not enter the SOF. Cavernous sinus thrombosis (CST) is a rare condition, with incidence of ~1.6 per 100,000 per year. SOFS is also uncommon with incidence of ~0.3% of maxillofacial fracture cases. To our knowledge, this is the first reported patient with both SOFS and CST.

Description of Case(s):

A 45-year-old male prisoner was admitted after an assault by 20 inmates. He presented with binocular diplopia, ophthalmoplegia, and complete ptosis of his left eye. He also sustained a pneumothorax, requiring chest tube placement. He was previously healthy without significant medical history. Physical exam demonstrated trace extraocular movements in all directions of the left eye. Initially, both pupils measured 2 mm with minimal reactivity to light but the left pupil enlarged to 6 mm by day 3 following trauma. Visual acuity was 20/20 OD and 20/25 OS at distance. Fundoscopy was normal bilaterally. Neurologic exam was otherwise normal except diminished sensation in left V1 distribution. Maxillofacial CT revealed a fracture fragment within the left SOF. Magnetic resonance imaging showed minimal flow through the cavernous sinus and left superior orbital vein and a T2 FLAIR hyperintensity in the left temporal pole. Cerebral angiography illustrated a mostly thrombosed cavernous sinus with only trickle flow. The patient was treated with IV dexamethasone for 5 days and anticoagulation with warfarin for 6 months.

Conclusions, including unique features of the case(s):

Sixty days following discharge, he returned full ocular motility and eyelid function with only occasional diplopia and mildly decreased sensation in V1 distribution.

References: 1. Rai S, Rattan V. Traumatic superior orbital fissure syndrome: Review of literature and report of three cases. *Natl J Maxillofac Surg.* 2012;3:222–225. 2. Lai PF, Cusimano MD. The spectrum of cavernous sinus and orbital venous thrombosis: a case and a review. *Skull Base Surg.* 1996;6:53-9. 3. Brismar G, Brismar J. Thrombosis of the intraorbital veins and cavernous sinus. *Acta Radiol Diagn (Stockh).* 1977;18:145-53.

Keywords: Ocular motility, Neuroimaging, Stroke trauma

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 71**Oscillopsia and Tinnitus in the Absence of Vertigo in Neurovascular Cross-Compression of the Vestibulocochlear Nerve**

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Introduction:

Neurovascular cross-compression (NVCC) of the vestibulocochlear nerve (CN-VIII) is thought to cause brief episodes of vertigo termed vestibular paroxysmia. We report a case of a patient with NVCC of CN-VIII who presented with frequent brief attacks of oscillopsia and non-pulsatile tinnitus without vertigo.

Description of Case(s):

A 65-year-old male presented with a 1-year history of concurrent brief episodes of binocular oscillopsia that can be either vertical or horizontal, around 10-20 times a day lasting a few seconds each, along with non-pulsatile tinnitus in about 70% of the episodes. The episodes would occur suddenly, any time of the day, but fatigue and sounds seemed to abate the episodes as he did not experience them while watching TV at night or exercising. The patient denied experiencing vertigo, and head position was not a trigger. On neuro-ophthalmic examination, afferent and efferent exams were within normal limits except for an ocular flutter that was observed with the naked eye and slit lamp as the patient experienced oscillopsia episodes that were occasionally associated with tinnitus during examination. A slow phase could not be identified, and the eye movement appeared to take the pattern of an ocular counter roll. There was no induction by Valsalva or handshaking, and no nystagmus was appreciated. MRI 6 months prior to the visit, indicated for enhancing small vessels along the superior right cerebellar hemisphere near the cerebellopontine angle (CPA), showed a vascular loop extending from the right CPA cistern into the porus acusticus, resulting in crowding of the structures in the right internal auditory canal. Treatment with carbamazepine was trialed abating the symptoms almost completely.

Conclusions, including unique features of the case(s):

Oscillopsia and non-pulsatile tinnitus can be associated with NVCC of CN VIII in the absence of vertigo. This unique case does not entirely fulfill the criteria of currently established syndromes but could be a spectrum of vestibular paroxysmia.

References: None.

Keywords: Ocular manifestations of vestibular disorders, Ocular motility, Vestibular, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 72**Oculopalatal tremor secondary to atypical cavernoma, precipitated by pregnancy.**

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Introduction:

Oculopalatal tremor typically encompasses a pendular nystagmus combined with continuous rhythmic movement of the soft palate. Disruption of the dentato-rubro-thalamic tract with secondary inferior olivary nucleus hypertrophy is a requirement for its evolution. We present an atypical case, first apparent during pregnancy.

Description of Case(s):

A 28 year old female, midway through her first pregnancy, reported to her Obstetrician, a sensation of her knees buckling during heightened emotional states. This was not associated with a loss of consciousness or day time somnolence. A review soon after delivery, revealed asymptomatic chaotic horizontal, vertical and rotatory ocular movements of both eyes. A neurological examination was otherwise unremarkable. Concern for opsoclonus prompted a paraneoplastic screen and was negative for anti-cerebellar (anti-Ri/Yo/Hu), anti-Ma2 (Ta), anti-CV2 and anti-amphiphysin antibodies. All other blood markers including ANA, ANCA, IgG, IgA, IgM, HIV and Syphilis serology were negative. An MRI revealed a high T2 signal abnormality extending from the lower midbrain / upper pontine tegmentum to the superior cerebellar peduncles bilaterally. Increased T2 signal and expansion of the inferior medullary olives were consistent with bilateral hypertrophic olivary degeneration. Subsequently, a rhythmic movement of the soft palate was noted, and the eye movements evolved into a synchronous vertical pendular nystagmus with superimposed gaze-evoked nystagmus and right sided internuclear ophthalmoplegia. A CT angiogram and venogram revealed the lesion to be heavily calcified with no associated vessels apparent, and an atypical cavernoma was thought most likely. Follow up imaging to assess for change was planned, particularly as the drop attacks ceased. The oculopalatal tremor was still present, but less pronounced 3 months post-partum.

Conclusions, including unique features of the case(s):

The Neuro-Ophthalmologist should be aware of the variable presentation and associations of oculopalatal tremor. This case additionally highlights the risk pregnancy poses to vascular malformations, as a result of increased circulating vascular growth factors.

References: 1) Talks SJ, Elston JS. Oculopalatal myoclonus: eye movement studies, MRI findings and the difficulty of treatment. *Eye*.11(1):19-24. 1997 2) Shaikh AG, Hong S, Liao K, et al. Oculopalatal tremor explained by a model of inferior olivary hypertrophy and cerebellar plasticity. *Brain* 133(1):923-940. 2010 3) Borruat, FX. Oculopalatal tremor: current concepts and new observations. *Curr Opin Neurol*. 26(1):67-73 2013 4) Jun B The Development of Hypertrophic Inferior Olivary Nucleus in Oculopalatal Tremor. *Neuroophthalmology* 40(6): 297–299 2016 5) Kilic T, Pamir MN, Kullu S, Eren F, Ozek MM, Black PM: Expression of structural proteins and angiogenic factors in cerebrovascular anomalies. *Neurosurgery* 46: 1179–1192 2000

Keywords: Neuroimaging, Nystagmus, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 73**Oculomotor Schwannoma Presenting as an Acute Painful Third Nerve Palsy**

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Introduction:

Oculomotor nerve schwannomas are exceedingly rare and the management of symptomatic tumors is challenging. We present a case of a painful third nerve palsy secondary to oculomotor nerve schwannoma that had significant improvement with partial resection.

Description of Case(s):

A 55-year old man with a history of hypertension and type 2 diabetes mellitus presented to the emergency department for acute-onset right periocular pain, binocular horizontal diplopia, and right ptosis. Examination was remarkable for visual acuity of 20/25 in the right eye and 20/20 in the left eye. Pupils were symmetric without a relative afferent pupillary defect (RAPD). Ocular ductions in the right eye showed deficits of 50% on adduction, 25% on supraduction, and 25% on infraduction. The remainder of the cranial nerve examination was unremarkable. The anterior and posterior segments were normal. MRI/MRA brain showed no intracranial aneurysm but was remarkable for a 2.5 x 0.9 x 1.1 cm mass in the right cavernous sinus with extension into the superior orbital fissure. Inflammatory, infectious, and neoplastic work-up was unremarkable. There was mild improvement of the ptosis after treatment with systemic steroids, although the eye movements and imaging findings did not change. He ultimately underwent trans-nasal trans-sphenoidal biopsy and partial resection of the mass. Histopathology confirmed a WHO grade I schwannoma. He elected to defer radiotherapy. Six weeks after surgery, examination was remarkable for visual acuity of 20/20 in each eye. Pupils were asymmetric - 2.5 mm larger in the right eye. There was a trace right RAPD. Ocular ductions were full in both eyes and there was trace right ptosis.

Conclusions, including unique features of the case(s):

In summary, both head imaging and biopsy were important for diagnosing this rare cause of an acute painful third nerve palsy. Although prior case reports have shown worsening symptoms with radical resection, our patient showed near-complete improvement with partial resection of the schwannoma.

References: None.

Keywords: Ocular motility, Tumors, Adult strabismus with a focus on diplopia, Skull base, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 74**Oropharyngeal Squamous Cell Carcinoma with Perineural Spread to the Cavernous Sinus**

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Introduction:

Metastatic disease involving the cavernous sinus is rare and most often associated with primary tumors of the lung, colon, and liver (1). Spread of oropharyngeal squamous cell carcinoma (OSCC) to the cavernous sinus is exceptionally rare, with only a handful of case reports available in the literature. We report a case of perineural spread of OSCC to the cavernous sinus discovered when the patient developed horizontal diplopia.

Description of Case(s):

A 48 year old man with a history of tobacco use and metastatic, moderately differentiated OSCC involving the tongue (T4aN2cMx) was admitted to the hospital for induction chemotherapy. During his hospitalization, Neuro-Ophthalmology was consulted for new onset binocular, horizontal diplopia. Visual acuity was 20/20 in both eyes with normal pupils and full color perception. Slit lamp examination and dilated ophthalmoscopy were normal. There was a complete abduction deficit on the right side, consistent with a 6th nerve palsy. An MRI of the brain with contrast showed a heterogeneously enhancing tumor arising from the tongue with extension of thickening and enhancement to Meckel's cave and the cavernous sinus on the right via the mandibular branch of the 5th cranial nerve, suggesting direct perineural invasion. Despite chemotherapy, the patient went on to develop complete ophthalmoplegia and fixed, dilated pupils bilaterally. With widely metastatic, treatment resistant disease the patient was ultimately transitioned to palliative measures and died approximately two months after onset of his double vision symptoms.

Conclusions, including unique features of the case(s):

Cavernous sinus involvement in the setting of oropharyngeal cancer is rare and presents with ocular motility deficits and trigeminal hypoesthesia. To our knowledge, this is the first reported case of direct perineural spread of OSCC to the cavernous sinus region. Cancer involving the cavernous sinus portends a very poor prognosis.

References: (1) Forner, D., Wilke, D., Rigby, M.H. et al. Cavernous sinus involvement in human papillomavirus associated oropharyngeal squamous cell carcinoma: case report of an atypical site of distant metastasis. *J of Otolaryngol - Head & Neck Surg* 47, 32 (2018) doi:10.1186/s40463-018-0280-0

Keywords: Neuroimaging, Ocular motility, Tumors, Adult strabismus with a focus on diplopia, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 75**Acute Vertigo from a Unilateral Middle Cerebellar Peduncle Demyelinating Lesion**

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Introduction:

The MCP is a major pathway for cortico-ponto-cerebellar connections that carry eye movement information. Unilateral MCP strokes are reported to cause acute vertigo with abnormal eye movements including spontaneous horizontal and/or torsional nystagmus, ocular tilt reaction, gaze-evoked nystagmus (GEN), abnormal head-impulse test and impaired smooth pursuit. Two-thirds of patients with MCP strokes showed GEN, indicating failure of neural integration.

Description of Case(s):

A 35-year-old woman with multiple sclerosis presented 3 months postpartum, off disease modifying therapy, with acute spinning, nausea, and a feeling of 'drunkenness.' Non-contrast MRI brain showed a medial right MCP diffusion-restricting lesion, consistent with an acute MS exacerbation. She was treated with steroids with minimal improvement. Ten months later, dizziness with motion continued. Exam revealed normal acuity, visual fields and color vision OU, and full ocular motor range without deterioration on dynamic acuity. On cross-cover testing there was a left hyperphoria that increased in left gaze and right head tilt, consistent with a skew deviation, and GEN (larger amplitude in right gaze). Occlusive ophthalmoscopy and horizontal headshaking unmasked right beat nystagmus. Head impulse test (HIT) was positive towards the right. Rightward pursuit was saccadic. Videonystagmography (VNG) confirmed impaired rightward pursuit, GEN, and spontaneous right-beat nystagmus suppressible with fixation. Calorics were normal. Video HIT several months after VNG and vestibular therapy suggested a left vestibulopathy. Rotary chair testing showed impaired VOR cancellation.

Conclusions, including unique features of the case(s):

Acute unilateral middle cerebellar peduncle pathology from ischemia or demyelination can cause an acute vestibular syndrome that can mimic peripheral vestibular neuropathy. A detailed exam seeking other centrally-mediated eye movement abnormalities, such as GEN, ipsilateral saccadic pursuit and skew deviation can assist with diagnosis.

References: Kim, S. H. and J. S. Kim (2019). "Eye movement abnormalities in middle cerebellar peduncle strokes." *Acta Neurol Belg* 119(1): 37-45.

Keywords: Nystagmus, Demyelinating disease, Ocular motility, Vestibular, Ocular manifestations of vestibular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 76

Checkpoint Inhibitor-associated Myositis of the Extraocular Muscles

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Introduction:

Immune checkpoint inhibitors (ICI) unleash the immune system by blocking signals that turn off the immune system. Without those signals, immune cells become activated against cells they would otherwise identify as “self.” The intended target is cancer cells, but activation against healthy cells results in adverse autoimmune reactions.

Description of Case(s):

A 78 year old man presented with double vision and ptosis. Six weeks prior to presentation, he had undergone his first cycle of pembrolizumab for melanoma. Within three weeks of his treatment, he developed severe progressive neck and back pain. Three days later, he developed ptosis and double vision. He had no eye pain. He did not undergo a second cycle. Ocular examination was notable for complete ophthalmoplegia and ptosis of both eyes with normal afferent visual function. Neurologic examination was notable for hoarse voice, weak swallow, and decreased strength in all extremities worse proximally. Bloodwork was notable for CK of 5,236 U/L (20-200 U/L). Negative testing included myositis panel, myasthenia panel (including Titin and MuSK), voltage-gated calcium channel antibody, TSH, and thiamine. EMG showed no decrement with repetitive stimulation. He had no objective improvement with ice test, or subjective improvement on pyridostigmine trial. Myalgias and weakness in his trunk and extremities improved with prednisone. His ptosis and diplopia had not improved at his 3 week follow-up.

Conclusions, including unique features of the case(s):

The unifying diagnosis was immune checkpoint inhibitor-associated myositis with ophthalmoplegia. Based on the time course, the inciting agent was felt to be the pembrolizumab. ICI, a class of cancer therapies first approved by the Food and Drug Administration in 2011, can cause oculobulbar symptoms via multiple mechanisms. Prior case reports describe myasthenia-like syndromes. Although not typical for systemic myositis, there are rare case reports of ICI myositis with ophthalmoplegia. In addition, ICI can cause severe systemic myopathy with negative antibody testing and negative pyridostigmine testing.

References: Hellman JB, Traynis I, and Lin LK. Pembrolizumab and epacadostat induced fatal myocarditis and myositis presenting as a case of ptosis and ophthalmoplegia. *Orbit*. 2019 Jun;38(3):244-247. Noda T, Kageyama H, Miura M, Tamura T, and Ito H. A case of myasthenia gravis and myositis induced by pembrolizumab. *Rinsho Shinkeigaku*. 2019 Aug 29;59(8):502-508. Onda A, Miyagawa S, Takahashi N, Gochi M, Takagi M, et al. Pembrolizumab-induced ocular myasthenia gravis with anti-titin antibody and necrotizing myopathy. *Intern Med*. 2019 Jun 1;58(11):1635-1638.

Keywords: Chemotherapy and radiation injury, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: Supported in part by an Unrestricted Grant from Research to Prevent Blindness, New York, NY, to the Department of Ophthalmology & Visual Sciences, University of Utah and the Utah chapter of the Achievement Rewards for College Scientists Foundation.

Contact Information: None provided.

Poster 77
Astigmatoma

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Introduction:

Parinaud's or dorsal midbrain syndrome is usually accomplished by abnormal eye movement and pupil dysfunction. The classic triad of upgaze paralysis, convergence retraction nystagmus and pupillary light-near dissociation are seen in 65% of patients. The common etiologies are hemorrhage, stroke and neoplasms in midbrain and pineal gland tumors. Germinoma is very rare accounting for less than 5% of all brain tumors. The tectal tumors may cause high intracranial pressure, obstructive hydrocephalus, up gaze palsy, and diplopia. We present a case of parinaud's syndrome with delayed in diagnosis.

Description of Case(s):

The patient is a 24 year-old Hispanic male who noticed difficulty in reading due to jumping words in January 2019. He was diagnosed with astigmatism and since the glasses did not resolve the issue, he underwent lasik surgery. As the complaint continued he was referred to neuro-ophthalmology service in May 2019. Past medical history was not significant. His VA was 20/20, color vision was full, visual field and dilated eye exam was within normal limits. His pupils were sluggish reactive to light with light-near dissociation. He was not able to look up. In attempt upgaze eyes were getting converged and retracted. MRI brain showed large posterior mid-brain tumor surrounded by edema. Craniectomy was done. Pathology showed nests and sheets of large epithelioid cells with numerous interspersed lymphocytes. Fibrous bands are seen in some areas. The neoplastic cells are characterized by large round and pleomorphic nuclei with prominent nucleoli and abundant clear cytoplasm. Immunohistochemistry confirms the diagnosis of germinoma, positive for PLAP, SALL4, OCT4, D240 and CD117. Pankeratin (AE1/AE3), CD45, GFAP, CD30 and Glypican 3 immunohistochemical markers are negative. The patient underwent radiotherapy.

Conclusions, including unique features of the case(s):

Motility and pupil exam is key part of ophthalmic evaluation. The diagnosis in the presented case was delayed due to lack of completion in eye exam.

References: 1. Gomez-Gonsalvez, Menor, Morant, et al. Tectal tumors in pediatrics. A review of eight patients. Rev Neurol. 33:605-611, 2001 2. Burgueño-Montañés, Santalla-Castro, Peña-Suárez. Parinaud «plus» syndrome in a patient with dysgerminoma. Arch Soc Esp Oftalmol;91(7):341-5, 2016 3. Hankinson, Lyons, Hukin, Cochrane. Ophthalmological outcomes of patients treated for pineal region tumors. J Neurosurg Pediatr. 17(5):558-63, 2016 4. Shields, Sinkar, Chan, Crompton. Parinaud syndrome: a 25-year (1991-2016) review of 40 consecutive adult cases. Acta Ophthalmol. 95(8): 792-793, 2017 5. Koizumi, Oka, Utsuki, Sato and et al. Primary germinoma arising from the midbrain. Acta Neurochir (Wien). 148(11):1197-200; 2006 6. Osorio and Allen. Management of CNS germinoma. CNS Oncol. 4(4): 273–279, 2015

Keywords: Neuroimaging, Ocular motility, Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 79**When Not to Sweat the Anisocoria: A Case Series of Anticholinergic Mydriasis**

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Introduction:

Causes of anisocoria range from benign to life-threatening, making it a common reason for urgent Neuro-Ophthalmology referrals. The pathways controlling pupillary size and reactivity are complex and affected by lesions along this pathway or by systemic or topical agents. We present three cases of pharmacologic anisocoria caused by inadvertent ocular exposure to a product marketed for axillary hyperhidrosis.

Description of Case(s):

1: A 15-year-old female had transient episodes of anisocoria and bilateral pupillary dilation. On exam, both pupils were mydriatic to 8.5 mm and nonreactive to light, without response to 1% pilocarpine eyedrops. 2: A 16-year-old female, referred for Adie tonic pupil, experienced a single episode of blurred vision, photophobia, and a dilated left pupil that lasted two days. She believed her symptoms were related to new contact lenses and had since worn her glasses without further recurrence. 3: A 38-year-old female noted three episodes of blurred vision accompanied by a dilated, nonreactive left pupil, lasting one to two days. Patient-provided photos showed a 4-mm right pupil and a fixed 7-mm left pupil. The rest of the exam for all three patients was normal. All three patients failed to list any medications that could explain their symptoms. Further questioning revealed the recent addition of an antiperspirant cloth wipe. Glycopyrronium (Qbrexza) cloth is an anticholinergic drug that received FDA approval in June 2018 for topical use to treat primary axillary hyperhidrosis.

Conclusions, including unique features of the case(s):

Mydriasis is a well-known side-effect of anticholinergic agents. This is one of the first case reports of pharmacologic anisocoria due to a new topical product intended for primary axillary hyperhidrosis. As more pharmacologic agents are incorporated into commercial beauty and hygiene products, clinicians should be mindful of this benign etiology to alleviate patient and physician worry and reduce unnecessary testing.

References: None.

Keywords: Pupils retina

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 80**Acquired Horner's Syndrome as a Presenting Sign of Dilatative Arteriopathy in PHACE Syndrome**

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Introduction:

We report a case of acquired Horner's syndrome associated with an increase in calibre of the internal carotid artery (ICA) in a child with PHACE (Posterior fossa brain malformations, Hemangioma, Arterial anomalies, Cardiac defect and aortic coarctation, Eye abnormalities) syndrome.

Description of Case(s):

A 1-month-old female was referred by Pediatric Medicine to screen for eye associations of PHACE syndrome. She was noted to have an isolated right periorbital hemangioma involving right forehead, upper and lower eyelids. The rest of the eye examination was unremarkable. The pupils were equal and briskly reactive to light. MRI/MRA of the brain and orbits showed tortuosity of the right cavernous ICA, and absent left ICA. An incidental enhancing lesion in the right cerebello-pontine angle (suspected hemangioma) was also noted. MRI orbits were unremarkable. She was treated with oral propranolol HCL over a period of 2 years, resulting in gradual resolution of the right periorbital hemangioma. Pupils were noted to be equal on all ophthalmology follow up visits during this period. At age 45 months, we found the right pupil smaller than the left, with anisocoria worse in the dark. Repeat MRI/MRA showed an increase in caliber of the tortuous right ICA along its cervical and cavernous segments. The previously noted enhancing mass at the right cerebello-pontine angle showed interval decrease in size and enhancement.

Conclusions, including unique features of the case(s):

Dolichoectatic arteries and dilatative arteriopathy is a rare manifestation of progressive arterial lesion in PHACE syndrome. To our knowledge, this is the first case that highlights Horner's syndrome as a presenting feature of dilatative arteriopathy of ipsilateral ICA in child treated with propranolol for periorbital hemangioma. Ophthalmologists should maintain a high index of suspicion despite resolution of periorbital hemangioma so that timely and effective interventions can be implemented.

References: 1. Baccin CE et al. A report of two cases with dolichosegmental intracranial arteries as a new feature of PHACES syndrome. *Child Nerv Syst.* 2007 May;23(5):559-67. 2. Samuelov L et al. Ocular complications in PHACE syndrome: A true association or a coincidence? *J Pediatr* 2019; 204:214-218 e2.

Keywords: Pediatric neuro-ophthalmology, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 81**Rapidly Progressive Primary Orbital Squamous Cell Carcinoma**

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Introduction:

Squamous cell carcinoma of the orbit is typically the result of perineural invasion or metastasis. We report a patient with a rapidly-progressive primary squamous cell carcinoma of the orbit, which is rare.

Description of Case(s):

A 74-year-old female presented with right-sided facial numbness, headaches, and visual loss following closed head trauma 8 months prior to visit. The patient bent over, struck her head sharply against a sink, and had brief loss-of-consciousness. Within 2 days, she developed numbness and tingling involving the right frontal head region extending into the right orbit and infraorbital rim. She had throbbing right-frontal and sharp stabbing periorbital pain. Four months later, she developed diplopia and right-sided ptosis. On exam, visual acuity OD: hand motion; OS 20/20. Reduced color vision OD and OS normal. Pupils were 3.75 mm OD and 3.5 mm OS. There was an afferent and efferent pupillary defect OD with complete internal ophthalmoplegia. There was marked ptosis OD, 3 mm of relative proptosis, and the eye was positioned down and out. Forced ductions were positive. Both optic nerves appeared healthy. A previous MRI scan of the brain showed a small soft tissue mass involving superior medial aspect of the right orbit. An MRI scan of the orbits showed a large extraconal mass located along the superior medial aspect of the right orbit. The mass extended into the anterior superior orbital apex as well as the anterior cavernous sinus. The patient underwent an orbital biopsy which confirmed invasive keratinizing squamous cell carcinoma. Subsequently, the patient underwent orbital exenteration OD and radiation therapy.

Conclusions, including unique features of the case(s):

We report a rare case of primary orbital squamous cell carcinoma with extension into the cavernous sinus. The patient was treated with orbital exenteration and radiation therapy. To our knowledge, this is the tenth case of primary orbital squamous cell carcinoma in the literature.

References: Ana L. Campos Arbulú, Sadava EE, Ruiz AS, Juan M. Fernández Vila, Dillon HS, Mezzadri NA. Primary orbital squamous cell carcinoma. *Medicina (Buenos Aires)*. 2017;77:37-39. Beaucaire MC, Mizen TR, Moftakhar R, Vreem D, Cohen AJ. Recurrent orbital squamous cell carcinoma with extension to the middle cranial fossa. *European Journal of Plastic Surgery*. 2014;37:241-244. Blandford AD, Bellerive C, Tom M, et al. Case Report: Primary Orbital Squamous Cell Carcinoma. *Ocular oncology and pathology*. 2019;5:60. Raevis J, Lin B, Shinder R. Rapidly Progressive Conjunctival Squamous Cell Carcinoma With Orbital Invasion. *Ophthalmic plastic and reconstructive surgery*. 2019. Sakashita T, Hayashi R, Homma A, et al. Multi-institutional retrospective study for the evaluation of ocular function—preservation rates in maxillary sinus squamous cell carcinomas with orbital invasion. *Head & Neck*. 2015;37:537-542.

Keywords: Orbit/ocular pathology, Orbit, Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 82
Seven Plus Seven Equals Four

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Introduction:

T helper type 2 cells (Th2) has strong correlation with IgG4 disease severity, where its production of the cytokine interleukin 4 (IL-4) is instrumental in the pathogenesis of IgG4-related disease. Dupilumab, a monoclonal antibody and antagonist of IL-4 and IL-13 receptors, is approved for treatment of chronic rhinosinusitis and should theoretically prevent development of IgG4-related disease. Our patient is a 59 year old male with eosinophilic asthma and chronic rhinosinusitis who developed severe progressive orbital inflammatory disease, initially presenting as eosinophilic granulomatosis with polyangiitis but ultimately diagnosed as IgG4 disease despite dupilumab.

Description of Case(s):

A 59-year-old male with adult-onset eosinophilic asthma, chronic rhinosinusitis, newly diagnosed right facial nerve palsy and trigeminal neuralgia who presented to the ED for new-onset diplopia and facial pain. Neuro-ophthalmic examination showed a right hypertropia and bilateral abduction deficit. MRI brain and orbits revealed extensive infiltration and enhancement of bilateral lateral recti muscles and orbit. Subsequent LP was unremarkable. Eosinophilic granulomatous polyangiitis and IgG4 disease were suspected. Serology revealed elevated IgG4 and IgG2 as well as elevated RF, ESR and CRP. Extensive infectious workup was revealing as were his serum and CSF ACE. He was discharged with plans for an outpatient lacrimal gland biopsy following steroid taper, but he developed new left facial weakness, worsening diplopia and severe right eye pain several days later. He was readmitted, underwent lacrimal biopsy and treated with intravenous methylprednisolone followed by oral prednisone for IgG-4 related disease.

Conclusions, including unique features of the case(s):

IgG4-related disease is a multisystem autoimmune disease with varied presentations. In a patient with orbital inflammation without evidence of infectious, granulomatous or neoplastic disease, IgG4-related disease should be considered. Involvement of cranial nerves such as the facial nerve, is rare but does not exclude the diagnosis. Although IL-4 plays a role in its pathogenesis, treatment with IL-4 antagonist may not prevent its occurrence.

References: None.

Keywords: Orbit, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 83**Painless Diplopia as Initial Presentation of Metastatic Lobular Breast Carcinoma**

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Introduction:

Intraorbital metastasis is a rare clinical finding present in 2-3% of cancer patients, with breast carcinoma accounting for up to 50% of cases. Orbital metastasis is primarily diagnosed in patients with a known history of metastatic malignancy. We present a case of previously undiagnosed diffuse metastatic lobular carcinoma presenting as subtle binocular diplopia.

Description of Case(s):

A 70 year old woman with a history of fibrocystic breast condition presented for cataract evaluation. She incidentally mentioned painless, binocular diplopia noticeable only in left gaze. Motility testing showed right hypertropia and she was referred to neuro-ophthalmology. Further examination showed left eye deficits in up and horizontal gaze as well as restriction on forced ductions testing. Pupil exam, slit lamp exam, and dilated fundus exam were unremarkable. CT orbits were obtained and revealed mass-like enhancement in the retrobulbar spaces bilaterally. In addition the globes appeared enophthalmic and cervical spine imaging showed diffuse sclerotic changes. High on the differential was metastatic carcinoma despite the patient having multiple negative routine screening exams including skin checks and mammograms. FNA of an enlarged cervical lymph node was unrevealing; excisional biopsy of the lymph node showed metastatic lobular breast carcinoma (ER+ PR+ Her2-). Systemic workup showed widespread metastasis. Further breast imaging including MRI and ultrasound revealed a 0.6cm primary right breast mass. The patient is now on palliative chemotherapy.

Conclusions, including unique features of the case(s):

This is a rare presentation of orbital metastasis as the initial manifestation of undiagnosed metastatic lobular breast carcinoma. The aggressive nature of the metastasis far outweighed the clinical presentation and was not identified prior despite negative mammograms and recent MRI brain with no osseous or orbital findings. Furthermore, this case supports studies showing ER+ lobular carcinoma has an affinity to the orbits and highlights the importance of monitoring these patients closely for orbital involvement.

References: None.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Orbit/ocular pathology, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 84**An Unusual Case of Sclerosing Inflammatory Pseudotumor in a 11-year-old Female**

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Introduction:

Idiopathic sclerosing orbital inflammation (ISOI) is an uncommon non-infectious condition with poorly understood pathogenesis distinct from the spectrum of orbital inflammatory disorders. It frequently affects anterior orbital structures and may masquerade as orbital cellulitis, lymphoma, or rhabdomyosarcoma. We describe a 11-year old girl with dacryoadenitis who presented with diplopia and proptosis.

Description of Case(s):

A 11-year-old healthy girl presented with painful right eyelid swelling, proptosis, and diplopia with concern for periorbital cellulitis and right sided pansinusitis. She received intravenous antibiotics with quick oral transition but was re-admitted due to little improvement with imaging concerning for chronic sinusitis and abscess formation in right orbit and paranasal sinus. She underwent abscess drainage with pathology revealing chronic inflammation and again only minimally improved. Concern remained for rhabdomyosarcoma or lymphoma of the orbit. Subsequently multiple biopsies revealed sclerosing orbital pseudotumor. She received intravenous methylprednisolone with oral taper with significant improvement. On outpatient neuro-ophthalmology evaluation she had 20/20 vision OU with normal color, no afferent pupil defect, and severe ptosis OD and vertical diplopia from downward displacement of the right globe relative to left. Anterior and posterior segment were unremarkable. Extensive autoimmune and infectious workup returned normal. Follow up exam revealed much improved ocular misalignment. Repeat MRI orbit shows residual soft tissue changes in the area of previous inflammation of right orbit. As she remains asymptomatic she has been off of steroids while being followed closely by neuro-ophthalmology and oculoplastics.

Conclusions, including unique features of the case(s):

This case is unique as ISOI rarely manifests in children. Typically it is bilateral rather than unilateral. The lacrimal gland may be the most commonly affected, as the only orbital structure containing lymphoid tissue. ISOI is treated primarily with steroids or steroid sparing agent, and rapid response typically points towards ISOI as the definitive diagnosis.

References: [1] S. A. Laponsie and P. K. Rabiah, "When an orbital infection isn't infectious at all: A review of orbital inflammatory syndrome," *Pediatr. Ann.*, vol. 46, no. 11, pp. e433–e436, 2017. [2] Z. Wallace, V. Deshpande, and J. Stone, "Ophthalmic Manifestations Of IgG4-Related Disease: A Single-Center Experience.," *Arthritis Rheum.*, vol. 65, no. s10, pp. S332–S333, 2013. [3] D. Pemberton John and D. Fay Aaron, "Idiopathic Sclerosing Orbital Inflammation: A Review of Demographics, Clinical Presentation, Imaging, Pathology, Treatment, and Outcome," *Ophthalmic Plast. Reconstr. Surg.*, vol. 28, no. 1, pp. 79–83, 2012. [4] H. Toprak, A. Aralasmak, T. Yilmaz, and H. Ozdemir, "Unusual Sclerosing Orbital Pseudotumor Infiltrating Orbits and Maxillofacial Regions," *J. Clin. Imaging Sci.*, vol. 4, no. 1, p. 30, 2014. [5] J. D. Hsuan, D. Selva, A. A. McNab, T. J. Sullivan, P. Saeed, and B. A. O'donnell, "Idiopathic Sclerosing Orbital Inflammation," *Arch. Ophthalmol.*, vol. 124, no. 9, pp. 1244–1250, 2006.

Keywords: Orbit/ocular pathology, Orbit, Neuroimaging, Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 85**Low-Grade Osteosarcoma: An elusive diagnosis**

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Introduction:

Low-grade Osteosarcoma is a rare entity that usually occurs on long bones and often has misleading radiographic and histopathologic findings that initially lead to misdiagnosis in 32-66% of cases^{1,2}. Here we present a patient whose histopathologic findings and clinical course differed significantly.

Description of Case(s):

A 29-year-old African American male without significant past medical history presented with months of progressive painless swelling of the right cheek. Computed tomography (CT) demonstrated an infiltrative, partially calcified, minimally enhancing mass involving the zygoma and extending through the lateral orbital wall. Visual acuity was 20/20 in both eyes without RAPD or proptosis with minimal limitation of abduction and supraduction. Biopsy revealed a grey mass with fibrous capsule. Histopathology showed monomorphic cells admixed with collagen fibers and small bone foci with peripheral rims of reactive bone. Immunohistochemical stains for MDM2/STAT6/CD34/S100/SMA/EMA/B-catenin were negative,¹ Ki67 index was low. The patient was diagnosed with fibrous dysplasia; excision and reconstruction was scheduled. Abnormal tissue extending into the orbit and infratemporal fossa was removed. Histopathology demonstrated a cellular lesion with focal necrosis and reactive bone. Malignancy was suspected but not diagnosed due to microscopic consistencies with fibrous dysplasia and no atypia. Six months later he redeveloped swelling and diplopia in primary gaze. Exam showed worse limitation of abduction and supraduction and now adduction. CT and magnetic resonance imaging (MRI) demonstrated an infiltrative osseous lesion emanating from the greater wing of the sphenoid. Exenteration and radical skull resection was performed. Tissue remained negative for osteosarcoma-specific stains, however hypercellular areas had a high Ki-67 index, confirming the suspicion of low-grade Osteosarcoma^{2,3}

Conclusions, including unique features of the case(s):

He received adjuvant ifosfamide, etoposide, and radiation and two years later remains disease-free. This case demonstrates the illusive nature of low-grade osteosarcomas and the need to tailor treatment to the behavior of the disease instead of assigned diagnosis.

References: 1. Dujardin, Fanny, Binh et al (2011). MDM2 and CDK4 immunohistochemistry is a valuable tool in the differential diagnosis of low-grade osteosarcomas and other primary fibro-osseous lesions of the bone. *Modern Pathology*. 24. 624-637. 10.1038/modpathol.2010.229. 2. Bertoni F, Bacchini P, Fabbri N, et al. Osteosarcoma. Low-grade intraosseous-type osteosarcoma, histologically resembling parosteal osteosarcoma, fibrous dysplasia, and desmoplastic fibroma. *Cancer* 1993;71:338–345. 3. Mankin HJ, Lange TA, Spanier SS. The hazards of biopsy in patients with malignant primary bone and soft tissue tumours. *J Bone Joint Surg* 1982;64: 1121–1127.

Keywords: Orbit/ocular pathology, Orbit, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 86**A Novel Treatment Approach in a Case of Mosaic Neurofibromatosis Type 2**

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Introduction:

Neurofibromatosis type 2 (NF2) is a genetic syndrome caused by mutations in the NF2 gene resulting in tumors of the nervous system. While NF2 is commonly thought to follow an autosomal dominant inheritance pattern due to a mutation on chromosome 22, we present a case of NF2 due to sporadic germline mosaicism. Our goal is to highlight the clinical presentation of a patient with radiological findings consistent with invasive meningioma in the setting of genetic features consistent with mosaic NF2, as well as novel treatment approaches for treatment of a complex high grade and refractory meningioma.

Description of Case(s):

A 60 year old female presented with a one week history of progressively worsening headache, right sided facial swelling, and proptosis. On examination exam, she was noted to have significant right sided facial edema, right eye proptosis, and a complete ptosis of the right eyelid. Additionally, noted to have a cranial nerve six palsy and a pupil-involving cranial nerve three palsy. Slit lamp and fundoscopic examination were otherwise normal. An MRI of the brain and orbits, revealed multiple large intracranial meningiomas, including an invasive cavernous sinus meningioma extending into the orbit and left vestibular schwannoma. The patient underwent debulking of tumors with tumor sampling revealing two mutations in the NF2 gene. Her serum genetic testing was negative for NF2. She was diagnosed with Mosaic Neurofibromatosis Type 2 based on clinical presentation, and genetic findings of the gross specimen and germline genetic testing. Rather than surgical resection alone, we opted to treat our case of NF-2 meningiomas with adjuvant chemotherapy (bevacizumab), radiation, and surgical resection.

Conclusions, including unique features of the case(s):

Our case highlights the unique findings of an ocular presentation leading to the diagnosis of mosaic NF2 with refractory meningiomas, indicating the use of a novel treatment modality, bevacizumab.

References: None.

Keywords: Tumors, Orbit/ocular pathology, Orbit, Genetic disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 87
A Sterile Environment

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Introduction:

This is an extremely challenging case involving multidisciplinary subspecialties of a patient presenting with multiple aseptic abscesses causing an orbital syndrome.

Description of Case(s):

A 54-year-old man presented with months of multifocal abscesses, and 5-weeks of right-sided periorbital pain, ophthalmoplegia, ptosis, and face sensitivity. His medical history included diabetes mellitus, hypertension, hepatitis C (HCV) with cirrhosis, & latent tuberculosis on rifampin. In December 2018, he was admitted for presumed bacteremia with fevers, chills, rigors, and back pain in the setting of a necrotic right 3rd toe & positive for Group B in serum. Imaging revealed multiple abscesses (psoas, C/T spine), early pancreatitis, enteritis, and lumbar discitis. He was treated with ceftriaxone, had C&T laminectomy and fusion, and thoracic incision/drainage but symptoms progressed. In February & March 2019, new abscesses of the elbow, wrist, thumb and sternoclavicular joints developed. Despite extensive workup and multiple joint washouts, no pathogenic infectious agent was identified. A prolonged course of antibiotics, antifungals and colchicine did not prevent progression. He was finally started on prednisone and slow taper. Once the prednisone taper was completed, he developed right-sided headache, binocular horizontal diplopia, pain on lateral gaze, photophobia, and nausea. Despite treatment, symptoms progressed over weeks to include a right ptosis, adduction deficit, and V1-V2 pain. CT head with venogram & MRI brain with contrast was unremarkable. Additional MRI orbit was obtained, which showed subtle STIR hyperintensity and enhancement of bilateral medial recti and right superior rectus-levator complex. Prednisone was restarted, with brisk resolution of symptom.

Conclusions, including unique features of the case(s):

Orbital involvement of a patient with aseptic abscess syndrome, a multifocal auto-inflammatory condition, is rare. This has previously been reported mostly (but not exclusively) in patients with inflammatory bowel disease. To our knowledge, orbital involvement has not been reported in literature.

References: 1. Andre MF, et al. Aseptic Abscesses. Medicine. 2007;86: 145-161. 2. Andre M. Aseptic systemic abscesses. Orphanet Encyclopedia.2005 3. Nicolas P, et al. - Unusual Neurologic Presentation of Aseptic Abscesses Syndrome. Neurol Neuroimmunology. Neuroinflamm.2018; e469.

Keywords: Neuroimaging, Ocular motility, Orbit/ocular pathology, Orbit, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 88**3, 2, 1...Blast Off!**

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Introduction:

Idiopathic orbital inflammation (IOI) is an entity characterized by orbital inflammation lacking an identifiable local or systemic etiology. Clinical presentation typically involves acute unilateral pain, redness, proptosis, and periorbital edema. Vision changes and diplopia may also occur. IOI is a diagnosis of exclusion. Work-up should focus on ruling out infectious, rheumatologic, or neoplastic causes.

Description of Case(s):

A 71-year-old male with history of bilateral pseudophakia, prior prostate cancer, and prior renal cell carcinoma presented with two weeks of left eye pain, redness, and blurred vision. He was started on oral antibiotics for preseptal cellulitis. Subsequent examination showed BCVA of 20/200 in the left eye without RAPD. Left eye motility was diffusely restricted with proptosis and periorbital edema. MRI of the orbits with contrast showed enhancement of the left choroid and sclera, as well as the left lacrimal gland. Further testing revealed mild anemia and elevated CRP. At this point, the presumed diagnosis was IOI. Intravenous methylprednisolone resulted in clinical improvement. Attempts at tapering off oral prednisone over months were met with recurrent symptoms. Biopsy of a persistently enlarged left lacrimal gland was deferred. Repeat testing then revealed severe anemia, thrombocytopenia, and leukocytosis with 11% blasts. Bone marrow biopsy was consistent with acute myeloid leukemia (AML). Chemotherapy was induced and the patient obtained remission. He also underwent stem cell transplant. Symptoms have not recurred off corticosteroids.

Conclusions, including unique features of the case(s):

Recurrent symptoms and repeat work-up led to a final diagnosis of AML-associated orbital inflammation. In patients with chronic, recurrent episodes of presumed IOI, extensive work-up should be performed to evaluate for underlying etiologies. AML can present with a multitude of ocular manifestations and should be considered in the differential for IOI.

References: None.

Keywords: Orbit, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 89**Invasive Sino-Orbital Aspergillosis in Immunocompetent Elderly Female**

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Introduction:

Invasive mycosis is historically considered a disease of the immunocompromised, however, there are reports in immunocompetent patients. The most common etiology of sino-orbital invasive mycosis is mucor, and rarely aspergillus. Invasive mycosis has high morbidity and mortality, therefore, high clinical suspicion of invasive mycosis is warranted in cases of rapidly progressive orbital apex syndrome.

Description of Case(s):

83 year old female initially treated in Bermuda for presumed orbital cellulitis, presented to outside hospital with left eye ptosis, upper lid swelling, and blurry vision. The initial acuity was 20/40, but rapidly declined to light perception vision within 4 days of hospitalization while on piperacillin / tazobactam and dexamethasone. Subsequent transfer to our institution revealed complete ptosis, NLP vision and complete ophthalmoplegia. MRI +/- contrast revealed infiltrative enhancing soft tissue within the left orbit extending through the orbital apex, pterygopalatine fossa and sphenoid, involving the optic canal with severe compression of the optic nerve. Steroids were discontinued immediately and empiric amphotericin was initiated given our high suspicion of invasive mycosis. Initial ENT evaluation and FESS reported low suspicion for invasive mycosis, however, biopsy results revealed aspergillus fumigatus, which warranted transition to voriconazole. Hospital course was complicated by fluctuating vision in the right eye, and subsequent MRI revealed progression of disease and spread to the right orbit. Source control was achieved by left orbital exenteration and sinus washout, and the patient stabilized. The postoperative course was complicated by superior orbital vein thrombosis and prolonged QTc interval, which warranted a switch to isavuconazole.

Conclusions, including unique features of the case(s):

Physicians should have high clinical suspicion of invasive mycosis in cases of orbital apex syndrome that present with rapidly progressive ophthalmoplegia and severe vision loss, even in immunocompetent patients. Invasive mycosis secondary to aspergillus is rare. Management in cases suspicious for invasive mycosis should involve immediate initiation of empiric antifungals and avoidance steroids.

References: Mukherjee B, Raichura ND, Alam MS. Fungal infections of the orbit. Indian J Ophthalmol. 2016;64(5):337–345.

doi:10.4103/0301-4738.185588 Farooq AV, Patel RM, Lin AY, Setabutr P, Sartori J, Aakalu VK. Fungal Orbital Cellulitis: Presenting Features, Management and Outcomes at a Referral Center. Orbit. 2015;34(3):152–159. doi:10.3109/01676830.2015.1014512

Chang YM, Chang YH, Chien KH, et al. Orbital apex syndrome secondary to aspergilloma masquerading as a paranasal sinus tumor: A case report and literature review. Medicine (Baltimore). 2018;97(30):e11650. doi:10.1097/MD.00000000000011650 Yip CM, Hsu SS, Liao WC, Chen JY, Liu SH, Chen CH. Orbital apex syndrome due to aspergillosis with subsequent fatal subarachnoid hemorrhage. Surg Neurol Int. 2012;3:124. doi:10.4103/2152-7806.102349

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Orbit/ocular pathology, Neuroimaging, Orbit, Orbit/ocular pathology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 90

Carotid Aneurysms as a Unique Presentation of Denys-Drash Syndrome

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Introduction:

Denys-Drash syndrome is a rare disease (~200 known cases) characterized by nephropathy, Wilms tumor, and hypogonadism. No known associations exist between Denys-Drash syndrome and vascular malformations, including carotid aneurysms.

Description of Case(s):

24 y/o Hispanic male presents with <1 day right-sided orbital pressure with ophthalmoplegia. Patient's medical history includes Denys-Drash syndrome with hypogonadism and Wilms tumor s/p nephrectomy and renal transplant 20 years ago on chronic immunosuppression. Initial CT brain was concerning for parasellar mass. Vital signs were stable. Ophthalmologic examination revealed visual acuity 20/30 OD and 20/20 OS, dilated but reactive pupil OD without RAPD, IOP 35 OD and 12 OS, motility with incomplete omnidirectional ophthalmoplegia OD but full motility OS, and full visual fields OU. Anterior segment notable for proptosis and significant ptosis OD (MRD1 -3mm). DFE unremarkable OU. Labs were notable only for elevated BMP and creatinine. MRI brain/orbits revealed large saccular aneurysm of cavernous right ICA, right orbital edema concerning for thrombosed right SOV, and fusiform aneurysm of cavernous left ICA. Cerebral angiogram showed right cavernous ICA aneurysm (18x28mm) with Type A CCF. Aneurysm was treated with pipeline stent placement and embolization with 52 coils. Repeat embolization with successful occlusion of SOV performed 5 days later with another 50 coils; IOP subsequently decreased to mid-teens. Follow-up examinations demonstrate improving chemosis with visual acuity 20/30, mid-teens IOP, and improving but mildly restricted EOMs OD.

Conclusions, including unique features of the case(s):

No association between Denys-Drash syndrome and carotid aneurysms is documented; however, only around 200 cases are reported. Recent literature suggests associations between AAA and immunosuppression for solid organ transplants^{1,2}, though there is no known association between transplant immunosuppression and carotid aneurysms. There is an association between AAA and CKD³, though no known association between CKD and carotid aneurysms. Overall, given the size and bilaterality of the patient's aneurysms, they are likely attributable to his Denys-Drash syndrome.

References: 1.) Lindeman, Jan H.n., Ton J. Rabelink, and J. Hajo Van Bockel. Immunosuppression and the abdominal aortic aneurysm. *Circulation* 124(18): e463-e465 (2011). 2.) Englesbe MJ, Wu AH, Clowes AW, Zierler R. The prevalence and natural history of aortic aneurysms in heart and abdominal organ transplant patients. *Journal of Vascular Surgery*. 37(1):27-31 (2003). 3.) Matsushita K, Kwak L, Ballew SH, Grams ME, Selvin E, et al. Chronic kidney disease measures and the risk of abdominal aortic aneurysm. *Atherosclerosis* 279: 107-113 (2018).

Keywords: Genetic disease, Vascular disorders, Orbit

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 91**A Case of Multiple Myeloma Relapse Presenting with Proptosis**

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Introduction:

Multiple myeloma is a plasma cell dyscrasia characterized by neoplastic monoclonal proliferation of plasma cells. In multiple myeloma abnormal plasma cell proliferation is generally confined to the bone marrow; however, 3% of cases may develop extramedullary involvement. Ocular involvement in multiple myeloma is exceptionally rare and if ocular involvement does occur, it typically presents with intraocular manifestations. We report a rare case of metastatic multiple myeloma with right orbital involvement, found to have multiple isolated right medial rectus masses.

Description of Case(s):

A 70 year-old female with a history of multiple myeloma who presented with a two month history of horizontal binocular diplopia and unilateral proptosis of right eye. There was no previous history of trauma, fevers, or chills. Examination revealed bilateral eyelid retraction, right eye proptosis, and restricted adduction of the right eye. Slit lamp and fundusoscopic examination were otherwise unremarkable. An MRI of the orbits was obtained which revealed multiple masses involving the medial rectus of the right orbit concerning for metastasis. Laboratory studies showed an elevated kappa free light chain, and an increased kappa/lambda ratio, indicating new disease activity. Notably, testing was negative for thyroid disorders and myasthenia gravis. The patient underwent positron emission tomography (PET), which revealed diffuse metastatic disease involving multiple organ systems. Her chemotherapy regimen was adjusted given evidence of newly discovered metastatic disease. The patient underwent external beam radiation therapy to the right orbit with improvement in her motility deficit.

Conclusions, including unique features of the case(s):

Our case highlights the rare findings of an ocular presentation of multiple myeloma including medial rectus enlargement and proptosis, which ultimately led to our patient's diagnosis of metastatic disease. Given the rarity of ocular involvement in multiple myeloma, we report this case to help characterize clinical manifestations of orbital multiple myeloma, and to highlight that proptosis can be an important indicator of metastasis and disease recurrence.

References: 1. Vatansever M, Bozkurt FM, Dinç E, et al. Orbital Metastasis of Multiple Myeloma: Case Report. Turk J Ophthalmol. 2016;46(3):148–150. doi:10.4274/tjo.73645 2. Knapp AJ, Gartner S, Henkind P. Multiple myeloma and its ocular manifestations. Surv Ophthalmol. 1987;5:343–51

Keywords: Paraneoplastic syndromes, Neuro-opth & systemic disease (eg. MS, MG, thyroid), Orbit, Tumors, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 92

Bilateral Segmental Optic Disc Edema in Vitamin B1 Deficiency

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Introduction:

Vitamin B1 deficiency/Wernicke's encephalopathy comprises the triad of ataxia, ophthalmoplegia and encephalopathy. We report a unique case of acute presentation and rapid progression of ocular signs and symptoms of vitamin B1 insufficiency.

Description of Case(s):

A 48-year-old woman presented to the hospital with intractable nausea and vomiting of unknown etiology. Ophthalmology was consulted for concerns of blurry vision and nystagmus. Ocular examination revealed horizontal gaze evoked nystagmus and partial horizontal gaze palsy with normal visual acuity (VA) at bedside and normal dilated fundus exam (DFE). Two days later, VA decreased to 20/60 right eye (OD) and 20/200 left eye (OS) with central and bitemporal defects on confrontation visual field testing. Repeat DFE showed symmetrical, segmental temporal disc edema involving the papillomacular bundle of both eyes (OU). Given the triad of nystagmus, horizontal gaze palsy, and optic nerve edema in addition to ataxia, we suspected Wernicke's encephalopathy. Urgent MRI brain and orbit showed T2 hyperintensity in medial thalami bilaterally. Vitamin B1 level was reduced to <10 ug/L. Patient was started on intravenous B1 supplementation for three days followed by oral supplement. Patient noted a rapid improvement in her visual symptoms with return of VA to 20/25 OD and 20/20 OS, resolution of the visual field defect and nystagmus, and improved gaze paresis within 20 days. Patient developed subtle temporal disc pallor with thinning of the temporal retinal nerve fiber layer bilaterally.

Conclusions, including unique features of the case(s):

1. Optic disc edema has rarely been reported in cases of acute Vitamin B1 deficiency. 2. The importance of high clinical suspicion for B1 deficiency in appropriate clinical setting cannot be overemphasized. 3. MRI brain needs to be reviewed with the neuro-radiologist personally in subtle cases of T2 hyperintensity which might be missed otherwise.

References: 1. Gratton SM, Lam BL. Visual loss and optic nerve head swelling in thiamine deficiency without prolonged dietary deficiency. *Clinical Ophthalmology* 8, 1021-1024. 2014. 2. Lawton AW, Frisard NE. Visual loss, retinal hemorrhages, and optic disc edema resulting from thiamine deficiency following bariatric surgery complicated by prolonged vomiting. *The Ochsner Journal* 17(1): 112–114. 2017. 3. Mun-Wei L, Gayathri G, et al. Optic discs swelling procrastinates wernicke's encephalopathy associated with hyperemesis gravidarum: A case report and review of literature. *Cureus* 10(6): e2793. 2018.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Nystagmus, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 93

RNFL Thickening: Not Always Optic Disc Edema

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Introduction:

Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay (ARSACS) is an autosomal recessive spastic ataxia associated with specific ocular findings, including significant peripapillary retinal nerve fiber layer (RNFL) thickening. Our aim is to increase awareness of retinal and OCT findings in ARSACS.

Description of Case(s):

A 17 year-old girl with genetically-confirmed diagnosis of ARSACS presented to the neuro-ophthalmology clinic for a screening dilated eye exam. She had no visual complaints. Her family history was notable for an older sister who also had a diagnosis of ARSACS with identical biallelic loss-of-function mutations previously not reported in the literature. On exam, visual acuity was 20/20 OD and 20/25 OS. Visual fields were full to confrontation, color vision was full, stereopsis was normal, and there was no relative afferent pupillary defect. Intraocular pressures were normal. Her extraocular motility was full with gaze-evoked nystagmus in right, left, and upgaze, saccadic smooth pursuit and abnormal vestibulo-ocular reflex (VOR) suppression. Dilated exam revealed normal anterior segment with healthy optic nerves with significantly increased striations of the peripapillary RNFL. There was no peripheral retinal hypermyelination. Optical coherence tomography (OCT) of the RNFL showed significant peripapillary RNFL thickening with average thicknesses of 244 μ m OD and 261 μ m OS. MRI brain demonstrated cerebellar atrophy with transverse linear pontine dark signals on T2 images.

Conclusions, including unique features of the case(s):

ARSACS is a rare diagnosis and not widely known in the neuro-ophthalmology community. There are several reported ophthalmic findings, including increased peripapillary RNFL thickness without myelination. RNFL thickening on OCT, particularly to the degree seen in ARSACS patients can be difficult to interpret and could potentially prompt a workup for papilledema, exposing the patient to unnecessary testing. This case highlights that peripapillary thickening of the RNFL is a common finding in patients with ARSACS, and that substantial thickening of the RNFL can be seen in conditions without optic disc edema.

References: Garcia-Martin E, Pablo LE, Gazulla J, Polo V, Ferreras A, Larrosa JM. Retinal nerve fibre layer thickness in ARSACS: Myelination or hypertrophy? Br J Ophthalmol. 2013;97(2):238-241. van Lint M, Hoornaert K, ten Tusscher MPM. Retinal nerve fiber layer thickening in ARSACS carriers. J Neurol Sci. 2016;370:119-122. Parkinson MH, Bartmann AP, Clayton LMS, et al. Optical coherence tomography in autosomal recessive spastic ataxia of charlevoix-Saguenay. Brain. 2018;141(4):989-999. Rezende Filho FM, Parkinson MH, Pedrosa JL, et al. Clinical, ophthalmological, imaging and genetic features in Brazilian patients with ARSACS. Park Relat Disord. 2019;62:148-155. Pablo LE, Garcia-Martin E, Gazulla J, et al. Retinal nerve fiber hypertrophy in ataxia of Charlevoix-Saguenay patients. Mol Vis. 2011;17:1871-1876

Keywords: Genetic disease, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 94**All signs point to Giant Cell Arteritis**

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Introduction:

Vision loss due to giant cell arteritis is a neuro-ophthalmology emergency requiring immediate attention, but if the disease course or response to treatment is atypical, alternative etiologies must be considered.

Description of Case(s):

A 67 y.o. female with history of hypertension, diabetes and recent diagnosis of fibromyalgia presented with sequential decrease of vision in both eyes. Vision decreased in the right eye 2-3 weeks prior, while in the left eye it decreased 5 days prior. Patient endorsed severe left sided temporal pain, jaw claudication, neck, shoulder and low back pain as well as recent weight loss. Her visual acuity was 20/200 in the right eye and hand motion in the left eye. She had a left relative afferent pupillary defect. Fundus exam of both eyes was remarkable for c/d 0.8 with pallid disc edema. ESR was 61. Given high clinical suspicion for anterior ischemic optic neuropathy, the patient was admitted for pulse IV solumedrol (1g daily x3) for possibility of vision preservation in the right eye. Left unilateral temporal artery biopsy was negative for temporal arteritis. CT Head was unremarkable. MRI was negative for any ischemic event, but did demonstrate abnormal signal and enhancement within the mid portion of the intraorbital optic nerves. A month after steroid treatment, her vision improved to 20/50 right eye and 20/25 left eye. Given the significant improvement, another etiology was considered and additional work up revealed positive Aquaporin-4 receptor antibody and SSA, SSB Immunoglobulin G. A diagnosis of Sjogren syndrome associated with Neuromyelitis Optica was established.

Conclusions, including unique features of the case(s):

Although the initial presentation of our patient was highly suspicious for arteritic anterior ischemic optic neuropathy, her drastic vision recovery in response to steroids treatment is atypical for that condition. This prompted work up for an alternative etiology which lead to the final diagnosis of Sjogren syndrome associated with Neuromyelitis Optica.

References: None.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 95**A Rare Presentation of Multiple Sclerosis Without Optic Neuritis**

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Introduction:

Multiple Sclerosis is a well known demyelinating disease commonly associated with periventricular plaques on MRI and painful optic neuritis. Many patients also present with visual field defects, most commonly diffuse loss or central defects in the affected eye.

Description of Case(s):

Patient is a 33 year old male with no past medical or ocular history presenting with 2 weeks blurring and fogging of the vision in the superior visual fields of both eyes. He had no localizing neurologic signs, exposures, recent trauma, or new medications. Initial outside HVF 24-2 demonstrating a dense left homonymous hemianopia. He had no afferent pupillary defect, pain with extraocular movement, color vision deficits, and fundus examination was unremarkable. An urgent MRI was performed demonstrating an ill-defined area of increased FLAIR signal inferior and posterior to the right basal ganglia of uncertain etiology. Infectious screening was negative and CSF analysis was unremarkable with the exception of elevated lymphocytes and total proteins, including negative malignant cytology. Subsequent MRI of cervical and thoracic spine was also within normal limits. The patient was started on IV Methylprednisolone 1g/day for a 3 day course, with significant improvement in visual field findings after the first two doses. One week after initial presentation, the Multiple Sclerosis panel from CSF resulted demonstrating elevated IgG of 8.3, increased IgG synthesis of 19.6, and negative oligoclonal bands. About 2 weeks after treatment he recovered full visual function and had complete resolution of his visual field abnormalities. He was diagnosed with presumed multiple sclerosis with ongoing investigation for Neuromyelitis Optica and MOG-antibody associated disease.

Conclusions, including unique features of the case(s):

We present an exceedingly rare presentation of Multiple Sclerosis with no clinical features of optic neuritis. Additionally, homonymous hemianopia is a very rare visual field defect associated with MS, found in only 1/448 patients in the Optic Neuritis Treatment Trial.

References: 1. The Clinical Profile of Optic Neuritis: Experience of the Optic Neuritis Treatment Trial. Arch Ophthalmol. 1991;109(12):1673–1678. doi:10.1001/archophth.1991.01080120057025 2. Keltner JL, Johnson CA, Cello KE, et al. Visual field profile of optic neuritis: a final follow-up report from the optic neuritis treatment trial from baseline through 15 years. Arch Ophthalmol. 2010;128(3):330–337. doi:10.1001/archophthalmol.2010.16

Keywords: Demyelinating disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 96**A rare presentation of Rhupus as an arteritic anterior ischemic optic neuropathy: A case report**

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Introduction:

Arteritic anterior ischemic optic neuropathy (AAION) is an ischemic optic neuropathy usually associated with giant cell arteritis (GCA). A few studies reported that AAION was found in systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). We report bilateral visual loss due to AAION as a rare presentation of Rhupus (SLE overlapping RA).

Description of Case(s):

A 52-year-old Thai male, no underlying disease, presented with sequential progressive visual loss of his both eyes for 5 days. He denied pain, fever, headache and malaise, except for chronic joint pain with stiffness. Best corrected visual acuity was 20/200 in the right eye and 20/25 in the left eye. Anterior segment examination was normal. Relative afferent pupillary defect was mildly positive in right eye. Fundus examination showed bilateral pallid disc swelling which worse in the right eye. Sectoral disc swelling in left superior disc was noted. Visual field test revealed tunnel pattern in right eye, inferior altitudinal in left eye. The presumptive diagnosis of anterior ischemic optic neuropathy was made. Laboratory investigations showed increased ESR and CRP. MRI and MRA of the brain and orbits were unremarkable. Fluorescein Angiography showed delayed choroidal and disc filling, confirm a diagnosis of AAION. Intravenous methylprednisolone (1g) was administered for 5 days then switched to oral prednisolone. Temporal artery biopsy was not performed since there was no suggestive sign of GCA and patient's disallowing. Special investigation showed increase ANA titer with specific pattern and positive for RF and dsDNA. Diagnosis of Rhupus was made. His visual acuity for both eyes slightly improved after treatment.

Conclusions, including unique features of the case(s):

Rhupus can be presented as AAION. Early diagnosis and prompt treatment may help preserve vision in some patients.

References: None.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 97**Granulomatous Amoebic Encephalitis**

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Introduction:

Here we report a case of granulomatous amoebic encephalitis (GAE) caused by *Balamuthia mandrillaris* in previously healthy 6-year-old Puerto Rican girl, which had a progressive and fatal outcome.

Description of Case(s):

The patient presented to the emergency department for right esotropia and blurry vision in the setting of recently resolved rash on the face and arms, morning headaches and emesis. MRI of the brain revealed infiltrative nodular enhancement along the walls of the 3rd and 4th ventricles and leptomeningeal enhancement. Initial concern for neoplasm, in particular CNS germinoma, was not supported by CSF analysis or histopathology of the brain lesion. Extensive infectious work-up was unrevealing, including tests for mycobacteria, atypical fungal meningoencephalitis and amoeba. Dedicated MRI of the orbits demonstrated diffuse enhancement of the peripheral margins of the optic nerves extending posteriorly to the optic chiasm and radiations. The patient was treated for NMO with methylprednisolone and PLEX. After a few days of subjective improvement in symptoms, the patient rapidly decompensated clinically. Interval MRI of the brain demonstrated new ring enhancing lesions with development of hemorrhage in several of the lesions. Ultimately, brain edema was refractory to all instituted measures and progressive brain damage led to death 25 days after admission to the hospital. Autopsy revealed widespread CNS necrosis with numerous leptomeningeal and parenchymal amoebic forms which were confirmed to be *Balamuthia mandrillaris* by DNA PCR.

Conclusions, including unique features of the case(s):

Balamuthia mandrillaris is a free-living amoeba and an uncommon agent of granulomatous encephalitis. GAE is rare with only about 200 total cases reported. CNS involvement often simulates a tumor or other granulomatous process making diagnosis challenging. The application of immunofluorescence staining and DNA detection techniques has led to increased awareness and case reports. The disease is mostly fatal, even when premortem diagnosis is made. Survivors have been treated with a combination of macrolide, anti-fungals and anti-protozoals.

References: None.

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 98**Emery-Dreifuss muscular dystrophy type 5 – a diagnostic challenge**

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Introduction:

Emery-Dreifuss muscular dystrophy is a rare and often slowly progressive genetic disorder that primarily affects skeletal muscles and cardiac muscle.

Description of Case(s):

A 38-year-old right-handed woman presented to Oculoplastics for consideration of ptosis surgery, and from there was referred further to Neuro-ophthalmology. She reported slowly progressive painless and non-fluctuating bilateral eyelid ptosis. On further questioning, she recently also started having difficulty in swallowing. She denied dysarthria, dysphonia, dyspnea or arm weakness, but did feel that her legs were weak at the end of the day. A review of prior photos of the patient confirmed gradual worsening of the ptosis since her 20s. The patient had no significant past medical history. She had immigrated from mainland Portugal. There was no family history of ocular, neurologic, or neuromuscular disease. The clinical examination showed asymmetric bilateral ptosis (left>right), minimal orbicularis oculi weakness, MRD1 of 2mm OD and 0mm OS, lid excursion of 13.5mm OD and 12mm OS. She had intact eye movements, and no ocular misalignment on cover testing. On neurological exam, there was neck weakness, bilateral weakness of deltoid, infraspinatus and hip abductor muscles, asymmetric bilateral triceps muscles weakness, bilateral biceps muscles weakness were also demonstrated. The reflexes were present but hypoactive. A laboratory work-up, including myasthenia gravis antibody panel with MuSK and LRP4 antibodies was negative, but creatine kinase level was elevated. In addition, MNG neurogenetic testing was positive for a variant of uncertain significance of muscular dystrophy in Syne2 and NEB genes. A muscular dystrophy gene panel was obtained, yielding a probable diagnosis of Emery-Dreifuss muscular dystrophy type 5.

Conclusions, including unique features of the case(s):

The rarity of muscular dystrophies and their variable presentation present a formidable diagnostic challenge. This case demonstrates the power of modern genetic screening techniques in the diagnosis of genetic muscle disease but also the challenges of appropriately interpreting genetic testing.

References: 1. Merlini L, Maraldi NM. Emery-dreifuss muscular dystrophy. In: Neuromuscular Disorders in Clinical Practice. ; 2014. doi:10.1007/978-1-4614-6567-6_61 2. Zhang Q, Bethmann C, Worth NF, et al. Nesprin-1 and -2 are involved in the pathogenesis of Emery–Dreifuss muscular dystrophy and are critical for nuclear envelope integrity. Hum Mol Genet. 2007;16(23):2816-2833. doi:10.1093/hmg/ddm238

Keywords: Genetic disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 99**Meige Syndrome Associated with Olivopontocerebellar Degeneration: Insight into Pathophysiology and Familial Association**

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Introduction:

Meige syndrome is a rare disorder of blepharospasm and oromandibular dystonia, thought to be idiopathic in etiology. Familial association is present in rare cases. We present a case of Meige syndrome associated with olivopontocerebellar degeneration, in a patient with a strong family history of similar symptoms. Our patient also had symptoms of episodic diaphragmatic dystonia which is a rare association with this condition.

Description of Case(s):

68-year-old right-handed woman with hypertension and major depressive disorder was evaluated in our neurology clinic for right eyelid spasms which started subacutely approximately twenty years ago and progressed to involve her left eye, making it difficult for her to carry out visually demanding functions such as driving. She had recently noticed a dry mouth with episodic nods and tongue protrusion. Additionally, she felt hard pressure in epigastric region, which was associated with phonation consistent with diaphragmatic dystonia. Her family history was significant as her father and a cousin on father's side exhibited similar symptoms of blepharospasm and oromandibular dystonia. MRI brain done to investigate secondary causes showed evidence of olivopontocerebellar degeneration. Her MRA head was unremarkable.

Conclusions, including unique features of the case(s):

There are rare reports of association of olivopontocerebellar degeneration in blepharospasm/Meige syndrome. Certain mutations including p.Gly213Ser or p.Ala353Thr mutations have been associated with the symptoms of Meige syndrome. Case presented here further strengthens this association and raises the possibility that symptoms in Meige syndrome could result from cranial nerve dysfunction as a consequence of brainstem degeneration. Familial association, at least in some cases of Meige syndrome may be by virtue of associated hereditary neurodegenerative disorders including olivopontocerebellar degeneration.

References: None.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 100**Bilateral Blindness: Mantle Cell Lymphoma Infiltration of the Optic Nerves**

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Introduction:

Mantle cell lymphoma (MCL) is a rare type of non-Hodgkin's lymphoma of B cell origin. It represents 3-6 % of all non-Hodgkin lymphomas and typically presents in older men. It is usually diagnosed in the advanced stages when diffuse lymphadenopathy and extranodal involvement is present. Central nervous system (CNS) involvement is very rare and portends an extremely poor prognosis. Furthermore, neuro-ophthalmic involvement of this disease is rarely discussed and only described in sparse case reports in the literature. We present the first noted case of bilateral blindness as the initial presentation for CNS infiltration of mantle cell lymphoma.

Description of Case(s):

An 84 year old male with Stage IV mantle cell lymphoma presented with vision loss in both eyes over 6 months. He was on bendamustine and rituximab treatment. His examination was significant for hand motion vision OD and count fingers vision OS, and bilateral optic nerve swelling with a peripapillary hemorrhage on the left side. Neuroimaging demonstrated markedly thickened prechiasmatic optic nerves bilaterally with reduced diffusion in keeping with lymphomatous involvement. A PET scan revealed numerous areas of hypermetabolic foci in the head, neck, chest and abdomen. CSF demonstrated elevated protein (134), low glucose, with the presence of CD-5 positive, kappa-restricted B cell lymphoma demonstrating leptomeningeal involvement of the disease.

Conclusions, including unique features of the case(s):

Mantle cell lymphoma is an exceptionally rare cause of central nervous system dysfunction. In patients who have a history of mantle cell lymphoma, regardless of how well they may appear to be responding to therapy, neurologic manifestations may be secondary to leptomeningeal or parenchymal involvement of the disease. In patients who present with worsening vision or optic disc swelling who have a history of this malignancy, it is important for physicians to consider optic nerve infiltration by the lymphoma so that early effective therapy can be initiated promptly.

References: 1. Bardenstein, D.S. Intraocular Lymphoma. *Cancer Control* 5, 317–325.1998 2. Coupland, S.E., Hummel, M., and Stein, H. Ocular adnexal lymphomas: five case presentations and a review of the literature. *Surv. Ophthalmol.* 47, 470–490.2002 3. Vali Khojeini, E., Durham, B.H., and Chen, M. Mantle cell lymphoma and involvement of the orbit and ocular adnexa. *Case Rep. Pathol.* 2013, 581856.2013 4. Iqbal, M., Castano, Y.G., Sher, T., and Kharfan-Dabaja, M.A. Intraocular involvement of Mantle cell lymphoma: A case report and literature review. *Hematol. Oncol. Stem Cell Ther.*2019. 5. Bedotto, J., Spier, Catherine., Paquin ML, Grogan, Ahmann FR, Greenberg BR. Mantle Zone Lymphoma with Central Nervous System Involvement. *Cancer.* 58: 2125-2129.1986

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 101**Everything that Glitters is not Gold**

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Introduction:

Syphilis is a great imitator. A high index of suspicion for infectious etiology of optic neuropathy in HIV patients is essential even if they are well controlled.

Description of Case(s):

60-yr-old homosexual man with diabetes, hypertension, prior intravenous drug abuse, gonorrhea and recently diagnosed HIV presented with 6-days of acute left eye vision loss with left occipital headache. He reported 6 weeks of decreased energy, light chills, cough and hypotension. He denied other symptoms of temporal arteritis. While he continued his antiretroviral therapy for HIV, he held his other medications. His exam showed CF vision in OS, left afferent pupillary defect, impaired color vision OS and optic disc edema with disc hemorrhages OS. OD was normal with crowded optic disc. His labs showed ESR 76, CRP 2.7, CD4 1393 and HIV viral load <20. VDRL and RPR were non-reactive. Contrast enhanced MRI head and orbits showed chronic white matter disease without optic nerve enhancement. Lumbar puncture revealed monocytic pleocytosis, elevated protein but no infection. Given the concern for temporal arteritis, he received intravenous Methyl Prednisone 1g daily for 3 days followed by oral steroids. When left temporal artery biopsy returned negative, steroids were tapered. He subsequently developed a rash on his palms, ankle and sole of his feet, biopsy was positive for syphilis. T pallidum particle agglutination and RPR then became reactive. Patient was treated with IM Benzathine Penicillin, 14 days of IV penicillin G followed by weekly bicillin. His vision improved to 20/400 OS and developed optic disc pallor OS.

Conclusions, including unique features of the case(s):

Syphilitic optic neuropathy in this case mimicked arteritic anterior ischemic optic neuropathy (AAION). This patient's initial RPR might have been non-reactive due to steroids he received for suspected AAION. If syphilis is suspected both treponemal and non-treponemal tests should be obtained and if possible before initiation of steroids.

References: None.

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 102**Transient Monocular Vision Loss Following Pipeline Embolization Device Placement**

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Introduction:

Flow-diverting stents are an emerging treatment option in the management of fusiform and saccular intracranial aneurysms, particularly involving the paraophthalmic internal carotid artery.[1] Despite low occlusion rates of the ophthalmic artery,[2] ophthalmic complications ranging from visual field deficits to transient monocular vision loss have been reported at both short-term[3] and long-term[4] follow-up.

Description of Case(s):

We review four cases of transient monocular vision loss following pipeline embolization device (PED) placement for ipsilateral paraophthalmic internal carotid artery aneurysms. Two female patients presented with an isolated episode of vision loss occurring 2 and 9 months following PED placement, with a superior visual field deficit noted in the former. Two female patients, both with prior history of migraine headaches, presented with recurrent episodes of vision loss over 2–4 months, occurring 10 and 29 months following PED placement; visual fields were full in both patients, and brain and vascular imaging did not reveal associated infarcts or sources of thromboembolism. Visual symptoms ultimately resolved without intervention in both cases.

Conclusions, including unique features of the case(s):

Flow diversion across paraophthalmic internal carotid artery aneurysms may be associated with remote isolated or recurrent episodes of transient monocular vision loss without evidence of ischemic complications.

References: 1. Bhogal P, Ganslandt O, Bänzner H, et al. The Fate of Side Branches Covered by Flow Diverters-Results from 140 Patients. *World Neurosurg* 2017; 103:789–98. 2. Griessenauer CJ, Ogilvy CS, Foreman PM, et al. Pipeline Embolization Device for small paraophthalmic artery aneurysms with an emphasis on the anatomical relationship of ophthalmic artery origin and aneurysm. *J Neurosurg* 2016; 125:1352–9. 3. Rouchaud A, Leclerc O, Benayoun Y, et al. Visual outcomes with flow-diverter stents covering the ophthalmic artery for treatment of internal carotid artery aneurysms. *AJNR Am J Neuroradiol* 2015; 36:330–6. 4. Touzé R, Touitou V, Shotar E, et al. Long-term visual outcome in patients treated by flow diversion for carotid-ophthalmic aneurysms. *J Neurointerv Surg* 2018; 10:1067–73.

Keywords: Vascular disorders, Interventional neuroradiology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 103**A novel mitochondrial mutation with recurrent inflammatory optic neuropathy**

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¹University of Calgary, Calgary, Canada, ²Mayo Clinic, Rochester, Minnesota, USA, ³University of Iowa, Iowa City, Iowa, USA

Introduction:

Mutations in the ND5 gene have been associated with MELAS-overlap syndromes, including MELAS-LHON.

Description of Case(s):

We present 2 patients with optic neuropathies associated with the mitochondrial DNA pathogenic variant m.13513 G>A, in the MT-ND5 gene. Case 1: A 28-year old man with chronic tubulointerstitial nephritis presented with bilateral sequential optic neuropathies over 18 months. Visual acuity evolved to count fingers bilaterally, with severe optic atrophy. Goldmann perimetry showed dense central scotomas. Serial MR imaging revealed enhancement of the left optic nerve, and progressed to demonstrate T2/FLAIR hyperintensities involving the left optic nerve, chiasm, tract; and, splenium of the corpus callosum. Extensive investigations [including aquaporin-4 and myelin oligodendrocyte glycoprotein antibodies, CSF analysis, LHON genetic testing, spinal MRI, and CT body imaging] were normal. Despite treatment with high dose corticosteroids and plasma exchange therapy, the patient manifested no visual improvement. Genetic testing revealed the m.13513G>A (p.D393N) mutation in the MT-ND5 gene. Case 2: A 63-year old woman presented with bilateral optic neuropathies, associated with recurrent vomiting and sensorineural hearing loss. Visual acuity was hand motions vision in the right eye and 20/200 in the left eye. Goldmann perimetry showed dense central scotomas. She developed severe optic atrophy. MRI revealed left optic nerve enhancement and nonspecific periventricular white matter lesions. Extensive investigations were unremarkable. Initial treatment with plasma exchange and corticosteroids was unhelpful, but the patient manifested modest visual improvement with rituximab therapy. Genetic testing demonstrated a mitochondrial DNA pathogenic variant m.13513 G>A in the MT-ND5 gene, most consistent with a LHON-MELAS overlap syndrome.

Conclusions, including unique features of the case(s):

In cryptogenic cases of acquired optic neuropathy, molecular genetic examination should be extended to other mtDNA encoded subunits of MTND5 complex I, in the mitochondrial DNA. The clinical spectrum associated with this pathogenic genetic mutation is expanding, and requires further study.

References: 1. Blok MJ, Spruijt L, de Coo IFM, et al. Mutations in the ND5 subunit of complex I of the mitochondrial DNA are a frequent cause of oxidative phosphorylation disease. *J Med Genet* 2007; 44: e74 2. Kolarova H, Liskova P, Tesarova M, et al. Unique presentation of LHON/MELAS overlap syndrome caused by m.13046T>C in MTND5. Genetic testing demonstrated a mitochondrial DNA pathogenic variant m.13513 G>A in the MT-ND5 gene, most consistent with a LHON-MELAS overlap syndrome. *Ophthalmic Genetics* 2016; 37(4): 419-423

Keywords: Optic neuropathy, Demyelinating disease, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 104

The Occam's razor. The simplest explanation is usually the correct one.

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Introduction:

Leptomeningeal carcinomatosis (LCM) is an uncommon site of metastasis in solid tumors. In gastric cancer (GC) it is associated with a devastating prognosis. We report a case of LMC secondary to GC, initially presenting as papilledema and then, the definitive diagnosis was reached.

Description of Case(s):

A 59-year old man, with unremarkable past medical and ocular history, with complainets for visual disturbances and floaters in his left eye for the past two weeks. Ophthalmoscopic examination revealed a swelling and blurred optic disc in his left eye. Twenty days later examination revealed a swelling and blurred optic disc in the other eye. A full work-up was performed including MRI, three LP, infectologic, hematologic and rheumatologic involving and no anomalies were detected. Consequently, a second MRI was performed which revealed signs of hydrocephalus and optic nerves sheaths thickening. The man was hospitalized after he lost weight and developed abducens nerve paresis. The PET Scan revealed an hyper-intense signal image in stomach and optic nerves sheaths. By biopsy, a gastric signet-ring cell carcinoma was diagnosed and the meningeal biopsy revealed meningeal carcinomatosis. No anomalies were detected in the optic nerve biopsy. Four month later the patient died.

Conclusions, including unique features of the case(s):

LMC presents in approximately 2% to 4% of all patients with cancer, but its incidence is much lower in GC. The LMC as an initial manifestation of metastatic GC has rarely been reported. Symptoms associated with LCP included not only headache, nausea and vomiting, altered mental status but also cranial nerve palsy and papilledema. MRI frequently revealed hydrocephalus. Treatment may consist of not only systemic as well as intratecal chemotherapy, radiotherapy but also palliative care. Prognosis of LMC due to GC is extremely limited.

References: Kawasaki A, Suzuki K, Takekawa H, et al. Co-occurrence of multiple cerebral infarctions due to hypercoagulability associated with malignancy and meningeal carcinomatosis as the initial manifestation of gastric cancer. *BMC Neurol.* 2014 Guo JW, Zhang XT, Chen XS, et al. Leptomeningeal carcinomatosis as the initial manifestation of gastric adenocarcinoma: a case report. *World J Gastroenterol.* 2014 Jay WM. *Neuro-Ophthalmology Illustrated*, 2nd Edition By Valérie Biousse and Nancy J. Newman: New York, Thieme Medical Publishers, Inc., 2015 Xu Q, Du W, Zhou H, et al Distinct clinical characteristics of paraneoplastic optic neuropathy *British Journal of Ophthalmology* 2019 Vergoulidou M. Leptomeningeal Carcinomatosis in Gastric Cancer: A Therapeutical Challenge. *Biomark Insights.* Published 2017

Keywords: Tumors, Neuroimaging, Optic neuropathy, High intracranial pressure/headache, Paraneoplastic syndromes

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 105

The Purple and Ugly are Hidden Inside

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Introduction:

T-cell prolymphocytic leukemia (T-PLL) is a rare, mature lymphoid neoplasm that affects males around age 60 and presents with leukocytosis, lymphadenopathy and hepatosplenomegaly (1–3). Although rare, direct invasion of the CNS can occur (3,4). We describe a case of a 57-year-old male with T-PLL with acute, bilateral, painful vision loss from infiltrative optic neuropathy without optic nerve sheath or CSF involvement.

Description of Case(s):

A 57-year-old male in remission from T-PLL presented with acute, bilateral, painful vision loss. Prior to presentation, the patient had one episode of acute, painful vision loss in the left eye that improved with high-dose IV steroids. During subsequent steroid taper, the patient developed recurrent symptoms. On presentation, BCVA was 20/40 OD and 20/150 OS. An afferent pupillary defect was present in the left eye. Examination showed bilateral optic disc edema with bilateral peripapillary hemorrhage and clear vitreous. MRI imaging demonstrated bilateral enhancement of the optic nerves and optic tract. CSF cytology remained negative for malignancy. Temporal artery biopsy was negative for giant cell arteritis. Upon initiation of radiation therapy, the patient lost complete vision in the left eye to no light perception. A left optic nerve sheath fenestration with biopsy was performed, which demonstrated necrosis and atypical lymphoid cells with CD2, CD4, and CD8 positivity in the optic nerve. There was no malignancy in the sheath. Final diagnosis was T-PLL infiltration of the left optic nerve. The patient succumbed to his disease two weeks later.

Conclusions, including unique features of the case(s):

To our knowledge, this is the first documented case of T-PLL with biopsy-proven optic nerve invasion without optic nerve sheath or CSF involvement. This case argues against leptomeningeal disease. Possible mechanisms include hematogenous seeding and entrapment within the optic nerve and eye, suggesting a sanctuary site from chemotherapy or perineural invasion. Histopathologic diagnosis is essential for guiding treatment and prognosis.

References: 1. Valbuena JR, Herling M, Admirand JH, Padula A, Jones D, Medeiros LJ. T-Cell Prolymphocytic Leukemia Involving Extramedullary Sites. *Am J Clin Pathol.* 2005;123(3):456-464. 2. Collignon A, Wanquet A, Maitre E, Cornet E, Troussard X, Aurran-Schleinitz T. Prolymphocytic Leukemia: New Insights in Diagnosis and in Treatment. *Curr Oncol Rep.* 2017;19:29. 3. Malkan UY, Gunes G, Yayar O, Demiroglu H, Yesilirmak A, Uner A. A T-cell prolymphocytic leukemia case with central nervous system involvement. *Int J Clin Exp Med.* 2015;8(8):14207-14209. 4. Göçmen S, Kutlay M, Erikçi A, Atabey C, Sayan O, Haholu A. Central nervous system involvement of T-cell prolymphocytic leukemia diagnosed with stereotactic brain biopsy: case report. *Turkish J Haematol Off J Turkish Soc Haematol.* 2014;31(1):75-78.

Keywords: Orbit/ocular pathology, Neuro-opth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 106**Ischemic Optic Neuropathy in Susac's Syndrome**

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Introduction:

Susac's syndrome (SS), an autoimmune disease affecting the microvasculature of the brain, retina, and inner ear, typically presents a clinical triad of symptoms: encephalopathy, branch retinal artery occlusion (BRAO), and depressed hearing. The reported symptoms are variable and may not all present concurrently. We examined a woman with classic features of SS who developed concurrent bilateral ischemic optic neuropathies.

Description of Case(s):

A 55 year old female complained of shaded areas in the right superior temporal and left inferior temporal visual fields. Background history included migraine, episodic vertigo, and low-frequency hearing loss AU. Retinal examination with fluorescein angiography demonstrated multiple branch retinal artery occlusions. Full cardiovascular evaluation included echocardiography and four vessel angiography. The latter showed small vessel infarcts along both posterior cerebral artery distributions. Comprehensive evaluations for vasculopathy and vasculitis were unremarkable, and the patient was referred for neuro-ophthalmologic examination. Central visual acuity: 20/20- OD, 20/25- OS. Funduscopy revealed superior disc head pallor OD and a swollen optic nerve OS confirmed by OCT. Humphrey's 24-2 visual fields demonstrated bilateral arcuate defects. Neurologic examination demonstrated no evidence of cognitive defects. High resolution MRI showed normal appearing optic nerves and callosal lesions, one in the lateral aspect of the splenium. Steroid therapy was initiated and continued at high dose for six weeks, followed by taper. Follow up examination at two months showed mild disc pallor OU without change in visual acuity or fields.

Conclusions, including unique features of the case(s):

The present case is unique in that signs typical for ischemic optic neuropathy accompanied classic features of SS, and it extends the spectrum of microvascular involvement in this syndrome.

References: Brandt, Zimmermann, Kaufhold, Promesberger, Schippling, Finis, ... Dörr. Patterns of retinal damage facilitate differential diagnosis between Susac syndrome and MS. PLoS one, 7(6), 2012. Dörr, Krautwald, Wildemann, et al. Characteristics of Susac syndrome: a review of all reported cases. Nat Rev Neurol 9, 307–316, 2013. Jarius, Kleffner, Dörr, Sastre-Garriga, Illes, Eggenberger, ... Wildemann. Clinical, paraclinical and serological findings in Susac syndrome: an international multicenter study. Journal of neuroinflammation, 11, 46, 2014. Khan, Allroggen, & Pagliarini. Susac's syndrome: the value of fundus fluorescein angiography. BMJ case reports, 2014.

Keywords: Optic neuropathy, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 107**Severe Papilledema with Vision Loss secondary to Guillain-Barre Syndrome: Management and Mechanism**

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Introduction:

Papilledema is a rare but well-recognized complication of Guillain-Barre Syndrome (GBS). Literature review suggests a female predilection although the reverse is true for incidence of GBS which is slightly more common in males. We discuss a 16-year-old female with GBS who developed papilledema and vision loss.

Description of Case(s):

A 16-year-old female presented with double vision, weakness in right upper limb with subsequent progression to involve other limbs, over two weeks. Pertinent findings were thin body habitus, no papilledema, bilateral abduction deficits, bi-facial palsies, severe limb weakness, absent deep-tendon reflexes. CSF analysis (normal cells and elevated protein of 2.29g/L (0.15-0.45 g/L)) and nerve conduction studies supported the diagnosis of GBS. She received intravenous immunoglobulins. She developed headaches and vision loss five weeks later. Funduscopic examination demonstrated Frisen grade-V papilledema. Visual acuity was 6/30 OU with bitemporal depression on visual fields. MRI-brain showed no venous sinus thrombosis. Opening CSF pressure was 39 cm of water, protein 1.76 g/L (0.15-0.45 g/L). She received acetazolamide (2g/day). There was steady improvement of papilledema with complete resolution at eight weeks. Acetazolamide was ceased. At 3-month follow-up, VA was 6/6 OU, normal visual fields and no papilledema or optic nerve pallor. OCT revealed mild superior retinal nerve fibre loss OU with borderline ganglion cell layer thinning OU.

Conclusions, including unique features of the case(s):

Funduscopy in patients with GBS is important. Early detection and prompt management of papilledema can prevent permanent vision loss in this usually monophasic disease. Close neuro-ophthalmic follow-up is paramount. Initial aggressive treatment with therapeutic lumbar punctures, high dose acetazolamide should be instituted. Lumbar drain, optic nerve sheath fenestration and CSF-flow diversion procedures are rarely required. Papilledema in GBS has been attributed to high CSF-protein, however, not all patients develop papilledema. We speculate the possibility of early cranial neuropathy, female gender and young age in addition to high CSF-protein as risk factors for papilledema in GBS

References: 1. Drew, Magee, Papilledema in Guillain-Barre Syndrome, Lancet 6,384-398,1943. 2. Reid, Draper, Pathogenesis of papilledema and raised intracranial pressure in Guillan Barre Syndrome, BMJ,281,1393-1394,1980. 3. Bruce, McClelland, Van Stavern, Papilledema in an otherwise clinically typical case of Miller Fisher syndrome, Can J Ophthalmol,50(5)e70-e7,2015 4. Sullivan, Reeves, Normal cerebrospinal fluid protein, increased intracranial pressure, and the Guillain-barre syndrome, Ann Neurol,1(1),108-9,1977. 5. Joynt, Mechanism of production of papilledema in the Guillain-Barre SYndrome, Neurology,8(1),8-12,1958 6. Neuwirth, Weber, GD1a-Associated pure motor Guillain barre syndrome with hyperreflexia and bilateral papillitis, J Neuromusc dis11(3),114-115, 2010

Keywords: High intracranial pressure/headache, Optic neuropathy, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 108**Tonic Water Toxic Optic Neuropathy Causing Vision Loss and Deafness**

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Introduction:

We describe a case of likely toxic bilateral optic neuropathy and deafness in a 40-year-old man from quinine toxicity from heavy ingestion of tonic water, substantial alcohol use and heavy smoking.

Description of Case(s):

A 40-year-old white man had progressive central vision loss in both eyes, followed 3 months later by progressive hearing loss in both ears, the former over 6 months and the latter over one year to complete deafness. On examination, vision was 20/300 OD and 20/400 OS, with profoundly reduced color vision, cecocentral scotomas, and temporally pale optic nerves. OCT RNFL was initially normal OU, but GCC was diffusely thin. MRI (twice) was normal and VEPs were severely delayed. Further questioning revealed he was drinking 4-6 cocktails per day of vodka and tonic water, ingesting about 2 liters of tonic water daily and smoking 2 packs of cigarettes daily for 20 years. LHON testing, inherited optic atrophy panel, B12, folate, zinc, copper, NMO/MOG, syphilis were normal or negative. LP (twice) showed normal CSF contents and normal cytology/flow-cytometry. Toxicology testing revealed blood quinine levels of 1mg/ml (assay detection limit 100ng/ml). He was immediately instructed to cease tonic water use, alcohol use and smoking. He stopped tonic water and alcohol ingestion. He decreased his smoking. Within one year, his vision improved to 20/80 OD and 20/40 OS, but his hearing loss was irreversible.

Conclusions, including unique features of the case(s):

Vision and hearing changes in overdose, and from therapeutic dosing from quinine and anti-malarials have been described. Chronic lower dose exposure is less well-recognized. We hypothesize that our patient represents a rare case of toxic optic neuropathy from chronic quinine use with a synergistic effect from heavy alcohol and tobacco exposure that was partially reversible with quinine cessation. This case emphasizes the need for a detailed dietary and environmental history in the setting of unexplained vision and hearing loss.

References: Horgan, SE; William, RW; Chronic retinal toxicity due to quinine in Indian tonic water. *Eye (Lond)*, 9, 637-8, 1995.

Bacon, P; Spalton, DJ; Smith, SE; Blindness from quinine toxicity. *British Journal of Ophthalmology*, 72, 219-224, 1988. Hall, AP; Williams, SC; Rajkumar, KN; Galloway NR; Quinine induced blindness. *British Journal of Ophthalmology*, 81(12), 1029, 1997. Wolf, LR; Otten, EJ; Spadafora, MP; Cinchonism: two case reports and review of acute quinine toxicity and treatment. *Journal Emergency Medicine*, 10(3), 295-301, 1992.

Keywords: Optic neuropathy, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 109**Ischemic Optic Neuropathy and Cilioretinal Artery Occlusion from Crohn's Disease**

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Introduction:

Crohn's disease is associated with ocular manifestations in 1-2% of patients, most commonly uveitis, retinal vasculitis and keratopathy. Optic neuropathy associated with Crohn's disease is rare and may take the form of optic neuritis or rarely, anterior ischemic optic neuropathy (AION). We describe a case of non-arteritic AION and cilioretinal artery occlusion associated with newly diagnosed Crohn's disease.

Description of Case(s):

A 57-year-old female presented with acute painless vision loss in the left eye (OS). In the weeks prior to presentation, she developed pruritic violaceous nodules in her lower extremity bilaterally suggestive of erythema nodosum. Three weeks prior to presentation, she had undergone colonoscopy for investigation of chronic diarrhea with occult blood; pathology confirmed a diagnosis of Crohn's disease. On neuro-ophthalmic examination, she was found to have hand motion visual acuity OS with a dense afferent pupillary defect. Fundus examination revealed pallid optic disc swelling associated with hemorrhages and ischemia in the cilioretinal artery distribution. Fluorescein angiogram demonstrated delayed and patchy choroidal perfusion. Laboratory studies demonstrated an ESR of 34mm/hr and CRP of 24.4mg/L with thrombocytosis; a temporal artery biopsy was normal. An extensive evaluation for infectious and inflammatory conditions was unremarkable. The patient was treated with high dose oral corticosteroids with no significant change in her visual function.

Conclusions, including unique features of the case(s):

There are only three previously reported cases of AION associated with Crohn's disease, and the mechanism is hypothesized to involve an occlusive vasculitis affecting the posterior ciliary arteries. In our patient, the involvement of both the cilioretinal artery and optic nerve would support this localization. While giant cell arteritis may present very similarly, the combination of intestinal and extra-intestinal manifestations of Crohn's disease, and a negative temporal artery biopsy, support a diagnosis of Crohn's-associated posterior ciliary artery vasculitis.

References: 1. Bernstein CN, Blanchard JF, Rawsthorne P, Yu N. The prevalence of extraintestinal diseases in inflammatory bowel disease: a population-based study. *Am J Gastroenterol*, 96:1116-22, 2001. 2. Barabino AV, Gandullia P, Calvi A, Vignola S, Arrigo S, et al. Sudden blindness in a child with Crohn's disease. *World J Gastroenterol*, 17:4344-6, 2011. 3. Heuer DK, Gager WE, Reeser FH. Ischemic optic neuropathy associated with Crohn's disease. *J Clin Neuroophthalmol*, 2:175-81, 1982. 4. Felekis T, Katsanos KH, Zois CD, Vartholomatos G, Kolaitis N, et al. Anterior ischemic optic neuropathy in a patient with Crohn's disease and aberrant MTHFR and GP11a gene variants. *J Crohns Colitis*, 4(4):471-4, 2010. 5. Coussa RG, Ali-Ridha A, Vila N, Alshareef R, Chen J. Simultaneous central retinal artery occlusion and optic nerve vasculitis in Crohn disease. *Am J Ophthalmol Case Rep*, 5:11-5, 2017.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 110**Monocular visual field defect (VFD) presenting feature of Neurovascular disorder.**

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Introduction:

Moyamoya disease (MMD) and Takayasu arteritis (TA) are occlusive neuro-vascular disease of brain. Our cases have monocular VFD as sole manifest of these vasculopathies.

Description of Case(s):

Case I: A ten year old girl patient presented with inability to see lower half of an object with right eye for 2 months with associated holocranial headache. On asking she admitted episodes of transient weakness of right upper and lower limb specially on playing. Examination showed normal vision OU with RAPD in OD. Fundus revealed mild disc pallor OD, perimetry showed inferior altitudinal defect OD with RNFL loss in corresponding area on OCT. Rest of the examination was normal. Lab tests were normal. MRI cranial revealed bilateral supraclinoid ICA occlusion with filling of ACA and MCA through collaterals and posterior communicating arteries. DSA showed clouds of smoke suggestive of MMD. Patient was referred to Neurosurgery for revascularization procedure. Case II: A thirty years old female had complaint of TVO in OS for six months followed by permanent loss of inferior field for last 2 weeks. Examination showed normal vision OU with mild RAPD in OS. Fundus revealed mild disc pallor OS while rest examination was normal. Perimetry showed inferotemporal constriction in OS with thinning of RNFL in the corresponding quadrant on OCT. Pulse on both upper limbs was feeble and there was cervical lymphadenitis on left side which on FNAC showed tubercular pathology. CTA revealed mild wall thickening with luminal narrowing of bilateral CCA and proximal ICA with significant narrowing of right subclavian artery suggestive of TA secondary to Tuberculosis. She responded well to anti tubercular drugs with ecospirin treatment.

Conclusions, including unique features of the case(s):

Neurovascular occlusive disease like MMD and Takayasu disease are an important cause of stroke in eye in younger age group. Thromboembolic phenomenon from carotid circulation is the cause of unilateral VFD in these cases.

References: 1. Chu MK, Lee IH, Kim KD et al. Moyamoya disease initially presenting VFD. Yonsei Medical Journal 2001, Vol 42, No 5, 566-570. 2. Dipankar Das, Sanjeev Kumar Handique, Harsha Bhattacharjee et al, Moyamoya disease with neuro-ophthalmic manifestations: a rare case report Eye Brain. 2010; 2: 63–65. 3. Jayanthi Peter, George Joseph, Vivek Mathew et al Visual loss in Takayasu Arteritis – Look Beyond the Eye. J Clin Diagn Res. 2014 Aug; 8(8): MD06–MD07. 4. Shiang-Yao Wu a,b , Chen-Hung Chen c,e , Cheng-Chung Cheng d et al Takayasu's Arteritis Presenting as Monocular Visual Loss Pediatrics and Neonatology (2015) 56, 435-438

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging, Optic neuropathy, Perimetry, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 111**Acute Vision Loss Associated With Hypereosinophilic Syndrome.**

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Introduction:

Primary HES is a rare idiopathic leukoproliferative disorder marked by an eosinophilia of greater than 1500 eosinophils/mm³ for more than 6 months with target organ damage. Stroke incidence in HES is estimated around 12%, and ophthalmologic manifestations are reported in 18% of cases. We will present a case of cortical blindness due to rapidly deteriorating HES.

Description of Case(s):

A 41-year-old female, with a history of chronic urticaria with angioedema, presented with polyarthralgia, splinter hemorrhage, elevated CRP and hypereosinophilia. Infectious serologies were negative, bone marrow biopsy showed non clonal eosinophilia. Positive LAC, ANA and capillaroscopy suggested vasculitis. Corticosteroid treatment was initiated, but eosinophil counts increased rapidly and the patient developed acute myocarditis, pulmonary edema and multiple embolic cerebral infarctions, manifested as left hemiplegia. Hypereosinophilic syndrome with secondary vasculitis was diagnosed. Patient was treated with Corticosteroids, Clexane, Hydroxyurea, Cyclophosphamide, Anti-IL-5 and Imatinib. Despite aggressive treatment, the patient developed fulminant eosinophilia (30,000/mm³), she became restless and her family suspected visual impairment. Neuro-ophthalmologic exam suggested cortical blindness, and an MRI showed multiple infarcts including bilateral occipital giant infarcts. The patient developed pancytopenia and suffered from respiratory failure which led to artificial respiration. Plasmapheresis was conducted and I.V Ig treatment was also given, while other drugs were carefully balanced in the intensive care unit. Eosinophilia resolved, cardiac function partially recovered and after weaning the patient from artificial ventilation, physician discovered she was no longer blind. After physical rehabilitation the patient is able to walk independently and has a residual left upper limb weakness. Three month after presentation, the patient has a visual acuity of 6/15, normal colour vision and a residual left lower quadrantanopia.

Conclusions, including unique features of the case(s):

Early recognition of HES and appropriate treatment, is crucial. Our case demonstrates a fulminant course with cortical blindness partially resolved, which was not reported before.

References: Hartej S 1. Hartej S, Sethi, James W. Schmidley. Cerebral Infarcts in the Setting of Eosinophilia. Three Cases and a Discussion. Arch Neurol. 2010;67(10):1275-1277 2. Norah S. Lincoff, David Schlesinger. Recurrent Optic Neuritis as the Presenting Manifestation of Primary Hypereosinophilic Syndrome: A Report of Two Cases. J Neuro-Ophthalmol 2005;25: 116–121 3. Bozkir N, Stern GA. Ocular Manifestations of the Idiopathic Hypereosinophilic Syndrome. Am J Ophthalmol 1992;113:456–58 4. Chaine G, Davies J, Kohner EM, et al. Ophthalmologic Abnormalities in the Hypereosinophilic Syndrome. Ophthalmology 1982;89: 1348–56 5. Dinc A, Soy M, Pay S, et al. A case of Churg-Strauss syndrome presenting with cortical blindness. Clin Rheumatol 2000;19:318–20 6. Eosinophilic vasculitis in an isolated central nervous system distribution. R B Sommerville, J M Noble, J P Vonsattel, R Delapaz, C B Wright. J Neurol Neurosurg Psychiatry 2007;78:85–88

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Stroke trauma, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 112**Blurred Margins: Cocaine Use Clouding the Diagnosis of Orbital Granulomatosis With Polyangiitis**

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Introduction:

Cocaine induced vasculitis and Idiopathic ANCA Associated vasculitis (AAV) share similar presentations which can be difficult to differentiate. We report the case of young woman presenting with right eye vision loss and severe pansinusitis in the setting of cocaine use, who was diagnosed with orbital granulomatosis with polyangiitis.

Description of Case(s):

A 32 year old woman presented with painless, progressive vision loss in the right eye over a course of 2 weeks. Ophthalmologic examination demonstrated no light perception and abduction deficit in the right eye. Fundoscopy demonstrated 270 degrees of blurred disc margins with frisen grade 2-disc edema. In the left eye visual acuity was 20/20 with normal fundus. Urine drug screen was positive for cocaine. CT sinuses and MRI orbit demonstrated destruction of the nasal septum, middle turbinates, lateral wall of right maxillary and sphenoid sinus. An enhancing soft tissue mass was seen extending through the right inferior orbital fissure into the orbital apex with significant compression/infiltration of right optic nerve. The lateral and medial rectus muscles also appeared enlarged. CT chest demonstrated tiny, non significant opacities. Renal function was normal without proteinuria. Labs included positive C-ANCA 1:20 titer (EIA positive for anti-PR3), negative Levamisole Ab, and negative Human Neutrophil Elastase Ab. Tissue biopsy and pathology demonstrated necrotizing granulomatous inflammation and vasculitis. As the biopsy was most consistent with GPA, patient was started on a lower dose of prednisone at 0.5 mg/kg daily due to concurrent MSSA infection.

Conclusions, including unique features of the case(s):

A comprehensive review of the clinical presentation, labs, and tissue biopsy is needed to reach diagnosis. Positive UDS for cocaine should not deter the clinician from considering ANCA Associated Vasculitis syndromes. In our case, evidence supporting GPA include minimally elevated Anti-PR3 antibodies, negative levamisole Ab, negative Human Neutrophil Elastase antibody and necrotizing granuloma on biopsy. Orbital involvement can occur in 60% of GPA cases.

References: Berman M, Paran D, Elkayam O. Cocaine-Induced Vasculitis. Rambam Maimonides Med J. 2016;7(4):e0036. Published 2016 Oct 31. doi:10.5041/RMMJ.10263 McGrath MM, Isakova T, Rennke HG, Mottola AM, Laliberte KA, Niles JL. Contaminated cocaine and antineutrophil cytoplasmic antibody-associated disease. Clin J Am Soc Nephrol. 2011;6(12):2799–2805. doi:10.2215/CJN.03440411 Muller K, Lin JH. Orbital granulomatosis with polyangiitis (Wegener granulomatosis): clinical and pathologic findings. Arch Pathol Lab Med. 2014;138(8):1110–1114. doi:10.5858/arpa.2013-0006-RS Subesinghe S, van Leuven S, Yalakki L, Sangle S, D'Cruz D. Cocaine and ANCA associated vasculitis-like syndromes – A case series. Autoimmunity Reviews.2018; 17(1):73-77. doi: 10.1016/j.autrev.2017.11.011 Wiesner O, Russell KA, Lee AS, Jenne DE, Trimarchi M, Gregorini G, et al. Antineutrophil cytoplasmic antibodies reacting with human neutrophil elastase as a diagnostic marker for cocaine-induced midline destructive lesions but not autoimmune vasculitis. Arthritis Rheum. 2004;50(9):2954–65. doi:10.1002/art.20479

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Orbit/ocular pathology, Optic neuropathy, Ocular motility, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 113**Recurrent Bilateral Papilledema Initially Mimicking Idiopathic Intracranial Hypertension In Granulomatosis With Polyangiitis**

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Introduction:

Granulomatosis with polyangiitis (GPA) may involve the central nervous system and manifest as pachymeningitis. Usual clinical findings include headaches and various cranial neuropathies. Although inconsistently reported, papilledema and intracranial hypertension may be a complication of GPA with pachymeningitis, as a result of the obstruction of venous outflow by thickened meninges. We describe a case of GPA that initially manifested with recurrent papilledema and intracranial hypertension, mimicking idiopathic intracranial hypertension.

Description of Case(s):

A 52-year-old overweight woman presented with a 7-year history of recurrent headaches, transient visual obscurations, and occasional haemorrhagic nasal discharges. She had been diagnosed with papilledema due to idiopathic intracranial hypertension with bilateral stenoses of transverse venous sinuses, for which she was treated with acetazolamide alone. The symptoms worsened in the past 3 months. Clinical examination revealed bilateral papilledema. Cerebral MRI exhibited thickened and enhanced meninges over the hemispheres and the cerebellum, and signs of elevated intracranial pressure. However, there was no meningeal enhancement on the MRI at the time of first symptoms 7 years ago. The lumbar puncture opening pressure was 300 mm H₂O. The laboratory workup yielded increased levels of PR3 cANCA titers. Biopsy of the temporal artery revealed necrotizing granulomas within the vasa vasorum. The patient received a treatment of steroids with slow tapering, and a long-term immunosuppressive treatment with rituximab.

Conclusions, including unique features of the case(s):

In retrospect, early symptoms indicate an early onset of GPA with upper airway involvement. This case suggests recurrent papilledema and intracranial hypertension might be signs of central nervous system involvement in GPA, prior to radiological evidence for pachymeningitis. This case prompts clinicians to look for treatable autoimmune conditions when confronted with recurrent papilledema despite acetazolamide treatment in patients diagnosed with idiopathic intracranial hypertension.

References: Choi HA, Lee MJ, Chung C-S. Characteristics of hypertrophic pachymeningitis in patients with granulomatosis with polyangiitis. *J Neurol*. 2017 Feb 20;264(4):724–32. Lam BL, Barrett DA, Glaser JS, Schatz NJ, Brown HH. Visual loss from idiopathic intracranial pachymeningitis. *Neurology*. 1994 Apr;44(4):694–8. Di Comite G, Bozzolo EP, Praderio L, Tresoldi M, Sabbadini MG. Meningeal involvement in Wegener's granulomatosis is associated with localized disease. *Clin Exp Rheumatol*. 2006 Mar;24(2 Suppl 41):S60–4. Arnaoutoglou MA, Xerras CG, Kalevrosoglou IK, Rafailidis VD, Notas KP, Tegos TI. Headache Linked to Intracranial Hypertension and Hypertrophic Pachymeningitis as the Initial and Dominant Presentation of Granulomatosis With Polyangiitis. Case Report and Review of the Recent Literature. *Headache*. 2018 Apr;58(4):589–95. Fain O, Mekinian A. [Pachymeningitis]. *Rev Med Interne*. 2017 Sep;38(9):585–91.

Keywords: High intracranial pressure/headache, Neuroimaging, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 114**A Case of T-cell leukemia/lymphoma Presenting as Acute Bilateral 3rd Nerve Palsy**

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Introduction:

Acute 3rd nerve palsy has been attributed to many etiologies including vasculopathic process, trauma, compression, infiltrative, inflammation, tóxico, etc. Bilateral acute 3rd nerve palsy is very rare an uncommon presentation of T-cell leukemia/lymphoma.

Description of Case(s):

A 29 year old apparently healthy man presented with a 10 days history of bilateral palpebral ptosis, horizontal binocular diplopia and blurred vision at near. Three years ago he had been treated for leukemia, responded well to chemotherapy and was about 15 months healthy. Examination demonstrated a complete bilateral ptosis, and adduction, supra and infraduction deficit in both eyes; His pupils were 5 mm symmetrical and no reactive to light or accommodation. Otherwise, neuro-ophthalmic examination, including cranial nerves, biomicroscopy and dilated fundus examination was unremarkable. Brain contrasted MRI showed enhancement of both 3rd nerves from their origin in the midbrain to the orbits. CSF analysis showed elevated white blood cells with undifferentiated lymphoid elements. Bone marrow biopsy and flow cytometry confirmed the the reappearance of T-cell leukemia/lymphoma. Other imaging studies reported no additional extramedullary disease.

Conclusions, including unique features of the case(s):

Bilateral 3rd nerve palsy is an uncommon presentation of T-cell leukemia/lymphoma. In young patients and those patient with history of T-cell malignancy, thorough and expedited evaluation of acute cranial nerve palsies, including contrasted MRI, is required to evaluate for life-threatening disease.

References: None.

Keywords: Adult strabismus with a focus on diplopia, Neuroimaging, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 115**Non-Arteritic Ischemic Optic Neuropathy in the setting of Optic Nerve Sheath Meningioma: a Case Report**

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Introduction:

Non-arteritic ischemic optic neuropathy (NAION) is the most common cause of acute optic neuropathy in patients over age 50. While crowded optic nerve heads are a risk factor for developing NAION, NAION in the setting of optic nerve sheath meningiomas (ONSM) is rare. We report a case of NAION in a patient with preexisting ONSM.

Description of Case(s):

58-year-old female with known left eye ONSM, status post radiation 5 years prior, and medically-controlled hypertension presented complaining of worsening vision. The patient's left eye was found to a visual acuity of 20/70, an afferent pupillary defect, dyschromatopsia, and normal intraocular pressure. Left eye fundus exam showed a cupless disc with elevated optic nerve head with blurred disc margins and an optociliary shunt vessel inferiorly. There was no obscuration of vessels. The right eye exam was normal. Humphrey visual field testing showed a full field in the right and a new dense superior hemifield defect in the left eye. Left visual fields 6 months prior had shown only an enlarged blind spot. Optical coherence tomography of the left optic nerve demonstrated <0.1 cup with elevated disc margins, while the right was normal. The differential diagnoses included compressive, radiation-induced, and ischemic optic neuropathies. MRI orbits with and without contrast showed no change in the size of ONSM. The patient was diagnosed with NAION secondary to preexisting ONSM. As neuroprotective therapy, the patient was given topical brimonidine drops, but she deferred oral steroids. The patient was referred back to her primary care physician for optimization of her blood pressure, sugar, and cholesterol.

Conclusions, including unique features of the case(s):

In patients with ONSM, the management of comorbidities such as hypertension, diabetes, and hypercholesterolemia should be emphasized to decrease the risk of further vision loss from optic nerve ischemia. Neuroprotective therapy for NAION remains controversial.

References: 1. Hattenhauer MG, Leavitt JA, Hodge DO, Grill R, Gray DT. Incidence of nonarteritic anterior ischemic optic neuropathy. *Am J Ophthalmol.* Jan 1997;123(1):103-107. PMID: 9186104. DOI:10.1016/s0002-9394(14)70999-7. 2. Guhlmann M, Kommerell G. Simulation of anterior ischemic optic neuropathy by optic nerve sheath meningioma. *Klin Monbl Augenheilkd.* 1995 Sep;207(3):200-2. German. PMID: 7474790. 3. Hayreh SS. Controversies on neuroprotection therapy in non-arteritic anterior ischaemic optic neuropathy. *Br J Ophthalmol.* 2019 Sep 5. pii: bjophthalmol-2019-314656. doi: 10.1136/bjophthalmol-2019-314656. [Epub ahead of print]

Keywords: Optic neuropathy, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 116**"Bilateral optic disc edema associated with Primary CNS Lymphoma"**

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Introduction:

Primary CNS lymphoma is a rare form of extranodal non-Hodgkin lymphoma that is typically confined to the brain, eyes, and cerebrospinal fluid without evidence of systemic spread.

Description of Case(s):

A 74 year old woman presented to us with complaints of bilateral decreased vision of 2 weeks duration along with word finding difficulty. Her past medical history includes signet ring adenocarcinoma of the stomach, s/p esophagojejunostomy. Her visual acuity was 20/25 OU, no RAPD. Fundus showed OU grade 3 disc edema with trace pallor and associated nerve fiber hemorrhages & cotton wool spots. Visual fields OD inferior arcuate, supero-nasal step and OS general depression. OCT RNFL diffuse thickening OU, normal GCL. MRI brain showed multifocal lesions of increased FLAIR including left basal ganglia, insular cortex, hippocampi, mesial temporal lobe with bilateral optic disc elevation and enhancement along the retrobulbar optic nerve on the left. Lumbar puncture normal, 2 unique oligoclonal bands in CSF, and serum pANCA was elevated 1:640, received methylprednisone. PET CT did not show recurrence of her gastric tumor, but there was hypermetabolic lesion in the left frontal lobe.

Conclusions, including unique features of the case(s):

Brain biopsy revealed atypical lymphoid cells with markedly irregular nuclei, multiple small nucleoli and angiocentric distribution. Immunohistochemistry shows the neoplastic cells are B-cells positive for CD20, CD10, BCL6 and MUM1, Repeat PET/CT scan revealed no development of metastases in the neck, chest, abdomen or pelvis. She was treated with intravenous rituximab and methotrexate with radiographic improvement of enhancing lesions. Corticosteroids can cause regression of lymphoma cells in the vitreous lowering biopsy yield and may also change the radiographic appearance as well as histopathology findings with numerous apoptotic bodies rather than typical large lymphoid cells in an angiocentric pattern. New imaging techniques (MRS, PWI and DWI) play important role in diagnosis of PCNSL, differentiate from high-grade gliomas and metastases

References: Asem, Monther, Hikmat et al, MR imaging features of intracranial primary CNS lymphoma in immune competent patients, *Cancer Imaging*. 2014; 14(1): 22 Sitaula R, Shrestha GB, Paudel N, Shrestha JK. Ocular and orbital metastases presenting as a first sign of gastric adenocarcinoma. *BMJ Case Rep*. 2011;422–425. Xu Q, Du W, Zhou, Distinct clinical characteristics of paraneoplastic optic neuropathy, *Br J Ophthalmol*. 2019 Jun;103(6):797-801 Giannini C1, Dogan A, Salomão DR, CNS lymphoma: a practical diagnostic approach, *J Neuropathol Exp Neurol*. 2014 Jun;73(6):478-94 Zou Y, Tong J, Leng H, Jiang J, Pan M, Chen Z. Diagnostic value of using 18F-FDG PET and PET/CT in immunocompetent patients with primary central nervous system lymphoma: a systematic review and meta-analysis. *Oncotarget*. 2017;8(25):41518–41528.

Keywords: Neuroimaging, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy, Paraneoplastic syndromes, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 117**Delayed Diagnosis of Cranial Neuropathies from Perineural Invasion of Skin Cancer**

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Introduction:

Perineural invasion (PNI) of cranial nerves (CNs) by cutaneous malignancies is difficult to diagnose given the indolent course and often late or absent findings on brain imaging. We present a case with multiple cranial neuropathies secondary to PNI of squamous cell carcinoma with negative imaging for 5.25 years.

Description of Case(s):

A 68-year-old white man presented with 39 months of left V1-V2 numbness and 1.5 months of left CN VI palsy. Examination showed normal afferent visual function, with left CNs V1-V3, VI deficits, and decreased left brow elevation. Repeat brain MRIs showed left atrophic lateral rectus and pterygoid muscles, but no CN abnormality. Full body PET and CSF studies were normal. Subsequent examinations over 2 years showed further involvement of CNs, including left CN VII, right V1-V3, and right CN VI, and generalized swallowing and speech difficulty and cachexia. Subsequent high-quality MRIs showed no changes. Paraneoplastic antibodies were negative. 5.25 years after initial onset of left clinical V2 dysfunction, MRI showed new enhancement along the proximal extracranial extent of right V3 (with foramen ovale widening). Given the patient's poor health, no biopsy was performed. The patient died a year later. Autopsy showed squamous cell carcinoma within bilateral cranial nerves VI.

Conclusions, including unique features of the case(s):

Our patient developed progressive multiple cranial neuropathies over 6.5 years (78 months) prior to death. Repeat high-quality brain imaging focused on the CNs remained normal for 5.25 years (63 months) and showed secondary effects (atrophic left lateral rectus and pterygoid muscles), but no CN enhancement. Literature review shows an average time to diagnosis of about one year, with a range of 0.5-84 months. A long interval to diagnosis is associated with high morbidity, emphasizing the need for earlier methods of detection, whether by enhanced neuroimaging (such as MR neurography) or "blind" biopsies of CNs V1, V2 or VII when clinical suspicion is high.

References: 1. Badger, D. and N. Aygun "Imaging of Perineural Spread in Head and Neck Cancer." *Radiol Clin North Am* 55(1): 139-149, 2017 2. Bourque, P. R., et al. "Combined isolated trigeminal and facial neuropathies from perineural invasion by squamous cell carcinoma: A case series and review of the literature." *Journal of Clinical Neuroscience* 35: 5-12, 2017 3. Leach, B. C., et al. "Cranial neuropathy as a presenting sign of recurrent aggressive skin cancer." *Dermatologic Surgery* 34(4): 483-497, 2008 4. Warner, G. C., et al. "Slowly progressive cranial nerve palsies." *Medical Journal of Australia* 184(12): 641-643, 2006 5. Warren, T. A., et al. "Insight into the epidemiology of cutaneous squamous cell carcinoma with perineural spread." *Head Neck* 38(9): 1416-1420, 2016

Keywords: Skull Base, Neuroimaging, Orbit/ocular pathology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 118**A Rare CN 6 Palsy**

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Introduction:

Horner's syndrome with ipsilateral CN VI palsy has significant localizing value.

Description of Case(s):

A 71-year-old woman presented with left temporal headache and horizontal diplopia. She had type 2 diabetes mellitus, chronic obstructive pulmonary disease, and hypothyroidism. Ophthalmic exam showed loss of left eye abduction. Initial workup showed erythrocyte sedimentation rate of 100 and C-reactive protein of 92. Complete blood count, comprehensive metabolic panel, and computed tomography scan of her head were normal. Empiric steroid treatment for giant cell arteritis (GCA) was initiated. Magnetic resonance imaging (MRI) of her brain as well as temporal artery biopsy (TAB) were interpreted as normal. Repeat exam 1 week later showed unchanged left eye abduction deficit with development of left upper eyelid ptosis and anisocoria. Right and left pupils measured 3mm and 2mm in dark, and 1.75mm and 1.5mm in light, respectively. This finding prompted re-evaluation of her MRI from 1 week prior, which was then found to have an abnormal enhancing signal in the left petrous apex extending towards the clivus, with possible involvement of the cavernous sinus. Subsequent imaging showed diffuse metastatic disease involving the liver, lungs, kidneys and bone. Liver biopsy confirmed metastatic adenocarcinoma of upper GI origin.

Conclusions, including unique features of the case(s):

This is a rare presentation of Parkinson syndrome with an isolated CN VI palsy and development of an ipsilateral Horner's syndrome 1 week later. The localizing value of this combination revealed the diagnosis. Parkinson Syndrome occurs with a lesion in the cavernous sinus where sympathetic plexus fibers from the carotid artery join CN VI before joining the ophthalmic division of the trigeminal nerve. It was first described as a theoretical syndrome by Dr. Dwight Parkinson in 1979 and subsequently described only in case reports. Etiology of these lesions include intracavernous carotid artery aneurysm or occlusion, cavernous sinus thrombosis, trauma, and neoplasm.

References: 1. Parkinson, Mitchell, Horner syndrome and others?, Surg Neurol., 11(3), 221-3, 1979 2. Tamhankar, Biousse, Ying, et al., Isolated third, fourth, and sixth cranial nerve palsies from presumed microvascular versus other causes: a prospective study, Ophthalmology, 120(11), 2264–2269, 2013

Keywords: Ocular motility, Neuroimaging, metastatic carcinoma, Tumors, Skull base

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 119**Myasthenic ptosis induced by bulb light**

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Introduction:

The ptosis in ocular myasthenia (OM) is fluctuating and could be bilateral or unilateral; symmetric or asymmetric. Cogan lid twitch, enhanced ptosis, peek sign, and lid fatigue are some of the findings that support the clinical diagnosis of myasthenia. The ice test is one of most useful test with 80% sensitivity and 100% specificity.¹

Description of Case(s):

A 50 year-old woman presented with a 1-month history of a drooping right eyelid that worsened in the afternoon but specially with incandescent light bulb exposure. Neurophthalmological examination showed right eyelid ptosis which worsened with sustained upward gaze. The exposure to the incandescent and halogen light of the bulb increase the ptosis until reach the total closing of the eyelid. When the light was removed the eyelid raised. Cogan lid twitch, peek sign, curtain sign and ice pack test were positive. The remain examination was normal and the only complementary test positive were anti-AChR antibody

Conclusions, including unique features of the case(s):

Ptosis in OM tend to improve with lower temperature probably because reduces the effects of acetylcholinesterase. A hot test provoke ptosis by warming the eyelid in OM patients with minimal fatigability.² Several mechanisms have been proposed to explain the effects of temperature on the neuromuscular junction, including temperature effects on the release of acetylcholine, endplate sensitivity, and differences in the activity of acetylcholinesterase.³ The light bulb energy is being transformed into light and thermal (heat) energy. Different wattages and types of bulbs give off varying amounts of light and also heat. Most of the light bulbs emitted heat in about 60-90% of the electricity; probably in our patient this heat is enough to increase de effect of acetylcholinesterase.

References: 1. Al-Haidar M, Benatar M, Kaminski HJ.: Ocular Myasthenia. *Neurol Clin.* 2018 May;36(2):241-251. 2. Komiyama A, Hirayama K.: Diagnostic usefulness of a hot test in patients with mild ocular myasthenia gravis. *No To Shinkei.* 1987;39(8):733-7. 3. Marinos E, Buzzard K, Fraser CL, Reddel S: Evaluating the temperature effects of ice and heats test on ptosis due to Myasthenia Gravis. *Eye.* 2018; 32(8):1387-1391.

Keywords: Graves (systemic disease), Myasthenia, Ocular motility, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 120**Metabotropic Glutamate Receptor Type 1 Autoimmune Encephalitis: A Treatable Cause of Neuro-ophthalmologic Manifestations**

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Introduction:

Antibodies directed towards metabotropic glutamate receptor type 1 (mGluR1) have been reported in association with a type of cerebellar-predominant autoimmune encephalitis, with less than twenty cases reported. Few data regarding symptoms, comorbid pathology, and response to treatment exists. We report a case of a woman with mGluR1 autoimmune encephalitis who presented with prominent neuro-ophthalmologic signs and symptoms. We report the first recognized association between mGluR1 encephalitis and concurrent metastatic ductal breast carcinoma.

Description of Case(s):

A 50 year-old woman presented to the emergency department with three months of worsening gait instability, dysarthria, oscillopsia, and vertigo. Two months prior to presentation, she was diagnosed with infiltrating ductal carcinoma with regional lymph node involvement and was treated with a left mastectomy and lymph node dissection. Neurologic examination demonstrated prominent downbeat nystagmus in all directions of gaze, ataxic dysarthria, mild appendicular ataxia of the lower limbs, and severe truncal ataxia precluding the ability to walk unassisted. Basic laboratory analysis, computed tomography, and magnetic resonance imaging of the brain were unremarkable. Cerebrospinal fluid (CSF) analysis revealed 28 nucleated cells with lymphocytic predominance, elevated oligoclonal bands and IgG index. CSF Cytology was negative. Empiric treatment with intravenous corticosteroids was initiated for suspected paraneoplastic syndrome with subsequent improvement of oscillopsia, downbeat nystagmus, dysarthria, and gait. After discharge, antibodies towards n-methyl-d-aspartate receptor (NMDAR) and mGluR1 were found in the CSF. Serum autoimmune panel was also positive for mGluR1 antibody. She subsequently relapsed and responded well to plasmapheresis. She has been on a corticosteroid taper of intravenous methylprednisolone with complete resolution of nystagmus with mild difficulty performing tandem gait but otherwise intact neurologic examination. She has initiated chemotherapy for metastatic ductal carcinoma.

Conclusions, including unique features of the case(s):

Antibodies directed towards mGluR1 can be detected in patients with prominent neuro-ophthalmologic symptoms. Early diagnosis and prompt institution of immunotherapy is associated with good neurologic outcomes.

References: Christ M, Muller T, Bien C, Hagen T, Naumann M, "Autoimmune Encephalitis Associated with Antibodies Against the Metabotropic Glutamate Receptor Type 1: Case Report and Review of the Literature", *Therapeutic Advances in Neurological Disorders*, 10, eCollection 2019.

Keywords: Paraneoplastic syndromes, Nystagmus

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 121**Dorsal Midbrain Syndrome Secondary to Pineal Glioblastoma**

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Introduction:

Glioblastomas of the pineal region make up less than one percent of intracranial tumors in adults.¹ To date, less than 100 cases of pineal glioblastoma have been reported worldwide.² These tumors often infiltrate upper portions of the midbrain and therefore can have ophthalmic complications such as dorsal midbrain syndrome.

Description of Case(s):

Here we report a case of a 24 year-old male who presented to the emergency room with blurry vision and a headache and was found to have an intracranial pineal gland mass. This was later diagnosed as glioblastoma on biopsy. On ophthalmologic evaluation, the patient notably had light-near dissociation, convergence retraction nystagmus, fixation instability, and vertical gaze palsy consistent with dorsal midbrain syndrome secondary to pineal glioblastoma. Dilated exam showed papilledema bilaterally consistent with increased intracranial pressure. A ventriculoperitoneal shunt was placed by neurosurgery to relieve intracranial pressure. He was instructed to patch for symptomatic relief of diplopia and was eventually started on radiation and chemotherapy given the unresectable nature of the tumor location.

Conclusions, including unique features of the case(s):

Dorsal midbrain syndrome, also known as Parinaud syndrome, can manifest most classically as light-near dissociation, convergence retraction nystagmus, and upgaze palsy. It can result from midbrain lesions secondary to mass compression, especially in the pineal gland, which has close anatomic proximity to the dorsal midbrain. Most pineal gland tumors originate from cells of the pineal parenchyma, but rarely, glioblastoma multiforme tumors can arise in the pineal gland and generally have a poor prognosis.¹

References: 1. Orrego, E., Casavilca, S., Garcia-Corrochano, P., Rojas-Meza, S., Castillo, M., & Castaneda, C. A. (2017). Glioblastoma of pineal region: report of four cases and literature review. *CNS oncology*, 6(04), 251-259. 2. Glioblastoma Multiforme of the Pineal Region. (n.d.). Retrieved from <http://www.ajnr.org/ajnr-case-collections-diagnosis/glioblastoma-multiforme-pineal-region>.

Keywords: Ocular motility, High intracranial pressure/headache, Tumors, Nystagmus, High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 123**Central Nervous System Leukemic Involvement Presenting as Unilateral Oculomotor Nerve Palsy without Imaging Findings**

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Introduction:

Cranial nerve palsies secondary to leukemia have been reported, rarely without magnetic resonance imaging (MRI) findings. We present the first known case of a unilateral pupil-involving oculomotor nerve palsy without any MRI findings, in a patient with acute myelogenous leukemia.

Description of Case(s):

A 32 year old female with history of acute myelogenous leukemia (AML), diagnosed 7 months prior and treated with chemotherapy and bone marrow transplant, presented with acute onset left sided ptosis, binocular diplopia worse in upgaze and ipsilateral headache. Visual acuity was 20/40 right eye (OD) and 20/60 left eye (OS). Pupils were brisk without a relative afferent pupillary defect. Left pupil mydriasis was noted and pharmacologic testing revealed pupillary constriction to pilocarpine (1%). Motility exam revealed a 75% supraduction deficit of the left eye. Remainder of the ocular examination was unremarkable. MRI brain and orbits and MRA head and neck were unremarkable. Lumbar puncture revealed cerebrospinal fluid leukemic infiltration on flow cytometry. The patient developed multiple complications refractory to treatment and was transitioned to hospice care, passing away 40 days after ophthalmologic examination.

Conclusions, including unique features of the case(s):

Cranial nerve palsies in AML are rarely reported but usually present with enhancement on MRI suggestive of leukemic infiltration. In the absence of such findings, cerebrospinal fluid studies proved essential in establishing a diagnosis of central nervous system involvement.

References: None.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Magnetic resonance imaging, Pupils retina, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 124**Carotid Cavernous Fistula: An Uncommon Etiology of a Common Presentation**

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Introduction:

Abducens nerve palsy is a common presentation and can be caused by various etiologies. A carotid-cavernous sinus fistula (CCF) is an abnormal communication between the cavernous sinus and the carotid arterial system. CCF is rare and initial symptoms can manifest as a painful or painless abducens nerve palsy.

Description of Case(s):

A 60 year-old woman with a past medical history significant for hypertension, hyperlipidemia and anxiety, presented with binocular, horizontal and diagonal diplopia for two days. Double vision was only evident when looking at distance and was associated with left facial pain and left peri-orbital pain. On exam, patient demonstrated complete left 6th nerve palsy with horizontal gaze. She had slow beat horizontal nystagmus in the right eye with left gaze. Intact vertical gaze. She had full visual fields and normal visual acuity. Intraocular pressure was OD 14, OS 15. Funduscopy exam showed a retinal micro hemorrhage and hyperemia in the left eye. Remainder of neurological exam was normal. Lyme profile negative, ESR normal. CT head and MRI brain interpreted as normal. Subsequent MR Venogram with IV contrast showed flow-related signal intensity/arterialized flow present in the left posterior cavernous sinus, retroclival venous plexus, and superior petrosal sinus consistent with carotid-cavernous fistula. Digital subtraction angiography (DSA) revealed indirect carotid-cavernous fistula with malignant cerebellar venous drainage. Trans-venous embolization of CCF was performed successfully.

Conclusions, including unique features of the case(s):

CCF can be unapparent or misdiagnosed at early stages, particularly in indirect, low-flow CCF, which typically manifest with more subtle initial symptoms. Painful diplopia due to abducens nerve palsy is a common presentation of this uncommon anomaly. When there is clinical suspicion for CCF, even with normal MRI and CT angiography, DSA should be considered.

References: None.

Keywords: Ocular motility, Interventional neuroradiology, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 125**Spontaneous Carotid-Cavernous Sinus Fistula Causing Fluctuating Ocular Symptoms**

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Introduction:

The symptomatology of carotid cavernous fistula is mainly based on the degree of neural or vascular involvement and can be classified based on its etiology (Traumatic or spontaneous), hemodynamic properties (High flow vs low flow) and anatomical features of the shunt. We report a patient with protracted course of ocular symptoms who was diagnosed to have carotid cavernous fistula.

Description of Case(s):

A 48 year old man presented with sudden onset horizontal diplopia at an outside facility. Patient was initially diagnosed with divergence insufficiency after MRI of the orbit and brain failed to show etiology. Double vision persisted for 3 weeks followed by complete resolution. Over a period of 3 months patient noticed intermittent and fluctuating right sided symptoms of face tingling, swelling, throbbing periorbital pain and headache. Gradually he also developed intermittent redness and lacrimation in right eye. Indomethacin was prescribed for suspicion of hemicrania continua with mild improvement of symptoms. Finally, he developed right upper eyelid droopiness, pulsatile tinnitus and horizontal double vision within a period of 10 days before he was seen in Neuro-ophthalmology clinic. Ocular examination revealed pupil sparing partial 3rd nerve palsy, proptosis, chemosis and elevation of IOP in right eye. Patient was admitted for urgent imaging studies which was positive for right carotid cavernous fistula. While patient was undergoing investigations in hospital, clinical deterioration occurred with complete droopiness, further limitation of extra-ocular eye movements and severely elevated IOP in right eye. Emergent embolization of carotid cavernous fistula was performed.

Conclusions, including unique features of the case(s):

1. Symptoms of spontaneous low flow carotid cavernous fistula can be subtle, making the diagnosis challenging. 2. Low flow fistula can switch into high flow fistula during the course of disease, causing sudden clinical deterioration. 3. Occasionally, repeat brain imaging studies is warranted, in cases of persistent ocular signs and symptoms to reach final diagnosis.

References: Leone, G., Renieri, L., Enriquez-Marulanda, A., Dmytriw, A. A., Nappini, S. (2019). Carotid Cavernous Fistulas and Dural Arteriovenous Fistulas of the Cavernous Sinus: Validation of a New Classification According to Venous Drainage. *World Neurosurgery*. Campbell, S., Hack, E., & Philip, B. (2019). A rare red eye: cavernous sinus dural arteriovenous fistula masquerading as conjunctivitis and sinusitis. *The Medical Journal of Australia*, 210(9), 398–399.e1. Chaudhry, I. A., Elkhayry, S. M., Al-Rashed, W., & Bosley, T. M. (2009). Carotid cavernous fistula: ophthalmological implications. *Middle East African Journal of Ophthalmology*, 16(2), 57–63. Fan, Y., Li, Y., Zhang, T., Jiang, C., & Zhang, P. (2019). Carotid-Cavernous Sinus Fistula caused by Persistent Primitive Trigeminal Artery Aneurysm rupture: A case report. *Journal of Stroke and Cerebrovascular Diseases: The Official Journal of National Stroke Association*, 104306.

Keywords: Neuroimaging, Vascular disorders, Ocular motility, Interventional neuroradiology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 126**An Unusual Presentation of Diplopia in the Setting of Idiopathic Intracranial Hypertension**

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Introduction:

Idiopathic Intracranial Hypertension (IIH) is a neuro-ophthalmic condition of raised intracranial pressure resulting in headache, papilledema, and potentially diplopia secondary to a sixth nerve palsy. The diagnostic criteria, or Dandy Criteria, specifically restricts focal neurologic deficits other than a sixth nerve palsy. A seventh nerve palsy has been well established as another possible isolated cranial neuropathy secondary to raised intracranial pressure (1, 2, 3, 4). The authors report a patient with fulminant IIH who presented with bilateral fourth and sixth nerve palsies but otherwise met the Dandy criteria and responded well to acetazolamide and ventriculoperitoneal (VP) shunting. This has rarely been presented in the literature prior (5, 6, 7, 8) and may be under recognized as a potential cranial nerve palsy in IIH.

Description of Case(s):

A 20-year-old female presented urgently for headache, attributed to migraine. Two weeks later she developed diplopia and an ophthalmology consult was obtained revealing grade V papilledema in both eyes and bilateral fourth and sixth nerve palsies with an esotropia of 20 prism diopters, a right hypertropia of 10 diopters, and 10 degrees of excyclotorsion. She underwent an MRI brain with and without contrast, showing no causative lesion. An MRV head showed significant venous sinus stenosis. A lumbar puncture showed an opening pressure of >85 cm of H₂O with normal CSF analysis. She was started on 2 grams of acetazolamide twice a day, however her visual field worsened with only mild improvement of her papilledema over 3 weeks. Ultimately, she was treated with a VP shunt and had rapid improvement in her papilledema and visual field.

Conclusions, including unique features of the case(s):

Similar to a sixth nerve palsy, we postulate a fourth nerve palsy is rare, but possible, secondary to elevated intracranial pressure. Clinicians should be aware of this unusual presentation of IIH.

References: 1. Bakshi S K, Oak J L, Chawla K P, Kulkarni S D, Apte N, Facial nerve involvement in pseudotumor cerebri, J Postgrad Med, 38(3), 144-5, 1992 2. Capobianco DJ, Brazis PW, Cheshire WP, Idiopathic Intracranial Hypertension and Seventh Nerve Palsy, Headache, 37(5), 286-288, 1997 3. Soroken C, Lacroix L, Korff CM, Combined VIth and VIIth nerve palsy: Consider idiopathic intracranial hypertension!, Eur J Paediatr Neurol, 20, 336-338, 2016 4. Samara A, Ghazaleh D, Berry B, Ghannam M, Idiopathic intracranial hypertension presenting with isolated unilateral facial nerve palsy: a case report, J Med Case Rep, 13, 94, 2019 5. Totuk OMG, Aldroubi N, Aykan U, A case of bilateral fourth nerve palsy associated with pseudotumor cerebri, Arq Bras Oftalmol, 82(4), 332-5, 2019 6. Lee AG, Fourth Nerve Palsy in pseudotumor cerebri, Strabismus, 3(2), 57-9, 1995 7. Speer C, Pearlman J, Phillips PH, Cooney M, Repka MX, Fourth cranial nerve palsy in pediatric patients with pseudotumor cerebri, Am J Ophthalmol, 127(2), 236-7, 1999 8. Patton N, Beatty S, Lloyd C, Bilateral sixth and fourth cranial nerve palsies in idiopathic intracranial hypertension, J R Soc Med, 93(2), 80-1, 2000

Keywords: Pseudotumor cerebri, Ocular motility, High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 127**Hypertestosteronism In Atypical Idiopathic Intracranial Hypertension (IIH): A Possible Alternative Pathophysiology**

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Introduction:

We present an atypical IIH patient with an underlying pathologic testosterone excess. Given recent data demonstrating the effects of testosterone on the production of cerebrospinal fluid (CSF) in the choroid plexus, this endocrinopathy may be contributing to the pathophysiology of IIH or a subset of IIH cases.

Description of Case(s):

A twenty year-old non-obese female who underwent female-to-male (FTM) gender reassignment, and self-treated with unmonitored exogenous testosterone, presented with headaches, bilateral severe visual field constriction, pulse-synchronous tinnitus, and bilateral papilledema for six months. She satisfied the Modified Dandy Criteria and was found to have an elevated serum testosterone level of 466 ng/dL (normal female range 15 - 70 ng/dL) after increasing her testosterone dose from 50 mg to 100 mg weekly. She was treated with acetazolamide and a gradual reduction of her exogenous testosterone. Although we were able to stabilize her vision loss on maximum doses of acetazolamide, her headaches persisted and she discontinued her acetazolamide due to significant side effects. She was found to have an elevated right transverse venous sinus pressure gradient of 15 mmHg, and underwent venous sinus stenting resulting in the resolution of signs and symptoms of IIH and remarkable improvement in visual field defects.

Conclusions, including unique features of the case(s):

Testosterone has been demonstrated to upregulate the activity and number of Na/K/ATPase pumps in the human choroid plexus, which increases CSF production, suggesting a possible link to the overproduction of CSF pathophysiology of IIH (1,2). An association between elevated active testosterone levels in fifty five women with IIH and in five other FTM gender-reassignment patients with IIH has recently been demonstrated (1,2). Our patient's unique presentation exemplifies an understudied potential endocrinological pathophysiology of IIH, which warrants further investigations. Spironolactone may be considered as an adjunctive therapy for IIH patients with hypertestosteronism.

References: O'Reilly M, Westage C, Hornby C, Botfield H, Sinclair A, et al. A Unique Androgen Excess Signature in Idiopathic Intracranial Hypertension is Linked to Cerebrospinal Fluid Dynamics. *JCI* 2019;4(6):e125348. Hornby C, Mollan S, Mitchell J, Markey K, Sinclair A, et al. What Do Transgender Patients Teach Us About Idiopathic Intracranial Hypertension? *NeuroOphthalmology*, 41:6, 326-329

Keywords: Pseudotumor cerebri, Visual fields, Interventional neuroradiology, High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 128**Idiopathic Intracranial Hypertension Secondary to Uremia**

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¹*University of Maryland School of Medicine, Baltimore, Maryland, USA*

Introduction:

Idiopathic intracranial hypertension (IIH) commonly occurs in obese women of childbearing age. We report a rare case of IIH due to a failing kidney transplant.

Description of Case(s):

A 24-year-old African-American male with a history of kidney transplant in 2011 presents with chronic headaches, transient visual obscurations, and pulsatile tinnitus for the past six months. Examination reveals visual acuity of 20/20 bilaterally, no APD, normal color perception, full extraocular movements, orthophoria, and full visual fields. Grade 3 optic disc edema is noted bilaterally with an otherwise normal appearing retina. The patient was lost to follow up for two months and then presents with “severe worsening” of his vision. Repeat examination shows decreased color vision and constricted visual fields of both eyes. In addition to persistent grade 3 optic disc edema bilaterally, there was newly noted retinal edema, vascular sheathing, and massive exudation in the right eye forming a partial macular star. OCT confirms significant optic disc and retinal edema concerning for neuroretinitis. Work-up reveals normal MRI/MRV of the brain, opening pressure of 40 cmH₂O with normal CSF composition, and negative Bartonella serology. Fluorescein angiography shows significant disc leakage with no macular leakage, consistent with primary disc edema rather than retinitis or neuroretinitis. The patient refused surgical management and was therefore started on oral Acetazolamide 1g daily, limited by his declining kidney function. Two weeks later he presents with persistent diarrhea, nausea, and vomiting, due to chronic progressive kidney transplant rejection resulting in uremia, requiring hemodialysis. Four weeks after hemodialysis is restarted, he reports improvement in his vision. Examination reveals resolution of papilledema, retinal edema, exudates, and recovery of color vision and visual fields.

Conclusions, including unique features of the case(s):

IIH due to uremia is rarely reported and may present with atypical features, which can imitate retinal disorders. Patients with chronic kidney disease may have multiples triggers of intracranial hypertension.

References: None.

Keywords: Pseudotumor cerebri, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 129**Multiple Recurrences of Cerebrospinal Fluid Rhinorrhea after Leak Repair**

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Introduction:

Idiopathic Intracranial Hypertension (IIH) is known to be associated with cerebrospinal fluid (CSF) leak. The standard of care in patients with CSF leak is to repair the leak in order to prevent complications such as meningitis. However, repairing the leak in IIH patients may worsen the intracranial hypertension.

Description of Case(s):

A 39-year-old female with a history of migraines, fibromyalgia, and polyneuropathy presented to the otolaryngology clinic for evaluation of headaches and left sphenoid sinus opacification. She had visited the emergency department multiple times for these headaches. An MRI done 8 months prior to her visit showed left sphenoid sinus opacification. She was started on topiramate by her neurologist but experienced worsening of headaches. A new MRI was ordered and showed skull base dehiscence. Her lumbar puncture (LP) opening pressure was 26. CSF rhinorrhea developed 2 months after her initial visit, and an endoscopic repair with fascia lata and fat was scheduled. One day post-operatively, the patient experienced recurrence of CSF rhinorrhea, and she underwent another repair with an allograft. She experienced worsening headaches and was started on acetazolamide with dose titrated up to 1000mg bid. CSF rhinorrhea recurred again. On examination, there was no papilledema present, and MRI of the orbits was ordered for further evaluation. LP opening pressure after 12 hours of lumbar drain clamping was elevated at 34. Multidisciplinary care was required for this patient, with input from otolaryngology, neurosurgery, neurology, ophthalmology, and rheumatology. The patient is currently admitted to the hospital with additional workup pending.

Conclusions, including unique features of the case(s):

This case demonstrates the need for integrated multidisciplinary care in patients with CSF leak in the setting of symptoms concerning for IIH. This patient had recurrence of leak immediately post-operatively with worsening headache after leak repair. The effects of CSF leak repair in IIH patients need to be further studied.

References: None.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 130**Are MRI Findings Sufficient To Allow A Diagnosis Of Idiopathic Intracranial Hypertension Without CSF Study?**

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Introduction:

Diagnostic criteria for IIH require normal CSF studies. NANOSNET discussions indicate some clinicians are satisfied in a typical patient if MRI is characteristic with dilated nerve sheaths, posterior globe flattening, and empty sella. We present two cases seen this year arguing otherwise.

Description of Case(s):

Case 1: A 21 y/o obese female had daily headache for several years. Exam showed enlarged blind spots and papilledema. MRI showed enlarged nerve sheaths, flattened posterior globes and normal sella without meningeal enhancement. Opening pressure was 38 cm; CSF RBC 0, WBC 325, Lymphocytes 85, monocytes 15; normal glucose, protein. Bacterial, fungal and TB studies were negative. Headache and papilledema improved with steroid treatment for chronic lymphocytic meningitis. Case 2: A 37 y/o obese female had headache, pulsatile tinnitus, and transient obscurations of vision. There was a vague history of numbness in fingers and toes and mild imbalance. Exam showed large blind spots and papilledema. MRI showed dilated nerve sheaths, flattened posterior globe, and empty sella. Administrative issues delayed her lumbar puncture for seven weeks. Opening pressure was 40 cm; CSF RBC 100, WBC 14, PMNs 1, lymphocytes 58, monocytes 41; protein 213; glucose 57. She subsequently developed CIDP and was treated with IVIg.

Conclusions, including unique features of the case(s):

Patient 1 had signs, symptoms, and MRI typical of IIH with no indication of any underlying disorder but turned out to have a chronic lymphocytic meningitis. Treatment resulted in improved symptoms and papilledema. Patient 2 had vague, unimpressive sensory symptoms when initially evaluated. After her lumbar puncture she had developed clear neurologic findings and would have been diagnosed with CIDP. Nevertheless, the diagnosis might have been further delayed had a lumbar puncture not been done as part of the initial evaluation.

References: None.

Keywords: High intracranial pressure/headache, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 131**Neuro-Imaging Evidence for Reversible Collapsibility of the Distal Transverse Sinuses in Spontaneous CSF Leak**

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Introduction:

Many patients who develop spontaneous CSF leaks have demographic similarities to IIH patients, and some patients develop symptoms of intracranial hypertension after leak repair. Spontaneous intracranial CSF leak is likely on the same spectrum disorder as idiopathic intracranial hypertension (IIH) and is sometimes a complication of definite IIH. Characteristic radiologic signs of IIH are common in spontaneous CSF leak patients, but little is known about changes in the distal transverse sinuses in patients with spontaneous CSF leak.

Description of Case(s):

A 48-year-old obese woman with a remote history of IIH presented with a low CSF pressure headache and was found to have a spontaneous right sphenoid CSF leak. Brain MRI/MRV were normal without stigmata of intracranial hypertension, and specifically no narrowing of the distal transverse sinuses. About 10 days after CSF leak repair, despite low-dose Diamox (250 mg BID) and a 5-pound weight loss, she developed symptoms of intracranial hypertension. Repeat MRI/MRV showed increased optic nerve angles OU with optic nerve sheath tortuosity and reduction in the caliber of the transverse sinuses bilaterally. Acetazolamide was increased (1500 mg/day) and she lost 30 lbs. Symptoms improved, and acetazolamide was successfully tapered off. Repeat MRV showed no stenosis of the distal transverse sinuses. She never developed papilledema.

Conclusions, including unique features of the case(s):

The MRI/ MRV imaging for this patient demonstrated the development of optic nerve sheath tortuosity and distal transverse sinus narrowing after repair of a spontaneous CSF leak, with the subsequent reversal of these findings after weight loss and treatment with Diamox, consistent with fluctuations in intracranial pressure. This case supports the connection between spontaneous CSF leak and IIH, and supports reversible collapse of the distal transverse sinuses as part of the pathophysiology of fluctuating intracranial pressure.

References: 1. Ducros A, Biousse V. Headache arising from idiopathic changes in CSF pressure. *Lancet Neurol.* 2015;14(6):655-68. 2. Bidot S, Saindane AM, Peragallo JH, Bruce BB, Newman NJ, Biousse V. Brain Imaging in Idiopathic Intracranial Hypertension. *J Neuroophthalmol.* 2015;35(4):400-11. 3. Holbrook J, Saindane AM. Imaging of Intracranial Pressure Disorders. *Neurosurgery.* 2017 ;80(3):341-354. 4. Hu R, Holbrook J, Newman NJ, Biousse V, Bruce BB, Qiu D, Oshinski J, Saindane AM. Cerebrospinal Fluid Pressure Reduction Results in Dynamic Changes in Optic Nerve Angle on Magnetic Resonance Imaging. *J Neuroophthalmol.* 2019;39(1):35-40. 5. Bidot S, Levy JM, Saindane AM, Oyesiku NM, Newman NJ, Biousse V. Do Most Patients With a Spontaneous Cerebrospinal Fluid Leak Have Idiopathic Intracranial Hypertension? *J Neuroophthalmol.* 2019 Feb 8. Epub ahead of print.

Keywords: High intracranial pressure/headache, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: This study was supported in part by an unrestricted departmental grant (Department of Ophthalmology) and by the NIH/NEI core grant P30-EY006360 (Department of Ophthalmology).

Contact Information: None provided.

Poster 132**Light After the Tunnel: Reversal of Fulminant IIH-Induced Severe Visual Loss, Diplopia and Hearing Loss**

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Introduction:

Idiopathic intracranial hypertension (IIH) is a rare disorder with significant morbidity, including rapid severe visual loss in fulminant IIH.

Description of Case(s):

A 22-year-old female, otherwise healthy on no medications, presented with a 1-month history of blurry vision and binocular oblique torsional diplopia. She endorsed muffled hearing, neck pain and pulsatile tinnitus but no headache. She was mildly overweight but had no other risk factors for IIH. Her review of systems was negative for meningitis, cerebral venous thrombosis, intracranial tumors, vasculitis and hypertension. She had excellent visual acuity and color vision with symmetric pupils bilaterally, but her visual fields by confrontation were severely constricted and a right RAPD was noted. Extraocular movements showed 50% abduction deficits bilaterally, with right inferior oblique overaction, and cover-uncover testing revealed bilateral CN-VI and right CN-IV palsy. The anterior segment and intraocular pressures were normal. The posterior segment exam showed severe optic nerve head swelling bilaterally, with hemorrhages, exudates, cotton wool spots, retinal and choroidal folds, venous dilation and vascular tortuosity, along with evidence of gliosis indicating chronicity. CN-V, VII and IX-XII were intact. CT head revealed partially empty sella with no space occupying lesion or hydrocephalus. Optic coherence tomography showed elevated RNFL and reduced GC-IPL (OS>OD). MRI/MRV showed vertical optic nerve tortuosity and transverse sinus stenosis, and DWI showed optic nerve ischemia bilaterally. Her audiogram revealed right mild low- and severe high-frequency sensorineural hearing loss. The patient was admitted for intravenous steroids, acetazolamide 4g and lumbar puncture which showed normal CSF composition but >50cmH₂O opening pressure, and she underwent optic nerve sheath fenestration. She stabilized, her visual fields improved and her diplopia, neck pain and pulsatile tinnitus resolved, with mildly reduced non-dysfunctional hearing.

Conclusions, including unique features of the case(s):

Recognition and immediate management can improve patients with fulminant IIH, including reversal of severe visual loss, diplopia and hearing loss in atypical presentations.

References: None.

Keywords: Pseudotumor cerebri, Magnetic resonance imaging, Visual fields, High intracranial pressure/headache, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 133**This ought to be a spinal reflex!**

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Introduction:

Spinal tumor is an important cause of bilateral papilledema and secondary intracranial hypertension. The proposed mechanisms include high protein content in cerebrospinal fluid(CSF) which impairs CSF absorption, mechanical obstruction to CSF drainage by the tumor or neoplastic arachnoiditis or meningeal tumoral infiltration.

Description of Case(s):

A 23-year-old obese female presented with headache, transient visual obscurations, pulse synchronous tinnitus, and intermittent binocular horizontal diplopia alongwith numbness in her legs and back pain over the last 2 months. On exam, vision was 20/30 OU, pupils were brisk and she was noted to have bilateral disc edema. Visual field testing revealed enlarged blind spots and superonasal field defect in both eyes. MRI of the brain and orbit with contrast and MR venogram (MRV) were normal. A lumbar puncture(LP) was schedule and there were four unsuccessful attempts. A fifth LP attempt now showed an opening pressure of 10 cm H2O, elevated CSF cell counts and protein. Patient was started empirically on Diamox. The patient then developed symptoms of cauda equina syndrome with acute onset rectal incontinence. An MRI of the lumbar spine showed a large intradural extramedullary mass with leptomeningeal spread along thoracic and cervical spinal cord. She underwent surgical resection of the tumor with L3-L5 laminectomy and tumor debulking. Biopsy revealed myxopapillary ependymoma, with immunohistochemistry positive for mucin (Periodic Acid Schiff) and S100.

Conclusions, including unique features of the case(s):

This young obese female presented with symptoms of raised intracranial pressure with normal MRI brain, orbits with normal MR Venogram of the brain. Multiple attempts at spinal tap were unsuccessful accounting for the false low opening pressure. Spinal fluid showed elevated protein and CSF pleocytosis. The patient then developed symptoms of cauda equina syndrome with acute onset rectal incontinence. MRI of the spinal axis revealed a myxopapillary ependymoma. Spinal tumor is an important cause of bilateral papilledema and secondary intracranial hypertension.

References: Marzban AN, Saxena A, Bhattacharyya D, Ivanov M. Hydrocephalus and Papilledema in Spinal Cord Tumors: A Report of Two Cases. Surg J (N Y). 2016;2(2):e51–e58. Published 2016 Jun 29. doi:10.1055/s-0036-1584584

Keywords: Tumors, High intracranial pressure/headache, Neuroimaging, Pseudotumor cerebri, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 134**Severe Intracranial Hypertension as a result of Topical Isotretinoin**

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Introduction:

Secondary intracranial hypertension occurs in patients taking oral isotretinoin and tetracyclines. In a small percentage of patients, this can be severe enough to cause irreversible optic nerve damage. It was previously thought that these medications had no cross-reactivity, thus patients with intracranial hypertension secondary to drug use have been prescribed medications from alternate drug classes. However, two cases demonstrate synergistic action between tetracycline and isotretinoin, even after the initial medications were withdrawn and visual function was recovered.

Description of Case(s):

Retrospective observational study. Two subjects were identified with drug-induced intracranial hypertension who presented to clinic with symptoms after using isotretinoin. Histories were reviewed for the beginning and end dates of precipitating therapy. Physical exam, OCT-RNFL, and Humphrey visual fields were compared at the time of diagnosis and after the patient was taken off Isotretinoin. One 19-year-old woman received treatment for acne with doxycycline and topical isotretinoin when she was referred by her PCP for elevated intracranial pressure and headaches. Imaging and examination revealed bilateral optic nerve swelling, which completely resolved after her medications were discontinued. Another 19-year-old woman was diagnosed with intracranial hypertension in 2014 after treatment with minocycline, which resolved after she stopped the medication. She presented to the ED in 2018 with severe papilledema, 6th nerve palsy and visual field changes requiring urgent surgical intervention. She improved after stopping isotretinoin which she has been taking for 1 year.

Conclusions, including unique features of the case(s):

These cases disprove the belief that patients who react to one precipitating cause of intracranial hypertension can be safely treated with alternate medication classes. For patients with refractory acne, the concern for potential vision loss in the context of prior drug-induced intracranial hypertension contraindicates the use of isotretinoin or tetracycline drugs. Furthermore, the studies show that the intracranial hypertension associated with these medications use is reversible after stopping the offending agent.

References: None.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 135**Recurrent Intracranial Hypertension in a Transgender Female-to-Male on Testosterone Therapy: A Case Report**

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Introduction:

Idiopathic intracranial hypertension (IIH) may lead to vision loss. Hormones, specifically androgens, may exert an effect on cerebrospinal fluid (CSF) regulation leading to increased intracranial pressure. We present a case of recurrent intracranial hypertension (IH) in a transgender female-to-male on testosterone therapy.

Description of Case(s):

A 24-year-old female, with a body mass index (BMI) of 37.3, presented with headaches, transient visual obscurations (TVOs), pulsatile tinnitus, Frisén 5 papilledema, and scotomas. She was diagnosed with idiopathic IH after a normal magnetic resonance imaging and venogram (MRI/V) of her brain, an elevated opening pressure of 27 cm. water, and normal CSF. Her IIH resolved with acetazolamide 4 g/day and an optic nerve sheath fenestration (ONSF) on the left. He then started testosterone therapy for female-to-male reassignment and was on this for 20 months when his headaches, pulsatile tinnitus, TVOs, and Frisén 3 papilledema recurred, at BMI of 31. Brain MRI/V were normal. Opening pressure was elevated at 31 cm. water. Free testosterone level was 177.8 picogram/ml (range 0.2-5), bioavailable testosterone 334.8 picogram/ml (range 0.5-8.5), total testosterone 511 picogram/ml (range 2-45). Acetazolamide 4 g/day did not improve the papilledema, thus a left ONSF was repeated. As of writing this abstract, 2 weeks after the repeat fenestration, there was no improvement in his papilledema, but the headaches and other symptoms have resolved. He has decided to continue testosterone therapy.

Conclusions, including unique features of the case(s):

We acknowledge that IIH may recur, but given his testosterone therapy for his gender reassignment, recurrent IH due to testosterone therapy should be strongly considered. This supports the theory that IIH may be due to hyper-androgenism and increased CSF testosterone. In-vitro studies in rats showed that testosterone increased CSF production. Thus, IIH patients undergoing hormonal therapy for gender reassignment should proceed with caution.

References: None.

Keywords: High intracranial pressure/headache, Pseudotumor cerebri, Optic nerve trauma and treatment

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 136**Delayed Onset Craniosynostosis Presenting as Idiopathic Intracranial Hypertension**

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Introduction:

Craniosynostosis refers to premature fusion of one or more cranial sutures, and typically presents with abnormal head shape within the first year of life. Management includes cranial vault reconstruction (CVR) or observation. Rarely, suture fusion may occur later in childhood or go unnoticed. These delayed cases may not be associated with changes in head shape and come to attention only because of an elevation in intracranial pressure. We present five children referred for presumed pediatric idiopathic intracranial hypertension (IIH) who fulfilled the modified Dandy criteria for the disease but were ultimately found to have sagittal craniosynostosis as the cause of papilledema. We review presenting symptoms and signs, associated radiological findings, management and clinical course.

Description of Case(s):

Age ranged from 3-6 years and 4/5 patients were male. Papilledema was noted on routine ophthalmological examination in all. One noted headaches and blurry vision and 1 horizontal diplopia. Three denied any symptoms. Automated perimetry performed in three patients showed enlarged blind spots and arcuate defects OU. All had either grade II or III papilledema and one had bilateral abducens palsies. MRI showed radiological papilledema in all but suggested craniosynostosis in only one. In the rest, craniosynostosis was diagnosed by CT. MRV showed venous sinus stenosis (VSS) in 3/5 and abnormal venous collaterals in one. Average opening pressure was 30.9 cm H₂O. Four underwent CVR with improvement in papilledema and one is under observation on acetazolamide. Intracranial hypertension persisted after CVR in one patient but improved following stenting of VSS.

Conclusions, including unique features of the case(s):

Occult delayed craniosynostosis may present in young children with isolated intracranial hypertension mimicking IIH. Poor response to acetazolamide should prompt consideration of the diagnosis, which may be confirmed with CT with 3D reconstruction, which has greater sensitivity than MRI. VSS does not preclude concomitant craniosynostosis and rarely, the two entities may both contribute to intracranial hypertension.

References: 1. Ortolani, Safier, Mitchell, Cleves-Bayon, Non-Syndromic Craniosynostosis Mimicking Primary Pseudotumor Cerebri Syndrome, Headache: the journal of head and face pain, 59(2): 264-265, 2019. 2. Bonfield, Tamber, Losee. Blindness from late presenting undiagnosed pancraniosynostosis mimicking pseudotumor cerebri, J Child Neurol, 29(8):NP24-7, 2014 3. Florisson, Barmpalios, Lequin, van Veelen, Bannink, Venous hypertension in syndromic and complex craniosynostosis: the abnormal anatomy of the jugular foramen and collaterals, J Craniomaxillofac Surg. 43(3):312-8. 2015

Keywords: Pseudotumor cerebri, Pediatric neuro-ophthalmology, High intracranial pressure/headache, Interventional neuroradiology

Financial Disclosures: The authors had no disclosures.

Grant Support: Supported by a departmental grant from Research to Prevent Blindness.

Contact Information: Marc Dinkin, MD- mjd2004@med.cornell.edu, 917-968-2358.

Poster 137**An Uncommon Cure For A Runny Nose**

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Introduction:

Spontaneous CSF leaks including CSF rhinorrhea are recognized but uncommon presentations of IIH. These leaks can recur if post-operative ICP is inadequately controlled, but no consensus exists on optimal ICP management following repair. We here describe a case of successful management of IIH in a patient who presented with CSF rhinorrhea and meningitis.

Description of Case(s):

A 20 year old female with a history of migraines noted new rhinorrhea for 1 month, and subsequently developed meningitis. A CT scan revealed an air-fluid level in her left sphenoid sinus with associated skull base defect and encephalocele. She was treated with antibiotics and sent for evaluation of IIH, but noted no typical symptoms. Her exam was notable for intact acuity, color plates, no RAPD and no evidence of disc edema or atrophy. Following repair of her skull base defect, she was started on acetazolamide, and 1 month following repair, her ophthalmologic exam was stable. As she tapered off acetazolamide she noticed new pulsatile tinnitus and a follow up exam revealed stable vision, but new grade 2 papilledema in both eyes. Her acetazolamide was restarted but she complained of side effects. A diagnostic venogram demonstrated elevated superior sagittal sinus pressures up to 32 mmHg and bilateral transverse sinus stenosis with predominantly right-sided drainage. She subsequently underwent right transverse sigmoid junctional stenting. Examination 2 weeks later revealed improvement in her symptoms and marked improvement in her papilledema.

Conclusions, including unique features of the case(s):

Diagnosing IIH in a patient with a spontaneous CSF leak can prove challenging as the leak can mask traditional signs and symptoms of elevated ICP. The diagnosis may reveal itself after repair, thus patients should be regularly monitored post-operatively by a neuro-ophthalmologist. For patients with persistent evidence of increased ICP who are unable to tolerate medical management, endovascular venous stenting may provide a viable treatment option.

References: 1. Bidot S, Levy JM, Saindane AM, Oyesiku NM, Newman NJ, Biousse V. Do Most Patients With a Spontaneous Cerebrospinal Fluid Leak Have Idiopathic Intracranial Hypertension? J Neuroophthalmol. 2019 Feb 8. 2. Iyer RR, Solomon D, Moghekar A, Goodwin CR, Stewart CM, Ishii M, Gailloud P, Gallia GL. Venous Sinus Stenting in the Management of Patients with Intracranial Hypertension Manifesting with Skull Base Cerebrospinal Fluid Leaks, World Neurosurg. 2017;106:103-112. 3. Kanagalingam S, Subramanian PS. Update on Idiopathic Intracranial Hypertension. Curr Treat Options Neurol. 2018;20(7):24. 4. Kenning TJ, Willcox TO, Artz GJ, Schiffmacher P, Farrell CJ, Evans JJ. Surgical management of temporal meningoencephaloceles, cerebrospinal fluid leaks, and intracranial hypertension: treatment paradigm and outcomes. Neurosurg Focus. 2012;32(6):E6 5.owler BK, Allan R, Parker G, Besser M. Br J Neurosurg. Pseudotumour cerebri, CSF rhinorrhoea and the role of venous sinus stenting in treatment. 2003;17(1):79-83.

Keywords: Pseudotumor cerebri, Interventional neuroradiology, High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: Unrestricted department grant from Research to Prevent Blindness.

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Poster 138**Idiopathic Intracranial Hypertension in the Setting of Hypertensive Emergency**

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Introduction:

Idiopathic intracranial hypertension (IIH) is typically slowly progressive allowing good response to treatment. Rarely, patients present with fulminant IIH in which vision loss is rapidly progressive. Fulminant IIH has been reported in association with malignant hypertension. Here we describe a case of fulminant IIH in a male patient with hypertensive emergency.

Description of Case(s):

A 45-year-old man with uncontrolled hypertension presented with two weeks of rapidly progressive bilateral visual decline. On presentation his systolic blood pressure was above 200 and he had acute kidney injury. Initial examination revealed vision of 20/40 in the right eye and 20/50 in the left eye with a right eye inferior paracentral scotoma. Fundus examination showed severe bilateral disc edema and hypertensive retinopathy. The patient had minimal IIH symptoms. Initially the working diagnosis was hypertensive retinopathy with neuroimaging findings concerning for low intracranial pressure including inferior displacement of the brainstem and cerebellar tonsils. After neuro-ophthalmic evaluation the case was felt to be more suggestive of increased intracranial pressure with imaging showing severe stenosis in the left transverse sinus and posterior flattening of the globes. Lumbar puncture was unsuccessful. The patient's hypertension was treated and he was initiated on high-dose acetazolamide. However, he had progressive vision loss and worsening of his kidney function. Therefore he underwent stenting of the left transverse sinus with postoperative improvement of his vision.

Conclusions, including unique features of the case(s):

Fulminant IIH when presenting with malignant hypertension can be a diagnostic dilemma and a treatment challenge. These patients may be misdiagnosed with hypertensive retinopathy and their comitant kidney dysfunction may limit treatment with acetazolamide. Prompt surgical management is often needed to prevent permanent vision loss.

References: None.

Keywords: Optic neuropathy, High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 139**Retinitis with Unilateral Abducens Nerve Palsy: a Rare Presentation of Cat Scratch Disease**

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Introduction:

Cat scratch disease (CSD) caused by *Bartonella henselae*, a zoonotic pathogen transmitted by cats, typically manifests with self-limiting fever and regional lymphadenopathy. Ocular CSD is reported in about 5% of cases and include: neuroretinitis, Parinaud oculoglandular syndrome and focal retinochoroiditis. Neurological complications are uncommon and include meningioencephalitis and encephalopathy. Peripheral facial nerve palsy is reported in a few CSD cases secondary to direct compression by the parotid gland. Bilateral abducens nerve palsy associated with CSD was reported in a single case secondary to increased intracranial pressure. We present a rare case of CSD with simultaneous bilateral retinitis and unilateral abducens nerve palsy.

Description of Case(s):

A 47-year-old previously healthy Caucasian woman presented with binocular diplopia and decreased vision. She reported recent contact with cats. Best corrected visual acuity was 20/40 in the right eye and 20/25 in the left eye. Examination revealed left abducens nerve palsy and white retinal lesions in both eyes, of which one was paramacular in the right eye. Optic nerve functions were normal and no papilledema was observed. Optical coherence tomography showed hyper-reflective lesions in the superficial retina, with intra-retinal fluid around the paramacular lesion. Visual field showed right central scotoma. Erythrocyte sedimentation rate was elevated. Cerebrospinal fluid analysis showed mononuclear pleocytosis and normal opening pressure. Brain magnetic resonance imaging was unrevealing, but chest computed tomography showed bilaterally enlarged axillary lymph nodes. Serological blood test was positive for *Bartonella henselae*. Her symptoms and imaging findings improved rapidly with oral corticosteroids and doxycycline treatment.

Conclusions, including unique features of the case(s):

Our case demonstrates a rare presentation of CSD with bilateral retinitis manifesting simultaneously with unilateral abducens nerve palsy. Increased intracranial pressure is unlikely to be the cause of her cranial neuropathy, given a normal opening pressure. Our patient's ocular motility rapidly improved with corticosteroids treatment, suggesting cranial mono-neuropathy of para-infectious origin.

References: 1. Habot-Wilner Z, Trivizki O, Goldstein M, Kesler A, Shulman S. Cat-scratch disease: ocular manifestations and treatment outcome. *Acta Ophthalmol.* ;96(4):e524-e532, 2018 2. Breitschwerdt E.B., Sontakke S, Hopkins S. Neurological Manifestations of Bartonellosis in Immunocompetent Patients: A Composite of Reports from 2005–2012. *Journal of Neuroparasitology.* Vol. 3 : 1-15, 2012. 3. Premachandra DJ, Milton CM. Cat scratch disease in the parotid gland presenting with facial paralysis. *Br J Oral Maxillofacial Surg.* 28: 413-415, 1990. 4. Ahmad A, Thavaratnam L, Ismail S, Wan Hazzabah W, Kandasamy R. Cat scratch disease presenting as increased intracranial pressure and aseptic meningitis. *Asian Pac J Trop Dis.* ;5(6): 500-501, 2015 5. Ksiai I, Abroug N, Mahmoud A, Zina S, Hedayatfar A. Update on *Bartonella* neuroretinitis. *J Curr Ophthalmol.* 6 ; 31(3): 254-261, 2019

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Ocular motility, Adult strabismus with a focus on diplopia

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 140**BILATERAL OPTICAL NEURITIS BY DENGUE. AN ATYPICAL CASE**

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Introduction:

Dengue is transmitted by a virus of the flaviviridae family, whose shedding is a hematophagous female arthropod called *Aedes aegypti* and *Aedes albopictus*; (2,3) Clinical presentation varies from febrile illness to hypovolemic shock. Symptoms appear 3-14 days after the sting characterized by fever, headache, myalgia, arthralgia, skin erythema and in more severe cases petechiae and mucosal bleeding (4,5). The diagnosis is clinical, but based on the guidelines of the World Health Organization, the detection of the virus by polymerase chain reaction or detection of antigens must be performed before the fifth day of the disease. There are few reports on the relationship of dengue infection and optic neuritis, which is considered an atypical manifestation of late onset, with a possible formation of auto-antibody, with serious sequelae, but with an adequate diagnosis and early intervention, visual sequelae may decrease (2).

Description of Case(s):

Male, 54 years old, from the Colombian coast, with a clinical picture consisting of headache, polyarthralgia and fever, sudden loss of left eye vision and vision of right eye shadows, associated with intense pain with eye movements; with positive IgM serology for dengue; leukopenia (4710) and thrombocytopenia (150000). Ophthalmic examination vision OD CD 1 mt OS CD 50 cm, normal anterior segment, intraocular pressure and normal fundus. Contrasting brain magnetic resonance: edema with optic nerve enhancement OS in the intracanal portion.

Conclusions, including unique features of the case(s):

There are case reports in the literature that relate dengue to ocular manifestations. Very little has been published about the relationship dengue and optic neuritis which is late in appearance by inflammatory immune mediation response and not a direct damage to the virus (2). Optic neuritis can be unilateral or bilateral. The estimated time between the onset of fever and eye symptoms can be understood in a period of 5 days to 7 months. The incidence report of optic neuritis is 0–1.5%. There is no specific antiviral treatment, only empirical use systemic steroids, since optic neuritis is an immune mediation process. So its use is justified.

References: 1. Farrar, Jeremy, y Patrick Manson, editores. *Manson's Tropical Diseases*. 23. ed, Elsevier Saunders, 2014:129-161, 2014. 2. Ng, Aaron W., y Stephen C. Teoh. Dengue Eye Disease. *Survey of Ophthalmology*, vol. 60, n.o 2, marzo de 2015, pp. 106-14. 3. Padilla JC, Lizarazo FE, Murillo OL, et al. Epidemiología de las principales enfermedades transmitidas por vectores en Colombia, 1990-2016: *Biomédica* 2017;37(Supl.2):27-40 4. Gulati, Sameer, et al. Ocular Manifestations of Dengue Fever. *Indian Journal of Medical Specialities*, vol. 7, n.o 4, octubre de 2016, pp. 155-59 5. Kapoor, Harpreet K., et al. Ocular Manifestations of Dengue Fever in an East Indian Epidemic. *Canadian Journal of Ophthalmology*, vol. 41, n.o 6, diciembre de 2006, pp. 741-46

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 141**Neurosyphilis with Concurrent Acetylcholine Receptor Binding Antibodies: Report of Two Cases**

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Introduction:

Development of neurologic autoimmunity following infectious disease is well known. Given recent advances in neuroimmunology and widespread availability of testing, there have been an increasingly large number of antibodies identified through investigations for a variety of clinical indications. We report two cases of neurosyphilis with concurrent acetylcholine (ACh) receptor binding antibodies without neuromuscular symptoms (false positive).

Description of Case(s):

Case 1: A 46 year-old man developed ankle pain followed by generalized arthralgia, night sweats, weight loss, vertigo, a rash on the trunk and hands, then blur in the right eye. Examination revealed visual acuity 20/80 OD, 20/30 OS, and optic disc edema OU. Reactive rapid plasma regain (RPR) and treponemal antibodies were positive; cerebrospinal fluid (CSF) pleocytosis of 23 nucleated cells was noted. Paraneoplastic testing revealed ACh receptor binding antibody of 1.08 nmol/L (reference OS. Laboratory investigation showed reactive RPR, CSF VDRL, and positive ACh receptor binding antibody at .44 nmol/L. N-type calcium channel antibodies and neuronal voltage-gated K⁺ channel antibodies were also positive at .05 and .13 nmol/L, respectively (reference < .03, .02 nmol/L). Neither patient had any historical or clinical features consistent with myasthenia gravis.

Conclusions, including unique features of the case(s):

We present two patients with neurosyphilis with concurrent positive AChR binding antibodies without features of myasthenia gravis. There are rare reports of neurologic autoimmunity following neurosyphilis, but the development of AChR antibodies has not been established in the literature. As previously proposed in other cases of neurologic autoimmunity, the mechanism may be molecular mimicry. The association illustrated by these cases provides a basis for further investigation in larger studies.

References: None.

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Neuro-ophth & systemic disease (eg, MS, MG, thyroid), Myasthenia, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease,

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 142**Inflammatory Orbital Apex Syndrome in the Setting of Recently Treated Herpes Zoster Ophthalmicus**

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Introduction:

Herpes Zoster Ophthalmicus (HZO) is a reactivation of varicella zoster virus (VZV) affecting the ophthalmic division of the trigeminal nerve. Rarely, VZV leads to severe sequelae such as Orbital Apex Syndrome (OAS), affecting cranial nerves II-VI.

Description of Case(s):

A 70-year old male, initially treated with a 2-day course of amoxicillin and oral steroids for left-sided sinusitis, presented with blisters on his nose and decreased vision. Exam was notable for rash in V1 distribution, 20/100 vision OS, positive Hutchinson's sign, "limited" ocular motility, and corneal dendrites. The patient was treated with IV acyclovir and piperacillin/tazobactam for 3 days and discharged on oral valacyclovir and erythromycin ointment. Over the next four weeks, he developed worsening left periorbital numbness, pain, and photophobia and presented to neuro-ophthalmology clinic. Vision OS was CF. There was complete third nerve palsy, partial sixth nerve palsy, and complete corneal anesthesia OS. Patient was admitted. Orbital CT ruled out orbital fungal superinfection. MRI of brain and orbit showed enhancement of the left optic nerve sheath extending to CNV into Meckel's cave. Lumbar puncture showed lymphocyte-predominant WBCs with negative HSV and VZV PCR. IV acyclovir and methylprednisone were started and PO antivirals were continued after discharge. One-week follow-up revealed VA OS 20/30 and significantly improved motility exam.

Conclusions, including unique features of the case(s):

This patient initially developed left-sided HZO after starting oral steroids. Despite treatment with antivirals, symptoms progressed. CSF analysis confirmed sterility. Only after treatment with intravenous steroids did the patient improve. Ironically, steroids were both the inciting factor and treatment. Judicious use of steroids for HZO is advised. The polyneuropathic presentation (CNII-VI) of this patient's illness suggests OAS, which was confirmed by MRI showing enhancement in the orbital apex. HZO related OAS is rare, having only been described in eight case reports in PubMed; this is the first case demonstrating involvement extending posteriorly to Meckel's cave.

References: None.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 143**Acute convergence and divergence paralysis in HIV-related rhombencephalitis.**

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Introduction:

Acute vergence disorders might be caused by CNS disease. Acute divergence paralysis has been associated with thalamic stroke, elevated intracranial hypertension, Miller-Fisher syndrome, and nucleus reticularis tegmenti pontis (NRTP) lesions, while acute convergence paralysis has been related to lesions in the corpora quadrigemina, cerebellar peduncles, rostral superior colliculus, third nerve nucleus, frontal eye field and the NRTP. Simultaneous acute divergence and convergence paralysis in the presence of CNS disease is extremely rare. We present a case of acute convergence and divergence paralysis, in a patient with an HIV-related pontine lesion involving the NRTP.

Description of Case(s):

A 50-year-old male recently diagnosed with HIV presented with a 2 week-history of horizontal binocular diplopia both at near and distance, dysarthria and imbalance. On exam, afferent visual function was normal OU. On video-oculography, there was left beating nystagmus on primary gaze, gaze-evoked nystagmus, and a hypoactive left head impulse. There was low gain horizontal pursuit and horizontal saccade hypometria. Saccade velocity was normal. Ocular ductions were full. Prism cover test showed a comitant 4-prism diopter exotropia at near and a comitant 4-prism diopter esotropia at distance. Fusional vergence amplitudes (cc) were completely lost both at distance (base-in) and near (base-out). Near point of convergence was 48cms. Beyond 54cms, diplopia would return (ie, the patient could maintain binocular single vision only between 48 and 54cms). Digital Hess Lancaster test at 30cms and 130cms from Hess screen replicated prism cover test findings. Brain MRI showed a diffuse pontine enhancing lesion involving the NRTP. The patient underwent additional extensive but unrevealing investigation. High dose IV steroids and empirical antibiotic and antiviral treatment showed no clinical benefit. The patient died 4 days later.

Conclusions, including unique features of the case(s):

Our findings support the hypothesis that the NRTP plays a role in the control of both convergent and divergent eye movements.

References: 1. Mays LE, Porter JD, Gamlin PD, Tello CA. Neural control of vergence eye movements: neurons encoding vergence velocity. J Neurophysiol. 1986. 2. Rambold H, Neumann G, Sander T, Helmchen C. Pontine lesions may cause selective deficits of "slow" vergence eye movements. In: Annals of the New York Academy of Sciences. ; 2005. 3. Thomson WD, Desai N, Russell Eggitt I. A new system for the measurement of ocular motility using a personal computer. Ophthalmic Physiol Opt. 1990

Keywords: Adult strabismus with a focus on diplopia, Neuro-ophth & infectious disease (eg, AIDS, prion), Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 144**Unilateral Disc Edema as the First Presentation of CML.**

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Introduction:

Papilledema has previously been reported as the initial presentation of chronic myeloid leukemia (CML). Reported cases of CML have demonstrated bilateral, symmetrically edematous optic nerves attributed to poor CSF absorption given the hyperviscosity induced by an elevated white blood cell (WBC) count. We report an interesting case of unilateral optic disc edema as the first presentation of CML approximately one year prior to substantial elevation of WBC count.

Description of Case(s):

An 18 year-old girl with history of polycystic ovarian syndrome and hypothyroidism presented with right eye pain, headaches, and vomiting found to have right optic disc edema in the setting of normal imaging results. The patient underwent lumbar puncture with cerebrospinal fluid (CSF) opening pressure of 21cm water, after which she was started on low-dose acetazolamide for presumed idiopathic intracranial hypertension (IIH). During that time, complete blood work evaluation showed WBC count of $13.2 \times 10^9/L$. Throughout the course of one year, the patient continued to have worsening headaches with transient episodes of vision loss and eventual bilateral optic disc edema in the setting of maximally up titrated acetazolamide therapy. Repeat imaging showed signs of elevated intracranial pressure, with repeat CSF opening pressure of 35cm water. Further investigation revealed WBC count $141.9 \times 10^9/L$. The patient then underwent bone marrow biopsy confirming CML, BCR-ABL1+, chronic phase, and was started on hydroxyurea and allopurinol with eventual transition to bosutinib. Acetazolamide was gradually tapered with interval improvement of bilateral optic disc edema.

Conclusions, including unique features of the case(s):

Complete blood count is an important diagnostic consideration in patients who present with unexplained worsening optic disc edema, but may not always initially confirm the diagnosis. Patients with CML may present with unilateral disc edema with symptoms mimicking IIH long before leukocytosis is seen. On the other hand, IIH may co-exist with CML, which requires careful evaluation and monitoring even in patients who achieve remission.

References: None.

Keywords: High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 145**A Case of Pituitary Non-Hodgkin's Lymphoma Presenting As Unilateral Optic Neuropathy**

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Introduction:

Primary lymphoma of the pituitary is a rare cause of a sellar mass in immunocompetent patients. Here, we present a case of unilateral optic neuropathy and enlarged pituitary gland as the presenting signs of Non-Hodgkin's Lymphoma.

Description of Case(s):

47-year-old woman with a history of seizures developed gradual painless blurry vision in the right eye. On examination, visual acuity was counting fingers in the right eye and 20/20 in the left eye. There was severe dyschromatopsia, a relative afferent pupillary defect and temporal optic atrophy in the right eye. Brain and Orbits MRI showed enlargement of the pituitary gland (16 mm in the largest dimension) and faint abnormal enhancement of the right optic nerve and meninges. Inflammatory, infectious and neoplastic work-up showed CSF with 8 white blood cells (100% lymphocytes), glucose 62, protein 79 and elevated IgG index. PET scan showed nonspecific hypermetabolic sub-centimeter lymph nodes. Endocrine derangements included mildly elevated prolactin at 41, hypogonadism, and a low-normal FT4. Without treatment, the sellar mass and enhancement decreased on Brain MRI. Visual acuity improved to 20/25 in the right eye. On follow up neuroimaging, the pituitary mass and areas of enhancement continued to fluctuate. Biopsies of hypermetabolic lymph nodes on PET scan were negative. Eventual pituitary biopsy revealed an atypical lymphoproliferative process. She underwent transsphenoidal subtotal resection and radiation to the pituitary. At a two-month follow up exam, visual acuity had improved in 20/20 in both eyes, smaller right RAPD, and mild right dyschromatopsia.

Conclusions, including unique features of the case(s):

In summary, this was an elusive case of right optic neuropathy and enlarged pituitary being the first manifestation of Non-Hodgkin's Lymphoma. Clinical examination, repeat head imaging and ultimately, biopsy were important for diagnosing this uncommon cause of optic neuropathy.

References: None.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 146**Vision Loss as the First Symptom of Metastatic Lung Adenocarcinoma in a Non-Smoking Asian Female**

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Introduction:

Fewer than 1 in 10 lung cancer patients present with orbital metastasis as the initial sign. We present a case of non-smoking previously healthy elderly Asian female with progressive vision loss who was found to have a large right orbital metastasis with intracranial extension from primary lung adenocarcinoma.

Description of Case(s):

A 68-year-old Asian female with no past medical history presented to our eye clinic complaining of worsening vision in her right eye over 6 months. Past surgical, social, and family histories were negative. She denied constitutional symptoms. Her right eye was bare light perception while her left eye was 20/50. There was an afferent papillary defect in her right eye, along nasal defect on visual fields to confrontation, and limited extraocular movement. Intraocular pressures were normal bilaterally. The right eye had 2+ posterior subcapsular cataract, a 0.3 cup-to-disc ratio, with 3+ disc pallor. Ishihara color plates were unable to be checked in the right eye, but were 13/14 in the left eye. The differential included ischemic, autoimmune, compressive optic neuropathies. ESR and CRP were normal. MRI of the orbits with and without contrast revealed a soft tissue mass in the upper right pterygopalatine region and involving the right greater wing of the sphenoid and orbital apex. Biopsy identified the mass as a metastasis from primary lung adenocarcinoma. Other metastases were found in her liver and bone.

Conclusions, including unique features of the case(s):

Patient underwent chemotherapy and whole brain radiation, but passed away three years after diagnosis. While smoking is one of greatest risk factors for developing lung adenocarcinoma, our patient was notably a non-smoker. Despite the size of her intracranial and orbital metastasis, her only complaint was progressive vision loss over 6 months. Careful optic nerve evaluation must be undertaken to determine other etiologies of vision loss, even in the presence of a significant cataract.

References: 1. Soeroso NN, Tarigan SP, Saragih W, Sari ND, Lubis N, Lubis H. Lung adenocarcinoma presenting with an orbital metastasis. *Respir Med Case Rep.* 2018 Aug 7;25:116-118. doi: 10.1016/j.rmcr.2018.08.005. eCollection 2018. PMID: 30112271 2. Sun L, Qi Y, Sun X, Yu J, Meng X. Orbital metastasis as the initial presentation of lung adenocarcinoma: a case report. *Onco Targets Ther.* 2016 May 9;9:2743-8. doi: 10.2147/OTT.S99583. eCollection 2016. PMID: 27274270 3. Zarogoulidis P, Terzi E, Kouliatsis G, Androuli S, Kontakiotis T, Zaramboucas T, Zarogoulidis K. Orbital metastases as the first manifestation of lung adenocarcinoma. *Case Rep Ophthalmol.* 2011 Jan 21;2(1):34-8. doi: 10.1159/000323945. PMID: 21347190

Keywords: Orbit/ocular pathology, Neuroimaging, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 147
Optic Glioma Gone Astray

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Introduction:

Malignant optic gliomas occur almost exclusively in adults but aggressive behavior has been reported by Bilgin et al in tumors that are histologically low grade (WHO I/II). Although it may occur with or without prior radiation therapy, intratumoral hemorrhage is rare.

Description of Case(s):

A 46 year old male was referred for decreased peripheral vision in the left eye. Exam showed a left afferent pupil defect, nerve fiber bundle defects on visual field, and sectoral optic disc pallor. MRI showed a large optic nerve mass and subsequent biopsy showed WHO grade 1 pilocytic astrocytoma. He was treated with radiation therapy. During week 5 of radiation therapy the patient developed decreased central vision and progressive proptosis. MRI showed enlargement of the heterogeneously enhancing mass, extending intracranially, with a rim of enhancement at the tumor margin. The patient subsequently underwent resection of the optic nerve from the globe to just short of the chiasm. Pathology showed numerous abnormally thickened blood vessels, pronounced vascular proliferation, and large regions of recent and remote hemorrhage infiltrating the intra-tumoral spaces and extending into the subarachnoid space. With the exception of a rim of enhancement of the tumor margin the enlarged tumor showed similar MRI characteristics, as seen initially, with markedly heterogenous enhancement, but was not characteristic of hemorrhage. Pathology remained grade I pilocytic astrocytoma.

Conclusions, including unique features of the case(s):

Uniquely, this is a rare case of WHO grade I pilocytic astrocytoma in an adult that exhibited indolent growth with progressive visual field loss for five years followed by rapid enlargement during radiation therapy due to intratumoral hemorrhage. Acute development of intratumoral hemorrhage, with or without prior radiation therapy, is rare. However, the hemorrhage within the tumor in our case was not well-delineated on magnetic resonance imaging, and this may represent a limitation of imaging in detecting this type of transformation.

References: None.

Keywords: Tumors, Orbit/ocular pathology, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 148**Duanes syndrome and a new neurodevelopmental disorder: the MED13L syndrome. A case report.**

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Introduction:

The Mediator complex is an important regulator of transcription. The activity of the Mediator complex is regulated by several subunits encoded by 26 genes in humans. In recent years, the Mediator complex subunit 13-like gene (MED13L MIM:608771) has been linked to congenital cardiac disease and neurodevelopmental delay.

Description of Case(s):

Our patient is a girl born at term. The child was born with a congenital diaphragmatic hernia known from prenatal ultrasounds. The child needed surgery for diaphragmatic repair at 2 days old. An atrial septal defect was observed but no intervention was needed. During the first months of life parents noticed intermittent strabismus and the patient was referred to our clinic at 18 months of age. At presentation, the child seemed to have normal visual behaviour and normal visual acuity in each eye tested with the Kasper-test which is a test based on preferential looking. The refraction was moderately hypermetropic(+2/+2). Fundoscopy was normal. Orthoptic evaluation revealed bilateral Duane syndrome with a bilateral abduction deficit and exophoria and hyperphoria. In the adducting eye, globe retraction, ptosis and upshoot was noted. In addition to Duane syndrome the patient had mild dysmorphic features and global developmental delay that prompted a genetic evaluation. Exome sequencing revealed a duplication in the MED13L gene resulting in a frame-shift error and a truncated protein with loss of normal function.

Conclusions, including unique features of the case(s):

The understanding of the clinical spectrum associated with MED13L syndrome is incomplete. There are only a few articles presenting in-depth phenotypic descriptions of patients, but intellectual disability, speech delay and facial dysmorphic features appear to be common. Duane syndrome have been previously reported in 3 cases which is interesting given the rarity of both Duane syndrome and MED13L syndrome. This case may contribute to our knowledge of symptoms associated with the MED13L syndrome.

References: Adegbola, Musante, Callewaert et al. Redefining the MED13L syndrome, *European Journal of Medical Genetics*, 23, 1308–1317, 2015 Snijders Blok, Hiatt, Bowling et al. De novo mutations in MED13, a component of the Mediator complex, are associated with a novel neurodevelopmental disorder, *Human Genetics*, 137, 375-388, 2018 Tørring, Larsen, Brasch-Andersen et al. Is MED13L-related intellectual disability a recognizable syndrome?, *European Journal of Medical Genetics*, 62, 129-136, 2019

Keywords: Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 149**A Pediatric Case of Tolosa-Hunt Syndrome**

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Introduction:

Tolosa-Hunt syndrome (THS) is a rare condition characterized by episodic, painful ophthalmoplegia secondary to idiopathic inflammation of the cavernous sinus, orbital apex, or superior orbital fissure, resulting in paralysis of the third, fourth, and/or sixth cranial nerves(2,3). The incidence of THS in the United States is one case per million people annually, with a mean onset of 38-41 +/- 14-16 years (1). Only 18 pediatric cases have been reported in the literature and there remains controversy regarding diagnostic approach and treatment strategies in children. We aim to offer an additional successful therapeutic approach.

Description of Case(s):

We present an eight-year-old Hispanic female with no significant past medical history who presented with a five-day history of right eye pain with extraocular movements, periorbital edema, and purulent white drainage that progressed to painful ophthalmoplegia, photophobia, blurry vision and horizontal diplopia. There was no previous history of trauma, rashes, headaches, or recent illnesses. Examination revealed right upper eyelid ptosis, impaired adduction, supraduction, and infraduction, with a 6mm dilated pupil with sluggish reaction to light. These findings were consistent with a pupil-involving right cranial nerve three palsy. Magnetic resonance imaging revealed inflammation of the right cavernous sinus with asymmetric thickening and enhancement, resulting in severe narrowing of the cavernous and petrous portions of the right internal carotid artery. Extensive rheumatologic, neurologic, oncologic, and infectious workup was negative. The patient was started on a five-day course of high dose intravenous methylprednisolone, 1 gram/day, and oral aspirin 81mg with resultant improvement in her motility deficit. She was subsequently transitioned to a prolonged oral steroid taper beginning with 100mg/day, decreasing by 20 mg per week until successfully being tapered off.

Conclusions, including unique features of the case(s):

Due to the rarity of this syndrome, we aim to shed light on diagnostic approaches and management options for THS in children, given the lack of consensus within the literature.

References: 1. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. Cephalalgia. 2018;38(1):1-211. 1. Pérez, Carlos A., and Monaliza Evangelista. "Evaluation and Management of Tolosa-Hunt Syndrome in Children: A Clinical Update." *Pediatric neurology* 62 (2016): 18-26. 2. Tolosa Hunt Syndrome. NORD. March 30, 2012; Retrieved from <http://www.rarediseases.org/rare-disease-information/rare-diseases/byID/399/viewAbstract>.

Keywords: Pediatric neuro-ophthalmology, Ocular motility, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: There is no grant support for this abstract submission.

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Poster 150**Splenium Involvement in Oculodentodigital Dysplasia**

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Introduction:

Oculodentodigital Dysplasia (ODDD) is a rare autosomal dominant disorder causing abnormalities in the face, eyes, skeleton, and nervous system and is associated with mutations in GJA1. Magnetic resonance imaging (MRI) typically demonstrates hyperintensity on T2 weighted imaging in the parieto-occipital white matter and hypointensity of the subcortical grey matter structures. Computed tomography has described calcifications of the basal ganglia. We present a novel finding not described previously which is the involvement of the splenium of the corpus callosum.

Description of Case(s):

A mother and daughter presented for evaluation of a gait disturbance. The mother complained of gait difficulties, but her gait was initially clinically normal but over two years follow up demonstrated mild spasticity. The daughter had a severely spastic gait. Both had skeletal abnormalities of the 5th digits with normal corneae. Magnetic resonance imaging demonstrated white matter abnormalities in the parieto-occipital region but also the splenium of the corpus callosum in both patients. Both carried the GJA1 mutation of c.443G>A; p.Arg148Gln. The mother's brother's grandson also had the disease genetically confirmed.

Conclusions, including unique features of the case(s):

We present a novel finding not described previously which is the involvement of the splenium of the corpus callosum. Review of the medical literature however reveals two cases previously published documenting parieto-occipital white matter lesions, but splenium involvement was also demonstrated in these two cases and unfortunately ignored. The mother initially presented with normal gait and a prior abnormal MRI which supports the notion that neuroimaging abnormalities in ODDD predate clinical symptomatology. Genetic anticipation has also been previously suggested which is present in this cohort.

References: 1) Loddenkemper T, Grote K, Evers S, Oelerich M, Stogbauer F. Neurological manifestations of the oculodentodigital dysplasia syndrome. J Neurol. 2002; 249: 584-595. 2) Park KW, Ryu HS, Kim J, Chung SJ. Oculodentodigital Dysplasia Presenting as Spastic Paraparesis: The First Genetically Confirmed Korean Case and a Literature Review. J Mov Disord. 2017; 10(3): 149-153.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Demyelinating disease, Neuroimaging, Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 151**Isolated Subdivision Third Nerve Palsies in Pediatric Autoimmune Disease**

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Introduction:

Oculomotor nerve palsies in a pediatric population have a wide range of etiologies, most commonly congenital and traumatic.¹ Partial oculomotor palsies represent 60% of all oculomotor nerve palsies in pediatric patients.¹ However, reports of pediatric oculomotor division palsies of an autoimmune etiology are rare.² Here, we describe two cases of isolated pediatric oculomotor division palsies, one superior and one inferior, of an autoimmune etiology.

Description of Case(s):

The first patient, at age 9, developed ptosis and limitation of elevation of her left eye without anisocoria, consistent with a superior division oculomotor nerve palsy. MRI demonstrated multiple foci of T2/FLAIR hyperintensity without enhancement and without oculomotor nerve or brainstem involvement. Workup was notable for multiple autoimmune markers including ANA, anti-dsDNA, rheumatoid factor, and anti-Ro IgG (SSA). Salivary biopsy was consistent with Sjogren's syndrome. Treatment with oral prednisone improved her chin-up posture and ptosis but left her with a residual esotropia and left hypotropia that have been stable over 8 years. The second patient, at age 4, developed vision changes, anisocoria, and eye pain. On exam she had right eye mydriasis, loss of accommodation, and impaired infraduction/adduction, consistent with inferior division oculomotor nerve palsy. MRI brain demonstrated edema, and enhancement of the inferior and superior branches of the right oculomotor nerve. Workup was notable for positive rheumatoid factor, ANA, and thyroid peroxidase antibody with subclinical hypothyroidism. Treatment included IV steroids with steroid taper, IVIG, plasma exchange, and amblyopia prophylaxis. Four months after symptom onset patient's motility and stereopsis had improved with a residual exotropia at near.

Conclusions, including unique features of the case(s):

We describe two unique cases of isolated subdivision palsies of the oculomotor nerve involving inflammatory etiologies in pediatric patients. For both patients, these neuropathies caused their presenting symptoms ultimately uncovering systemic autoimmune conditions.

References: 1. Schumacher-Feero LA, Yoo KW, Solari FM, Biglan AW. "Third cranial nerve palsy in children." *Am J Ophthalmol.* 1999 Aug;128(2):216-21. 2. Go T. "Partial oculomotor nerve palsy associated with elevated anti-galactocerebroside and anti-GM1 antibodies." *J Pediatr.* 2000 Sep;137(3):425-6.

Keywords: Pediatric neuro-ophthalmology, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging, Ocular Motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 152**Comparative Changes In The Vestibular Response Following Horizontal Pursuit And Saccadic Eye Movements**

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¹*Biomedical Engineering Program, University of Manitoba, Winnipeg, Canada,* ²*Section of Neurology, Department of Medicine, University of Manitoba, Winnipeg, Canada*

Introduction:

The role of the vestibular system in generating and calibrating eye movement is well-established. However, the reciprocal effect of eye movements on vestibular system is less known. We investigated the influence of visual/ocular information on vestibular efferents and afferents.

Description of Case(s):

Vestibular responses to horizontal smooth pursuit and saccades were measured in nineteen healthy individuals. We used VR environment and a headset to show the stimuli. To generate the pursuit eye movement, a green circle moved with the angular velocity of 22°/sec from left-to-right across a grey background. For the saccadic eye movement, the target moved horizontally between two fixed points located 50 degrees apart (angular velocity > 100°/sec). Vestibular responses were recorded bilaterally and simultaneously using Electrovestibulography (EVestG) prior, during and within 30 seconds of cessation the eye movements.

Conclusions, including unique features of the case(s):

Pursuit and saccadic eye movements resulted in similar effect on the vestibular responses generating smaller action potential (AP) area on the ear contralateral to the direction of the eye movement (p<0.05) showing longer time intervals between the hypothesized efferent mediated afferent detected FPs bilaterally, compared to those spontaneously recorded as backgrounds (intervals were calculated between each 33 detected vestibular firings). To the best of our knowledge this is the first report that shows pursuit and saccade eye movements can selectively suppress the activity of the brainstem and peripheral vestibular systems unilaterally. The psychological role of this suppression is unclear but it is conceivable that eye movement calibrates the vestibular system for a possible future vestibular stimulation through head or body movements e.g. reducing VOR response if the head movement follows a gaze.

References: None.

Keywords: Ocular motility, Vestibular, metastatic carcinoma

Financial Disclosures: The authors had no disclosures.

Grant Support: NSERC (# 950-229260)

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Poster 153**In Eye pain, confocal microscopy can come to the rescue**

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Introduction:

Hydrocarbons are soluble in lipids and may cross cellular membranes without direct signs of damage. We describe how ocular pain may result from a chemical injury that did not produce initial corneal ulceration.

Description of Case(s):

A 39 year old healthy man, presented after exposure to alkylate while wearing contact lenses after his eyes had been flushed with saline. His Vision OD 20/40 OS 20/25. SLE showed diffuse injection of the conjunctiva, but no corneal defects were described. Corneal sensitivity was normal OU. On follow up visits patient consistently reported worsening eye pain and severe photophobia and he developed severe inferior punctate keratitis in both eyes. Severe eye pain and photophobia resistant to management even after punctal plugs continued. Corneal expert diagnosed severe dry eyes and meibomitis. Keratography showed left eye with mild inferior paracentral steepening, otherwise normal. Patient started on Doxycycline, Gabapentin, Fluorometholone and plasma tears with no improvement in eye pain. At this time specular microscopy of corneas showed tortuous stromal nerve with increased branch points and reduction in the number of keratocytes consistent with ocular neuropathic pain. Patient was treated with amniotic membrane contact lens with marked improvement of all symptoms.

Conclusions, including unique features of the case(s):

In our patient ocular neuropathic pain was diagnosed, a condition where there is response to normally non-painful stimuli due to damage to corneal nerves resulting in aberrant regeneration and upregulation of nociceptors. The diagnosis was confirmed with confocal microscopy and this has been associated with allodynia and photoallodynia as presented in our patient. Confocal microscopy is an important tool to define damage in small fibers, allows in-vivo imaging and a direct examination of unmyelinated nerve fiber damage in a non-invasive technique. Given the lipophilic nature of the agent, corneal nerve damage without initial signs of injury was a possibility since the compound can pass through normal tissue.

References: 1. American Academy of Ophthalmology. Pain in Eye (<https://www.aao.org/eye-health/symptoms/pain-in-eye-list>). American Academy of Ophthalmology. 2. Aggarwal S et al; Autologous Serum Tears for Treatment of Photoallodynia in Patients with Corneal Neuropathy: Efficacy and Evaluation with In Vivo Confocal Microscopy. Ocul. Surf. 2015. 3. Singh, P., Tyagi, M., Kumar, Y., Gupta, K. K., & Sharma, P. D. (2013, May). Ocular chemical injuries and their management. Retrieved October 14, 2019, from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3779420/> 4. Eguchi H, Hiura A, Nakagawa H, Kusaka S, Shimomura Y. Corneal Nerve Fiber Structure, Its Role In Corneal Function, And Its Changes In Corneal Diseases. BioMed Research International. Volume 2017, Article ID 3242649, 15 pages. Retrieved October 14, 2019, from <https://doi.org/10.1155/2017/3242649> 5. Müller L J, Marfurt C F, Kruse F, Tervo T MT. Corneal nerves: structure, contents and function. Experimental Eye Research 2003; 76:521-542.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Orbit/ocular pathology, Miscellaneous,

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 154**Hemi-Cloverleaf Pattern on Static Perimetry as an Indicator of Posterior Cortical Atrophy**

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Introduction:

Posterior cortical atrophy (PCA) is a rare, progressive, degenerative disease that initially manifests with visual dysfunction. Since its description over thirty years ago, debate remains over whether this is a variant of Alzheimer disease or a distinct entity, with pathology similar to Alzheimer's. Initially characterized by progressive impairment in many aspects of cortical visual function, in the early stages there is relative sparing of memory and executive function. Patients commonly present with non-descript visual complaints, often resulting in delayed diagnosis. On automated (Humphrey) visual field testing a majority demonstrate some degree of homonymous deficiency. The cloverleaf pattern on automated (Humphrey) visual fields is recognized as artifact of non-physiologic vision loss or visual inattention. This artifact results from the algorithm commonly used in static perimetry. We report a similar pattern where the affected field demonstrates a superimposed hemi-cloverleaf pattern from patients affected by PCA.

Description of Case(s):

Observation was made during the evaluation of three patients recently diagnosed with PCA. Chart review was conducted to determine initial visual field pattern and accuracy of diagnosis. Neuro-imaging was reviewed to ensure no alternate etiology for observed visual field defects. All patients were seen in the neuro-ophthalmic clinic and alternative ocular pathology to account for the visual field findings has been excluded. We identified individuals with new diagnosis of likely PCA, with supporting evidence to include neuro-psychiatric testing (3/3), MRI imaging (3/3), neuro-ophthalmologic examination (3/3) excluding alternate causes, and FDG-PET (2/3). All three were seen to have homonymous visual field defects with artifact in the affected field consistent with a cloverleaf pattern.

Conclusions, including unique features of the case(s):

PCA should be suspected in patients presenting with a hemi-cloverleaf pattern superimposed on their homonymous hemi-field defects that is not otherwise explained by an obvious lesion of the visual cortex.

References: 1. Pelak VS, Smyth SF, Boyer PJ, Filley CM. Computerized visual field defects in posterior cortical atrophy. *Neurology*. 2011 Dec 13;77(24):2119-22. 2. Tang-Wai DF, et al. Clinical, genetic, and neuropathologic characteristics of posterior cortical atrophy. *Neurology*. 2004 Oct 12;63(7):1168-74. 3. Crutch SJ, et al. Posterior Cortical Atrophy. *Lancet Neurol*. 2012 February; 11(2): 170–178. 4. Maia da Silva MN, Visual Dysfunction in Posterior Cortical Atrophy. *Front Neurol*. 2017; 8: 389. 5. Frisen L, Identification of functional visual field loss by automated static perimetry. *Acta Ophthalmol*. 2014; 92: 805–809.

Keywords: Visual fields, Higher visual cortical functions, Perimetry, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 155
Nest of Evil

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Introduction:

83-year-old Caucasian female presented with headaches, fatigue and vision loss in the right eye. PMH is significant for HTN, HLD, meningioma, lumpectomy and radiation for breast cancer 1994&1998. No history of smoking. Meds: lisinopril, atorvastatin and metoprolol. ROS: fatigue, dizziness, balance problem and anxiety. Her recent MRI showed a plaque-like homogeneous enhancing dural based mass at the planum sphenoidale with involvement of left cavernous sinus measuring 3.6x 1.8x 3.8 cm only 0.2cm increase in each dimension compare to the imaging 6 months prior. BCVA 20/150, 20/40, 3+ RAPD OD, diffuse optic atrophy OD, sup optic atrophy OS. Visual field showed generalized constriction OD, inferior arcuate defect OS. OCT optic nerve: diffuse RNFL thinning OD, superior thinning OS. MRI orbit revealed involvement of orbital apex on the right side. She underwent surgical resection of tumor. Tumor progression in 3 months caused third N. palsy and vision loss on the left eye. VA 20/250 OD, LP OS. Pathology read as malignant tumor.

Description of Case(s):

The patient had vision loss despite "stable meningioma" on the brain MRI. The tumor started to grow 3 months after surgery. Pathology reported poorly differentiated adenocarcinoma. Molecular testing pointed towards head and neck (90%) or breast (6%) adenocarcinoma. The patient had breast cancer treated by lumpectomy and radiation 20 years ago. The oncology work up did not reveal any tumor in the breast or salivary gland. The patient deferred treatment and passed away 3 month later.

Conclusions, including unique features of the case(s):

Tumor to tumor metastasis in Meningiomas by adenocarcinoma is a rare phenomenon. The hypervascularity and low metabolic activity of meningioma makes it an ideal nest for metastatic cells. The most common reported tumor to tumor intracranial metastases are from primary breast and lung neoplasms. This is the first report of Salivary gland tumor metastasizing to meningioma.

References: 1. Syed, Karambizi, Baker, Groh, Toms. A Comparative Report on Intracranial Tumor-to-Tumor Metastasis and Collision Tumors. World Neurosurg. 116, 454-463, 2018. 2. Rao, Giordano, Liu, McCutcheon. The association of breast cancer and meningioma in men and women. Neurosurgery. 65, 483-9, 2009 3. Caroli, Salvati, Giangaspero, Ferrante, Santoro. Intrameningioma metastasis as first clinical manifestation of occult primary breast carcinoma. Neurosurg Rev. 29, 49-54, 2006. 4. Farrag, Ansari, Ali, Sunbuli, Kassem, Al Hamad. Intracranial meningioma as primary presentation for an undiagnosed collision metastatic breast cancer: Case report and literature review. Mol Clin Oncol. 8, 661- 664, 2018. 5. Pham, Kim, Nguyen, Bota, Kong. Intracranial meningioma with carcinoma tumor-to-tumor metastasis: two case reports. CNS oncology, Vol.7(2),2018

Keywords: Tumors, Orbit/ocular pathology, Optic neuropathy, Ocular motility, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 156**An atypical case of Lyme Neuroborreliosis**

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Introduction:

Lyme neuroborreliosis in adults most commonly affects the facial cranial nerve but oculomotor or trigeminal nerve palsies have been reported in the medical literature. Interestingly, there is one case of an adult patient who was diagnosed with Lyme disease, and presented with isolated trochlear nerve palsy and normal MRI of the brain.

Description of Case(s):

A 24-year-old right-handed woman presented to the Neuro-Ophthalmology department with acute binocular diplopia when looking down and to the left. Ophthalmic examination was significant for visual acuities of 20/20 OU. The neuro-ophthalmic examination showed a right hypertropia in left gaze, downgaze and right head tilt, conforming to the pattern of a right fourth nerve palsy. In addition, she had subjective and objective excyclotorsion OD. No ocular signs of myasthenia, thyroid eye disease or other ocular or systemic complaints were elicited. An MRI of the brain with and without contrast was notable only for an incidental pituitary cyst, and left-sided paranasal sinus disease with normal orbits and brain parenchyma. MRA of the brain was unrevealing. However, a repeat MRI of the brain and orbit with high-resolution T2 and post-contrast T1 sequences of the skull base and cranial nerves demonstrated enhancement along the course of the right 4th cranial nerve at the right tentorium in the region of the trochlear groove and the right trochlear cistern. Laboratory testing for Lyme disease was positive, with 5 IgG bands and 0 IgM bands. The patient was started on 30-days course of doxycycline and symptoms completely resolved within 2 weeks.

Conclusions, including unique features of the case(s):

Lyme disease with isolated trochlear nerve palsy can be a diagnostic challenge due to absence of more typical neuroborreliosis symptoms. This is the first case of Lyme in the medical literature presenting with fourth intracranial nerve enhancement on MRI of the brain.

References: 1. Hildenbrand P, Craven DE, Jones R, Nemeskal P. Lyme neuroborreliosis: Manifestations of a rapidly emerging zoonosis. *Am J Neuroradiol.* 2009. doi:10.3174/ajnr.A1579 2. Bababeygy SR, Quiros PA. Isolated trochlear palsy secondary to Lyme neuroborreliosis. *Int Ophthalmol.* 2011. doi:10.1007/s10792-011-9482-4 3. Bunch PM, Kelly HR, Zander DA, Curtin HD. Trochlear groove and trochlear cistern: Useful anatomic landmarks for identifying the tentorial segment of cranial nerve IV on MRI. *Am J Neuroradiol.* 2017. doi:10.3174/ajnr.A5117

Keywords: Lyme, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 157**Bilateral Acute Retinal Necrosis After HSV Encephalitis Post Craniotomy For Planum Meningioma**

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Introduction:

Acute retinal necrosis (ARN) is a rapidly progressive condition causing vitritis, occlusive vasculitis, and progressive peripheral necrotizing retinitis. Infectious agents include herpes simplex virus (HSV), herpes zoster virus (VZV), and cytomegalovirus (CMV). The pathway through which the virus gains access to the retina has not been completely elucidated. We present a case of bilateral ARN after HSV encephalomeningitis which occurred shortly after routine craniotomy for a planum meningioma resection suggesting a mode of transmission from the central nervous system via blood flow or directly through the optic nerves into the retina.

Description of Case(s):

A 49-year-old female with a history of a planum meningioma resection discovered after left sided compressive optic neuropathy, presented with three weeks of bilateral decreased visual acuity. Six weeks previously, she had undergone meningioma resection and after the third post-operative week, she was readmitted with mental status changes and diagnosed with HSV encephalomeningitis treated with intravenous acyclovir. Vision at presentation was light perception in both eyes. Examination showed bilateral anterior uveitis, and vitritis. Posteriorly, nasal retinal whitening and retinal detachments were present in both eyes with left optic nerve pallor. Given poor acuity in the left eye from prior compressive optic nerve atrophy, the decision was made to surgically intervene to repair the detachment in the right eye. Both eyes were treated with intravitreal ganciclovir. Polymerase chain reaction testing of vitreous sampling was positive for HSV2 and negative for HSV1, VZV, and CMV.

Conclusions, including unique features of the case(s):

This is a unique case of bilateral ARN in a patient with recent HSV encephalomeningitis that occurred after routine craniotomy for a planum meningioma. This case highlights the importance of suspecting post-operative CNS infection with consequent eye involvement even in an immune competent patient to allow for aggressive and prompt treatment in order to reduce the risk of vision loss.

References: None.

Keywords: Optic neuropathy, Neuro-ophth & infectious disease (eg, AIDS, prion), Neuroimaging, Tumors, Pupils retina

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 158**Successful Treatment of Multiple Sclerosis Associated Panuveitis with Rituximab**

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Introduction:

The most common ocular manifestation of multiple sclerosis (MS) in the eye is optic neuritis, but MS may much more rarely be associated with uveitis or panuveitis. Treatment of uveitis typically includes corticosteroids or TNF- α inhibitors. Rituximab (RTX), is an anti-B cell antibody that may be used as a treatment for MS, but its use in uveitis is limited.

Description of Case(s):

A 45-year-old female with a history of recurrent bilateral panuveitis, previously treated with topical, intravitreal, and sub-Tenon's corticosteroids, presents with 2 days of injection and decreased vision OU. Visual acuity was 20/200 and IOP 38 OD, 20/25 and IOP 49 OS. Slit lamp exam revealed injection with 1+ flare and 360 degrees of posterior synechiae OU. Fundus exam was limited OD and revealed foveal mottling with focal areas of peripheral depigmentation OS. The patient was diagnosed with uveitic glaucoma and was started on topical therapy. Infectious workup was negative. Further imaging revealed leakage at the optic nerve and inferotemporal macula and subretinal fluid OS. Prior to planned initiation of adalimumab, an MRI brain with contrast was obtained, which showed FLAIR signal hyperintensities consistent with a demyelinating process, and the patient was referred for further evaluation by neurology with an eventual diagnosis of MS. Treatment with rituximab was initiated by neurology. After 2 infusions of rituximab, subsequent ophthalmic examination and imaging demonstrated resolution of intraocular inflammation, subretinal fluid, and vascular leakage. The patient underwent synechiolysis and cataract extraction OD with a resultant visual acuity of 20/20.

Conclusions, including unique features of the case(s):

Panuveitis is rarely associated with MS, but in this case preceded the diagnosis of systemic disease. RTX it is not routinely used in the treatment of uveitis, however there are prior reports of its successful use in non-infectious disease. This appears to be the first report of case of MS-associated panuveitis successfully treated with primary RTX.

References: Lasave AF, You C, Ma L, et al. Long-Term Outcomes of Rituximab Therapy in Patients with Noninfectious Posterior Uveitis Refractory to Conventional Immunosuppressive Therapy. *Retina* 38(2):395-402, 2018. Smith JR, Stempel AJ, Bharadwaj A, Appukuttan B. Involvement of B cells in non-infectious uveitis. *Clin Transl Immunology* 5(2):e63, 2016. Salzer J, Svenningsson R, Alping P, et al. Rituximab in multiple sclerosis: A retrospective observational study on safety and efficacy. *Neurology* 87(20):2074-81, 2016.

Keywords: Demyelinating disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Pupils Retina

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 159**Cerebral Venous Thrombosis: Rare Complication of High Dose Corticosteroids in a Patient with IRVAN Syndrome**

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Introduction:

Cerebral venous thrombosis (CVT) after undergoing lumbar puncture (LP) with no prothrombotic risk has been previously reported, attributing its effect to increased venous stasis in dural sinuses along with venodilation. We described a case in which high-dose steroids along with LP may play a role in the development of CVT.

Description of Case(s):

28-year-old woman with a history of left optic neuritis presented with progressive right vision loss and headache. Magnetic resonance (MR) imaging showed T2 hyperintensities in the right corona radiata. Cerebrospinal fluid and serum studies were unremarkable. She was discharged on day 5 after a course of high-dose intravenous methylprednisolone (IVMP) however returned on day 8 with recurrent symptoms. MR venogram showed transverse and superior sagittal sinus thromboses. LP revealed an opening pressure of 60cm H₂O. Patient was placed on heparin infusion. Extensive work up was unremarkable except for decreased Protein S and elevated Factor VIII/IX. Fibrinogen was 403 mg/dL. Angioplasty of venous sinus without stent placement was performed. Repeat MR imaging redemonstrated improved areas of nonocclusive thrombus. On day 13, patient was given 1 gm IVMP for persistent headaches. Follow up MR venogram showed recurrence of dural sinus thrombosis. Fibrinogen levels were 525 mg/dL. Ophthalmologic evaluation showed bilateral ischemic optic neuropathy with numerous macroaneurysms, concerning for IRVAN (idiopathic retinitis, vasculitis, aneurysms, and neuroretinitis). Optic angiogram revealed three aneurysmal dilations in right retinal arterioles, no leakage of fluorescein at either of the optic nerve heads. Three months later, right-sided vision improved mildly; and repeat imaging showed interval decrease in venous thrombus.

Conclusions, including unique features of the case(s):

This case suggests the possible procoagulant role of high-dose steroids, especially in patients during a pro-inflammatory state. The use of steroid-sparing agents could be an important aspect to consider to avoid such adverse effect in high risk patients.

References: None.

Keywords: Optic neuropathy, Vascular disorders, Interventional neuroradiology, Neuroimaging, High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 160**A case of presumed sildenafil induced maculopathy**

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Introduction:

Ophthalmic effects of pulmonary hypertension and phosphodiesterase (PDE) inhibitors are unclear. PED-5 inhibitors are known to be associated with non-arteritic anterior ischemic optic neuropathy. Its association with maculopathy has not been well-studied. We report a case of presumed sildenafil induced maculopathy in a female patient with pulmonary hypertension.

Description of Case(s):

A 47-year-old female with pulmonary hypertension presented with vision changes for 1 year after initiating sildenafil. Her vision was a "total blur" with black dots all over the visual fields. She had no double vision, sudden onset vision loss, pain with eye movement, or transient visual obscuration. The visual changes worsened with increased sildenafil dose. On exam, her best-corrected visual acuity was 20/30 in each eye. Intraocular pressures were 17 mmHg in each eye. She had normal color and stereo perception. The pupil exam was normal without relative afferent pupillary defect. The anterior segment showed no signs of infection or inflammation. The ocular motility was normal and there was no misalignment. Her fundus exam was normal with healthy optic nerves and maculae in each eye. Goldmann visual field showed full field in the right eye and generalized mild constriction in the left eye. Neuroimaging was normal. Full field electroretinography (ERG) showed normal amplitude, wave form, and timing. Multi-focal ERG showed blunting of the foveal peaks in both eyes, with focal depression in the macula, more prominent in the left eye. After discussion with her pulmonologist, sildenafil was discontinued. At 2 months follow-up, her visual symptoms did not change.

Conclusions, including unique features of the case(s):

Our patient's maculopathy is likely sildenafil-related given the timing of onset. However, as the presence of maculopathy cannot be proven absent prior to sildenafil. The decision to discontinue sildenafil should be made with pulmonology.

References: None.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Pupils retina

Financial Disclosures: The authors had no disclosures.

Grant Support: Research to Prevent Blindness Unrestricted Grant to Stanford Department of Ophthalmology, NIH P30 EY 026877.

Contact Information: None provided.

Poster 161**Treatment Of Horizontal Binocular Diplopia With Prismatic Contact Lenses**

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Introduction:

Binocular diplopia from horizontal strabismus often requires treatment including monocular occlusion, strabismus surgery, and prismatic spectacles. We report the novel use of ground-in-prisms (GIP) in scleral contact lenses using a retrospective, observational case report.

Description of Case(s):

A 39-year-old woman noted constant, stable, horizontal, omnidirectional binocular diplopia for 6 months. Examination showed full extraocular motility and a comitant 8-prism diopter (PD) esotropia in all gazes at distance for which she successfully wore plano glasses with an 8 PD base out (BO) Fresnel prism over her contact lenses. Due to glasses intolerance, she elected to discontinue prism glasses and declined strabismus surgery. Anterior segment impressions were sent for custom three-dimensional printed scleral lenses. There was 4 PD BO GIP in each lens, for a total of 8 PD BO overall. Two months later, wearing GIP contacts her acuities were 20/20 and cover testing revealed orthophoria in all directions.

Conclusions, including unique features of the case(s):

Prisms incorporated into scleral contact lenses represent a novel, viable treatment of symptomatic horizontal strabismus. To our knowledge, this has not been previously reported in the peer-reviewed literature. Further study of scleral lenses may improve treatment options for binocular diplopia as an alternative to spectacles or strabismus surgery.

References: 1. Iliescu DA, Timaru CM, Alexe N, et al. Management of diplopia. Rom J Ophthalmol. 2017;61(3):166–170. 2. Vincent SJ, Fadel D. Optical considerations for scleral contact lenses: A review. Cont Lens Anterior Eye 2019. doi:10.1016/j.clae.2019.04.012. 3. Nguyen MTB, Thakrar V, Chan CC. EyePrintPRO therapeutic scleral contact lens: indications and outcomes. Can J Ophthalmol. 2018;53(1):66-70.

Keywords: Adult strabismus with a focus on diplopia, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 162**Diplopia and Infraorbital Nerve Paresthesia Following Calcium Hydroxylapatite Filler Injection**

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Introduction:

Calcium hydroxylapatite (CaHa) filler is the third most requested dermal fillers for moderate to severe facial rhytids. We describe a rare case of vision loss, diplopia and infraorbital nerve paresthesia following CaHa injection of the palpebro-malar groove.

Description of Case(s):

A 41-year-old female presented with a one-day history of double vision and right facial pain immediately after injection of CaHa to bilateral palpebro-malar groove. Visual acuity was 20/30 OD and 20/20 OS, and IOP was 15 OD and 17 OS. There was no visual field, color vision or pupillary abnormalities. External examination revealed edema, ecchymosis of the right lower lid and malar area with blanching, right lower lid retraction, a -1/2 superior gaze deficit OD along with 3PD hypotropia OD. Paresthesia was noted along right nasal bridge and down to her maxillary teeth. Hertel measurement was 18mm OD and 16mm OS. SLE was notable for conjunctival injection and 3 scattered white creamy plaques in the conjunctival vessels OD. Fundus examination was unremarkable. Orbital CT showed multifocal calcific densities within the inferior periorbital soft tissues OU without intraorbital FB. CTA was negative. She initially had injection of sodium thiosulfate to the affected area by the original injector within 1 hour of CaHa placement and was started on Sildenafil 100mg qd, Prednisone 60mg qd, Nitropaste BID to the affected area of the cheek, and ASA 325mg qd. ENT consultation revealed a small ulceration on the roof of her mouth one week after injection. Resolution of visual disturbance and diplopia was seen at 1 week along with sloughing of small scabs and resolution of blanching. She had partial resolution of paresthesia and conjunctival vessel emboli, and complete resolution of ectropion at 3 month follow up.

Conclusions, including unique features of the case(s):

This case highlights the importance of early recognition and aggressive management of complications with CaHa filler injection.

References: 1. Aldabagh, Bishr, et al. "Temporary Infraorbital Nerve Sensory Disturbance Following Perioral Injection of a Soft Tissue Filler." *Cosmetic Dermatology*. May 2013. 2. Glass, Lora R. Dagi, et al. "Orbital Complication Following Calcium Hydroxylapatite Filler Injection." *Ophthalmic Plastic and Reconstructive Surgery*, vol. 33, 2017, doi:10.1097/iop.0000000000000584. 3. Urdiales-Gálvez, Fernando, et al. "Treatment of Soft Tissue Filler Complications: Expert Consensus Recommendations." *Aesthetic Plastic Surgery*, vol. 42, no. 2, 2018, pp. 498–510., doi:10.1007/s00266-017-1063-0. 4. Robinson, Deanne M. "In Vitro Analysis of the Degradation of Calcium Hydroxylapatite Dermal Filler." *Dermatologic Surgery*, vol. 44, 2018, doi:10.1097/dss.0000000000001683. 5. Sandoval, Laura F., et al. "Trends in the Use of Neurotoxins and Dermal Fillers by US Physicians." *Journal of the American Academy of Dermatology*, vol. 72, no. 5, 2015, doi:10.1016/j.jaad.2015.02.095.

Keywords: Orbit

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 163**Ischemic Third Nerve Palsy Due to Midbrain Stroke**

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Introduction:

The most common cause in adults of a neurologically isolated, pupil-spared and complete third nerve palsy is ischemia. Some authors have recommended that neuroimaging in this setting is not necessary and that close observation for improvement over time along with treatment of vasculopathic risk factors is sufficient. We describe a midbrain infarct as the etiology of an isolated, acute, third nerve palsy.

Description of Case(s):

A 48-year old female with diabetes presented with acute, painless horizontal binocular diplopia. The patient reported difficulty with gait instability which was attributed to diplopia. Past ocular history included end-stage primary open angle glaucoma OU, cataract surgery OU, vitrectomy OS, chronic 20/200 vision due to laser treated proliferative diabetic retinopathy OU and macular ischemia. The pupils were isocoric (3 to 2 mm OU) with sluggish reactivity OD, and there was a relative afferent pupillary defect OS. Extraocular motility exam showed a complete ptosis OS and adduction, supraduction and infraduction deficits OS. A computed tomography (CT) scan was negative. Cranial magnetic resonance imaging (MRI) however showed a midbrain ischemic stroke involving the fascicle of the third nerve OS.

Conclusions, including unique features of the case(s):

Midbrain infarct is an uncommon cause for a third nerve palsy. Although some texts advocate for observation for presumed ischemic acute third nerve palsy with pupil sparing, the presence of any other neurologic symptom including gait difficulty should prompt consideration for MR imaging.

References: None.

Keywords: Neuroimaging, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 164**Anterior Ischemic Optic Neuropathy in End Stage Renal Disease**

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Introduction:

Ischemic optic neuropathy was described in patients with end stage renal disease (ESRD). They usually suffer from chronic anemia and fluctuating blood pressure. These patients are vulnerable to ischemic complications including ischemic optic neuropathy. The pathophysiology arises from interruption of the posterior ciliary artery blood supply to the prelaminar optic nerve due to atherosclerosis, and is exacerbated by episodic hypotension and severe anemia. Although this is a form of non-arteritic ischemic optic neuropathy (NAION), they lack the general features including the disc at risk appearance. They are often misdiagnosed as giant cell arteritis (GCA), or idiopathic intracranial hypertension (IIH). Ischemic optic neuropathy in ESRD is an important entity to recognize as it influences the management of these medically fragile patients.

Description of Case(s):

Retrospective Case Series. We present the history, OCT, GCL, and HVF of four patients with ESRD found to have ischemic optic neuropathy. All four patients show expected OCT NFL thinning, GCL atrophy, and HVF deficits consistent with optic neuropathy. Three of the four patients were under the age of 35, putting them in an atypical age category for more common types of optic neuropathy. When the correct diagnosis was made, the neuro- ophthalmologic recommendation was to improve anemia and decrease risks of hypotension (particularly during dialysis) to avoid damage to the fellow eye.

Conclusions, including unique features of the case(s):

This case series highlights the importance of considering acute or chronic optic nerve hypoxia in patients with end stage renal disease, anemia, and hypotension presenting with signs and symptoms of optic neuropathy. These patients often do not fit the typical patient demographics for NAION, GCA, or IIH. Because they are chronically ill, misdiagnoses can result in harmful and unnecessary treatment. Understanding the pathophysiology of this process will lead to fewer misdiagnoses, and will direct treatment at the true causes- severe anemia and intermittent hypotension.

References: Shemesh A, Margolin E. Sequential nonarteritic anterior ischemic optic neuropathy in patient on chronic hemodialysis. CEN Case Reports, 8(2); 89-94. 2019. Zubidi et al. Pallid disc edema and choroidal perfusion delay in posthemodialysis nonarteritic ischemic optic neuropathy. CJO, 48(5); 120-123. 2013. Nieto J, Zapata MA. Bilateral anterior ischemic optic neuropathy in patients on dialysis: a report of two cases. Indian Journal of Nephrology, 20(1); 48-50. 2010. Baile C et al. Anterior ischemic optic neuropathy and dialysis: role of hypotension and anemia. Journal of Nephrology, 14(5); 420-423. 2001. Haider S et al. Optic neuropathy in uraemic patients on dialysis. Eye, 7; 148-153. 1993.

Keywords: Optic neuropathy, Visual fields, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: Dr. Eman Hawy- EHawy@llu.edu

Poster 165

CONE ROD DYSTROPHY Two associated mutations, two different phenotypes

Jean-Philippe Woillez¹

¹*Centre Hospitalo universitaire de Lille, Lille, France*

Introduction:

Cone rod dystrophy is a rare genetic isolated inherited retinal disorder characterized by primary cone degeneration with significant secondary rod involvement, with a variable fundus appearance. Typical presentation includes decreased visual acuity, central scotoma, photophobia, color vision alteration, followed by night blindness and loss of peripheral visual field.

Description of Case(s):

Two sisters (1942, 1944) have a very slowly progressive and late-onset bilateral vision loss. A visual field, a multifocal ERG, a global ERG, an OCT and eye fundus photos show very different clinical facts. Biomolecular sampling finds two mutations, one known (mutation c.5928-2A) and one unknown (mutation c.6609_6612del). A genealogical tree is constituted.

Conclusions, including unique features of the case(s):

Phenotype of each patient and each daughters are confronted with genotypic results after a review of the relevant literature. A late phenotypic involvement is found in the 2 affected sisters. Daughters carrying only one of the two mutations do not present any abnormal phenotype.

References: None.

Keywords: Genetic disease, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Visual fields, Perimetry, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 166**Every lock has a key: Unusual presentation of tuberculosis**

Gunjan Saluja¹, Swati Phuljhele¹, Pradeep Sharma¹, Rohit Saxena¹

¹*Dr. Rajendra Prasad Centre for Ophthalmic Sciences and Research, AIIMS, New Delhi, India*

Introduction:

Diagnosis of intraocular tuberculosis is always a diagnostic dilemma, lack of a diagnostic criteria adds to the confusion. Management is further tricky when there is no sign of pulmonary involvement.

Description of Case(s):

A 4 year old presented to the emergency department of our institute with complaints of sudden onset blurring of vision, since 4 days. There was a history of febrile illness 1 week back, following which the symptoms developed. There was no history of recent vaccination or weight loss. On examination, the child was not following light and objects, pupil were fixed and dilated in both eye, intraocular pressure was normal, and anterior segment was within normal limit. Fundus examination revealed blurring of disc margins in both eye with temporal disc pallor in the left eye. Complete blood count, C-reactive protein, erythrocyte sedimentation rate, chest xray were within normal limit. Contrast enhanced MRI revealed presence of a mass lesion with inflammation and surrounding edema arising from the orbital apex, causing compression of optic nerve, this further lead us to a differential diagnosis of lymphoma, soft tissue tumor and tuberculosis. Peripheral blood smear did not show presence of any blasts, cerebrospinal fluid analysis was within normal limits. Chest X-ray was within normal limits. Abdominal ultrasonography (USG) revealed the presence of multiple splenic abscess, USG guided fine needle aspiration cytology of the splenic abscess was done, which was positive for TB polymerase chain reaction (PCR), thus a diagnosis of disseminated tuberculosis was made and patient was started on anti-tubercular regimen with steroids, and responded well.

Conclusions, including unique features of the case(s):

Our case was unique as patient presented with optic neuritis like features but later found to have extrapulmonary tuberculosis, imaging in our case played an important role in making a differential diagnosis, the presence of splenic abscess was another surprising finding and helped us to reach the diagnosis.

References: None.

Keywords: Optic neuritis, Neuro-ophth & infectious disease (eg, AIDS, prion), Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 167
Enigmatic Optic Neuritis

Priyanka Kukkar¹, Gabrielle Bonhomme¹, Jamie Odden¹, Frank Lieberman¹

¹UPMC Eye Center, Pittsburgh, Texas, USA

Introduction:

We report a case of optic neuritis with subsequent development of right sixth nerve palsy and internuclear ophthalmoplegia.

Description of Case(s):

A 60 year-old woman presented with subacute vision loss in upper left field of view, associated with unsteadiness and depth perception changes. She denied classic symptoms associated with Giant Cell Arteritis. Medical History revealed hypertension, asthma, basal cell carcinoma and squamous cell carcinoma of the skin, central adrenal insufficiency, pituitary adenoma, and MGUS. Exam revealed visual acuity of 20/30 in the right eye and 20/200 which improved to 20/50 in the left eye with correction, with an altitudinal visual field deficit in the left eye. She perceived 11/11 colors in the right eye and 2/11 in the left eye which improved to 6/11 at 3 month follow up with stable 0.3-0.6 log RAPD in the left eye. Dilated ophthalmoscopy revealed a healthy-appearing optic disk in the right eye and sectoral left disk pallor infero-temporally. Six months later, she presented urgently with acute dizziness. Exam revealed reduced vision in her left eye (20/100 from 20/50), worsened dyschromatopsia, cognitive impairment, hypo-metric saccades, internuclear ophthalmoplegia(INO), and right sixth nerve palsy. MRI findings were initially suggestive of optic neuritis. Repeat MRI at subsequent visit revealed waxing and waning pattern of multiple frontal lobe foci of variable onset of age concerning for vasculitis or demyelinating disease. She underwent a lumbar biopsy, which revealed persistent plasma cell neoplasm. Six months later she succumbed to multi-organ failure secondary to influenza sepsis. Autopsy revealed relapsing necrotizing encephalopathy with myelopathy and optic neuropathy.

Conclusions, including unique features of the case(s):

While MRI suggested optic neuritis or inflammatory papillitis, funduscopy exam and persistent visual field defect supported an ischemic optic neuropathy associated with plasma cell neoplasm. Clinicians must maintain broad diagnostic approach in evaluating optic neuritis in patients with diagnosed blood dyscrasias, lymphoproliferative disorders, or cancer.

References: None.

Keywords: Optic neuropathy, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 168

RESECTION OF EXTRAOCULAR MUSCLES IN PATIENTS WITH THYROID EYE DISEASE

George Saitakis¹, Yael Redler¹, Suzanne Freitag¹, Jin Ma¹, Dean Cestari¹

¹*Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, USA*

Introduction:

In Thyroid Eye Disease (TED), the most common strabismus procedure performed is a recession of the tight extraocular muscle in order to lessen its force on the globe. Traditionally, there has been a concern that performing resections in these patients can cause further restriction and further ignite the inflammation, thus worsening the restrictive process. From a neuro-ophthalmic perspective, there has been a concern that performing resections could cause a compressive optic neuropathy by applying pressure on the optic nerve in the orbital apex. We present two cases of patients with TED who underwent strabismus surgery involving resection of one or two muscles using the adjustable suture technique.

Description of Case(s):

Our first case is a 44-year old female with TED, who had a residual esotropia, after maximal bimedial rectus recession due to an initial esotropia of approximately 90 prism diopters. Sequentially, we performed a bilateral lateral rectus resection to correct the residual 15 PD esotropia. The second case is a 70-year old male with TED, who initially underwent both right inferior rectus recession twice for right hypotropia and medial rectus recession for esotropia as well. A new right hypotropia developed 3 years later and the patient underwent a third surgery, this time a right superior rectus resection.

Conclusions, including unique features of the case(s):

We suggest obtaining VFs and color vision testing before and after strabismus surgery using the hang-back technique with adjustable sutures. This way if a compressive optic neuropathy develops as a complication, the resected muscle can be recessed back in the outpatient post-op appointment up to 5 days later. Both of our patients were orthophoric postoperatively in all directions of gaze without evidence of optic nerve compromise. These cases demonstrate that resections can be safely performed in patients with TED without compromise of optic nerve function.

References: None.

Keywords: Adult strabismus with a focus on diplopia, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Orbit

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 169**Preventing physician burnout by owning a vineyard**

Mitchell Strominger¹

¹*Renown Medical Center, Reno, Nevada, USA*

Introduction:

Physician burnout is becoming a national emergency. Its rising prevalence is now estimated at 50 percent in some studies. Its effect on access to care, patient safety, and quality care are concerning and there is a concerted effort to educate physicians about the signs and symptoms as well as to create an environment and systems to reduce the effect. These include improving communication, changing workflow, and addressing clinician concerns via quality improvement. The author took another route. This included leaving a large academic medical center, and moving to a small western town, inheriting a vineyard and enrolling in a vineyard maintenance and wine academy. The practice of Neuro-ophthalmology was continued at a smaller regional hospital.

Description of Case(s):

The author relocated to the high desert region of the United States where he purchased a small farm and realized that he owned a neglected vineyard. This included 107 vines of a number of varieties including Chardonnay, Fosh, Zieglet Merlot and Cabernet. Enrollment in the local Vines and Wines Academy aided in the redevelopment of the vineyard and in the process of wine making. The life cycle of the vineyard will be discussed including types of trellising, irrigation methods, row placement, pruning, fertilization, pest control, netting, picking, crushing, fermentation and pressing as it pertains to the high desert region. The 2 plus hours the author used to spend in the car commuting were now devoted to working the vineyard. His stress level and degree of burnout dropped precipitously.

Conclusions, including unique features of the case(s):

Despite the recommendations of experts in developing systems to reduce physician burnout, sometimes change in environment and another avocation outside medicine is required. Additionally learning the particular aspects of vineyard maintenance and wine making that is regionally dependent is rewarding.

References: None.

Keywords: Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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North American Neuro-Ophthalmology Society

46th Annual Meeting

March 7– March 12, 2020

Omni Amelia Island Plantation • Amelia Island, FL

Monday, March 9

6:00 am – 6:45 am	Yoga	Oceanview Room (Sunrise Tower, B level next to workout room)
6:30 am – 7:30 am	Breakfast with Exhibitors	Magnolia Ballroom
6:30 am – 7:30 am	Breakfast with the Novices	Magnolia Ballroom

Join us in the reserved YONO area at breakfast for table discussions led by senior members and /or YONOs to discuss topics relevant to aspiring or current YONOs.

6:30 am – 7:30 am	Tips to Building an Academic Career <i>Nagham Al-Zubidi, MD, PhD, John Chen, MD, PhD and Lanning Kline, MD</i>	
6:30 am – 7:30 am	Tips on Publishing and Performing Reviews <i>Laura Balcer, MD, MSCE, Robert M Mallory, MD and Heather E. Moss, MD, PhD</i>	
6:30 am – 5:00 pm	Registration/Help Desk	Amelia Foyer
6:30 am – 7:30 am	NOVEL/Editorial Board/Curriculum Committee Meeting	Talbot
7:30 am – 9:30 am	Hot Topics [2.0 CME] <i>Moderators: Julie Falardeau, MD and Devin Mackay, MD</i>	Amelia Ballroom

This session is designed to provide the audience with a practical, evidence-based discussion on how to manage important clinical scenarios, which are of specific and contemporary interest to the neuro-ophthalmic community. “Hot topics” will be presented by established experts and thought-leaders for the respective conditions.

Upon completion of this session, participants should be able to: (1) identify why an empty sella occurs, (2) explain how an empty sella influences the management of a patient with or without intracranial hypertension, (3) identify a subset of risk factors for anterior ischemic optic neuropathy, (4) distinguish various forms of hereditary optic neuropathies, (5) identify differences between hereditary optic neuropathies that influence patient education and treatment, and (6) describe the role of vascular imaging in the diagnosis, monitoring, and assessment of GCA disease activity and related vascular complications.

7:30 am – 7:35 am	Introduction
7:35 am - 7:55 am	I Have an Empty Sella, What Does This Mean? <i>Susan Mollan, MBChB, FRCOphth</i>
7:55 am – 8:15 am	DOA, Wolfram, Is It All the Same? <i>Nancy J. Newman, MD</i>
8:15 am – 8:50 am	AION Precipitants

	Nocturnal Hypotension <i>Anthony Arnold, MD</i>	
	Obstructive Sleep Apnea <i>Clare Fraser, FRANZCO</i>	
	PDE5 Inhibitors , <i>Howard Pomeranz, MD, PhD</i>	
	Cataract Surgery <i>Helen Danesh-Meyer, MD, PhD</i>	
8:50 am – 9:10 am	Vessel Imaging for the Diagnosis of Giant Cell Arteritis	
	<i>François-Xavier Borruat, MD</i>	
9:10 am – 9:30 am	Q&A	
9:30 am – 10:00 am	Coffee with Exhibitors (with support from EMD Serono)	Magnolia Ballroom
10:00 am – 12:00 pm	Telemedicine and Neuro-Ophthalmology 20/20 in 2020 [2.0 CME]	Amelia Ballroom
	<i>Moderators: Melissa W. Ko, MD, FAAN, CPE and Kevin Lai, MD</i>	

Telemedicine has been growing as a robust and vital part of clinical medicine in its ability to provide high-quality care to patients. This session will provide up-to-date information regarding the implementation of telemedicine in various clinical settings and specialties, discuss the medicolegal aspects of utilizing telemedicine in clinical practice, explore the financial feasibility of telemedicine, and demonstrate ways telemedicine enhances the care that we can deliver to patients in need of neuro-ophthalmic care.

Upon completion of this session, participants should be able to: (1) discuss various methods of telemedicine use, (2) recognize how telemedicine fits into neuro-ophthalmology practice, (3) detail the process of implementing telemedicine into clinical practice, (4) enumerate medicolegal considerations and how to address these concerns, and (5) evaluate the financial benefits and costs of incorporating telemedicine into clinical practice

10:00 am – 10:10 am	Telemedicine 20/20 in 2020: How Far Have We Come, Where Are We Headed and How Is It Relevant to Neuro-Ophthalmology? <i>Melissa W. Ko, MD, FAAN, CPE</i>	
10:10 am – 10:55 am	Panoramic View of a System-Wide Telemedicine Program at an Academic Medical Center <i>Ingrid Zimmer-Galler, MD</i>	
10:55 am – 11:05 am	Teleconsultation in the ED for Neuro-Otology at JHU <i>Dan Gold, DO</i>	
11:05 am – 11:20 am	Telemedicine: Does It Pay to Play? Billing, Coding, Reimbursement <i>Ingrid Zimmer-Galler, MD and Kevin Lai, MD</i>	
11:20 am – 11:40 am	Neuro-Ophthalmology Digital Consultations: The Stanford Model <i>Heather E. Moss, MD, PhD</i>	
11:40 am – 12:00 pm	Panel Discussion/Q&A	
12:00 pm – 1:00 pm	Lunch break	Magnolia Garden
	Lunch will be available for purchase in the meeting space. Credit card or room charge only.	
12:15 pm – 1:00 pm	Update ABO Certification/Re-certification,	Cumberland Ballroom
	<i>Jane Bailey, MD, and Lanning Kline, MD</i>	
12:15 pm – 1:00 pm	Update ABPN Certification/Re-certification,	Ossabaw
	<i>Yanjun (Judy) Chen, MD, PhD, Christopher Glisson, DO, MS, FAAN and</i>	

Heather E. Moss, MD, PhD

1:00 pm – 2:25 pm **Medicine Beyond Diagnosis: Skills for Handling Challenging Clinical Situations** (organized by the WIN Committee) **[1.5 CME]** **Amelia Ballroom**

The main purpose of this optional symposium is to help develop “EQ” emotional quotient skills to assist in clinical decision making and conduct with regards to the doctor-patient relationship and interactions, focusing on patient interactions and communication.

Upon completion of this session, participants should be able to: (1) identify common heuristic decision-making errors with relevance to neuro-ophthalmology, (2) employ skills to avert making medical errors, (3) demonstrate empathy when delivering bad news, and (4) communicate efficiently with patients who have specific challenges with communication.

1:00 pm – 1:05 pm	Introduction
1:05 pm – 1:30 pm	Legalese-Ease: Practices to Minimize Risk for Litigation <i>Barbara Yates, MD, Sophia Chung, MD, Howard R. Krauss, MD, BEEE, SM</i>
1:30 pm – 1:55 pm	The Art of Breaking Bad News <i>Madhura Tamhankar, MD, Jane Bailey, MD</i>
1:55 pm – 2:20 pm	Word of Mouth: Communicating With Patients Who Have Dementia or Language Difficulties <i>Kimberly Wings, MD, Victoria Pelak, Lynn Gordon, MD, PhD</i>
2:20 pm – 2:25 pm	Closing Remarks

2:30 pm – 4:45 pm **Coding and Billing Symposium [2.25 CME]** **Cumberland Ballroom**
(advanced registration required)
Moderators: Mark Moster, MD and John Pula, MD

This session will feature an introductory lecture on the nuts and bolts of billing as well as hot topics in coding and billing.

Upon completion of this session, participants should be able to: (1) recognize how to properly code for different types of clinical encounters, (2) describe the differences between levels of coding, and (3) interpret medical decision-making tiers to properly define a patient encounter.

2:30 pm – 2:35 pm	Introduction <i>Mark Moster, MD and John Pula, MD</i>
2:35 pm – 3:05 pm	Coding Update/Nuts and Bolts of Billing <i>Sue Vicchilli, AAO Director</i>
3:05 pm – 3:10 pm	Q&A
3:10 pm – 3:40 pm	Hot Topics <i>Sue Vicchilli, AAO Director</i>
3:40 pm – 4:05 pm	MACRA/MIPS (Why Some Do/Don't Need to Know It), Prolonged Codes, Telephone Codes, and Electronic Visit Coding <i>Sue Vicchilli, AAO Director</i>
4:05 pm – 4:10 pm	Q&A
4:10 pm – 4:30 pm	Typical Coding Conundrums <i>Mark Moster, MD and John Pula, MD</i>

4:30 pm – 4:45 pm

Q&A

2:30 pm – 4:45 pm

**Lonely Planet's Guide to
Neuro-Ophthalmology [2.25 CME]**

Amelia Ballroom

Moderators: Clare Fraser, FRANZCO and Susan Mollan, FRCOphth

The International Relations Committee of the North American Neuro-Ophthalmology Society presents an interactive case-based symposium that will discuss neuro-ophthalmology disorders associated with the perils of vacations and world-wide travel. Cases will include post-immunization optic neuritis, traumatic optic neuropathy, food borne toxins and unusual headaches.

Upon completion of this course, participants should be able to: (1) identify vaccine related problems, (2) summarize the concepts on traumatic optic neuropathy management options, (3) recognize food borne related neuro-ophthalmic conditions, and (4) recognize CSF diversion related complications and visual loss.

2:30 pm - 2:52 pm

Pre-Vacation Immunization Triggered Neuro-Ophthalmic Conditions Including Optic Neuritis *Fayçal Mokhtari, MD*

2:52 pm – 3:14 pm

Holiday Headaches: From Ice-Cream to Caffeine Withdrawal, Holidays Don't Always Mean Less Headache. Highlighting Common Headache Disorders and How to Manage Them *Alex Sinclair, MRCP, FRCP, PhD*

3:14 pm – 3:36 pm

Holiday Hell: Highlighting Underlying Neuro-Ophthalmic Disorders That May Surface Causing Holiday Mayhem *Laura Bonelli, MD*

3:36 pm – 3:58 pm

Trauma On Your Travels: An Update On the Latest Thinking About Traumatic Optic Neuropathy *Richard Blanch, MD, PhD*

3:58 pm – 4:20 pm

Maybe It Was Something I Ate? An Update on Food Borne Neuro-Ophthalmic Conditions *Christian Lueck, PhD, FRACP, FRCP(UK), FAAN*

4:20 pm – 4:42 pm

Flight Level in NA10N - A380, 747, 777..... Does It Matter? *Rustum Karanjia, MD, PhD*

4:42 pm – 4:45 pm

Q&A

5:00 pm – 7:00 pm

Scientific Platform Session I [2.0 CME]

Amelia Ballroom

Moderators: Nagham Al-Zubidi, MD, PhD and Beau Bruce, MD, PhD

5:00 pm - 5:15 pm

Optic Chiasm Involvement Associated with Myelin Oligodendrocyte Glycoprotein and Aquaporin-4 Antibodies, *Deena Tajfirouz, MD*

5:15 pm - 5:30 pm

Resveratrol Nanoparticles are Neuroprotective in Experimental, Optic Neuritis, *Ehtesham Shamsher*

5:30 pm - 5:45 pm

Efficacy and Safety of Satralizumab From Two Phase 3 Trials in Neuromyelitis Optica Spectrum Disorder, *Benjamin M. Frishberg, MD*

5:45 pm - 6:00 pm	Teprotumumab Effect on Proptosis, Diplopia and Quality of Life in Active Thyroid Eye Disease (TED), <i>Jade S. Schiffman, MD</i>
6:00 pm - 6:15 pm	Neuro-ophthalmic Complications in Patients Treated with CTLA-4 and PD-1/PD-L1 Checkpoint Blockade Inhibition, <i>Eduardo Nicolás Seleme, MD</i>
6:15 pm - 6:30 pm	Novel Biomarkers in Human and Murine Nonarteritic Anterior Ischemic Optic Neuropathy, <i>Y. Joyce Liao, MD, PhD</i>
6:30 pm - 6:45 pm	AAION Shows Profound Reduction in Disc and Choroidal Blood Flow Vs. NAION and Normal Eyes, <i>Randy Kardon, MD, PhD</i>
6:45 pm - 7:00 pm	Optic Disc Drusen in Young Adults with Anterior Ischemic Optic Neuropathy: A Multicenter Study, <i>Steffen Hamann, MD, PhD</i>
7:00 pm – 8:00 pm	WIN Reception - sponsored by Horizon Therapeutics (advanced registration required) Cumberland Ballroom

I HAVE AN EMPTY SELLA, WHAT DOES THIS MEAN?

*Susan P. Mollan, MBChB FRCOphth
Queen Elizabeth Hospital
Birmingham, United Kingdom*

LEARNING OBJECTIVES

1. Summarize the prevalence of the presence of empty sella
2. Differentiate between primary and secondary empty sella syndrome
3. Describe the controversy in the management of primary empty sella

CME QUESTIONS

1. What is NOT typically associated with secondary empty sella?
 - A. Post-radiotherapy of a pituitary adenoma
 - B. Presence of a craniopharyngioma
 - C. Sheehan syndrome
 - D. Traumatic brain injury
2. What is NOT a typical MRI characteristic of raised intracranial pressure?
 - A. Distention of the perioptic subarachnoid space with or without a tortuous optic nerve
 - B. Enlargement of the pituitary gland
 - C. Empty sella
 - D. Flattening of the posterior aspect of the globe
3. How many neuroimaging features of raised intracranial pressure need to be present to make a probable diagnosis of pseudotumor cerebri syndrome (PTCS) in the absence of papilledema or sixth nerve palsy, when all the other criteria of PTCS are met?
 - A. 1
 - B. 2
 - C. 3
 - D. 4
4. What is reported to be the commonest hormone to be affected in those with primary empty sella syndrome?
 - A. Adrenocorticotrophic hormone
 - B. Growth hormone
 - C. Progesterone
 - D. Thyroxine

KEYWORDS

1. Primary empty sella (PES)
2. Secondary empty sella (SES)
3. Magnetic Resonance Imaging (MRI)
4. Pituitary
5. Pseudotumor Cerebri Syndrome (PTSC)

HIGHLIGHTS

The sellar region is of extreme importance to neuro-ophthalmologists: the optic chiasm lies directly above the sella turcica and many pathological processes that arise in this region cause visual dysfunction. The sella turcica or “Turkish saddle” of sphenoid bone lies above and behind the sphenoid sinus. Anterolaterally on either side of the sella are the anterior clinoid processes, with the posterior limit being the dorsum sellae. The pituitary gland is contained within the sella and a sheet of dura called the diaphragma sellae frames the superior opening and connects the clinoid attachments of the tentorium cerebelli above the gland. The diaphragma sellae is perforated to allow the infundibular stalk of the pituitary gland to connect to the hypothalamus.

“Empty sella” was probably first documented formally by Sheehan and Summer in 1949. They described the empty appearance of the sella turcica found at autopsy in females following postpartum pituitary necrosis.[1] The term “empty sella” was popularized in 1951 by Busch who observed it in 40 of 788 autopsy specimens. He graded the appearance of the sella region (appendix 1) where an empty sella turcica is partially or completely filled with cerebrospinal fluid (CSF) and the pituitary gland is compressed against the sellar wall with or without enlargement of the sella turcica.[2] There are, of course, earlier radiographic and surgical descriptions of empty sella prior to these descriptions seen in other publications such as Twining’s case within his description of the third and fourth ventricles in 1939.[3]

Definition

When 50% of the sella turcica is filled with CSF and the pituitary gland thickness is 3 mm or more, the condition is called partial empty sella. If over 50% of the sella is filled with CSF and the pituitary gland thickness is <2 mm, the condition is called complete empty sella.

Prevalence of PES

The debate regarding how common the finding of PES is not new: in 1968 Kaufman and Chamberlin titled their publication “the ubiquitous empty sella turcica”. [4] PES is a common incidental finding, though estimates of prevalence vary according to the definition of empty sella, the detection method and publication bias. (Table 1) Most agree that the prevalence increases with age, and is more commonly found in women.[5,6]

Table 1: Variation in presence of complete empty sella and partially empty sella.

Author	Study period	Method	Country	Number of Patients	Complete Empty sella (partially ES)	Male:Female
Busch W [2]	1951	Autopsy	USA	788	5.5%	1:6
Bergland <i>et al.</i> [7]	1968	Autopsy	New York, USA	225	(23%)	Not reported.
Kaufman and Chamberlin [4]	1966-1968	Autopsy	Cleveland, USA	89	23.6% (6.7%)	Not reported.
Foresti <i>et al.</i> [5]	1991	MRI	Italy	500	12.4% (15.6%)	1:1.2
Freund <i>et al.</i> [6]	15–26 February, 2018	MRI	Biberach, Germany	100	13% (88%)	Not reported.

Debnath <i>et al.</i> [8]	2006-2015	MRI	India	12,414	1.94%	1:4
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Classification

- Primary empty sella (PES)

This is where there appears to be no previous pituitary pathologies that could cause an empty sella. It is characterized by the herniation of the subarachnoid space within the sella, which is often associated with variable degree of flattening of the pituitary. There are 3 postulated mechanisms for PES:

- Congenital nonappearance of the diaphragma sellae;
- Incomplete formation of diaphragma sellae;
- Expansion of the suprasellar subarachnoid space into the sella.

In the pre-MRI era Foley and Posner postulated a mechanism where by chronically raised intracranial pressure from pseudotumor cerebri syndrome (PTCS) may produce an empty sella if the diaphragma sella is incompetent and the subarachnoid space herniates into the sella turcica.[9] In the case of PTCS, some have shown reversibility of the pituitary gland height suggesting that the pituitary gland is only temporarily deformed, however it may not completely return to its pre-disease height following treatment.[10]

- Secondary empty sella (SES)

SES may be caused by a number of etiologies such as

- pituitary adenomas undergoing spontaneous necrosis (ischemia or hemorrhage),
- infective causes,
- autoimmune causes,
- traumatic brain injury,
- post-treatment (radiotherapy and/or surgery) regression of pituitary tumors.

Of note, as SES most commonly occurs following spontaneous or post-treatment regression of pituitary tumors and is more likely to be associated with visual field defects than PES.

Neuroradiology findings of an empty sella

Empty sella can be observed on:

- **Plain radiograph**

Lateral skull x-ray appearance is indistinguishable from those of patients with a pituitary mass, for example a pituitary macroadenoma. The fossa may be enlarged to a variable extent with thinned remodelled margins but no evidence of a bony destructive process.

- **CT**

CT generally shows a fossa occupied by material with the attenuation coefficients of CSF. This can be confirmed by coronal and sagittal sections or reconstructions. If thin section imaging (5mm) is obtained the infundibulum may be seen coursing through the “empty” sella.

- **MRI**

MRI will demonstrate the sella to be filled with CSF and the infundibulum can be seen to traverse the space, thereby excluding a cystic mass.

Differential diagnosis

The main differential of an empty sella would be other cystic lesions within this region. All of which displace the infundibulum off midline within the fossa. Differential diagnosis of an empty sella are included in Table 2.

Table 2: Differential diagnosis of an empty sella

Pathology	MRI characteristics
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Arachnoid cyst	Displacement of the infundibulum. High-resolution imaging may show the margins of the cyst superiorly.
Craniopharyngioma	Displacement of the infundibulum. Typically have visible solid components The cystic components may not have similar signal to CSF. Often calcified (better seen on CT imaging)
Cystic pituitary macroadenoma	Displacement of the infundibulum. May not have similar signal to CSF within the cystic component. Usually have visible solid components.
Epidermoid	Displacement of the infundibulum. May not have similar signal to CSF. Readily demonstrates restricted diffusion
Rathke cleft cyst	Displacement of the infundibulum. May not have similar signal to CSF. May contain a small T2-hypointense dot.

PES and visual loss

The prevalence of field defects in patients with PES is not known. Almost every type of visual field defect has been described in association with empty sella including arcuate scotomas, binasal defects, bilateral blind spot enlargement, homonymous achromatopsia, central scotoma and unilateral temporal defects. Note that cases with visual field defects, may have included SES within their descriptions. One small study of 31 cases of PES did not disclose any fields defects attributable to the empty sella. [11]

Two mechanisms have been suggested to account for visual failure in PES: prolapse of the suprasellar visual system into the empty sella causing injury; and ischemia due to stretching of perforating vessels which arise from the infundibular stalk.

PES and endocrine disturbances

Early studies suggested endocrine disturbances were uncommon in PES, but mostly these were based on clinical symptomatology. Symptoms arising from endocrine dysfunction are rarely observed in adults with PES compared with the pediatric age group. In adults mild hyperprolactinemia, and/or various degrees of hypopituitarism have been reported to varying degrees.[11-14] For example, in one cohort with total and partial primary empty sella: 59% and 8% had GH/IGF-I deficiency; 47% and 4% had TSH/FT4 deficiency; 15% and 4% had ACTH/cortisol deficiency and 55.9% and 10.6% had gonadotropin/testosterone or estrogen deficiency, respectively [12] Overall panhypopituitarism is thought to be rare in PES, whereas Growth Hormone (GH) deficiency is the most commonly described biochemical abnormality. The most typical characteristics are symptoms that may evolve as a result of secondary amenorrhea, loss of libido, and loss of hypophysis reserve.

Diagnosis of hypopituitarism in PES requires the measurement of basal anterior pituitary and their target hormones. Therefore, some endocrinologists have advocated that all with PES should be evaluated. They also suggest that non-symptomatic cases do not necessarily require treatment, but may need periodical follow-up by an appropriate specialist. [13,14] In response to this, some have cautioned regarding overdiagnosis.[6]

PES and Idiopathic Intracranial Hypertension (IIH)

The neuro-ophthalmologist has long been the receipt of referrals in patients where an incidental empty sella has been found[15], and the link between IIH and PES often cited. Bidot et al[16] calculated the sensitivity of the presence of an empty sella in IIH as ranging from 65% to 80%,

depending on the definition used. Complete empty sella with lack of visible pituitary gland was found to be uncommon, found in less than 10% of cases.[16]

The 2013 revised criteria for pseudotumor cerebri syndrome (PTSC) recommend 3 or more neuro-imaging criteria being present in order to make a probable diagnosis of IIH without papilledema, where there was no sixth nerve palsy and when all the other criteria for PTSC were met.[17] This has been recently validated. A combination of any 3 of 4 MRI features was found to be nearly 100% specific, with a sensitivity of 64%, for a diagnosis of IIH without papilledema in patients with chronic headache, no papilledema and elevated lumbar puncture opening pressure. In isolation no individual MRI feature of intracranial hypertension had sufficient specificity to be diagnostic of raised intracranial pressure. Reduced pituitary gland height (less than 4.8mm) was moderately sensitive at 80% but had a low specificity of 64%. [18] In addition no single MRI characteristics associated with PTSC have been found to be predictive of visual outcomes. [19]

SUMMARY

Practically, as neuro-ophthalmologists, the sella is our shared territory with the endocrinologists, neurologists and neurosurgeons. To quote Kaufman and Chamberlin's ubiquitous empty sella paper "Empty sellas are part of everyday medical practice and are not rare or mysterious"![4] More evidence needs to be acquired to understand the medical implications of PES, and the related impact on the visual and endocrine systems for our patients.

CME ANSWERS

1. B

A craniopharyngioma could be part of a differential diagnosis for empty sella, but has striking MRI and CT characteristics (Table 2) to distinguish the two. Pituitary adenomas undergoing spontaneous necrosis (ischemia or hemorrhage), traumatic brain injury; post-treatment (radiotherapy and/or surgery) regression of pituitary tumors are associated with secondary empty sella syndrome.

2. B

Enlargement of the pituitary gland is a feature of intracranial hypotension. Empty sella; flattening of the posterior aspect of the globe and distention of the perioptic subarachnoid space with or without a tortuous optic nerve may be observed on MRI in raised intracranial pressure.

3. C

Three or more neuro-imaging criteria should be present in order to make a probable diagnosis of PTSC, in the absence of papilledema or sixth nerve palsy, when all the other criteria for PTSC are met (namely normal neurologic examination; normal brain parenchyma without evidence of hydrocephalus, mass, or structural lesion; normal CSF composition and elevated lumbar puncture opening pressure in a properly performed lumbar puncture).

4. B

Adrenocorticotrophic hormone is the least affected. Growth hormone is reported the most affected. Progesterone and Thyroxine are not produced by the pituitary gland.

REFERENCES

1. Sheehan HL, Summers VK. The syndrome of hypopituitarism. Q J Med 1949, 18: 319-78.
2. Busch W. [Morphology of sella turcica and its relation to the pituitary gland]. Virchows Arch Pathol Anat Physiol Klin Med. 1951; 320(5):437-58.

3. Twining EW. Radiology of the third and fourth ventricles. *Brit J Radiol* 1939. 12: 385.
4. Kaufman B, Chamberlin WB Jr. The ubiquitous "empty" sella turcica. *Acta Radiol Diagn (Stockh)*. 1972;13(1):413-25.
5. Foresti M, Guidali A, Susanna P. Primary empty sella. Incidence in 500 asymptomatic subjects examined with magnetic resonance. *Radiol Med*. 1991;81:803–807.
6. Freund W, Nonn T, Weber F. Overdiagnosis is Stressful. *Dtsch Arztebl Int*. 2018;115(18):324–325.
7. Bergland RN, Ray BS, Torack RM. Anatomical variation in pituitary gland and adjacent structures in 225 human autopsy cases. *J Neurosurg* 1968;28:93-9.
8. Debnath J, Ravikumar R, Sharma V, et al. 'Empty sella' on routine MRI studies: An incidental finding or otherwise? *Med J Armed Forces India*. 2016;72(1):33–37.
9. Foley KM, Posner JB. Does pseudotumor cerebri cause the empty sella syndrome? *Neurology*. 1975;25(6):565-9.
10. Batur Caglayan HZ, Ucar M, Hasanreisoglu M, Nazliel B, Tokgoz N. Magnetic Resonance Imaging of Idiopathic Intracranial Hypertension: Before and After Treatment. *J Neuroophthalmol*. 2019;39(3):324-329.
11. Neelon FA, Goree JA, Lebovitz HE. The primary empty sella: clinical and radiographic characteristics and endocrine function. *Medicine* 1973;52:73-92.
12. Zuhur SS, Kuzu I, Ozturk FY, Uysal E, Altuntas Y. Anterior pituitary hormone deficiency in subjects with total and partial primary empty sella: do all cases need endocrinological evaluation? *Turk Neurosurg*. 2014;24:374–379.
13. Auer MK, Stieg MR, Crispin A, Sievers C, Stalla GK, Kopczak A. Primary Empty Sella Syndrome and the Prevalence of Hormonal Dysregulation. *Dtsch Arztebl Int*. 2018 Feb 16;115(7):99-105.
14. Giustina A, Aimaretti G, Bondanelli M, Buzi F, Cannavò S, Cirillo S, Colao A, De Marinis L, Ferone D, Gasperi M, Grottoli S, Porcelli T, Ghigo E, degli Uberti E. Primary empty sella: Why and when to investigate hypothalamic-pituitary function. *J. Endocrinol. Invest*. 2010;33(5):343-6.
15. Griffiths PG, Dayan M, Coulthard A. Primary empty sella: cause of visual failure or chance association? *Eye (Lond)*. 1998;12:905-6.
16. Bidot S, Saindane AM, Peragallo JH, Bruce BB, Newman NJ, Biousse V. Brain Imaging in Idiopathic Intracranial Hypertension *J Neuroophthalmol*. 2015;35(4):400-11.
17. Friedman DI, Liu GT, Digre KB. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. *Neurology* Sep 2013, 81 (13) 1159-1165.
18. Mallery RM, Rehmani OF, Woo JH, Chen YJ, Reddi S, Salzman KL, Pinho MC, Ledbetter L, Tamhankar MA, Shindler KS, Digre KB, Friedman DI, Liu GT. Utility of Magnetic Resonance Imaging Features for Improving the Diagnosis of Idiopathic Intracranial Hypertension Without Papilledema. *J Neuroophthalmol*. 2019;39(3):299-307.
19. Saindane AM, Bruce BB, Riggeal BD, Newman NJ, Biousse V. Association of MRI findings and visual outcome in idiopathic intracranial hypertension. *AJR Am J Roentgenol*. 2013;201(2):412–418.

Appendix:

Busch's criteria (1951) of the extent of diaphragma sellae deficiency and the state of the pituitary gland [2]

Order	Description
Type 1 A	The diaphragma sellae forms a complete covering.
Type 1 B	A slight funnel-shaped depression is present in the intact diaphragma sellae.
Type 2 A	A 3 mm or less opening in the diaphragma sellae exists around the hypophyseal stalk.
Type 2 B	A slight funnel-shaped indentation toward the middle of the diaphragma sellae is present.
Type 3 A	The diaphragma sellae is a peripheral rim of tissue 2 mm or less in extent with the pituitary gland freely exposed, and covered with arachnoid.

Type 3 B	The diaphragma sellae deficiency is the same as Type 3 A, but the pituitary gland is indented, often eccentrically.
Type 3C	In addition to the deficient diaphragma sellae characteristic of Type 3, the remodelling of the pituitary gland is marked and the gland may not be apparent on visual inspection.

INHERITED OPTIC NEUROPATHIES: DOA, WOLFRAM, IS IT ALL THE SAME?

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LEARNING OBJECTIVES

1. Describe the classic presentations of the most common inherited optic neuropathies
2. Recognize that mutations in the same gene may result in different phenotypes and even different patterns of inheritance
3. Appropriately test for the different causes of inherited optic atrophy

CME QUESTIONS

1. Mutations in which of the following genes can cause isolated optic atrophy:
 - A. OPA1
 - B. WFS1
 - C. DNML
 - D. MTND4
 - E. All of the above
2. True or False: All patients with Wolfram syndrome will have a mutation in the Wolframin gene (*WFS1*)
3. True or False: Syndromic optic atrophy can occur in patients with point mutations in the *OPA1* gene

KEYWORDS

1. Optic neuropathy
2. Optic atrophy
3. Inherited
4. Dominant optic atrophy
5. Wolfram syndrome

HIGHLIGHTS

Amongst the many causes of optic neuropathies, the inherited optic neuropathies are figuring more commonly in the differential diagnosis of otherwise unexplained optic atrophy, despite there often being no recognized family history. While in the past this diagnosis was often one of exclusion or presumption, modern advances in the detection of genetic abnormalities in both the nuclear and mitochondrial genomes have allowed for a veritable revolution in the genetic diagnosis of inherited causes of optic nerve disease (1-3). Linkage analysis requiring large pedigrees and clinical syndrome recognition, although still often important to alert the astute clinician that a disorder might be genetic and prompt appropriate testing, have largely yielded to strategies that go even beyond targeted gene sequencing to gene panel screening with next generation sequencing (NGS) (1). As accessibility increases, costs decrease, and these tests are becoming more frequently used in routine neuro-ophthalmologic practice.

The two most common forms of inherited isolated optic neuropathy are Leber hereditary optic neuropathy (LHON) and dominant optic atrophy (DOA), the former caused by point mutations in the mitochondrial DNA (mtDNA), and the latter most often due to mutations in the *OPA1* gene on chromosome 3 of the nuclear DNA (1-4). The diagnosis of each of these disorders is easy if there is a classic clinical presentation and a family history that follows the maternal lineage in LHON and the rules of autosomal dominant mendelian inheritance in DOA. However, genetic analysis has allowed for the accurate diagnosis of singleton cases and has widened the clinical phenotype of both disorders to include neurologic and systemic manifestations which previously would have guided the clinician toward alternative syndromic diagnoses. For example, up to 30% of DOA patients will have additional, usually neurologic, findings, especially over time, hearing loss, myopathies/neuropathies, and even chronic progressive external ophthalmoplegia and ptosis (5). Alternatively, genetic analysis has also demonstrated that disorders we had previously recognized as invariably syndromic may actually manifest as isolated optic atrophy (1). The most striking example of this are disorders related to mutations in the Wolframin gene (*WFS1*) which classically present with the syndrome of juvenile onset optic atrophy and diabetes mellitus, with subsequent development of hearing loss and diabetes insipidus, as well as other neurologic, renal and psychiatric abnormalities (6). It is now recognized that mutations in the *WFS1* gene are responsible for isolated nonsyndromic optic neuropathies, as well as limited forms of the syndrome, including many patients with no optic nerve involvement (1). Furthermore, mutations in the same genes can be inherited both autosomal dominantly and recessively, sometimes resulting in the same clinical phenotype, but often not. In general, when the mutation causes a recessively-inherited disorder, the clinical phenotype is likely to be that of a more severe multisystem disease, whereas autosomal dominantly inherited disorders from the same mutation are more likely to have isolated optic atrophy, or optic atrophy and one other defining characteristic, such as hearing loss, but this is not entirely predictable. Underlying most, if not all, of these inherited optic atrophy disorders is a proven or presumed final common pathogenesis via mitochondrial dysfunction (2).

So what's a busy clinician to do? New technologies that rely on massively parallel NGS methodologies are fast becoming the "new" standard for mtDNA and nuclear genome sequencing (7). Next-generation sequencing of the entire mtDNA genome is now commonly applied in the detection of mtDNA point mutations associated with mitochondrial diseases such as LHON. Most laboratories continue to report a first line screening for LHON to include the three primary mtDNA mutations associated with the disease (accounting for about 90% of all cases), but complete analysis of the mitochondrial genome is no longer a difficult or exceptional process. It should be emphasized that although newer technologies make mapping an individual's mitochondrial genome feasible, interpretation of what is found still requires an expertise in mitochondrial genetics, physiology and pathophysiology (3).

When screening for nuclear DNA mutations associated with mitochondrial disorders, such as DOA, NGS screening of the entire gene(s) in question should be performed (1). Often, phenotypic panels for a variety of nuclear genes in which mutations have been associated with a particular clinical feature are offered commercially. At Emory University, for example, an "optic atrophy" panel includes NGS screening of the genes *MFN2*, *OPA1*, *OPA3*, *TIMM8A*, *TMEM126A*, and *WFS1*, while in the UK, there is access to panels assessing the genes *ACO2*, *AFG312*, *ATAD3A*, *AUH*, *C12ORF65*, *C19ORF12*, *CISD2*, *DNAJC19*, *DNM1L*, *MFN2*, *MTPAP*, *NDUFS1*, *NEFH*, *NR2F1*, *NUTF2*, *OPA1*, *OPA3*, *POLG*, *SLC25A46*, *SPG7*, *TIMM8A*, *TMEM126A*, *TSFM*, and *WFS1* (Patrick Yu-Wai-Man, personal communication). Optic atrophy genes are also included in oculome panels which assess hundreds of genes associated with developmental eye disorders and inherited disease (8). Analyses of known positive and negative control

samples are required for validation of any diagnostic genetic testing. Causative variants discovered with NGS are usually verified using Sanger sequencing (1). If a patient already has a known mutation either in mtDNA or nuclear DNA, a family member can be specifically tested for that mutation without the expense and delay of NGS screening of multiple genes.

Finally, it is important to remember, especially when a family history is not apparent, that other causes of optic neuropathy must still be ruled out, in particular those optic neuropathies that are believed to also have a final common pathogenesis of mitochondrial dysfunction, such as those of toxic/metabolic/nutritional origin (2). Even if an underlying genetic mutation associated with optic atrophy is discovered, these other causes of mitochondrial dysfunction may contribute to phenotypic expression and provide therapeutic opportunities not yet available for the inherited optic neuropathies in isolation.

SUMMARY

- Many cases of inherited optic neuropathy have no known or recognized family history.
- The same mutation can cause different clinical expression, even within the same pedigree.
- Different mutations can cause the same phenotype, even isolated optic atrophy.
- Autosomal dominant and autosomal recessive inheritance can result from mutations in the same gene and although the phenotypes will likely be different (with the autosomal recessively-inherited disorders usually more likely syndromic), this is not entirely predictable.
- Various screening “panels” are available commercially to test for mutations expected to cause inherited optic neuropathy

CME ANSWERS

1. E
2. False
3. True

REFERENCES

1. Jurkute N, Majander A, Bowman R, Votruba M, Abbs S, Acheson J, Lenaers G, Amati-Bonneau P, Moosajee M, Arno G, Yu-Wai-Man P. Clinical utility gene card for: inherited optic neuropathies including next-generation sequencing-based approaches. *Eur J Hum Genet*, 2019;27:494-502.
2. Yu-Wai-Man P, Griffiths PG, Chinnery PF. Mitochondrial optic neuropathies - Disease mechanisms and therapeutic strategies. *Progress in Retinal and Eye Research* 2011; 30:81-114.
3. Newman NJ. Diagnosis and management of mitochondrial neuro-ophthalmologic disorders: translating scientific advances in the clinic. *J Neuro-ophthalmol* 2016;37:56-69.
4. Fraser JA, Biousse V, Newman NJ. The neuro-ophthalmology of mitochondrial disease. *Surv Ophthalmol* 2010; 55:299-334.
5. Ham M, Han J, Osann K, Smith M, Kimonis V. Meta-analysis of genotype-phenotype analysis of OPA1 mutations in autosomal dominant optic atrophy. *Mitochondrion* 2019;46:262-269.
6. Moosajee M, Yu-Wai-Man P, Rouzier C, Bitner-Glindzicz M, Bowman R. Clinical utility gene card for: Wolfram syndrome. *European Journal of Human Genetics*, 2016;24: doi: 10.1038/ejhg.2016.49.
7. Wong L-JC. Challenges of bringing next generation sequencing technologies to clinical molecular diagnostic laboratories. *Neurotherapeutics* 2013; 10:262-272.

8. Patel A, Hayward JD, Tailor V, Nyanhete R, Ahlfors H, Gabriel C, Jannini TB, Abbou-Rayyah Y, Henderson R, Nischal KK, Islam L, Bitner-Glindzicz M, Hurst J, Valdivia LE, Zanolli M, Moosajee M, Brookes J, Papadopoulos M, Khaw PT, Cullup T, Jenkins L, Dahlmann-Noor A, Sowden JC. The oculome panel test: next-generation sequencing to diagnosis a diverse range of genetic development eye disorders. *Ophthalmology* 2019;126:888-907.

PRECIPITANTS FOR NAION: NOCTURNAL HYPOTENSION

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LEARNING OBJECTIVES

1. Explain the proposed rationale for nocturnal hypotension as a causal factor in NAION
2. Describe the limitations of the data supporting nocturnal hypotension as a causal factor
3. Summarize the evidence and limitations for the theory that visual loss in NAION occurs more frequently on awakening

CME QUESTIONS

1. Which of the following is a limitation of data proposing nocturnal hypotension as a precipitant of NAION?
 - A. Lack of evidence of increased nocturnal “dip” in blood pressure in NAION compared to controls
 - B. Incorrect rationale for decreased blood pressure as a casual factor for NAION
 - C. Inaccuracy of 24 hour BP monitoring to assess nocturnal hypotension
 - D. Presence of systemic hypertension renders measurements of nocturnal changes inaccurate
2. Which of the following is a limitation of the theory that visual loss in NAION occurs more frequently on awakening and is the result of nocturnal hypotension?
 - A. There are no data to support the increased frequency
 - B. Data from the IONDT do not support the increased frequency
 - C. There is no evidence of nocturnal hypotension
 - D. Systemic hypotension has not been associated with NAION
3. Which of the following factors has been proposed to contribute to the effect of nocturnal hypotension in the development of NAION?
 - A. Carotid artery insufficiency
 - B. ?zone parapapillary atrophy
 - C. Decreased intraocular pressure
 - D. Impaired disc vascular autoregulation

KEYWORDS

1. NAION
2. Nocturnal hypotension
3. 24 hour blood pressure monitoring
4. Time of onset visual loss

HIGHLIGHTS

The September 2016 issue of the Journal of Neuro-Ophthalmology included a Point-Counter-Point section entitled “Does Nocturnal Hypotension Play a Causal Role in Nonarteritic Anterior Ischemic Optic Neuropathy?”¹ The following includes an excerpt from that paper. A followup Letter to the Editor from Dr. Hayreh and Response from Dr. Arnold were published subsequently.²⁻³

The etiology of nonarteritic anterior ischemic optic neuropathy (NAION) remains unclear. While there is evidence in fluorescein angiographic studies that optic disc perfusion is impaired⁴, the precise location of the vasculopathy is unproven, and features predisposing or inciting the ischemic event lack clear substantiation. Suggested contributing factors have included the so-called “crowded disc,” lipohyalinosis of the disc microvasculature with decreased flow and impaired autoregulation, and the presence of nocturnal hypotension with associated impaired optic disc perfusion. The relation of nocturnal hypotension to NAION has been controversial, and the evidence inconclusive.

The purported link of decreased systemic blood pressure (and by implication, optic disc perfusion pressure) to the development of optic disc ischemia is certainly reasonable, particularly in view of the clear association of severe hypotensive episodes with the development of optic disc infarcts. Ischemic optic neuropathy following severe blood loss with anemia and hypotension, after GI bleed or cardiac surgery, is well documented, and the pathogenetic mechanism appears clear. To extrapolate from this scenario to one in which an exaggerated physiologic drop in blood pressure at night results in an inability to maintain adequate perfusion to the optic disc, however, is more difficult; the available data are not compelling.

In 1994, Hayreh⁵ proposed supportive evidence for a causal relationship, not only in nonarteritic anterior ischemic optic neuropathy (NAION), but also both normal tension glaucoma (NTG) and primary open angle glaucoma (POAG). He suggested that the drop in blood pressure might either be a precipitating event for NAION in patients predisposed to it by vasculopathic and other risk factors or that chronic relative hypotension may compromise optic disc circulation, particularly in those patients with an exaggerated “dip” or in patients, such as those with systemic hypertension, in which optic disc circulation autoregulatory mechanisms are impaired. Twenty-four hour ambulatory monitoring was performed in 52 subjects with NAION. Mean decrease in systolic and diastolic blood pressure of 25.3% and 31.2% respectively were noted. Similar monitoring was performed in 19 subjects with POAG and 65 subjects with NTG. Mean systolic blood pressures decreased at night 25.8% and 27.6% respectively, with diastolic decrease 33.2% and 36.0% respectively. In general, no significant differences in pressure decrease were observed between NAION, NTG, and POAG.

Hayreh interpreted these data to show that nocturnal hypotension plays a significant role in the development of NAION, but the data have significant limitations. No controls were monitored. The nocturnal drop in pressure for all 3 groups was substantially larger than the reported figures for normotensive or hypertensive patients without ocular disease; a large meta-analysis of 24-hour ambulatory blood pressure measurement revealed averages of 14% and 16% nocturnal drop in systolic and diastolic blood pressure respectively⁶. However, techniques in measurement vary greatly, and without a control group, it is difficult to assess the significance of the absolute level of nocturnal decrease seen in his subjects. He measured peak daytime levels vs trough nighttime levels, whereas most investigators compared mean levels of blood pressure day vs night. Moreover, the findings, if significant, would suggest with equal if not greater significance that nocturnal hypotension plays a pathogenetic role in the development of both NTG and POAG. While a number of studies of ambulatory

blood pressure measurement in these diseases have been performed, the role of nocturnal hypotension remains unproven.

Landau et al⁷ performed 24 hour ambulatory blood pressure monitoring in 24 subjects with NAION and 24 controls matched for age, disease, and medication. Mean decreases of 11% systolic and 18% diastolic were measured in NAION, compared with 13% and 18% respectively in controls, showing no significant difference. They concluded that nocturnal hypotension was not established as a cause of NAION, although there was some evidence that lower daytime mean blood pressure was present in NAION patients compared with controls. The contradicting results regarding level of nocturnal “dip” in NAION and whether chronic or intermittent low systemic blood pressure is a factor in etiology remain unresolved. A lively discussion between Drs. Hayreh and Landau was published in 1997⁸⁻⁹. In 1999, Hayreh published a continuation of his study with a larger number of subjects¹⁰, along with a review paper of the same data that same year¹¹, but no additional features were presented to support his theory.

In 1997, Hayreh¹² reported a detailed study of time of onset of visual loss in NAION. Of 544 episodes of visual loss in 635 subjects with NAION studied over 20 years, “discovery” of visual loss was reported on awakening either from nighttime sleep or a daytime nap in 52%, during the first “critical” use of vision in the morning in an additional 21.5%. He interpreted these data to show that the development of NAION was related to hypotension in approximately 73% of patients. In contrast, the Ischemic Optic Neuropathy Decompression Trial (IONDT) reported that 174/418 (42%) of subjects described onset of visual loss within two hours of awakening in the morning, while 170/418 (41%) reported that it did NOT occur during the 1st two waking hours¹³. Dr. Hayreh attributed the differences in the two studies to the focus of the interviewers in obtaining the information, suggesting that he was more specific and detailed in his discussions with subjects than the investigators in the IONDT. One could just as easily suggest that a broader base of interviewers might result in less biased results. Moreover, a portion (not detailed in the paper) of the 52% of his cases reported on awakening followed not a nighttime prolonged sleep, but a nap of undetermined length. The relation of short-term sleep to the development of systemic hypotension is not established. If these cases may be discounted, it is possible that the percentage of patients noting visual loss on awakening from nocturnal sleep is similar to that reported in the IONDT and does not support a causal link.

SUMMARY

In summary, the theory that nocturnal hypotension is a significant contributor to the development of NAION is based on very limited data from a single series of studies and is not corroborated by others. While isolated cases of severe systemic hypotension may result in ION, the normal or even mildly exaggerated nocturnal dip in blood pressure seen in the population has not been established as a cause in routine NAION.

CME ANSWERS

1. A
2. B
3. D

REFERENCES

1. Arnold AC. Con: Nocturnal hypotension is not causally related to nonarteritic anterior ischemic optic neuropathy. *J Neuro-Ophthalmol* 2016;36:329-333.
2. Hayreh SS. Role of nocturnal arterial hypotension in nonarteritic anterior ischemic optic neuropathy. *J Neuro-Ophthalmol* 2017;37:350-351.
3. Arnold AC. Does nocturnal hypotension play a causal role in nonarteritic anterior ischemic optic neuropathy? Response. *J Neuro-Ophthalmol* 2017;37:352-353.
4. Arnold AC, Hepler RS. Fluorescein angiography in acute nonarteritic anterior ischemic optic neuropathy. *Am J Ophthalmol* 1994;117:222-230.
5. Hayreh SS, Zimmerman MB, Podhajsky P, et al. Nocturnal arterial hypotension and its role in optic nerve head and ocular ischemic disorders. *Am J Ophthalmol* 1994;117:603-624.
6. Staessen JA, Fagard RH, Lijnen PJ, et al. Mean and range of the ambulatory pressure in normotensive subjects from a meta-analysis of 23 studies. *Am J Cardiol* 1991;67:723-727.
7. Landau K, Winterkorn JMS, Mailloux LU, et al. 24-hour blood pressure monitoring in patients with anterior ischemic optic neuropathy. *Arch Ophthalmol* 1996;114:570-575.
8. Hayreh SS, Zimmerman MB, Podhajsky P, et al. Nonarteritic anterior ischemic optic neuropathy: role of nocturnal hypotension (letter). *Arch Ophthalmol* 1997;115:942-943.
9. Landau K, Winterkorn JMS, Napolitano B. Nonarteritic anterior ischemic optic neuropathy: role of nocturnal hypotension (reply to letter). *Arch Ophthalmol* 1997;115:943-945.
10. Hayreh SS, Podhajsky PA, Zimmerman B. Role of nocturnal arterial hypotension in optic nerve head ischemic disorders. *Ophthalmologica* 1999;213:76-96.
11. Hayreh SS. Role of nocturnal arterial hypotension in the development of ocular manifestations of systemic arterial hypertension. *Curr Opin in Ophthalmol* 1999;10:474-482.
12. Hayreh SS, Podhajsky PA, Zimmerman B. Nonarteritic anterior ischemic optic neuropathy: Time of onset of visual loss. *Am J Ophthalmol* 1997;124:641-647.
13. IONDT Study Group. Characteristics of patients with nonarteritic anterior ischemic optic neuropathy eligible for the Ischemic Optic Neuropathy Decompression Trial. *Arch Ophthalmol* 1996;114:1366-1374.

PRECIPITANTS FOR NAION: OBSTRUCTIVE SLEEP APNEA

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LEARNING OBJECTIVES

1. Recognize the key diagnostic tests for OSA
2. Describe the link between OSA and NAION
3. Explain how OSA may affect the vasculature at the optic disc

CME QUESTIONS

1. Which is the best clinical test in the office for OSA?
 - A. Ask about a history of snoring
 - B. Stop-Bang Questionnaire
 - C. Pulse oximetry
 - D. Look at the optic discs
2. Which condition does not have an increased odds ratio for OSA?
 - A. Glaucoma
 - B. NAION
 - C. Cataract
 - D. CSR
3. 3. Obstructive sleep apnea
 - A. Causes increased arterial stiffness
 - B. Increases risk of stroke
 - C. Alters cerebral vasoreactivity
 - D. All of the above

KEYWORDS

1. Sleep apnea
2. Snoring
3. Continuous positive airway pressure
4. NAION
5. Ischemic

HIGHLIGHTS

Obstructive sleep apnea is a nocturnal breathing disorder characterised by repetitive episodes of partial or complete collapse of the pharynx during sleep, resulting in intermittent hypoxia (IH). Initial OSA prevalence reports from the mid 1990's gave figures that ranged from 3-7% for men and 2-5% for women. However, more recent American studies estimated the prevalence to be between 17-31% for

men and 6.5-9% for women. The increasing prevalence may be due to the increased sensitivity of newer recording equipment but are also linked increasing obesity.

The widely accepted definition of OSA is an apnea-hypopnea index (AHI) >5, associated with daytime symptoms such as excessive daytime sleepiness. The gold-standard measure of AHI is made with an overnight dPSG. Questionnaires including STOP-Bang (SBQ), the Epworth Sleepiness Scale (ESS) and the Berlin Questionnaire (BQ) are used for OSA screening. A recent study compared their use, and concluded that compared with the BQ, and ESS, the SBQ is a more accurate tool for detecting mild, moderate, and severe OSA. The STOP items are snoring, daytime tiredness, observed apneas and high blood pressure. The BANG items are body mass index (BMI) >35 kg/m², age >50 years, neck circumference >40 cm and male gender.

There are several pathophysiological explanations for why OSA may affect the microvasculature at the optic disc, triggering NAION. Firstly, OSA is associated with increased inflammatory marker expression, increased arterial stiffness, altered endothelial function and increased blood pressure, increasing the risk of cardiovascular disease and stroke. Vascular endothelial growth factor (VEGF) is reported to stimulate the progression of cardiovascular disease. Levels of VEGF are significantly decreased in OSA patients after CPAP therapy of more than 1 year. In addition, impaired cerebral vasoreactivity is thought to render the brain more vulnerable to ischaemic events. Using near-infrared spectroscopy, patients with moderate to severe OSA have been shown to have altered cerebral vasoreactivity.

A 2016 meta-analysis (1) showed that OSA subjects have increased odds ratio (OR) of a diagnosis of glaucoma and floppy eyelid syndrome. In reverse, those patients with ophthalmic disease, the OR for OSA was increased in those with glaucoma (OR=1.7), non-arteritic anterior ischaemic optic neuropathy (NAION) (OR=3.1) and central serous retinopathy (OR=2.0). In a Korean paper, the 10-year incidence probability of NAION was significantly higher in a group of patients with OSA (0.92% versus 0.42%) even after adjusting for other risk factors (2).

Specifically looking at NAION, analysis of 4 prospective studies and one case-control study found that patients with OSA had a more than six-fold increase of NAION compared to non-OSA patients (3). Two older prospective case-control studies using dPSG have reported a significantly higher prevalence of OSA in patients with NAION compared to matched controls (4,5). The prevalence of OSA ranged from 55.6%-71% for NAION patients and 18%-22.2% for controls. In another study (6) no significant difference in OSA rates was found in patients with NAION and controls. In the baseline data for the NORDIC Quark trial of NAION, presented at NANOS in 2019, it was reported that of the first 400 patients 40% reported snoring and 20% had a diagnosis of OSA. In a study published this year, Chang and Keltner reported that non-compliance with CPAP in patients with moderate-severe OSA was a significant risk for second eye involvements over a 3.5-year period. (7)

The two management options shown to improve outcomes in patients with OSA are weight loss and continuous positive airway pressure (CPAP). Interestingly a review of obesity, OSA and cardiovascular events, found that while the gold standard treatment for moderate-to-severe OSA is CPAP, significant reductions in major cardiovascular events were not observed in clinical trials. However, they did show that weight control was essential to decrease the risk of cardiovascular events and mortality.

SUMMARY

There is now increasing evidence that OSA risk should be assessed in all patients with NAION, and it has even been recommended that dPSG should be performed in all patients (8).

CME ANSWERS

1. B
2. C
3. D

REFERENCES

1. Huon LK, Liu SY, Camacho M, Guilleminault C. The association between ophthalmologic diseases and obstructive sleep apnea: a systematic review and meta-analysis. *Sleep Breath*, 20(4):1145-54. 2016.
2. Yang HK, Park SJ, Byun SJ, Park KH, Kim JW, Hwang JM. Obstructive sleep apnoea and increased risk of non-arteritic anterior ischaemic optic neuropathy. *Br J Ophthalmol*. 103(8):1123-1128. 2019
3. Wu Y, Zhou LM, Lou H, Cheng JW, Wei RL. The Association Between Obstructive Sleep Apnea and Nonarteritic Anterior Ischemic Optic Neuropathy: A Systematic Review and Meta-Analysis. *Current eye research*. 41(7):987-92. 2016
4. Bilgin G, Koban Y, Arnold AC. Nonarteritic anterior ischemic optic neuropathy and obstructive sleep apnea. *J Neuroophthalmol*. 33(3):232-4. 2013
5. Mojon DS, Hedges TR, Ehrenberg B, Karam EZ, Goldblum D, Abou-Chebl A, et al. Association between sleep apnea syndrome and nonarteritic anterior ischemic optic neuropathy. *Arch Ophthalmol*. 120(5):601-5. 2002.
6. Arda H, Birer S, Aksu M, Ismailogullari S, Karakucuk S, Mirza E, et al. Obstructive sleep apnoea prevalence in non-arteritic anterior ischaemic optic neuropathy. *Br J Ophthalmol*. 97(2):206-9. 2013.
7. Chang MY, Keltner JL. Risk Factors for Fellow Eye Involvement in Nonarteritic Anterior Ischemic Optic Neuropathy. *J Neuroophthalmol*. 39(2):147-152. 2019.
8. Mentek M, Aptel F, Godin-Ribuot D, Tamisier R, Pepin JL, Chiquet C. Diseases of the retina and the optic nerve associated with obstructive sleep apnea. *Sleep medicine reviews*. 38:113-30. 2018

PRECIPITANTS FOR NAION: PDE5 INHIBITORS

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LEARNING OBJECTIVES

1. The attendee will be able to list the phosphodiesterase-5 (PDE5) inhibitors that have been associated with developing non-arteritic anterior ischemic optic neuropathy (NAION).
2. The attendee will be able to identify the medical conditions for which PDE5 inhibitors are prescribed and which patients taking PDE5 inhibitors might be at potential risk for developing NAION.
3. The attendee will be able to explain the relative risk of developing NAION after use of PDE5 inhibitors.

CME QUESTIONS

1. PDE5 inhibitor medications that have been associated with developing NAION include
 - A. Sildenafil
 - B. Vardenafil
 - C. Tadalafil
 - D. All of the above
2. Male patients with erectile dysfunction who use PDE5 inhibitors are the only group of patients at risk for developing NAION.
 - A. True
 - B. False
3. According to two prospective studies, the relative risk of developing NAION after ingestion of a PDE5 inhibitor within one half-life of the medication is:
 - A. no risk
 - B. 2-3 fold over control
 - C. 3-4 fold over control
 - D. 5-6 fold over control

KEYWORDS

1. Non-arteritic anterior ischemic optic neuropathy (NAION)
2. Phosphodiesterase-5 (PDE5) inhibitor
3. Sildenafil
4. Viagra

HIGHLIGHTS

Cases in the peer reviewed medical literature:

The first case of NAION associated with sildenafil was documented by Egan and Pomeranz in 2000¹. Within the next few years several other case reports followed which were summarized in two case series reports^{2,3}. Cases of NAION associated with tadalafil have been documented as well⁴⁻⁶. In a review

published in 2016⁷, it was documented that a total of 39 case reports were published in the peer reviewed medical literature as of 2014. Since that time, 4 additional cases have been published⁸⁻¹¹ and other cases have been reported at NANOS Annual Meeting poster sessions. Several of the published cases were challenge/re-challenge cases either involving the same eye or bilateral sequential NAION after repeated sildenafil or tadalafil use. These cases strongly suggest an association between use of PDE5 inhibitors and development of NAION.

Cases reported to the FDA

In addition to cases published in the peer-reviewed medical literature, cases of NAION associated with PDE5 inhibitor use have been reported to the FDA. Pomeranz reviewed these cases in 2016¹² and reported that 448 cases of sildenafil, 71 cases of tadalafil and 39 cases of vardenafil associated ischemic optic neuropathy were reported to the FDA as of 2014. These cases reports are likely underestimates of the true number of cases since only FDA reports that had completely unambiguous data identifying ischemic optic neuropathy were included in the reported data.

Prospective Case studies

There have been two studies (one published and one not published) to date that report data collected by the FDA mandate to the pharmaceutical companies that manufacture PDE5 inhibitors. One study¹³, sponsored by Pfizer, concluded that there was an odds ratio of 2.15 for the daily relative risk for acute NAION within five half-lives of PDE5 inhibitor use among definite NAION cases, and an odds ratio of 2.36 when possible NAION cases were included. The other study, sponsored by Eli Lilly, was not published in the peer reviewed medical literature, but was included as a revision to the drug insert. This study concluded that there was an odds ratio of 2.27 for the daily relative risk for acute NAION within five half-lives of PDE5 inhibitor use among definite NAION cases; thus, the result was virtually identical to the Pfizer sponsored study.

What should be discussed with patients in whom a diagnosis of NAION is made?

In addition to making an assessment of the “disk at risk” and vascular risk factors in a patient with NAION, we should be asking patients whether a PDE5 inhibitor is being used for treatment of erectile dysfunction or pulmonary hypertension and when the medication was last used relative to the onset of symptoms of vision loss due to NAION. An inquiry could also be made as to whether the patient has used some other “sexual enhancer” drug or supplement as some of these have been found to include a PDE5 inhibitor among its ingredients. The patient should be counseled about the future increased risk of NAION in the fellow eye with continued PDE5 inhibitor use. It is not known exactly how PDE5 inhibitor use changes that potential future risk (15% over 5 years per the IONDT) other than the two to three-fold odds ratio discussed above.

SUMMARY

Forty-two cases of ischemic optic neuropathy associated with PDE5 inhibitor use to date have been documented in the peer reviewed medical literature. There have been 558 cases of ischemic optic neuropathy associated with PDE5 inhibitor use reported to the FDA. Two observational case crossover studies have concluded that there was a two to three-fold increased risk of NAION within five-half-lives of PDE5 inhibitor use. When a diagnosis of NAION is made, an inquiry should be made as to whether any PDE5 inhibitor was used prior to onset of vision loss. If so, the patient should be counseled as to the possibility that continued PDE5 inhibitor use may increase the risk of NAION in the fellow eye. Patients with a known history of previous NAION should be cautioned regarding the use of PDE5 inhibitors for

treatment of erectile dysfunction or pulmonary hypertension because of the potential increased risk of fellow eye involvement.

CME ANSWERS

1. D
2. False
3. B

REFERENCES

1. Egan RA, Pomeranz HD. Sildenafil (Viagra) associated anterior ischemic optic neuropathy. *Arch Ophthalmol* 118: 291-292, 2000.
2. Pomeranz HD, Smith KH, Hart WM, Egan RA. Sildenafil-associated non-arteritic anterior ischemic optic neuropathy. *Ophthalmology* 109: 584-587, 2002.
3. Pomeranz, HD, Bhavsar A. Non-arteritic anterior ischemic optic neuropathy developing shortly after use of sildenafil (Viagra). *J Neuroophthalmol* 25: 9-13, 2005.
4. Bollinger K, Lee MS, Recurrent visual field defect and ischemic optic neuropathy associated with tadalafil rechallenge. *Arch Ophthalmol* 123: 400-1, 2005.
5. Escaravage GK Jr, Wright JD Jr, Givre SJ. Tadalafil associated with anterior ischemic optic neuropathy. *Arch Ophthalmol* 123: 399-400, 2005.
6. Peter NM, Singh MV, Fox PD. Tadalafil-associated anterior ischaemic optic neuropathy. *Eye* 19: 715-7, 2005.
7. Pomeranz, HD. State of the Art Review: The relationship between phosphodiesterase-5 inhibitors and non-arteritic anterior ischemic optic neuropathy, *J Neuroophthalmol* 36: 193-196, 2016.
8. Neufeld A, Warner J. Case of bilateral sequential nonarteritic ischemic optic neuropathy after rechallenge with sildenafil, *J Neuroophthalmol* 38: 123-24, 2018.
9. Zheng L, Miller KM, Kotlyar E, Garrick R, Sildenafil-induced nonarteritic anterior ischemic optic neuropathy in a patient with pulmonary hypertension. *J Neuroophthalmol* 36: 348-9, 2016.
10. Coca MN, Morgan ML, Gupta P, Elkeeb A, Lee AG. Bilateral posterior ischemic optic neuropathy associated with use of sildenafil for pulmonary hypertension. *Can J Ophthalmol* 5: e96-9, 2016.
11. Dehghani A, Alemzadeh-Ansari MH, Masjedi M, Amirkhani A, Pourazizi M. Anterior ischemic optic neuropathy in a patient with erectile dysfunction: tadalafil as an offending medication. *J Res Pharm Pract* 7: 164-167, 2018.
12. Pomeranz, HD. Cases of ischemic optic neuropathy associated with phosphodiesterase-5 inhibitor use reported to the Food and Drug Administration Adverse Event Reporting System. *J Neuroophthalmol* 36: 221-222, 2016.
13. Campbell UB, Walker AM, Gaffney M, Petronis KR, et al. Acute nonarteritic anterior ischemic optic neuropathy and exposure to phosphodiesterase type 5 inhibitors. *J Sex Med* 12: 139-51, 2015.

PRECIPITANTS FOR NAION: CATARACT SURGERY

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LEARNING OBJECTIVES

1. The attendee will be able to explain the theoretical basis upon which cataract surgery has been considered as a precipitant of NAION.
2. The attendee will be able to identify risk factors that have been considered to increase the risk of NAION following cataract surgery.
3. The attendee will be able to explain the relative risk of developing NAION following cataract surgery.

CME QUESTIONS

1. Which of the following statements is true?
 - A. NAION following cataract surgery can be decreased by using non-steroidal anti-inflammatory drops
 - B. Patients with NAION following cataract surgery will have symptoms of pain on eye movement
 - C. Changes in surgery techniques and anesthesia have been considered to have decreased the rate of NAION following cataract surgery
 - D. Vitrectomy decreases the risk of NAION following cataract surgery.
2. True or False: There is prospective, randomized clinical evidence that connects NAION to cataract surgery.
3. Which of the following theories have been put forward to explain how NAION could theoretically be precipitated by cataract surgery:
 - A. Increased intraocular pressure
 - B. Raised intraorbital pressure from peribulbar or retrobulbar anaesthetic
 - C. Systemic perioperative hypotension
 - D. All of the above

KEYWORDS

1. Non-arteritic anterior ischemic optic neuropathy (NAION)
2. Cataract surgery
3. Post-cataract surgery ischemic optic neuropathy

HIGHLIGHTS

Non-arteritic ischemic optic neuropathy (NAION) is a relatively common optic neuropathy in patients over the age of 50 with an estimated annual incidence of around 10 per 100 000.¹ Cataract surgery is the most common ophthalmic surgical procedure in patients over the age of 50. The question has been raised as to whether there is a possible association between NAION and cataract extraction.

There are no prospective randomized trials that address this question therefore, the association is at best presumptive. However, there is a body of evidence that suggests there may be some association and causality.

Proposed Mechanism:

1. Immediate NAION: Intraocular pressure elevation
2. Delayed NAION: Intraocular inflammation: delayed reaction to inflammation similar to cystoid macular edema. Local vasoactive peptide release during and after uncomplicated cataract surgery may be responsible for the development

Evidence Available:

1. Case reports:
 - A. Townes reported 4 cases in 1951- 3 associated with uveitis.²
 - B. Serrano 1982: one patient who developed NAION following ICCE cataract surgery in first eye four weeks after surgery. There had been some IOP spikes. One year later had surgery in his other eye with control of IOP spikes with acetazolamide and Timolol. He developed NAION in the second eye within 4 weeks of surgery.³
 - C. O’Keeffe 1966: one patient with bilateral NAION each within 3 months of ICCE.⁴
2. Case series
 - A. Rees & Carroll (1958)⁵ reported 17 cases of ‘optic neuritis’ occurring 6-12 weeks following uncomplicated intracapsular cataract extraction.
 - i. 3 patients had bilateral NAION after cataract surgery
 - B. Hayreh (1980):⁶ hours to days after intra-capsular cataract surgery
 - i. Associated with peri-operative IOP spikes
 - ii. Occurred within days of cataract surgery.
3. Retrospective Cohort Study (McCulley et al 2001):⁷ 3 patients developed NAION out of 5787 cases within 1 year of cataract extraction. They suggested that the incidence of NAION increased after cataract extraction and a potential risk factor may be a history of NAION in the fellow eye.
4. Retrospective Cohort Study (Lam et al 2007):⁸ 325 patients who had NAION in one eye between 1986-2001: Findings: 17 patients underwent uncomplicated ECCE cataract surgery on the contralateral eye, 9 (53%) then developed NAION in the operated eye compared to 308 who did not undergo surgery 19% developed contralateral NAION
5. Retrospective nationwide cohort study 12 years in South Korea (Yang et al 2019)⁹: 40,356 patients who had undergone cataract surgery and matched non-cataract surgery controls
 - A. The 10-year incidence probability of NAION was 0.70% in the cataract surgery group and 0.27% in the non-cataract surgery group (P < .0001).
 - B. Unusual Features/Limitations of Study
 - i. The prevalence of glaucoma same in both groups
 - ii. 78% had NAION greater than one year after cataract surgery
 - iii. Diagnosis of NAION did not have any set criteria

Evidence Against:

1. Nguyen et al 2006¹⁰: Retrospective review of Neuro-ophthalmology Department
 - A. All patients had ‘typical risk factors’: 7 eyes identified
 - B. One patient had bilateral NAION- both 4 months after surgery (and 4 years apart)
2. Retrospective cohort study (Moradi et al 2017)¹¹

- A. 188 patients with NAION: Of these, 18 (9.6%) underwent cataract surgery during the year prior to developing NAION, while the remainder developed NAION spontaneously.
- B. No significant temporal patterns associated with subsequent NAION in the operated eye.
- C. No increased risk of PCSON to the fellow eye.

SUMMARY

It is extremely difficult to establish a causal relation based on available evidence.

- 1. Cataract surgery has changed with significantly less inflammation and IOP fluctuation
- 2. It is very difficult to ascribe the occurrence of NAION greater than one year after cataract surgery to the surgery.
- 3. There are a few case reports that suggest possible temporal relationship
- 4. However, one cannot exclude a weak association between modern cataract surgery and NAION. If there is a causal association, the risk is very low.

CME ANSWERS

- 1. C
- 2. False
- 3. D

REFERENCES

- 1. Hattenhauer MG, Leavitt JA, Hodge DO, et al. Incidence of nonarteritic anterior ischemic optic neuropathy. *Am J Ophthalmol* 1997;123:103-7.
- 2. Townes CD, Moran CT, Pfingst HA. Complications of cataract surgery. *Trans Am Ophthalmol Soc* 1951;49:91-107.
- 3. Serrano LA, Behrens MM, Carroll FD. Postcataract extraction ischemic optic neuropathy [letter]. *Arch Ophthalmol* 1982; 100:1177-8.
- 4. O'Keeffe D, Choudhury KC. Bilateral optic neuritis following cataract surgery. *Br J Ophthalmol* 1966;50:608-609
- 5. Reese AB, Carroll FD. Optic neuritis following cataract extraction. *Am J Ophthalmol* 1958;45:659-62.
- 6. Hayreh SS. Anterior ischemic optic neuropathy. IV. Occurrence after cataract extraction. *Arch Ophthalmol* 1980;98: 1410-6.
- 7. McCulley TJ, Lam BL, Feuer WJ. Incidence of nonarteritic anterior ischemic optic neuropathy associated with cataract extraction. (*Ophthalmology* 2001;108:1275-8.)
- 8. Lam BL, Jabaly-Habib H, Al-Sheikh N, Pezda M, Guirgis MF, Feuer WJ, et al. Risk of non-arteritic anterior ischaemic optic neuropathy (NAION) after cataract extraction in the fellow eye of patients with prior unilateral NAION. *Br J Ophthalmol* 2007;91:585-7.
- 9. Yang HK; Park SJ; Byun SJ; Park KH; Hwang JM. Risk of Nonarteritic Anterior Ischemic Optic Neuropathy after Cataract Surgery. *AJO* 2019;307:343-348.
- 10. Nguyen LT, Taravella MJ, Pelak VS. Determining whether delayed nonarteritic ischemic optic neuropathy associated with cataract extraction is a true entity. *J Cataract Refract Surg* 2006;32(12):2105-2109.

11. Moradi A, Kanagalingam S, Diener-West M, Miller NR. Post-cataract surgery optic neuropathy: prevalence, incidence, temporal relationship, and fellow eye involvement. *Am J Ophthalmol* 2017;175(3):183-193.

VESSEL IMAGING IN GIANT CELL ARTERITIS

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LEARNING OBJECTIVES

1. List the various vessels which can be involved in giant cell arteritis.
2. Identify the advantages/disadvantages of the various imaging techniques available to the clinician when investigating a patient suspected of giant cell arteritis.
3. Use the proper imaging techniques for a patient suspected to harbour giant cell arteritis, according to the clinical presentation.

CME QUESTIONS

1. True or False: The rate of detection of choroidal non-perfusion on retinal angiography is higher when using indocyanine green than fluorescein.
2. True or False: Temporal artery ultrasound can replace the need for temporal artery biopsy when suspecting giant cell arteritis.
3. True or False: OCT angiography is a sensitive and specific test to diagnose arteritic AION.

KEYWORDS

1. Giant cell arteritis
2. MRI
3. PET/CT
4. Ultrasound
5. OCTA

HIGHLIGHTS

Giant cell arteritis (GCA) is the most frequent vasculitis in patients aged 50 and above, affecting large- and medium-sized arteries. GCA has a predilection for the extracranial branches of the carotid arteries and visual loss is the most feared complication of GCA. Recent studies demonstrated that up to 70% of GCA patients present also involvement of other arterial territories (aorta, vertebral, axillary, subclavian, iliofemoral, renal, mesenteric arteries).¹⁻⁶ Visual loss results most frequently from ocular ischemia, whereas cerebral ischemia is rare. Ocular ischemic events result from an occlusive arteritis of the ophthalmic artery and/or its branches (central retinal artery, short and long posterior ciliary arteries, anterior ciliary arteries). Arteritic anterior ischemic optic neuropathy (AAION) is the most common presentation of visual loss in GCA, accounting for > 80% of cases. Other mechanisms of visual loss include central retinal artery occlusion (5-15%), choroidal ischemia, posterior ischemic optic neuropathy (<3%), cotton-wool spots. It is not rare to encounter a combination of such ischemic events in the same eye. Amaurosis fugax has been reported in 15-25% of patients who later developed permanent visual loss. Stroke and/or transient ischemic attacks occur less frequently than ocular ischemia, the incidence

of cerebral complications ranging from 2-4%.⁷⁻⁹ Cerebral ischemic events result from arteritis involving the extradural portions of either the vertebral or carotid arteries.

Vessel imaging in GCA is essential not only to promptly establish a correct diagnosis of GCA but also to detect and follow the presence of occult arterial involvement in extracranial arterial territories such as the aorta.

Temporal artery (TA) is frequently involved in GCA, but not always. Imaging TA is an important step in diagnosing GCA. TA biopsy (TAB) is still the gold standard but is invasive. A useful and non-invasive alternative to TAB is ultrasonography which can demonstrate the “halo sign” (vessel wall thickening). However it is operator-dependent and both sensitivity and specificity are lower than TAB. Cerebral MRI and CTA can demonstrate extracranial artery involvement, but like for ultrasonography, both sensitivity and specificity are lower than TAB.

In the presence of transient or permanent visual loss, retinal and choroidal angiography can reveal either papillary, retinal or choroidal delayed perfusion.¹⁰ Fluorescein angiography is sufficient, as the use of indocyanine green does not increase the rate of detection of choroidal non-perfusion.¹¹

OCTA has been recently used in a few patients with AAION. OCTA can disclose choroidal nonperfusion, but its sensitivity is lower than retinal/choroidal angiography. It is too early to determine whether AAION has a specific presentation on OCTA and larger prospective studies are needed to determine the potential role of OCTA in GCA.

Aortitis can be found in up to 70% of patients at the time of the initial diagnosis of GCA, whereas a clinical manifestation of aortitis is much lower (3-18%). Aortitis is associated with an increased risk of developing aneurysm or dissection with potentially dramatic complications. Whereas routine imaging of the aorta at the time of GCA diagnosis is recommended by the American Cardiology guidelines, the European League Against Rheumatism (EULAR) does not reach the same conclusions. Apart from the cost and the potential difficulties/risks to image (i.e. PET/CT), it is not yet determined whether routine imaging of the aorta is beneficial or not to the patient. Aorta imaging should be performed in patients with symptoms of aortic ischemia, inflammatory flare (ESR, CRP, thrombocytes) or a chronic form of GCA necessitating steroids/immunosuppression for more than two years.

SUMMARY

Vessel imaging is of prime importance in the diagnosis and management of GCA and new imaging techniques are emerging. For the neuro-ophthalmologist facing a patient with transient or permanent visual loss, OCTA is a promising new and non-invasive imaging technique, but cannot replace retinal/choroidal fluorescein angiography. The gold standard for confirming a clinical suspicion of GCA remains temporal artery biopsy, even if temporal artery ultrasonography is recommended by non-ophthalmologists. Neuro-ophthalmologists should be aware of frequent aortic involvement in GCA.

CME ANSWERS

1. False: the use of indocyanine green dye does not increase the rate of detection of choroidal non perfusion when compared with fluorescein.

2. False: temporal artery biopsy remains the gold standard and cases of positive temporal artery with negative ultrasound studies have been reported.
3. False: the vascular anomalies which can be detected either on the optic disc or around the optic nerve head are nonspecific. Further studies are needed to determine whether OCTA might be of help to diagnose GCA.

REFERENCES

1. Blockmans D, de Ceuninck L, Vanderschueren S, et al. Repetitive 18F-fluorodeoxyglucose positron emission tomography in giant cell arteritis: a prospective study of 35 patients. *Arthritis Rheum* 2006;55:131–7.
2. Prieto-Gonzalez S, Arguis P, Garcia-Martinez A, et al. Large vessel involvement in biopsy-proven giant cell arteritis: prospective study in 40 newly diagnosed patients using CT angiography. *Ann Rheum Dis* 2012;71:1170–6.
3. Schmidt WA, Seifert A, Gromnica-Ihle E, et al. Ultrasound of proximal upper extremity arteries to increase the diagnostic yield in large-vessel giant cell arteritis. *Rheumatology* 2008;47:96–101.
4. Aschwanden M, Kesten F, Stern M, et al. Vascular involvement in patients with giant cell arteritis determined by duplex sonography of 2×11 arterial regions. *Ann Rheum Dis* 2010;69:1356–9.
5. Lie JT. Aortic and extracranial large vessel giant cell arteritis: a review of 72 cases with histopathologic documentation. *Semin Arthritis Rheum* 1995;24:422–31.
6. Brack A, Martinez-Taboada V, Stanson A, Goronzy JJ, Weyand CM. Disease pattern in cranial and large-vessel giant cell arteritis. *Arthritis Rheum* 1999;42:311–7.
7. Frohman L, Wong ABC, Matheos K, Leon-Alvarado LG, Danesh-Meyer HV. New developments in giant cell arteritis. *Surv Ophthalmol* 2016;61:400–421.
8. Salvarani C et al. Risk factors for severe cranial ischemic events in an Italian population-based cohort of patients with giant cell arteritis. *Rheumatology* 2009 ;48 :250–253.
9. Gonzalez-Gay MA et al. Strokes at time of disease diagnosis in a series of 287 patients with biopsy-proven giant cell arteritis. *Medicine* 2009 ;88 :227–235.
10. Samson, M. et al. Stroke associated with giant cell arteritis: a population-based study. *J. Neurol. Neurosurg. Psychiatry*. 2015 ;86 : 216–221.
11. Ball EL, Walsh SR, Tang TY, Gohil R, Clarke JM. Role of ultrasonography in the diagnosis of temporal arteritis. *Br J Surg* 2010;97:1765–71.
12. Arida A, Kyprianou M, Kanakis M, Sfrikakis PP. The diagnostic value of ultrasonography-derived edema of the temporal artery wall in giant cell arteritis: a second meta-analysis. *BMC Musculoskeletal Disord* 2010;11:44.
13. Bley T, Uhl M, Carew J, et al. Diagnostic value of high-resolution MR imaging in giant cell arteritis. *AJNR Am J Neuroradiol*. 2007;28:1722e7.
14. Kawasaki A, Michel P, Maeder P, Borruat F-X. Visualizing the skip lesions of giant cell arteritis with CT angiography. *Eur Neurol* 2009;61:374.
15. Siatkowski RM, Gass JD, Glaser JS, Smith JL, Schatz NJ, Schiffman J. Fluorescein angiography in the diagnosis of giant cell arteritis. *Am J Ophthalmol* 1993 ;115 :57–63.
16. Valmaggia C, Speiser P, Bischoff P, Niederberger H. Indocyanine green versus fluorescein angiography in the differential diagnosis of arteritic and nonarteritic anterior ischemic optic neuropathy. *Retina* 1999;19:131–134.
17. Balducci N et al. Optical coherence tomography angiography in acute arteritic and non-arteritic anterior ischemic optic neuropathy. *Graefes Arch Clin Exp Ophthalmol* 2017 ;255 :2255–2261.

18. Cerda-Ibanez M et al. Correlation between ischemic retinal accidents and radial peripapillary capillaries in the optic nerve using optical coherence tomographic angiography : observation in 6 patients. *Ophthalmol Eye Dis* 2017;9:1-3.
19. Gaier ED et al. Optical coherence tomographic angiography identifies peripapillary microvascular dilation and focal non-perfusion in giant cell arteritis. *Br J Ophthalmol* 2018;102 :1141-1146.
20. Rougier MB et al. OCT angiography and choroidal ischemia related to arteritic anterior ischemic optic neuropathy. *J Fr Ophtalmol* 2017 ;40 :438-439.
21. Hiratzka LF, Bakris GL, Beckman JA, et al. *J Am Coll Cardiol.* 2010;55:e27–e129.
22. DeJaco C, Ramiro S, Duftner C et al. EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice. *Ann Rheum Dis* 2018;77:636-643.
23. Chen JJ, Warrington KJ, Garrity JA, Prasad S. Is routine imaging of the aorta warranted in patients with giant cell arteritis? *J Neuro-Ophthalmol* 2017;37:314-319.

TELEMEDICINE 20/20 IN 2020: HOW FAR WE HAVE COME, WHERE ARE WE HEADED AND HOW IS IT RELEVANT TO NEURO-OPHTHALMOLOGY?

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LEARNING OBJECTIVES

1. Describe and provide an overview of the spectrum of telemedicine interactions
2. Grasp the current landscape of patient expectations and healthcare delivery that is shaping the future of telemedicine for ophthalmology and neuro-ophthalmology
3. Understand the current landscape of physician readiness to adopt and integrate telemedicine into their workflow

CME QUESTIONS

1. True or False: The age distribution of physicians interested and willing to engage in telemedicine skews towards the millennial generation and younger.
2. True or False: While the technological advances exist and are ready for synchronous live audio-video telemedicine, 66% percent of consumers surveyed state they prefer seeing their physician in person in the office.
3. True or False: Presently, only 8% of consumers surveyed have actually used telemedicine services, despite a majority expressing willingness to use it.

KEYWORDS

1. Telemedicine
2. Teleconsultation
3. Consumer Telehealth Trends

HIGHLIGHTS

Advances in technology, demographic shifts, market changes and patient/consumer demands are all forces propelling delivery of health care in ways towards telemedicine, requiring neuro-ophthalmologists to consider how we will adapt to these changes while facing challenges of physician shortage, limited patient access, limited reimbursement and regulatory demands.

SUMMARY

Telehealth is a broader definition of health care delivery over distance or time using electronic communication technologies, which serve to enhance health care access, quality, and patient satisfaction. It encompasses diagnosis, management, education and administration. Telehealth can be delivered through live audio-video (synchronous), store-and-forward (asynchronous), remote patient monitoring (RPM) or mobile health (mHealth) formats. **Telemedicine**, is more narrowly defined as the provision of traditional clinical service using electronic communication technology via one of the above formats.¹

Telemedicine Trends

In the last decade, with advancements in technology, there has been a dramatic increase in the use of telehealth and telemedicine in the private and academic sectors. In 2018, the U.S. telemedicine market was valued at \$21.5 million and is expected to grow to \$60.5 million by 2024.² Globally, in 2018 the telemedicine market was valued at \$38.5 billion and this is projected to be \$130.5 billion by 2025.² Canada has been at the forefront of telemedicine for decades and is more integrated compared to the United States, with a telemedicine network within each province. In 2017, the Ontario Telemedicine Network conducted nearly 900K patient consultations and 20K of those visits occurred within the patient's home with 270 million kilometers avoided in patient travel.³ The rapid expansion and projected hypergrowth of telemedicine is due to multiple factors including a growing need to access medical care along with the introduction of technologies that allow for physicians to do clinical work remotely. Geographic boundaries are removed and patients and physicians can now reliably connect in real-time.

Are Patients Ready for Telehealth/Telemedicine?

The dramatic increase in telehealth use can also be attributed to change in consumer demand for telemedicine as younger generations and digital natives are receptive and even prefer to receive their health care delivered in telehealth formats. In 2019, American Well conducted a survey in collaboration with Harris Interactive polling 2,000 U.S. consumers.⁴ Sixty-six percent of respondents said they are willing to use telemedicine services. These respondents named convenience, faster service, cost savings and better access to professionals as top reasons for that willingness. Cost savings was the top reason for telehealth use in the 35 to 44 age group, convenience was the top reasons among the 45 to 54 age group, and faster service was cited as the main driver in the 65-plus age group. Compared with the results from American Well's 2017 survey, the number of consumers who said they would be willing to switch primary care providers for access to telehealth services increased from 50 million in 2017 to 64 million in 2018.⁴ Experts state that these trends suggest that it will be increasingly important for health care plans, systems and individual practices to have telemedicine as one of the treatment care options available to patients.

According to one JAMA study, telemedicine patient visits increased annually by 261 percent between 2015 and 2017.⁵ Despite the meteoric rise of telemedicine use by patients, there still remains a gap between willingness to use telemedicine versus actual use—66% of consumers are willing to use telemedicine but only 8 percent actually do.⁴ This can be attributed to lack of patient awareness as many patients do not know that their hospital or physician practices offers telehealth services. Another cited reason is that when surveyed consumers are asked where they would seek care if they or a loved one have a perceived health care issue during evening hours, 52% of consumers state they would go to an emergency room and only 18% stated they would utilize a virtual healthcare visit.⁶ Public awareness and patient education of when to utilize telemedicine versus urgent care or the emergency room may alter this perception.

Are Physicians ready for Telehealth/Telemedicine?

There is limited research regarding the population of physicians delivering care through telemedicine. The American Medical Association (AMA) recently reported in a national physician survey that 15% of physicians have used telemedicine in clinical settings for the purpose of diagnosing or treating patients.⁷ Doximity published the first analysis of U.S. physician interest in telemedicine clinical work in a recent report.⁸ They cited that between 2015-2018, physicians who self-reported telemedicine as one of their skills doubled and is increasing by about 20 percent per year. When looking at gender, Doximity

reported that female physicians were 10% more interested in telemedicine job opportunities relative to male physicians. Interestingly, in the Doximity report, physicians across all age groups had nearly equal interest in telemedicine, with 28.4% of doctors between the ages of 31-40 years old showing interest in telemedicine, 26.5% of doctors between the ages of 41-50 years, 24.5% of doctors between the ages of 51-60 years, and 17.6% of doctors between the ages of 61-70 years.

2020 and Beyond—What to Expect

1. Telehealth is health, and will be the standard of care. It will be just as commonplace for a doctor to see the first two patients in person as it will be to see the next two via the computer screen integrated with the electronic medical record.
2. Home telehealth and remote patient monitoring will continue to expand⁹
3. E-consultations will continue to grow. This is becoming a trend not only in direct-to-consumer telemedicine, but also among hospitals and academic medical centers where they have realized high satisfaction ratings from patients and providers alike.

What does this mean for neuro-ophthalmology?

We live in interesting times and are at an inflection point in medicine, specifically within our field of neuro-ophthalmology. Advances in technology, demographic shifts, market changes and patient/consumer demands are all forces propelling delivery of health care in new ways, requiring neuro-ophthalmologists to consider how we will adapt.

Within ophthalmology, there exists well documented applications of telemedicine in screening for diabetic retinopathy and retinopathy of prematurity.^{10,11} Within neurology, availability of telestroke care is widespread and have been in place for more than a decade demonstrating improved time to needle administration of tissue plasminogen activator (tPA) and patient neurological outcomes.¹²

There are limited numbers of neuro-ophthalmologists worldwide and they are mainly concentrated in larger metropolitan areas. Patient access and wait times for neuro-ophthalmic appointments are easily on the order of several months. Barriers of geographical distance and technological capabilities are reduced through telemedicine via live audio-video or electronic consultations. The future and survival of our field will be supplemented by telemedicine and will need to become part of our standard of care. The challenges of reimbursement and payment within the United States (see Dr. Kevin Lai's syllabus) remain, but the national and global marketplace is more ready than ever before. As increasing data emerge demonstrating that ophthalmic telemedicine is non inferior to in-office examinations, reduces cost curves, improves patient access, patient visual outcomes, and patient experience, it is only a matter of time that commercial and government payors will follow suit and expand payment of tele ophthalmic services. With such a future within near grasp, we should consider and identify ways for neuro-ophthalmology to be at the ready to integrate and promote the use of telemedicine as a conduit for patients to access our subspecialized clinical expertise.

CME ANSWERS

1. False
2. False
3. True

REFERENCES

1. Telemedicine for Ophthalmology Information Statement. Task Force on Telemedicine in Ophthalmology: American Academy of Ophthalmology. <https://www.aao.org/clinical-statement/telemedicine-ophthalmology-information-statement>. (Accessed on 23 September 2019).
2. Gminsights.com (2019). Telemedicine Market Share Report: Global 2019-2025 Industry Data. <https://www.gminsights.com/industry-analysis/telemedicine-market> (Accessed on 23 September 2019).
3. Ontario Telemedicine Network Annual Report 2017-2018 <https://www.otn.ca/wp-content/uploads/2017/11/otn-annual-report.pdf> (accessed on 19 September 2019).
4. Telehealth Index: 2019 Consumer Survey <https://static.americanwell.com/app/uploads/2019/07/American-Well-Telehealth-Index-2019-Consumer-Survey-eBook2.pdf> (accessed on 23 September 2019).
5. Barnett ML, Ray KN, Souza J, Mehrotra A. Trends in Telemedicine Use in a Large Commercially Insured Population, 2005-2017. JAMA. 2018;320(20): 2147-2149.
6. Vaidya, A. "Market your telehealth program with precision using these 5 consumer profiles." Becker Hospital Review. <https://www.beckershospitalreview.com/hospital-management-administration/market-your-telehealth-program-with-precision-using-these-5-consumer-profiles.html> (accessed on 19 September 2019).
7. Kane, CK. "The Use of Telemedicine by Physicians: Still the Exception Rather Than the Rule." Health Affairs. (December 1, 2018) <https://www.healthaffairs.org/doi/abs/10.1377/hlthaff.2018.05077> (accessed 31 October 2019).
8. Doximity 2019 Telemedicine and Locum Tenens Opportunities Survey: Measuring Physician Interest in Emerging Employment Areas (July 2019) <https://s3.amazonaws.com/s3.doximity.com/press/2019TelemedicineAndLocumTenensOpportunitiesStudy.pdf> (accessed on 31 October 2019).
9. Holekamp NM. Moving from Clinic to Home: What the Future Holds for Ophthalmic Telemedicine. Am J Ophthalmol 2018 Mar; 187: xxviii-xxxv.
10. American Telemedicine Association. Telehealth Practice Recommendations for Diabetic Retinopathy, 2nd edition. 2011.
11. Biten H, Redd TK, Moleta C, et al. Diagnostic Accuracy of Ophthalmoscopy vs Telemedicine in Examinations of Retinopathy of Prematurity. JAMA Ophthalmol 2018; 136(5) 498-504.
12. Schwamm LH, Holloway RG, Amarenco P, et al. A review of the evidence for the use of telemedicine within stroke systems of care: A scientific statement from the American Heart Association/American Stroke Association. Stroke 2009; 40: 2616-34.

PANORAMIC VIEW OF A SYSTEM-WIDE TELEMEDICINE PROGRAM AT AN ACADEMIC MEDICAL CENTER

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LEARNING OBJECTIVES

1. The attendee will be able to list the modalities of telemedicine.
2. The attendee will be able to describe components of building a successful telemedicine program.
3. The attendee will be able to describe regulatory issues to consider in providing virtual care.
4. The attendee will be able to describe reimbursement challenges for telemedicine programs.
5. The attendee will be able to explain how to assess the value of a telemedicine program.

CME QUESTIONS

1. Legislation and regulations to consider when implementing telemedicine include:
 - A. Licensure
 - B. Informed consent
 - C. HIPAA
 - D. a, b and c
2. Diabetic retinopathy screening and ROP screening are examples of which telemedicine modality?
 - A. Synchronous
 - B. Asynchronous (store and forward)
 - C. Remote patient monitoring
3. In addition to direct revenue from reimbursement, which of the following are examples of how telemedicine can add value to a health system?
 - A. Increased patient access and convenience
 - B. Cost avoidance through less expensive care and avoiding unnecessary care
 - C. Increased provider satisfaction
 - D. a, b and c

KEYWORDS

1. Telemedicine
2. Tele-ophthalmology
3. Telehealth
4. Virtual care

HIGHLIGHTS

Health care systems are increasingly recognizing the benefits of incorporating telemedicine offerings into their delivery of health care. The main telemedicine modalities include virtual video visits, store-and-forward platforms and remote patient monitoring. The programs that succeed are the programs that manage change well by defining a mission and establishing goals that align with institutional

strategic priorities. Developing a plan and a roadmap to success includes managing implementation, minimizing disruption, providing training and support, leveraging reimbursement, measuring outcomes and satisfaction, and publishing results. In parallel, establishing evidence-based standards and working with government affairs to improve the regulatory environment for telehealth legislation are important roles which academic health system telemedicine programs can fill to amplify the return on investment in digital health technology.

SUMMARY

Definition and modalities

The American Telemedicine Association defines telemedicine as “the remote delivery of health care services and clinical information using telecommunications technology”¹ while the World Health Organization defines telemedicine simply as “healing at a distance.”² The primary elements of telemedicine are to provide clinical support, overcome geographical barriers by connecting users in different locations, use of telecommunications technology and improved health outcomes. Some of the main benefits of telemedicine are increased access to care, expansion of populations served, lowered total cost of care, and increased patient and provider satisfaction. Major academic health systems across the US are increasingly implementing telehealth programs and integrating digital health solutions to enhance their delivery of care while meeting the growing consumer demand for convenient access to services and to leverage finite health care resources.

Health systems using telemedicine typically have multiple virtual care offerings allowing provider-to-provider and direct-to-consumer interactions. The telehealth tools or modalities that allow these virtual healthcare delivery options include:

- synchronous or real-time virtual video visits between patient and provider or between two or more providers [eg primary care and specialty care video visits, e-consults],
- asynchronous or store-and-forward transmission of diagnostic images and patient data usually via a patient portal for later (not in real time) review by a health care professional [eg telemedicine diabetic retinopathy and retinopathy of prematurity screening, e-visits, medical second opinions],
- remote patient monitoring of chronically ill patients utilizing technology to remotely collect and send data to a home health agency, diagnostic testing facility or critical care command center [eg tele-ICU], and
- mobile or mhealth using mobile devices to improve health outcomes, health care services and health research with a large educational component.³

Implementing telehealth programs at academic medical centers

In the US, 91% of academic medical centers have a telehealth system, many of which are already at an advanced level.⁴ Most are integrated with an electronic health record and most have centralized teams providing core services and telehealth support. The operational framework and organizational structure of telehealth program for large health systems are typically tailored to the specific mission, long-term goals and strategic plan of the institution. The telemedicine program governance sets priorities for the initiatives of highest value to the health system. To build a feasible, leadership needs to be engaged and willing to commit the investment of resources with the knowledge that the return on investment may require time. Setting up a telemedicine program and embedding it into an academic health system requires a team of experts. Coordination is vital with a highly collaborative telemedicine program or office to bridge the university and health system and to work closely with its various entities including all inpatient and outpatient facilities. The organizational structure should define key members including a medical director supported by an administrative director, project manager(s), technology manager(s),

trainers and staff dedicated to integrating the virtual care platform(s) with the electronic health record. Staff may be divided into inpatient and outpatient teams. The team(s) should be advised by telehealth experts comprising legal, compliance, payor, government affairs, operations, finance, security, quality and safety, clinical champions and information technology workgroups. All telemedicine projects should be vetted by each team of experts to ensure adherence to the same standard of care as delivery of in-person care.

Drivers and barriers to telehealth adoption

Key drivers to telehealth adoption include new advancements in technology that improve usability and decrease costs, health system transformation with incorporation of telemedicine into standard of care practices, consumer demand, and interest in technology. Healthcare consumers are changing and their expectations for convenience, affordability and quality are redefining how they engage in their care.⁵ Younger patients, especially millennials and generation X, acquire goods and services electronically and are also more willing to seek out non-traditional healthcare services electronically or in retail space. Healthcare systems, providers, and payers who deliver what patients are looking for, rather than expecting only a return on investment, will be the ones to earn loyalty and will be well-positioned as the future of healthcare consumerism unfolds.

Key barriers to widespread telehealth adoption are federal and state policies governing telehealth activities, sustainability due to financial and reimbursement challenges, and the need for solid published evidence on the benefits of care delivery by telemedicine. A major policy barrier is the requirement for state medical licensure at the patient's originating site, which often limits the locations in which a provider may perform telehealth services. Medicine occurs where the patient, not the provider, is located. This limits the utility of telemedicine options to provide specialty care from academic institutions to areas where specialists may not be available. Interstate licensure compacts are improving the landscape but do not eliminate the potential need for multiple state licenses to utilize telemedicine modalities over a wide geographic area. While early changes have been implemented in 2019, statutory restrictions on coverage for telemedicine services by the Centers for Medicare and Medicaid Services still need to expand payment to all geographic areas and appropriate telehealth services. Commercial payers have generally embraced the adoption of telehealth models of care more openly and reimbursement is becoming more common but payment parity with services that are delivered in person is not always present. Other challenges include lack of broadband service to support telehealth in some areas, high cost of technologies and infrastructure, inadequate clinical engagement, poor leadership vision, and lack of standardized measures of success.

Scaling and optimizing telehealth programs to support health system transformation

Telehealth networks can be leveraged to connect emergency departments, hospitals, outpatient offices, diagnostic centers and skilled nursing facilities to help provide a continuum of care across the enterprise. Specific opportunities to grow telemedicine programs at academic centers include achieving cost savings by treating low acuity patients remotely with synchronous or asynchronous care leaving in-person appointments for higher acuity patients. Reducing readmissions and hospitalizations with remote monitoring of patients with chronic illnesses, improving care coordination, and incorporating telehealth services into value-based care lowers the total cost of care. Increasing patient engagement with digital health and making care more convenient improves patient satisfaction. Finally, combining virtual care with advanced analytics and artificial intelligence provides an opportunity for personalized precision medicine.

However, full adoption of telemedicine by all stakeholders requires a culture shift. Clinical champions who demonstrate the benefits and power of telehealth and integration of telemedicine into the clinical workflow help providers to understand and accept this new health care delivery model as a routine

process to provide care. More importantly, high quality economic evaluation and implementation science studies are needed to better understand the complexities in scaling up digital health technologies and developing effective pathways for change.⁶ Academic institutions are particularly well-situated to help develop standards and guidelines for implementation of telemedicine programs such as has been accomplished for diabetic retinopathy and retinopathy of prematurity screening.^{7,8} Standardized reporting metrics and dashboards to monitor the quality and success of telemedicine programs have been less clearly identified. On an institutional level, reporting metrics and dashboards should be part of every telemedicine program. Return on investment is measured not only with financial metrics but also with value metrics. At a minimum, financial metrics should include direct revenue (reimbursement), indirect revenue (new patients, retention of patients), total cost of care (burden on patient, payer and provider), and cost avoidance (avoiding unnecessary care, less costly care). Equally important to measure, although not in dollars and cents, are value metrics including patient access and convenience, clinical quality, provider satisfaction, and competitive advantage.⁹

Telehealth is likely the disruptive technology that will have the biggest impact on health care delivery in the years to come. Telemedicine has been shown to optimize delivery of care, increase access, reach patients at distant locations, improve quality of care and increase patient satisfaction. Academic institutions are increasingly leveraging telemedicine to achieve these benefits. The merits of implementing and scaling telehealth services are based not solely on reimbursement but also on value and financial benefits from changes to patient acuity levels and increased new and retained patient volumes.

CME ANSWERS

1. D
2. B
3. D

REFERENCES

1. The American Telemedicine Association: About telemedicine, available from: <http://legacy.americantelemed.org/main/about/about-telemedicine/telemedicine-faqs>
2. World Health Organization: Telemedicine: Opportunities and developments in member states, available from: https://www.who.int/goe/publications/goe_telemedicine_2010.pdf
3. Classification of digital health interventions, Geneva: World Health Organization, (WHO/RHR/18.06), licence CC BY-NC-SA 3.0 IGO, 2018.
4. American Hospital Association: Telehealth: A path to virtual integrated care, available from https://www.aha.org/system/files/media/file/2019/02/MarketInsights_TeleHealthReport.pdf
5. Gill L, Minchak M, Samuel A: Healthcare Technology & Disruption, 2019 Outlook: Disruption = Opportunity; Follow the consumer in 2019, JP Morgan, Dec 2018.
6. Labrique A, Vasudevan L, Weiss W, et al: Establishing standards to evaluate the impact of integrating digital health into health systems, Global Health: Science and Practice, Vol 6, S5, 2018.
7. Li H, Horton M, Bursell S, et al: Telehealth practice recommendations for diabetic retinopathy, second edition, Telemedicine and eHealth, Vol 17, 10, 2011.
8. Fierston W, Capone A, American Academy of Pediatrics, et al: Telemedicine for evaluation of retinopathy of prematurity, Pediatrics, 135, 1, e238, 2015.
9. Arkwright B, Leslie M, Light M: Telehealth finance variables and successful business models, Telehealth and Medicine Today, Vol 4, 2019.

10. Ellimootil C, An L, Moyer M, et al: Challenges and opportunities faced by large health systems implementing telehealth, *Health Affairs*, 37, No 12:1955, 2018.
11. Kruse C, Krowski N, Rodriguez B, et al: Telehealth and patient satisfaction: a systematic review and narrative analysis, *BMJ Open*, 7:e016242. doi:10.1136/bmjopen-2017-016242, 2017.
12. Agarwal S, Lefevre A, Labrique A: A call to digital health practitioners: new guidelines can help improve the quality of digital health evidence, *JMIR Mhealth Uhealth*, Vol 5, 10, e136, 2017.
13. AHA Center for Health Innovation: Telehealth: A path to integrated virtual care, https://www.aha.org/system/files/media/file/2019/02/MarketInsights_TeleHealthReport.pdf

A NOVEL TELE-DIZZY CONSULTATION PROGRAM IN THE EMERGENCY DEPARTMENT USING PORTABLE VIDEO-OCULOGRAPHY

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LEARNING OBJECTIVES

1. The attendee will be able to identify those patients who would benefit the most from a Tele- dizzy consultation.
2. The attendee will be able to describe the workflow of a Tele-dizzy consultation service.
3. The attendee will be able to describe the equipment and personnel necessary to perform a Tele-dizzy consult.

CME QUESTIONS

1. Which of the following patients presenting to the Emergency Department with new onset vertigo would benefit the most from having their eye movements recorded (using video-oculography [VOG] and video head impulse test [vHIT])?
 - A. A patient presenting with acute onset continuous vertigo and spontaneous nystagmus
 - B. A patient with horizontal canal benign paroxysmal positional vertigo
 - C. A patient with posterior canal benign paroxysmal positional vertigo
 - D. All of these patients would benefit from VOG and/or vHIT
2. True or False: Stroke neurology should be consulted immediately (prior to VOG/vHIT) in a patient presenting with acute vertigo and vision loss due to a homonymous hemianopia.
3. What are challenges associated with the implementation of a Tele-Dizzy consultation service ?
 - A. The testing is technique dependent
 - B. A patient can have dizziness or vertigo due to a stroke and have normal eye movements
 - C. There are too few vestibular subspecialists to staff these consults (i.e., automated algorithms - “ECG of the eyes” - must be developed and refined)
 - D. a, b, and c are challenges

KEYWORDS

1. Vertigo
2. Video-oculography
3. Dizzy
4. Video head impulse test

HIGHLIGHTS

Background

Dizziness and vertigo leads to 4.4 million emergency department (ED) visits annually in the US.¹ Nationally, up to one-third of these patients have benign inner ear conditions while about 5% have strokes, which in some cases could be life threatening or cause long-term morbidity.² The tools utilized for ED diagnosis in distinguishing ear from brain disorders is often low quality (inaccurate) and expensive (test overuse). At the national level, it has been estimated that approximately 50,000 strokes are missed annually in patients presenting with the chief complaint of dizziness or vertigo.³ There are also significant value consequences for the diagnostic process of dizzy patients with an estimated \$1 billion spent nationally on unnecessary scans (obtained roughly half of the time¹) and unnecessary admissions in patients ultimately diagnosed with inner ear diseases.

The first description of the “HINTS” (Head Impulse, Nystagmus, Test of Skew) exam came in 2008.⁴ In the acute vestibular syndrome (AVS) - acute prolonged vertigo, spontaneous nystagmus, imbalance, head motion intolerance, nausea - the HINTS three step ocular motor exam has superior sensitivity and specificity in the detection of stroke as compared to the current “gold standard” MR-diffusion weighted imaging. In the hands of eye movement experts, HINTS is proven. However, its implementation has been limited for a variety of reasons including: many emergency medicine frontline providers are unfamiliar with the exam; improper technique (especially with the head impulse test [HIT]); improper interpretation (especially when abnormalities are mild, or when spontaneous nystagmus is robust); HINTS is misused – e.g., using it to triage patients with the episodic vestibular syndrome (EVS), when triggered (e.g., benign paroxysmal positional vertigo) or when spontaneous (e.g., TIA, vestibular migraine). Although HINTS has a very high sensitivity (96.5%) and specificity (84.4%) to detect stroke in the acute vestibular syndrome,⁴ it is not widely utilized. This work strives to leverage technology to bring the expertise of eye movement specialists to the bedside.

A ‘Tele-Dizzy’ Service

Technological advances in portable video-oculography (VOG) equipment have made it possible to record eye movements. VOG technology is FDA-approved and is currently in routine clinical use with human interpretation by neuro-otology experts. In fact, many vestibular experts have supplanted caloric and rotary chair testing with VOG-based video head impulse testing (vHIT) as the initial test given its portability, speed of testing, and favorable tolerability.

Implementation of a ‘tele-dizzy’ clinical service would enable a single expert to drastically expand their clinical reach through simultaneous coverage of multiple EDs. A tele-dizzy service could reliably, inexpensively, and quickly distinguish ear and brain etiologies of dizziness and vertigo since experts are providing the interpretation. Eye movement specialists can now almost instantaneously review a VOG exam remotely in minutes, enabling rapid tele-diagnosis. Addition of a standardized dizzy questionnaire (in a user-friendly kiosk format) would enhance localization and the ability to generate an accurate differential diagnosis, especially in patients with transient symptoms or in those without spontaneous nystagmus where HINTS cannot be relied upon.

Tele-Dizzy Workflow

ED providers would rule out medical and obvious neurologic causes of dizziness or vertigo (e.g., patient with vertigo and hemiparesis would immediately have a stroke consult, not a tele-dizzy consult). The triggers for a tele-dizzy consult would include:

- 1) Suspicion for a central cause of dizziness is high enough that a neuroimaging study would normally be ordered.

- 2) If a patient is diagnosed by an EM provider with a peripheral vestibular disorder, a tele-dizzy consult should be requested prior to discharge.

Once the tele-dizzy consult service is paged, a technician trained to operate the VOG would go to the bedside and perform eye movement testing. Historical data (using an evidence-based timing and triggers approach) would be collected in a standardized kiosk-style questionnaire by the same technician operating the VOG, and the history and exam elements would be securely transferred to the physician for review. Within a set period of time, the consulting physician would make recommendations regarding diagnosis and further evaluation largely based on the following:

- 1) Patients with ***acute, prolonged symptoms consistent with the AVS*** – differentiation between central (stroke) and peripheral (vestibular neuritis) based on the HINTS exam.
- 2) Patients with ***episodic vestibular syndrome (EVS, first attack or recurrent)*** – because the vast majority of patients with EVS that is *spontaneous* in onset will be asymptomatic at the time of the exam (and will have a normal VOG/vHIT), an accurate history and risk factor stratification using ABCD2 would be essential to diagnose the most common conditions including vestibular migraine, Meniere's, or TIA. Most of the patients with EVS that is *triggered* will be diagnosed with posterior or horizontal canal variants of benign paroxysmal positional vertigo (BPPV) based on Dix-Hallpike and supine roll testing, respectively.
- 3) Patients with ***subacute to chronic persistent imbalance or vestibular symptoms*** – this category requires a more in depth history and general neurologic examination. However, a tele-dizzy service could easily identify patients with bilateral vestibular loss or a cerebellar condition (e.g., gaze-evoked nystagmus, spontaneous downbeat nystagmus). These patients are the least common in the ED setting and can usually be discharged and worked up as outpatients.

Based on the above categorization, triage would be possible in the following way:

- 1) **Green light** – a benign condition like BPPV or vestibular neuritis is diagnosed and the patient is discharged with specific instructions for follow-up.
- 2) **Yellow light** – a clear diagnosis cannot be made at the time of the exam, but suspicion for a dangerous etiology is not high enough to necessitate neuroimaging or an admission. These patients can be seen expeditiously in an oto-neurology urgent clinic. An example would be a patient with a presumed first attack of vestibular migraine.
- 3) **Red light** – a central HINTS exam was demonstrated, or central positional nystagmus was seen. Neuroimaging is required to rule out an acute stroke.

SUMMARY

While a tele-dizzy service at present would rely upon manual review of the data by eye movement experts, in the future, automation could be used to diagnose many of the 'green light' (BPPV) and 'red light' (AVS due to stroke) cases. This would allow tele-dizzy consultants to spend most of their time sorting out the most difficult 'yellow light' cases. The work to refine algorithms necessary for effective automation is currently ongoing in AVERT (Acute Video-oculography for Vertigo in Emergency Rooms for Rapid Triage), which is a multicenter, Phase II clinical trial comparing VOG-rapid triage to standard ED diagnostic care. By using automation, this 'Eye-ECG' approach could drastically extend the reach of a single eye movement specialist.

CME ANSWERS

1. D
2. True
3. D

REFERENCES

1. Saber Tehrani AS, Coughlan D, Hsieh YH, et al. Rising annual costs of dizziness presentations to U.S. emergency departments. *Acad Emerg Med* 2013;20:689-696.
2. Newman-Toker DE, Hsieh YH, Camargo CA, Jr., Pelletier AJ, Butchy GT, Edlow JA. Spectrum of dizziness visits to US emergency departments: cross-sectional analysis from a nationally representative sample. *Mayo Clin Proc* 2008;83:765-775.
3. Newman-Toker DE, Curthoys IS, Halmagyi GM. Diagnosing Stroke in Acute Vertigo: The HINTS Family of Eye Movement Tests and the Future of the "Eye ECG". *Semin Neurol* 2015;35:506-521.
4. Kattah JC, Talkad AV, Wang DZ, Hsieh YH, Newman-Toker DE. HINTS to diagnose stroke in the acute vestibular syndrome: three-step bedside oculomotor examination more sensitive than early MRI diffusion-weighted imaging. *Stroke* 2009;40:3504-3510.

**TELEMEDICINE: DOES IT PAY TO PLAY?
BILLING, CODING, AND REIMBURSEMENT**

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LEARNING OBJECTIVES

1. Describe the models of reimbursement for telemedicine
2. Identify considerations for each model of reimbursement
3. Describe encounters that may be reimbursable by various insurance modalities

CME QUESTIONS

1. What determines if an E/M service provided via telemedicine is reimbursed at the same price as an in-office visit?
 - A. The patient lives in a Health Professional Shortage Area
 - B. The -GT (synchronous telemedicine) modifier is appended to the E/M code
 - C. The Place of Service on the claim form is 02 (Telemedicine)
 - D. If the patient's state of residence has parity laws
2. How many days after an office visit must elapse before a provider can bill Medicare for G2012, "Virtual check-in?"
 - A. 1 day
 - B. 3 days
 - C. 7 days
 - D. 15 days
3. An established patient calls and speaks with the neuro-ophthalmology about new abrupt-onset vision loss. He is seen a few days later and had a comprehensive exam; the neuro-ophthalmologist ordered an MRI. What should the neuro-ophthalmologist code for the phone call and encounter?
 - A. G2012 for the day of visit, 99215 for the day of visit
 - B. G2012 for the day of phone call, 99215 for the day of visit
 - C. 99215 for the day of visit
 - D. G2012 for the day of phone call

KEYWORDS

1. Telemedicine
2. Billing
3. Coding
4. Reimbursement

HIGHLIGHTS

- Reimbursement for telemedicine services typically comes from grant funding, third-party payors (Medicare/Medicaid/commercial insurance), or the patient (self-pay).
- Medicare limits reimbursement of conventional telemedicine (“live video” examinations with the patient) based on Health Professional Shortage Areas and types of facilities.
- Medicare allows reimbursement for outpatient E/M codes (99201-99205, 99211-99215, etc.) via telemedicine by changing the Place of Service on the claim to “02” (office visits are “11”).
- Medicare has also approved reimbursement for “virtual check-ins,” remote interpretation of photos and video data submitted by patients, and provider-to-provider consultation on previously unseen patients.

Introduction

Telemedicine reimbursement in the United States has changed in many ways, with many recent positive changes facilitating an ongoing shift in the culture of medical practice. According to the Center for Connected Health Policy, more than 100 state and federal bills related to telehealth implementation have been introduced annually in the last several years.¹ As AMA President Patrice A. Harris, MD, MA, said in a press release: “With the advance of new technologies for e-visits and health monitoring, many patients are realizing the best access point for physician care is once again their home.”²

While some countries and U.S.-based integrated health systems have already embraced and incorporated telehealth services into their practice and reimbursement structure,³ telemedicine reimbursement in the U.S. from an insurance standpoint is still in need of more refinement. State-to-state differences are one of those areas that needs refinement; because of the variations in regulations for each state, it is very important to look at the telemedicine laws pertinent to each state in which services are provided (in-person or remote).⁴ Because telemedicine services have not been specifically described for neuro-ophthalmology practice, general principles for coding and determining reimbursement structure may be more clinically relevant than delving into every code or modifier. As such, this syllabus and the associated presentation will highlight specific billing, coding, and reimbursement information that may be applicable to the U.S.-based neuro-ophthalmologist. Discussion of eligibility, licensure requirements, equipment requirements, legal/malpractice issues, and implementation are outside the scope of this presentation.

The information provided is intended as education and not meant to provide specific coding advice; consult with a coding specialist or with Medicare/Medicaid/commercial insurance specialist for advice.

Who pays?

There are essentially three major sources of reimbursement for telemedicine services:

1. Research grants
2. Commercial insurance/Medicare/Medicaid
3. Patients (self-pay)

While there are grants available to research and develop telemedicine infrastructures for various situations,^{5,6} this funding is not intended to be perpetual, and thus more self-sustaining models must be considered before using a grant to “jump-start” an implementation of telemedicine.

Third-party payors such as commercial insurance, Medicare, and Medicaid carry the most stipulations and regulations for reimbursement; the majority of this presentation is dedicated to expounding on

some of these considerations for neuro-ophthalmic practice. The key advantage to billing a patient's commercial insurance, Medicare, or Medicaid is that the full cost burden of the telemedicine service may not be shouldered by the patient alone. However, there are currently very limited applications and strict conditions for telemedicine when billing through one of these entities, which will be discussed below.⁷ Because Medicaid laws vary from state-to-state, it is important to research and understand state laws to avoid licensing or reimbursement problems. Additionally, some commercial insurances may allow for a looser interpretation of regulations that Medicare or Medicaid may not allow; for example, video conferencing with patient while the patient is at home through a HIPAA-compliant system is not allowed by Medicare or Medicaid but may be allowed by some commercial insurances (Medicare/Medicaid require the patient to be at a qualified facility).

Self-pay or “concierge” forms of telemedicine may provide a more direct source for reimbursement; prices are the most transparent in this model and are not subject to the limitations in the types of encounters that could be charged. State laws and institutional regulations must still be followed, and these encounters should still be accompanied by appropriate documentation.

Considerations for telemedicine reimbursement⁷

Telemedicine Modalities

There are several modalities used in telemedicine; the two most applicable to neuro-ophthalmology are **synchronous** (“live video”) and **asynchronous** (“store and forward”).

Synchronous Telemedicine

Live video telemedicine for neuro-ophthalmic consultation is not well-described, though it is conceivable that applicable programs could be created. Medicare covers telehealth consultations by physicians for emergency department and hospital inpatient encounters, as well as office/outpatient visits for eligible Medicare beneficiaries at eligible facilities. However, there are several stipulations that may affect the ease of implementation:

1. *Location of the patient:* CMS limits the use of telehealth codes to patients who are located in a rural Health Professional Shortage Area (HPSA). These are defined as areas where there are health care provider shortages in primary care, dental health, or mental health, and may be based on geographic area, specific population groups within a geographic area, or specific types of facilities.⁸ Because HPSAs are not defined by the shortage of a particular specialty (such as neuro-ophthalmology), it may not be readily apparent if a particular area is considered an HPSA without looking it up.⁹
2. *Where the patient is “seen”:* CMS allows the patient to be seen at physician offices, hospitals, critical access hospitals, rural health clinics, skilled nursing facilities, and several other locations. However, CMS does not allow the patient to be “seen” when they are at home; they must go to a qualified location that can facilitate the encounter.
3. *Where the provider is located:* If the provider and the patient are located in the same state, the telemedicine regulations are the same as that of routine face-to-face care. However, if the provider and the patient are located in different states, there are licensure and credentialing considerations that may need to be addressed, depending on the state. Similarly, the provider must be credentialed with each eligible facility (where the patient is located); in 2011, CMS allowed “privileging by proxy,” which in essence allows eligible hospitals (where the patient is located) to grant privileges to telemedicine providers without going through a separate credentialing process, as long as the provider's credentialing process with their hospital meets or exceeds CMS standards.¹⁰

4. *What service is provided:* CMS allows evaluation/management (E/M) codes (99201-99205, 99211-99215) as well as inpatient hospital subsequent care codes (99231-99233), prolonged services (99354-99357) by means of telemedicine. The documentation requirements for those codes is the same as that of an in-person visit, and coding simply requires a change of location of service to 02 (Telemedicine). The -GT modifier (signifying synchronous/live video) is no longer needed.
5. *Parity laws:* Not every state reimburses telemedicine encounters at the same amount as in-person visits (i.e., a telemedicine New Level 5 E/M may reimburse at a lower price as it might have in-person). In some states, **parity laws** require payors to reimburse telemedicine services at the same price as in-person visits.

Asynchronous Telemedicine

Asynchronous telemedicine, or “store-and-forward,” refers to the collection of clinical data from the patient and transmission of that information to a telemedicine provider separately from a live video. An example of this would be retinopathy of prematurity (ROP) screening, in which the fundus photography may be collected at a site and a provider may view the images and provide interpretation or recommendations later. Asynchronous telemedicine is still not very widely accepted by third-party payors but may be a modality used in self-pay models. As of 2019, Medicare does not allow asynchronous telemedicine (evaluation/management) with the exception of fundus photos for retinopathy, or federal demonstration projects in Hawaii or Alaska (using 02 as the location of service and adding the -GQ modifier, which signifies asynchronous/store-and-forward).^{7,11} There are some other asynchronous telehealth services that CMS recently approved, which will be discussed below.

Recipient(s) Of Telehealth Services

While the patient is generally going to be the primary recipient of telemedicine services, Medicare now also allows for reimbursement of “provider-to-provider” consults, in which a requesting provider can request an “E-consult” of a specialist or subspecialist (see below).

Informed Consent

Regardless of who is paying for the services, the patient must give informed consent before a provider may bill for telemedicine services. Depending on the institution, verbal or written informed consent is allowed. The logistics of providing this informed consent may be challenging, especially in forms of telemedicine in which the patient is not directly involved (such as in provider-to-provider “E-consults”). The patient needs to be aware of any potential co-pays for which they may be responsible.

Culture Shift

In the conventional practice of medicine, there are some cultural barriers to charging for telemedicine services, especially for services such as E-consults and patient-related communications. Patients may not be willing to pay (or be partially responsible for payment via their medical insurance) to communicate with their doctor when this was previously a free service. Likewise, physicians may feel like it is more financially advantageous to have patients return for an office visit than to receive a lower reimbursement for an e-mail correspondence.

The challenge is to reframe these concerns from the standpoint of opportunity cost. For the patient, being responsible or partially responsible for an e-mail exchange with their physician costs far less than the total expense of taking a half or full day off from work, travel expenses (including food and possibly lodging), and the cost of an office visit. For the physician, spending a few short minutes on an e-mail exchange may seem less financially productive than having the patient in the office, but may provide the opportunity for seeing additional new patients, which would be more financially productive.

Relevant coding updates for the u.s.-based neuro-ophthalmologist

In 2019, CMS made several changes that may allow neuro-ophthalmologists to consider billing for services that are often already performed. Because the services listed below are not full patient evaluations, CMS determined that these services do not fall under the same geographic or provider shortage requirements that telemedicine E/M visits have.^{13,14}

CPT code G2012: Brief Communication Technology-based Service (e.g., “Virtual Check-In”)

The “virtual check-in” is a brief communication with **established patients** to “decide whether an office visit or other service is needed.”¹⁴ Table 1 lists approved and unapproved communication modalities.

Table 1. Approved communications modalities for “virtual check-ins”

Approved Modalities	Unapproved Modalities
<ul style="list-style-type: none">• Real-time, audio-only telephone conversations• Real-time, two-way audio + video interactions	<ul style="list-style-type: none">• E-mail• Text message• Voicemail

There are some additional caveats:

- *The “virtual check-in” cannot relate to an E/M service provided to the patient in the prior 7 days.* Communication with the patient after an office visit to discuss matters related to the office visit are not reimbursable. This includes calling the patient with test results.
- *The “virtual check-in” cannot relate to an E/M service or procedure performed within 24 hours after the communication.* If the discussion with the patient results in an urgent evaluation or treatment, the “virtual check-in” is considered “bundled” in with the urgent visit.
- *The physician must perform the “virtual check-in.”* This service cannot be performed by technicians or office staff. CMS does not specify whether or not this service must be physician-initiated (“Practitioners could be separately paid...**when the patient checks in with the practitioner** via telephone or other telecommunications device...”)¹⁴
- *The “virtual check-in” must be medically reasonable and necessary.* CMS has created this code as a way to “increase efficiency for practitioners and convenience for beneficiaries.”¹⁴
- *The patient will have a co-pay for this charge.* Although this co-pay will be relatively small (around \$2.50), informed consent from the patient and acceptance of payment responsibility need to be documented.¹⁵

If the patient communication qualifies, the conversation and medical decision making are documented, and the patient gives verbal (or written) consent for the charge, G2012 could then be submitted to Medicare for reimbursement, with the date of service being on the day of the phone call. The place of service would be the same as that for the E/M visit (office or hospital). For 2019, the CMS Fee Schedule lists national reimbursement for G2012 at \$14.78.¹²

CPT code G2010: Remote Evaluation of Pre-Recorded Patient Information

CMS also now allows for the remote evaluation of pre-recorded patient information, which specifically specifies **photos or videos from established patients** to “assess whether visit is needed.”¹⁴ The photos or videos must be transmitted from patients. As with the “virtual check-ins,” the remote evaluation

charge will come with a co-pay, and the evaluation cannot be performed within 7 days after the last E/M visit, or within 24 hours before an upcoming E/M visit.

If the evaluation qualifies, the interpretation is documented, and the patient gives verbal (or written) consent for the charge, G2010 could then be submitted to Medicare for reimbursement, with the date of service being on the day of the interpretation. The place of service would be the same as that for the E/M visit (office or hospital). For 2019, the CMS Fee Schedule lists national reimbursement for G2010 at \$12.61.¹²

CPT code 99446-99449, 99451-99452: Interprofessional Consult (“E-consult”)

CMS also provides reimbursement now for provider-to-provider consultation (“E-consults”) by telephone, internet, or by two-way audio/video, for **new or established patients** to provide expert non-face-to-face consultation for **new or exacerbated problems** and determine if a visit is necessary.¹⁶

There are several considerations:

- *The “E-consult” must be requested by a referring physician/qualified healthcare provider.*
- *An “E-consult” cannot be reported more than once per seven days for the same patient.*
- *The “E-consult” is reported based on total (cumulative) time spent on the consult, even if occurring over several days.*
- *The “E-consult” does not qualify if there is a transfer of care or a face-to-face consult occurs as a result of the consultation within the next 14 days.*
- *The consultant cannot have seen the patient within the past 14 days.*
- *The consultant must document at least 5 minutes spent on the consult.* This includes review of pertinent medical records, lab/imaging studies, medication profile, etc., and medical consultative discussion either via verbal or internet discussion.
- *The referring provider cannot initiate this consult while the patient is on-site, and cannot be reported more than once every 14 days per patient.*
- *The referring provider must document at least 16 minutes of time spent in preparing the referral and/or communicating with the consultant, and non-face-to-face prolonged services (99358-99359) may be added if the services exceed 30 minutes in one calendar day (99358) or 74 minutes (99358+99359).*

The referring provider must document communication with the consulting provider, and the consulting provider must provide a written report to the referring provider. Patient consent for billing (and acceptance of any possible co-pays) must be documented but can be given verbally. While the language is not exact, interprofessional consults that result in a decision for evaluation may be considered “bundled” into the office visit. Reimbursement is available to both the referring provider and the consulting provider:

- Referring providers bill 99452 for initiating the consult. For 2019, the CMS Fee Schedule lists national reimbursement for 99452 at \$37.48.¹²
- For consulting providers, there are several different codes available, based on time spent (Table 2).

Table 2. CPT Codes For Interprofessional Consults, Consultant Codes

CPT Code	Time Required	CMS 2019 Fee Schedule (National)	Considerations
99451	≥ 5 minutes	\$37.48	<ul style="list-style-type: none"> No verbal report to referring provider required >50% of the time spent must be in consultation and not time used to review data (if more time is spent in data review, use 99451 +/- prolonged services non-face-to-face codes)
99446	5-10 minutes	\$18.38	
99447	11-20 minutes	\$36.40	
99448	21-30 minutes	\$54.78	
99449	≥ 31 minutes	\$72.80	

SUMMARY

There is no question that telemedicine is becoming more prevalent across the world; Canada, the U.K., and the U.S. are just some examples of countries who are striving to incorporate telehealth services into their existing medical infrastructure, with some regions having more success than others.¹⁶⁻²⁰ Within the U.S., changes both at the federal and state levels are improving payment from Medicare, Medicaid, and private insurances for telehealth services.²¹⁻²³

As of 2019, there are 3 areas of telehealth services that present potential advances to insurance reimbursement that could benefit neuro-ophthalmology practice: “virtual check-ins,” remote patient photo/video interpretations, and “E-consults” (interprofessional consultations). While these codes do not reimburse at the same levels as in-person office visits, they generally take far less time, and allow physicians to potentially optimize their clinics to only see patients who need the in-person expertise.

Self-pay models and research grants are some of the other options to consider when looking at reimbursement for telemedicine services. These models may have fewer restrictions but are still subject to state and federal laws for the practice of telemedicine.

As the culture shifts towards the adoption and widespread use of virtual medicine, it is ever more important for us to creatively consider how to enhance our patient care with these technologies, as well as ensuring that our expertise continues to be appropriately valued.

Coding reference

Table 3. CPT Codes For Telemedicine Applicable For U.S. Neuro-Ophthalmology^{12-15,22-23}

CPT/HCPCS Code(s)	Description	CMS 2019 Fee Schedule (National)	Considerations
99201-99205 99211-99215 99231-99233 99354, 99355 99356, 99357	Office/Outpatient E/M, New Office/Outpatient E/M, Established Inpatient Hospital Evaluation Prolonged Services, Outpatient Prolonged Services, Inpatient	\$46.49- \$209.75 \$23.07- \$147.76 \$40.00- \$105.59 \$132.26, \$100.91	<ul style="list-style-type: none"> Change Place of Service to “02” (Telemedicine) -GT modifier no longer used

		\$93.70, \$94.06	
G2010	Remote Evaluation of Pre-Recorded Patient Information	\$12.61	<ul style="list-style-type: none"> • The patient must submit photos or videos for interpretation • Must be at least 7 days after an E/M visit or unrelated to an upcoming E/M visit • Decision for subsequent visit must be made based on evaluation
G2012	Brief Communication Technology-based Service, e.g. Virtual Check-In	\$14.78	<ul style="list-style-type: none"> • Must be either real-time telephone or synchronous two-way audio +/- video interaction • Communication cannot be through RN, tech, office staff • Must be at least 7 days after an E/M visit or unrelated to an upcoming E/M visit • Decision for subsequent visit must be made based on evaluation
99452 99451 99446-99449	Interprofessional Consult, Referring Interprofessional Consult, Consultant Interprofessional Consult, 5 min-31+ min	\$37.48 \$37.48 \$18.38-\$72.80	<ul style="list-style-type: none"> • Written report must be provided to treating/requesting physician • These codes only apply to patients who have not been seen by the consulting physician (if a decision was made by the consulting physician to see the patient, then these codes do not apply)

OTHER TELEMEDICINE RESOURCES

- 15 Key Steps for Creating a Business Proposal to Implement Telemedicine. National Consortium of Telehealth Resource Centers. <https://www.telehealthresourcecenter.org/wp-content/uploads/2019/01/15-Steps-Jan.-2019.pdf>.
- Telehealth 101. National Consortium of Telehealth Resource Centers. <https://www.telehealthresourcecenter.org/wp-content/uploads/2018/09/Telehealth-101-pdf.jpg>.
- Telehealth Policy Issues. National Consortium of Telehealth Resource Centers. <https://www.telehealthresourcecenter.org/wp-content/uploads/2019/09/Policy-Fact-Sheet-2019.pdf>.
- HIPAA and Telehealth. National Consortium of Telehealth Resource Centers. <https://www.telehealthresourcecenter.org/wp-content/uploads/2019/07/2019-HIPAA.pdf>.

CME ANSWERS

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REFERENCES

1. State Telehealth Laws and Reimbursement Policies. Center for Connected Health Policy. https://www.telehealthpolicy.us/sites/default/files/2019-05/cchp_report_MASTER_spring_2019-FINAL.pdf.
2. Press Release: AMA Releases 2020 CPT code set. 4 September 2019. <https://www.ama-assn.org/press-center/press-releases/ama-releases-2020-cpt-code-set>. Accessed 11/1/19.
3. Wicklund E. Kaiser CEO: Telehealth Outpaced In-Person Visits Last Year. mHealthIntelligence. 2016 October 11. <https://mhealthintelligence.com/news/kaiser-ceo-telehealth-outpaced-in-person-visits-last-year>. Accessed 11/2/19.
4. Current State Laws & Reimbursement Policies. Center for Connected Health Policy, The National Telehealth Policy Resource Center. <https://www.cchpca.org/telehealth-policy/current-state-laws-and-reimbursement-policies#>. Accessed 10/29/19.
5. NIH Funding Opportunities & Notices Search Results: Telemedicine. https://grants.nih.gov/grants/guide/search_results.htm?sort=rel&scope=pa-rfa&year=active&text_curr=telemedicine. Accessed 10/29/19.
6. Funding Sources for Telehealth. National Consortium of Telehealth Resource Centers. November 2017. <https://www.telehealthresourcecenter.org/wp-content/uploads/2019/01/Funding-Jan.-2019.pdf>. Accessed 10/29/19.
7. Telehealth Reimbursement. National Consortium of Telehealth Resource Centers. February 2019. <https://www.telehealthresourcecenter.org/wp-content/uploads/2019/09/Reimbursement-Final-2019.pdf>. Accessed 10/29/19.
8. Health Professional Shortage Areas (HPSAs). Health Resources & Services Administration. <https://bhw.hrsa.gov/shortage-designation/hpsas>. Accessed 10/29/19.
9. Find Shortage Areas. Health Resources & Services Administration. <https://data.hrsa.gov/tools/shortage-area>. Accessed 10/29/19.
10. Credentialing and Privileging. Center for Connected Health Policy. The National Telehealth Policy Resource Center. <https://www.cchpca.org/telehealth-policy/credentialing-and-privileging>. Accessed 10/29/19.

11. Medicare Reimbursement for Ophthalmic Telemedicine. Corcoran Consulting Group. <https://www.corcoranccg.com/products/faqs/ophthalmic-telemedicine/>. Last updated 26 January 2015. Accessed 10/29/19.
12. CMS Physician Fee Schedule Look-Up Tool, <https://www.cms.gov/apps/physician-fee-schedule/overview.aspx>. Accessed 10/29/19.
13. O'Connor C. Medicare's New Virtual Check-In Code: 7 Things You Need to Know. Lexology. Published 12 November 2018. <https://www.lexology.com/library/detail.aspx?g=4fccb1b9-2de2-4822-95e1-80494bcc72a4>. Accessed 10/30/19.
14. Final Policy, Payment, and Quality Provisions Changes to the Medicare Physician Fee Schedule for Calendar Year 2019. Centers for Medicare & Medicaid Services. Published 2018 November 1. <https://www.cms.gov/newsroom/fact-sheets/final-policy-payment-and-quality-provisions-changes-medicare-physician-fee-schedule-calendar-year>. Accessed 10/30/19.
15. Dacey B. The reality of virtual check-in coding. Physicians Practice. Published 4 March 2019. <https://www.physicianspractice.com/article/reality-virtual-check-coding>. Accessed 10/30/19.
16. Glauser W, Nolan M, Remfry A. Telemedicine on the rise across Canada. *healthydebate.ca*. 2015 June 25. <https://healthydebate.ca/2015/06/topic/telemedicine-across-canada>. Accessed 11/2/19.
17. Owens B. Telemedicine on the rise but lagging in Canada. *CMAJ News*. 2018 September 6. <https://cmajnews.com/2018/09/06/telemedicine-on-the-rise-but-lagging-in-canada-cmaj-109-5634/>. Accessed 11/2/19.
18. Donnelly L. Skype GP consultations will be the norm within 10 years, head of NHS review says. *The Telegraph*. 2018 April 27. <https://www.telegraph.co.uk/news/2018/04/26/skype-gp-consultations-will-norm-within-10-years-head-nhs-review/>. Accessed 11/2/19.
19. Vogel L. Task force launching to examine national licensure for virtual care. *CMAJ News*. 2019 March 26. <https://cmajnews.com/2019/03/26/task-force-launching-to-examine-national-licensure-for-virtual-care-cmaj-109-5738/>. Accessed 11/2/19.
20. AAP Division of Health Care Finance. 2 new codes developed for interprofessional consultation. American Academy of Pediatrics. 4 January 2019. <https://aappublications.org/news/2019/01/04/coding010419>. Accessed 11/1/19.
21. 2019 State of the States Report: Coverage and Reimbursement. American Telemedicine Association. <https://www.americantelemed.org/initiatives/2019-state-of-the-states-report-coverage-and-reimbursement/>. Accessed 11/2/19.
22. Big Changes in 2019 for Medicare Telehealth Policy. National Consortium of Telehealth Resource Centers. <https://www.telehealthresourcecenter.org/big-changes-in-2019-for-medicare-telehealth-policy/>. Accessed 10/30/19.
23. The Rules Are Changing: The Truth About Telemedicine Revenue and Reimbursement. GlobalMed. <http://globalmed.actonservice.com/acton/openapi/form/v1/gated/33826/ea694839-57ed-4317-85ca-44be2d942e9f/p-005f/f-8249cf84-5d54-44ea-9040-c6f5c186c911>.
24. Fact Sheet: Finalized CY 2019 Physician Fee Schedule. Center for Connected Health Policy. Published November 2018. https://www.cchpca.org/sites/default/files/2018-11/FINAL%20PFS%20CY%202019%20COMBINED_0.pdf. Accessed 10/30/19.

NEURO-OPHTHALMOLOGY DIGITAL TELECONSULTATION: REAL WORLD EXPERIENCE

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LEARNING OBJECTIVES

1. To describe different technological approaches for improving access to neuro-ophthalmic care
2. To understand an approach for non-synchronous telemedicine consultation
3. To understand an approach for synchronous telemedicine visits

CME QUESTIONS

1. Asynchronous telemedicine includes:
 - A. review of medical information that has been collected, stored and forwarded to the provider, who then provides a report
 - B. remote monitoring of patient data
 - C. virtual office visits where the provider and patient communicate by video chat

KEYWORDS

1. Tele-medicine
2. Neuro-ophthalmology
3. Medical records
4. Expert opinion
5. Video visit

HIGHLIGHTS

- Telemedicine models are one strategy for improving access to neuro-ophthalmic care
- Telemedicine models differ from traditional medical encounter models by eliminating the requirement for patient and provider to be in the same location.
- IT and administrative support are critical to successful telemedicine implementation

Introduction

There are less than 500 neuro-ophthalmologists in the US and less than half as many clinical full-time equivalents, concentrated in major academic or urban centers. Routine outpatient evaluations often schedule 3-4 months ahead. This leaves many patients, referring providers and neuro-ophthalmologists frustrated regarding poor access to care. Many of the limitations of the current practice of consultative neuro-ophthalmology stem from a traditional model of medical care where patient and provider are in the same physical space at the same time to facilitate communication of symptoms, performance of the physical exam, review of testing and communication of recommendations. Being in the same space often requires extensive travel for the patient and allocation of space for the encounter. Meeting at the same time requires schedule coordination. Telemedicine approaches can eliminate the need for the patient and provider to be spatially coincident. In asynchronous approaches the requirement for being temporally coincident is also relaxed.

At Stanford we have implemented or are implementing three telemedicine strategies:

- We have installed ophthalmic testing devices (OCT, visual field) in the neuroscience clinic, which is 3 miles away from the ophthalmology clinic. This allows select neurosurgery and neurology patients to have a neuro-ophthalmology visit replaced by testing only with remote interpretation.
- The medical center offers a second opinion program, whereby providers review electronic copies of records and respond to a list of patient questions in an asynchronous manner.
- We are arranging to provide video visits through our electronic medical record and patient portal.

Remote ophthalmic testing

Ancillary ophthalmic testing plays an important role in neuro-ophthalmic practice and is the cornerstone of certain categories of neuro-ophthalmic consultation (i.e. visual fields for patients with pituitary tumors and OCT for MS patients on fingolimod). Typically, the neuro-ophthalmologist is both the ordering and interpreting provider. In contrast, radiologists serve mainly as the interpreting provider for their tests. Many practices, including ours, allow scheduling of photo only or visual field only visit in our department by both internal and external providers (Lossen, 2014).

Remote ophthalmic testing is typically reported as an outreach service, for example to screen for diabetic retinopathy in primary care clinics, or retinopathy of prematurity in resource poor regions. Familiar to neuro-ophthalmology is the FOTO-ED study, which studied non-mydratic photography in the ER in the triage of patients (Bruce, 2015). We installed automated perimetry and OCT devices in the neuroscience clinic to assist in providing ophthalmic evaluations remotely. Tests are scheduled at the request of neurosurgery or neurology providers order the tests. Medical assistants complete the test, transmit the result electronically to the ophthalmic PACS sever and transmit the EMR encounter to the neuro-ophthalmologist. Similar to a radiology report, the neuro-ophthalmologists review the images, enter a report into the EMR and forward this to the requesting provider. If further evaluation is deemed necessary, then an outpatient neuro-ophthalmology appointment is scheduled. The most common uses are SP1 inhibitor macula screening OCT, supra-sellar tumor visual fields/OCT and hemispheric space occupying lesion visual field.

On-line second opinions

Many patients have questions about their medical care that are unanswered by their own providers (sometimes because they are not asked) causing them to seek subspecialty care or second opinion. If there is poor access to subspecialty providers in their geographic region this can be challenging. Multiple companies have addressed this need by offering electronic second opinions (Reddy, 2015). Typically, the companies contract with employers as an employee health benefit and also contract with health care providers in a fee for service structure, which is typically not covered by insurance. Stanford, in partnership with one such entity, offers a second opinion service directly to patients. Requests are typically patient initiated and about a specific diagnosis or symptom. The company collects and digitizes relevant medical records including images and interviews the patient about their condition and questions. The second opinion provider reviews this information through a web portal and provides written answers to the patient, who then has an opportunity to submit follow up questions.

Video visits

With the exception of many parts of the physical exam, most office visit information and interaction can occur remotely. Video visits are standard in some managed health systems and have been studied for

multiple neurological conditions including migraine (Friedman, 2019). This method of care is getting more traction in neurology than ophthalmology, likely due to the nature the examination required and the amount of counselling provided. We are offering neuro-ophthalmology video visits targeting appointments that are primarily counselling or discussion based. These are scheduled in the same manner as office visits (i.e. on a template) and are conducted through the EMR (provider) and EMR patient portal (patient). At the appointed time both provider and patient log on. Documentation is the same as for an outpatient visit and billing is done through E&M codes. At this time, it is only an option for follow up visits for patients who have non-governmental insurance.

CONCLUSION

Both synchronous and asynchronous telehealth approaches can improve access to neuro-ophthalmic care and expand the practice of neuro-ophthalmologists.

CME ANSWERS

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REFERENCES

1. Afshari M, Witek NP, Galifianakis NB, Education Research: An experiential outpatient teleneurology curriculum for residents/ *Neurology* 93(4), 170-175, 2019
2. Baum S, Can a virtual specialist consult program help hospitals break down geographic barriers/ *MedCity News*, November 19, 2015 <https://medcitynews.com/2015/11/virtual-specialist-consults/>
3. Bruce BB, Nonmydriatic Ocular Fundus Photography in the Emergency Department: How It Can Benefit Neurologists/ *Seminars Neurologym* 35(5), 491-5, 2015
4. Friedman DI, Rajan B, Seidmann A, A randomized trial of telemedicine for migraine management/ *Cephalgia*, 31(12), 1577-85, 2019.
5. Lossen VI, Leavitt JA, Visual Fields with interpretation only – a preliminary evaluation, NANOS 2014 poster presentation. <https://collections.lib.utah.edu/ark:/87278/s6sx9kzz>
6. Rathi S, Tsui E, Mehta N, Zahid S, Schuman JS, The current state of teleophthalmology in the United States, *Ophthalmology*, 124(12), 1729-34, 2017
7. Reddy S, New ways for patients to get a second opinion: online services from established medical centers and independent businesses, *Wall Street Journal*, August 24, 2015 <https://www.wsj.com/articles/new-ways-to-get-a-second-opinion-1440437584>
8. Wechsler LR, Advantages and limitations of teleneurology, *JAMA Neurol*, 72(3), 349-54, 2015



North American Neuro-Ophthalmology Society

46th Annual Meeting

March 7 – March 12, 2020

Omni Amelia Island Plantation Resort • Amelia Island, FL

SCIENTIFIC PLATFORM SESSION I

Monday, March 9, 2020 - 5:00–7:00 pm

Amelia Ballroom

Moderators: Nagham Al-Zubidi, MD, PhD and Beau Bruce, MD, PhD

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Monday, March 9th from 5:00 - 5:15 pm

Optic Chiasm Involvement Associated with Myelin Oligodendrocyte Glycoprotein and Aquaporin-4 Antibodies

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Introduction:

To describe and compare the pattern of optic chiasm involvement in patients with myelin oligodendrocyte glycoprotein antibody associated optic neuritis (MOG-ON) with aquaporin-4 antibody associated optic neuritis (AQP4-ON). MOG-IgG associated disease (MOGAD) has been demonstrated to be a distinct entity from AQP4-IgG positive neuromyelitis optica spectrum disorder (NMOSD). Optic neuritis is often the presenting symptom in NMOSD. It has been previously reported that chiasmal involvement is seen in at least 50% of AQP4-ON compared to a minority of patients with MOG-ON.

Methods:

A retrospective review of all patients evaluated at three academic centers for the diagnosis of ON with positive serum testing for either MOG-IgG or AQP4-IgG by a cell-based assay. Inclusion criteria included the availability of MRI brain/orbits at the time of ON. These were reviewed for optic chiasm involvement and the morphology of the chiasmal involvement.

Results:

One-hundred and fifty nine patients (77 AQP4-ON and 82 MOG-ON) were identified that fulfilled inclusion criteria. Among patients with AQP4-ON, 15 of 77 (19%) were found to have chiasmal involvement, with 14 of 15 present in the first ON attack. Isolated chiasmal involvement was observed in 4 of 15 (27%). Among patients with MOG-ON, 12 of 82 (15%) had chiasmal involvement, with 11 of 12 present in the first ON attack. Isolated chiasmal involvement was present in 2 of 12 (17%) patients. In patients with chiasmal involvement, longitudinally extensive lesions (from globe to chiasm) were identified in 7 of 12 (58%) MOG-ON patients, compared to 0% AQP4-ON patients ($p < 0.001$).

Conclusions:

In this large cohort, chiasmal involvement of ON in MOGAD and AQP4-IgG positive NMOSD occur at more similar frequencies than have previously been reported, emphasizing the need for appropriate diagnostic testing when this clinical feature is present. If MOG-ON has chiasmal involvement, it is more likely to be part of a longitudinally extensive lesion.

References: None.

Keywords: Demyelinating disease, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: Stanford data funding: Research to Prevent Blindness and NIH P30 026877

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Monday, March 9th from 5:15 - 5:30 pm

Resveratrol Nanoparticles are Neuroprotective in Experimental Optic Neuritis

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Introduction:

Optic neuritis is the most common clinical manifestation of multiple sclerosis. Axonal damage and neuronal loss lead to permanent neurological disability in patients and its animal model, experimental autoimmune encephalomyelitis (EAE). Presently, treatments of this condition aim to reduce inflammation without showing any neuroprotection. Resveratrol is a natural polyphenol found in red wine with neuroprotective effects but poor solubility in water. Thus, a novel nanoparticle formulation of resveratrol was developed and assessed in a mouse model of EAE.

Methods:

Resveratrol nanoparticles (RNs) were formulated using a thin rehydration technique and assessed for stability with spectrophotometric techniques. C57/BL6 mice were immunized with the myelin oligodendroglial glycoprotein peptide. From EAE induction, mice were treated daily for 30 days by oral gavage of RNs (n=6), vehicle (n=5) or unconjugated resveratrol (UnRSV) (n=6). Mice were assessed for EAE signs daily and for visual function weekly by optokinetic responses (OKR). Optic nerve and spinal cord inflammation were assessed by hematoxylin and eosin (H&E). Retinal ganglion cells were immunostained with Brn3a.

Results:

RNs containing >10 mg/ml resveratrol were stable over 3 months with an encapsulation efficiency >70%. 16.9 mg/kg RNs reduced the EAE clinical score at day 30 compared to 16.9 mg/kg vehicle (1.4 ± 0.4 vs 3.0 ± 0.4 , $p < 0.05$) whereas up to 100 mg/kg UnRSV did not lead to reduction of EAE scores. OKR, optic nerve inflammation and spinal cord inflammation were not significantly modified by oral administration of RNs. 16.9 mg/kg RNs reduced RGC loss compared to 16.9 mg/kg vehicle (347 ± 12 vs 172 ± 12 cells/standardized field, $p < 0.0001$). Importantly, to get a similar reduction, at least 100 mg/kg of UnRSV were needed suggesting that RNs increase resveratrol bioavailability.

Conclusions:

RNs increase resveratrol solubility and bioavailability. They show neuroprotection by reducing RGC loss. However, as previously reported for resveratrol, these nanoparticles do not have any anti-inflammatory effect.

References: None.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Demyelinating disease

Financial Disclosures: The authors had no disclosures.

Grant Support: Swiss Study Foundation Scholarship Janggen-Pöhn Foundation Scholarship University College London Overseas Research Scholarship

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Monday, March 9th from 5:30 - 5:45 pm

Efficacy and Safety of Satralizumab From Two Phase 3 Trials in Neuromyelitis Optica Spectrum Disorder

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Introduction:

Satralizumab is a humanized recycling monoclonal antibody that binds to the interleukin-6 (IL-6) receptor; IL-6 has been implicated in the pathophysiology of neuromyelitis optica spectrum disorder (NMOSD). Satralizumab was evaluated in patients with NMOSD in two Phase 3 studies: SAKuraSky (NCT02028884) and SAKuraStar (NCT02073279). In this analysis, we assessed the efficacy and safety of satralizumab in the individual study and pooled patient populations, including the subgroup of patients who were seropositive for aquaporin-4 immunoglobulin G (AQP4-IgG).

Methods:

Patients were randomized 1:1 (SAKuraSky; N=83) or 2:1 (SAKuraStar; N=95) to satralizumab (120 mg as monotherapy [SAKuraStar] or in combination with baseline immunosuppressants [SAKuraSky]) or placebo. The primary endpoint of both studies and the pooled analysis was time to first protocol-defined relapse (PDR). Between-group hazard ratios (HRs) were calculated based on Cox proportional hazards models.

Results:

Compared with placebo, satralizumab reduced the risk of PDR by 62% (HR, 0.38 [95% CI 0.16–0.88]) in SAKuraSky and by 55% (HR, 0.45 [95% CI 0.23–0.89]) in SAKuraStar (both p=0.018). In AQP4-IgG–seropositive patients, risk of PDR was reduced in SAKuraSky (satralizumab, n=27; placebo, n=28) by 79% (HR 0.21 [95% CI 0.06–0.75]) and in SAKuraStar (satralizumab, n=41; placebo, n=23) by 74% (HR 0.26 [95% CI 0.11–0.63]). In the pooled analysis, HR for time to first PDR was 0.42 (95% CI 0.25–0.71; 58% risk reduction satralizumab vs placebo). In AQP4-IgG–seropositive patients, the HR was 0.25 (95% CI 0.12–0.50; 75% risk reduction). Incidence of adverse events was similar in satralizumab and placebo groups; there were no deaths or anaphylactic reactions.

Conclusions:

This analysis of data from two Phase 3 studies demonstrated the efficacy of satralizumab in reducing relapse risk in patients with NMOSD, particularly in AQP4-IgG–seropositive patients. Satralizumab had a favorable safety profile as monotherapy or in combination with immunosuppressants.

References: None.

Keywords: Optic neuritis, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic nerve trauma and treatment, Non-organic visual disorders, Miscellaneous

Financial Disclosures: Is a consultant, investigator and speaker for Genentech, Inc., investigator and speaker for Alexion and Biogen, and speaker for Genzyme and EMD Serono

Grant Support: This study was funded by Chugai Pharmaceutical Co., Ltd., a member of the Roche Group; ClinicalTrials.gov, NCT02028884/NCT02073279; writing and editorial assistance was provided by Health Interactions, Inc.

Contact Information: None provided.

Monday, March 9th from 5:45 - 6:00 pm

Teprotumumab Effect on Proptosis, Diplopia and Quality of Life in Active Thyroid Eye Disease (TED)

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Introduction:

Active thyroid eye disease (TED), a progressive, autoimmune condition, produces retro-orbital inflammation/tissue expansion. Patients present with ocular pain, redness, and swelling. Retro-orbital fat/muscle expansion produces subsequent proptosis, diplopia, and strabismus. These manifestations can persist after inflammation is no longer evident. A phase 3 placebo-controlled trial recently confirmed that teprotumumab, an IGF-1R inhibitory antibody, significantly reduced TED-associated proptosis and improved other outcomes.[1] Key TED outcomes (proptosis [mm], subjective Bahn/Gorman diplopia grade, and GO-QOL) from the teprotumumab phase 2 and 3 trials are reported here.[1,2]

Methods:

Two 24-week randomized, double-masked, placebo-controlled, parallel-group, multicenter, (phase 2 [NCT01868997] and 3 [NCT03298867]) studies included adults with recent-onset active, moderate-to-severe TED. Patients were treated with teprotumumab or placebo every 3 weeks (8 infusions). Data from both trials were pooled for these analyses.

Results:

Of the 171 patients (84 teprotumumab, 87 placebo) characteristics were similar between treatment groups. More teprotumumab patients had a ≥ 2 mm proptosis reduction (77.4% vs. 14.9%), and mean reduction was greater (3.14 vs. 0.37 mm) in the teprotumumab than placebo group (both $p < 0.001$) at week 24. Median time to first proptosis response was 6.4 weeks in the teprotumumab group (placebo not estimable). At week 24, there was a higher rate of diplopia improvement (≥ 1 grade) (69.7% vs. 30.5%) and complete resolution (53.0% vs. 25.4%) in the teprotumumab group (both $p < 0.001$). Median time to first diplopia improvement was 11.9 and 25.1 weeks in the teprotumumab and placebo groups, respectively (based on Kaplan-Meier estimates of survival). Additionally, overall GO-QOL (19.01 vs. 6.30), GO-QOL-visual function (19.68 vs. 6.95), and GO-QOL-appearance (17.73 vs. 5.64) scores improved more with teprotumumab than placebo (all $p < 0.001$) at week 24.

Conclusions:

This combined analysis of two placebo-controlled trials demonstrates that the more impactful, difficult to treat sequelae of TED (proptosis, diplopia) improve with teprotumumab and result in dramatically improved QOL.

References: Douglas RS, et al. [AACE 2019 abstract], 2. Smith TJ, et al. NEJ M 2017;376:1748–1761.

Keywords: Graves (systemic disease), Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy, Adult strabismus with a focus on diplopia, Orbit/ocular pathology

Financial Disclosures: Horizon provided funding to the author's research company for research services in the conduct of the study and for activities that the author does related to being a consultant.

Grant Support: Funding for the Phase 2 study was provided by River Vision; funding for the Phase 3 study was provided by Horizon Therapeutics plc

Contact Information: None provided.

Monday, March 9th from 6:00 - 6:15 pm

Neuro-ophthalmic Complications in Patients Treated with CTLA-4 and PD-1/PD-L1 Checkpoint Blockade Inhibition

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Introduction:

In recent years, the use of CTLA-4 and PD-1/PD-L1 checkpoint blockade inhibitors have proven to be effective and become increasingly widespread treatment options for metastatic melanoma and other cancers by enhancing autologous anti-tumor immune responses. Immune related ophthalmologic complications have been reported in association with checkpoint inhibitor use but remain incompletely characterized. This study seeks to investigate and further characterize the neuro-ophthalmic adverse effects from immune checkpoint blockade treatment.

Methods:

A survey was distributed through the secure electronic data collection tool REDCap to neuro-ophthalmology specialists in the North American Neuro-Ophthalmology Society (NANOS) listserv. The study received human subjects approval through the UCLA institutional review board. The survey identified specific neuro-ophthalmic findings in patients who developed ocular complications while receiving either PD-1 inhibitors pembrolizumab and nivolumab; PD-L1 inhibitors atezolizumab, avelumab, and durvalumab; or the CTLA-4 inhibitor ipilimumab.

Results:

Twenty-nine patients from 14 institutions were identified. The most common treatment was with pembrolizumab (13/29) followed by nivolumab, alone or in combination with ipilimumab (12/29). Most patients were treated for malignant melanoma (15/29) or non-small cell lung carcinoma (6/29). The median time between first drug administration and the time of ophthalmological symptom onset was 14.5 weeks. We identified six cases of papillitis/optic neuritis, seven cases of myasthenia gravis with ocular manifestations, six cases of inflammatory orbitopathy / thyroid-like ophthalmopathy, and five cases of other optic neuropathy. Disease was bilateral in 72% of cases. Patients with optic nerve involvement generally had favorable outcomes with steroid treatment, however the outcome for other neuro-ophthalmic complications was variable.

Conclusions:

This study describes the variable neuro-ophthalmic adverse events associated with use of immune checkpoint inhibitors, and contributes a more thorough understanding of their clinical presentations and treatment outcomes. We expect this will increase awareness of these drug complications and guide specialists in the care of these patients.

References: None.

Keywords: Optic neuritis, Myasthenia, Ocular motility, Orbit, Chemotherapy and radiation injury

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Monday, March 9th from 6:15 - 6:30 pm

Novel Biomarkers in Human and Murine Nonarteritic Anterior Ischemic Optic Neuropathy

Yaping Liao¹, Mohammed Shariati¹, Louise Louro¹

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Introduction:

Nonarteritic anterior ischemic optic neuropathy (NAION) the most common acute optic neuropathy in those older than 50 (1-3), and there is currently no diagnostic test or effective treatment. In this study, we identified novel plasma biomarkers for NAION using human and photochemical thrombosis animal model of NAION.

Methods:

We collected blood from 17 NAION and 10 age-matched control patients. We also collected blood and retina from 5 adult C57BL/6 mice with unilateral NAION induced by photochemical thrombosis and 5 control mice. Plasma was processed within 2 hours of collection. Three human samples and all animal plasma have been analyzed using 62-plex (human) or 39-plex (mice) cytokine liquid array (Luminex). Biological activity of extracellular vesicles (EVs) from NAION and control human plasma was analyzed using cultured human retinal endothelial cells for vessel formation and breakdown of blood-brain barrier.

Results:

Cytokine profiling of NAION plasma (one acute, one subacute, one chronic) showed many cytokines that were increased or decreased compared with controls (N = 3), and these changes were most prominent in acute NAION. Eotaxin was the most upregulated cytokine in all stages of human NAION and in acute murine NAION. We prepared plasma EVs, which are small membrane-bound particles thought to be new signaling organelles that function at the paracrine and systemic level (3-4) from the same 3 NAION patients and tested them for biological activity on human retinal endothelial cells in vitro. We found that human AION EVs in acute, subacute, and chronic AION all led to increased angiogenesis and increased endothelial leakage.

Conclusions:

Eotaxin, the protein most correlated with human aging (5) was elevated in the plasma in all stages of human NAION and in acute murine NAION. Eotaxin may be a novel biomarker and therapeutic target of NAION.

References: 1. Hayreh SS. Ischemic optic neuropathy. *Prog Retin Eye Res* 2009;28:34-62. 2. Arnold AC. Pathogenesis of nonarteritic anterior ischemic optic neuropathy. *J Neuroophthalmol* 2003;23:157-163. 3. Yanez-Mo M, Siljander PR, Andreu Z, et al. Biological properties of extracellular vesicles and their physiological functions. *J Extracell Vesicles* 2015;4:27066. 4. van Niel G. Study of Exosomes Shed New Light on Physiology of Amyloidogenesis. *Cell Mol Neurobiol* 2016;36:327-342. 5. Villeda SA, Luo J, Mosher KI, et al. The ageing systemic milieu negatively regulates neurogenesis and cognitive function. *Nature* 2011;477:90-94.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: Translational Research and Applied Medicine grant, Anonymous gift grant

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Monday, March 9th from 6:30 - 6:45 pm

AAION Shows Profound Reduction in Disc and Choroidal Blood Flow Vs. NAION and Normal Eyes

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Introduction:

We sought to differentiate patients with arteritic anterior ischemic optic neuropathy (AAION) from patients with non-arteritic anterior ischemic optic neuropathy (NAION) and age-matched normal eyes during the acute and post-treatment stages of giant cell arteritis by non-invasive quantification of choroidal and optic nerve blood flow using laser speckle flowgraphy (LSFG).

Methods:

laser speckle flowgraphy (Softcare, Japan) was used to quantify blood flow to the choroid and optic nerve head simultaneously during the cardiac cycle. Eyes from the following patient groups were compared: acute AAION (n=23; positive biopsy), acute NAION (n=15) and normal (n=20;>50 years of age). A subset of AAION and NAION eyes also had fluorescein angiography and 6 AAION eyes with posterior ciliary artery occlusion were studied acutely and with at least one subsequent visit following optic nerve atrophy (2,3,4,7, 8 and 10 months later).

Results:

Areas of slowed or non-filling on fluorescein angiography spatially correlated with areas of low blood flow using LSFG. Acutely, choroid and optic disc rim blood flow were both significantly and profoundly reduced compared to NAION and normal eyes (p=0.0001). Blood flow in the peripapillary choroid sectors highly correlated with corresponding adjacent disc sectors in AAION eyes (R=0.89; p=0.0001). Areas of reduced choroidal blood flow from posterior ciliary artery occlusion remained abnormal in 5 out of 6 eyes on follow up LSFG measurements.

Conclusions:

Measurement of choroid and optic nerve blood flow with LSFG provides an alternative to fluorescein angiography for diagnosis of AAION. Even after steroid treatment there is usually persistent hypoperfusion, aiding diagnosis even after acute vision loss.

References: None.

Keywords: Optic neuropathy, Vascular disorders, Neuro-ophth & infectious disease (eg, AIDS, prion)

Financial Disclosures: The authors had no disclosures.

Grant Support: Iowa City VA Center for the Prevention and Treatment of Visual Loss Alcon Scholarship for Visiting Professor (Dr. Hashimoto) University of Iowa Levitt Fund (Dr. Chung) Busse Foundation and Mintzer Family Neuro-ophthalmology Research Funds

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Monday, March 9th from 6:45 - 7:00 pm

Optic Disc Drusen in Young Adults with Anterior Ischemic Optic Neuropathy: A Multicenter Study

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Introduction:

Anterior ischemic optic neuropathy (AION) usually occurs in patients over the age of 50 with systemic vascular disease. Less commonly, AION occurs in patients younger than 50 years with few or no vascular risk factors. Optic disc drusen (ODD), present in 2% of the general population, have occasionally been reported with AION. The purpose of this study was to examine the prevalence of ODD in young patients with AION.

Methods:

In this retrospective study, all patients with AION age 50 years or less, seen in the neuro-ophthalmology clinics of the international ODDS (Optic Disc Drusen Studies) consortium between April 1, 2017, and March 31, 2019, were identified. Patients were included if ODD were diagnosed by any method, or if ODD were excluded by enhanced-depth imaging optical coherence tomography (EDI-OCT) using the ODDS consortium guidelines. AION eyes with ODD were termed ODD-AION, AION eyes without ODD were termed NODD-AION.

Results:

Sixty-five patients (128 eyes) with AION in one or both eyes were included (mean age 41 years). Seventy-four eyes were diagnosed with AION; of these 52% had ODD (ODD-AION), while 44% of eyes without AION had ODD (P=0.36). A significant difference in Snellen BCVA was found between NODD-AION (0.53) and ODD-AION (0.73) (P=0.047). No significant difference in perimetric mean deviation was found between eyes with NODD-AION (-13.5 dB) and ODD-AION (-10.4 dB). On EDI-OCT, 28% of eyes with NODD-AION had peripapillary hyperreflective ovoid mass-like structures (PHOMS) and 7% had hyperreflective lines while 54% with ODD-AION had PHOMS and 63% had hyperreflective lines (P=0.046 and P<0.001, respectively).

Conclusions:

The majority of our AION patients age 50 years and younger have ODD. This indicates that ODD may have a causative role in the development of AION, at least in younger patients. We suggest ODD-AION be recognized as a novel diagnosis.

References: None.

Keywords: Optic neuropathy, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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North American Neuro-Ophthalmology Society

46th Annual Meeting

March 7– March 12, 2020

Omni Amelia Island Plantation • Amelia Island, FL

Tuesday, March 10

6:00 am – 6:45 am	Yoga	Oceanview Room (Sunrise Tower, B level next to workout room)
6:30 am – 7:30 am	Breakfast with Exhibitors	Magnolia Ballroom
6:30 am – 7:30 am	Breakfast with the Novices	Magnolia Ballroom

Join us in the reserved YONO area at breakfast for table discussions led by senior members and /or YONOs to discuss topics relevant to aspiring or current YONOs.

6:30 am – 7:30 am	Combining Neurology Subspecialties with Neuro-Ophthalmology <i>Nathan Kung, MD and Stacy Smith, MD</i>	
6:30 am – 7:30 am	Job Hunting and Your First Year in Practice <i>Melinda Y. Chang, MD and Evan Price, MD</i>	
6:30 am – 1:30 pm	Registration/Help Desk	Amelia Foyer
6:30 am – 7:30 am	JNO Editorial Board Meeting	Talbot A
7:30 am – 9:30 am	Scientific Platform Session II [2.0 CME]	Amelia Ballroom
	<i>Moderators: Stacy Pineles, MD, MS and Alex Sinclair, MBChB, FRCP, PhD</i>	
7:30 am – 7:45 am	Retinal Microvascular Changes Differentiate Transient Ischemic Attack from Mimics in the Emergency Department: FOTO-TIA Study , <i>Beau Bruce, MD, PhD</i>	
7:45 am – 8:00 am	Human vs. Machine: The Brain and Optic Nerve Study with Artificial Intelligence (BONSAI) , <i>Valerie Biousse, MD</i>	
8:00 am – 8:15 am	Time is vision: early training enhances vision restoration after occipital Stroke , <i>Elizabeth L. Saionz, PhD</i>	
8:15 am – 8:30 am	Measuring Torsion with a Mobile App Compared to Double Maddox Rod , <i>Michael S. Lee, MD</i>	
8:30 am – 8:45 am	Quantitative Visual Assessment in Children with Cortical/Cerebral Visual Impairment (CVI) Using Eye Tracking , <i>Melinda Y. Chang, MD</i>	
8:45 am – 9:00 am	Anterograde Axonal Degeneration in Children with Vision Loss Secondary to NF1 Associated Optic Pathway Glioma , <i>Robert Avery, DO</i>	
9:00 am – 9:15 am	Is Visual Snow a thalamo-cortical dysrhythmia of the visual processing system – a magnetoencephalogram study , <i>Jenny L. Hepschke, MBBS, BSc(Med), PhD</i>	
9:15 am – 9:30 am	Gender distribution of speakers at the North American Neuro-	

Ophthalmology Society annual meetings,
Obadah Moushmoush, BS

9:30 am - 10:00 am	Coffee with Exhibitors (with support from GenSight Biologics S.A.)	Magnolia Ballroom
10:00 am – 12:00 pm	Scientific Platform Session III [2.0 CME] <i>Moderators: Ruth Huna-Baron, MD and Kenneth Shindler, MD, PhD</i>	Amelia Ballroom
10:00 am – 10:15 am	Static and Abduction Versus Adduction Dynamic Ocular Motor Abnormalities in Spinocerebellar Ataxia Type 3, <i>João Lemos, MD, PhD</i>	
10:15 am – 10:30 am	The 100,000 Genomes Project – Uncovering Pathogenic Variants in inherited Optic Neuropathies with Whole-Genome Sequencing, <i>Neringa Jurkute, MD, FEBO</i>	
10:30 am – 10:45 am	Progressive Optic Atrophy in a Retinal Ganglion Cell-Specific Mouse Model of Complex I Deficiency, <i>Sidney M. Gospe, III, MD, PhD</i>	
10:45 am – 11:00 am	Development of a Retinal Ganglion Cell Specific Gene Therapy Using SIRT1 Signaling for Neuro-Protection, <i>Ahmara G. Ross, MD, PhD</i>	
11:00 am – 11:15 am	Bilateral Visual Improvement with Unilateral Gene Therapy for Leber Hereditary Optic Neuropathy (LHON), <i>Nancy J. Newman, MD</i>	
11:15 am – 11:30 am	Expanded access program (EAP) in Leber’s hereditary optic neuropathy (LHON) patients treated for 24 months, <i>Xavier Llòria</i>	
11:30 am – 11:45 am	Proof of Concept for Levodopa Treatment in Rescuing Retinal Morphology and Visual Function in Albinism, <i>Helena Lee, PhD, FRCOphth</i>	
11:45 am – 12:00 pm	Ectopic Melanopsin For Visual Restoration: Comparisons With Alternative Optogenetic Tools, <i>Michael J. Gilhooley, MA, MB, BChir, FRCOphth</i>	
12:00 pm – 12:10 pm	JNO Update, <i>Laura Balcer, MD, MSCE</i>	Amelia Ballroom
12:10 pm – 6:00 pm	Afternoon free for activities	
6:00 pm – 6:30 pm	Meet the Legends of Neuro-Ophthalmology	Magnolia Ballroom
6:30 pm – 8:30 pm	Poster Session II: Scientific Advancements (heavy hors d’oeuvres buffet included)	Magnolia Ballroom
6:30 pm – 7:30 pm	Odd Numbered Posters	
7:30 pm – 8:30 pm	Even Numbered Posters	
8:30 pm – 9:30 pm	Abstract Committee Meeting	Talbot B



North American Neuro-Ophthalmology Society

46th Annual Meeting

March 7 – March 12, 2020

Omni Amelia Island Plantation Resort • Amelia Island, FL

SCIENTIFIC PLATFORM SESSION II

Tuesday, March 10 - 7:30 – 9:30 am

Amelia Ballroom

Moderators: Stacy Pineles, MD, MS and Alex Sinclair, MBChB, FRCP, PhD

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Tuesday, March 10th from 7:30 - 7:45 am

Retinal Microvascular Changes Differentiate Transient Ischemic Attack from Mimics in the Emergency Department: FOTO-TIA Study

Beau Bruce¹, Samuel Bidot¹, Fadi Nahab¹, Jeffrey Siegelman¹, Nicolas Bianchi¹, Kaitlin Sandor¹, Mung Lin¹, Sharrill Bell¹, Michael Ross¹, David Wright¹, Valerie Biousse¹, Nancy Newman¹

¹*Emory University, Atlanta, Georgia, USA*

Introduction:

About 10% of the 250–500,000 Americans who experience transient ischemic attack (TIA) annually have a stroke within 90 days. Clinical scores and MRI-DWI findings are routinely used to help triage patients with suspected TIA, although categorizing DWI-negative spells as TIAs or non-cerebrovascular events (CVE) is challenging. A primary aim of the FOTO-TIA study was to investigate a possible role for retinal microvascular findings in this risk stratification.

Methods:

FOTO-TIA was a cohort study of adult patients with a NIH Stroke Scale ≤ 3 admitted to three emergency departments' (EDs') observation units for an accelerated diagnostic protocol for suspected TIA or stroke. Clinical and imaging results were recorded prospectively. Non-mydratic fundus photographs were obtained as part of the accelerated diagnostic protocol and reviewed for retinal microvascular findings, defined as retinal hemorrhages, cotton wool spots, retinal emboli or occlusions, hard exudates, or microaneurysms. A neurologist rated the probability each patient's presentation (masked to fundus photography) represented a CVE on a visual analogue scale.

Results:

395 patients were enrolled (median age: 57 years (interquartile range [IQR]: 50–66); 219 (55%) women; 253 (64%) black; 34 (9%) retinal microvascular findings present; median CVE probability assessment 22% (IQR: 5–100)). Controlling for the individual components of the ABCD2 score (age, systolic and diastolic blood pressure, clinical symptoms, duration of symptoms, and diabetes) and presence of a MRI-DWI positive lesion, any retinal microvascular finding increased the CVE probability assessment by 15.6% (95%CI: 4.2–27.1%, $p=0.008$).

Conclusions:

Retinal microvascular findings assessed by nonmydratic ocular fundus photographs during the evaluation of suspected TIAs in the ED are an independent factor differentiating TIA and stroke from mimics.

References: Vuong LN, Thulasi P, Biousse V, Garza P, Wright DW, Newman NJ, Bruce BB. Ocular fundus photography of patients with focal neurologic deficits in an emergency department. *Neurology*. 2015 Jul 21;85(3):256-62.

Keywords: Vascular disorders, Stroke trauma

Financial Disclosures: The authors had no disclosures.

Grant Support: NIH R01-NS089694.

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Tuesday, March 10th from 7:45 - 8:00 am

Human vs. Machine: The Brain and Optic Nerve Study with Artificial Intelligence (BONSAI)

Valerie Biousse¹, Raymond Najjar², Caroline Vasseneix², Jiang Zhu³, Daniel Ting⁴, Yon Liu³, Tien Wong⁴, Nancy Newman¹, Dan Milea⁴, For the BONSAI Study Group⁵

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³Institute of High Performance Computing, Agency for Science, Technology and Research, Singapore, Singapore, Singapore, Singapore, ⁴Singapore National Eye Centre, Singapore, Singapore, ⁵International BONSAI Study Group, Singapore, Singapore

Introduction:

We developed and validated an artificial intelligence deep learning system (AI-DLS) to automatically classify optic discs as “normal” or “abnormal”, and specifically detect “papilledema”, but direct comparison of the diagnostic accuracy of a DLS versus expert neuro-ophthalmologists using the same sample is warranted. Our objective was to compare the diagnostic performance of an AI-DLS versus expert neuro-ophthalmologists in classifying optic nerves as “normal”, “papilledema” (optic nerve edema from proven intracranial hypertension), and “other optic nerve abnormalities” on ocular fundus photographs.

Methods:

Eight-hundred digital fundus photographs (400 “normal optic discs”, 201 “papilledema”, 199 “other optic disc abnormalities”) taken using multiple cameras with various fields were selected from the BONSAI multi-ethnic population. The image-naïve AI-DLS and expert neuro-ophthalmologists independently classified the optic discs on the randomly presented photographs as “normal”, “papilledema”, or “other optic disc abnormalities”, without any additional clinical information.

Results:

Classification by the machine took 25 seconds, compared to 61-74 minutes by humans for each of the tasks. The AI-DLS successfully classified 678/800 (84.7%) images, compared with 675/800 (84.4%) for human-1 and 641/800 (80.1%) for human-2. Agreement between the two humans was 656/800 (82%); between machine and human-1, 660/800 (82.5%); and between machine and human-2, 624/800 (78%). The machine’s performance in identifying papilledema was similar to humans’ (accuracy 91.5% vs. 89.0% and 89.6%, sensitivity 83.1% vs. 85.1% and 76.6%, specificity 94.3% vs. 90.3% and 94.0% for machine vs. human-1 and human-2, respectively). Similar results were observed for identification of normal optic discs (accuracy 92.1% vs. 93.1% and 88.6%, sensitivity 91.0% vs. 94.5% and 86.3%, specificity 93.3% vs. 91.8% and 91.0%).

Conclusions:

The classification performance of our trained AI-DLS was at least as good as two expert neuro-ophthalmologists lacking additional clinical information. Ongoing studies of machine versus non-ophthalmologic personnel will likely confirm the obvious superiority of AI-DLS over ophthalmoscopy in many clinical settings.

References: 1. Ting DSW, Peng L, Varadarajan AV, et al. Deep learning in ophthalmology: The technical and clinical considerations. *Prog Retin Eye Res* 2019 Sep;72:100759. doi: 10.1016/j.preteyeres.2019.04.003. Epub 2019 Apr 29. Review. PubMed PMID: 31048019. 2. Liu X, Faes L, Kale AU, et al. A comparison of deep learning performance against health-care professionals in detecting diseases from medical imaging: a systematic review and meta-analysis. *Lancet Digital Health* 2019; 1: e271–97.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: -NIH/NEI core grant P30-EY06360 (Department of Ophthalmology, Emory University School of Medicine), and by NIH/NINDS (RO1NS089694). -Singapore National Medical Research Council, CS-IRG grant (CIRG18Nov-0013), and Duke-NUS Ophthalmology and Visual Sciences Academic Clinical Programme grant (05/FY2019/P2/06-A60).

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Tuesday, March 10th from 8:00 - 8:15 am

Time is vision: early training enhances vision restoration after occipital stroke

Elizabeth Saionz¹, Matthew Canavuaugh¹, Michael Melnick¹, Berkeley Fahrenthold¹, Duje Tadin¹, Krystel Huxlin¹

¹University of Rochester, Rochester, New York, USA

Introduction:

Hemianopia is a common sequela of occipital stroke. After a brief period of spontaneous improvement, hemianopic defects are assumed to become stable and permanent. Lengthy, intensive visual training can induce partial recovery in chronic (>6 months) hemianopes, though restored vision is not entirely normal. In contrast, little is known about visual properties early after stroke or whether early training, as in sensorimotor stroke, could induce greater visual recovery. Here, we characterized vision in subacute (<3 months) hemianopic fields, before contrasting the relative efficacy of training in subacute versus chronic post-stroke patients.

Methods:

Baseline automated perimetry and psychophysical testing were performed before in-home, self-administered training in the blind field on either a global direction discrimination task at 100% luminance contrast (n[subacutes]=8, n[chronics]=14) or simple direction and orientation discrimination tasks at varying contrasts (n[subacutes]=5, n[chronics]=5). Five subacutes served as untrained controls.

Results:

At baseline, no chronic hemianopes performed better than chance within perimetrically-defined blind fields, but 7/18 subacutes retained conscious global motion discrimination and 5 retained contrast sensitivity for motion. Global motion training recovered similar performance in all chronics and subacutes, but subacutes recovered faster (16 *versus* 93 sessions; Student's t-test, $p < 0.0001$) and with greater spatial generalization (Student's t-test, $p < 0.0001$). Contrast training improved contrast sensitivity in all subacutes, but only in 2/5 chronics. Contrast-trained subacutes recovered dramatically more of their automated deficit than other groups, improving on average $61 \text{deg}^2/\text{month}$ of training (untrained[subacutes]= $7 \text{deg}^2/\text{month}$, global-motion-trained[subacutes]= $14 \text{deg}^2/\text{month}$, global-motion-trained[chronics]= $16 \text{deg}^2/\text{month}$, contrast-trained[chronics]= $7 \text{deg}^2/\text{month}$; ANOVA, $p = 0.001$). Importantly, untrained subacutes exhibited spontaneous recovery on automated perimetry, but not on discrimination tasks; in fact, absent training, preserved blind field discrimination abilities were lost by 6 months post-stroke.

Conclusions:

Our results suggest gradual vision loss that preserves motion sensitivity after occipital stroke. They also show that, similar to sensorimotor stroke rehabilitation, early visual training recruits preserved vision, preventing its degradation and enhancing recovery.

References: Das A, Tadin D, Huxlin KR. Beyond blindsight: properties of visual relearning in cortically blind fields. *J Neurosci.* 2014;34(35):11652–11664. doi:10.1523/JNEUROSCI.1076-14.2014 Cavanaugh MR, Huxlin KR. Visual discrimination training improves Humphrey perimetry in chronic cortically induced blindness. *Neurology.* 2017;88(19):1856–1864. doi:10.1212/WNL.0000000000003921 Elizabeth Saionz, Matthew Cavanaugh, Krystel Huxlin; Different properties of training-induced visual recovery in sub-acute and chronic stroke patients. *Journal of Vision* 2017;17(15):30-31. doi: 10.1167/17.15.30a. Elizabeth Saionz, Duje Tadin, Krystel Huxlin; Relative efficacy of global motion versus contrast training early after stroke for recovering contrast sensitivity in cortical blindness. *Journal of Vision* 2018;18(10):267. doi: 10.1167/18.10.267.

Keywords: Stroke trauma, Visual fields, Higher visual cortical functions, Perimetry

Financial Disclosures: The authors had no disclosures.

Grant Support: The present study was funded by NIH (EY027314 and EY021209, T32 EY007125 to Center for Visual Science, T32 GM007356 to the Medical Scientist Training Program, TL1 TR002000 to the Translational Biomedical Sciences Program, a pilot grant from University of Rochester CTSA award UL1 TR002001 to ELS), and by an unrestricted grant from the Research to Prevent Blindness (RPB) Foundation to the Flaum Eye Institute.

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Tuesday, March 10th from 8:15 - 8:30 am

Measuring Torsion with a Mobile App Compared to Double Maddox Rod

Michael Lee¹, Michael Koller¹, Anna Schweigert¹, Kimberly Merrill¹, Laura May¹, Noor Ismaiel¹, Mai Lor¹, Collin McClelland¹, Samuel Lee¹

¹University of Minnesota, Minneapolis, Minnesota, USA

Introduction:

The double Maddox rod (DMR) traditionally measures torsion. It requires a red Maddox rod, a white Maddox Rod, and a trial frame in good working order. We compared a new iPhone app to DMR to measure torsion, time to administer the test, and patient satisfaction.

Methods:

We created iTorsion (available free in the app store). Using red-green glasses with the red lens over the right eye, the patient aligns the lines on the app parallel to each other and to the floor. We randomized patients (n=18) with a vertical misalignment for testing with iTorsion or DMR followed by the other modality. This procedure was followed again by a second masked examiner. We measured time to administer test, test-retest variability, and then conducted a survey of patients regarding their experience.

Results:

There were 11 (61%) women, and the mean age of cohort was 47.1 years (range 9-74). Excyclotorsion (minus degrees) and incyclotorsion (plus degrees) were measured for RE1 (right eye, first trial), LE1 (left eye, first trial), RE2 (right eye, second trial), and LE2 (left eye, second trial) for both DMR and IT, compared using paired t-tests. The mean DMR results were -1.44°, -2.42°, -1.50°, and -1.47°, respectively. The mean IT results were -0.89° (p=0.404), -1.06° (p=0.383), -0.11° (p=0.095), and -0.67° (p=0.300), respectively. Mean time to administer the test was longer for DMR compared to IT (71.2 vs. 56.6 seconds, p = 0.12). There was no significant difference between tests using a Likert scale regarding ease of use, comfort, length of time, learning curve, efficiency, and confidence in the results. However, with a forced choice preference, 8 of 9 respondents chose iTorsion.

Conclusions:

iTorsion represents a new iPhone app to measure torsion. It is equivalent to DMR for measuring torsion, faster to use, requires less equipment, and patients prefer it to DMR.

References: None.

Keywords: Ocular motility, Adult strabismus with a focus on diplopia

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Tuesday, March 10th from 8:30 - 8:45 am

Quantitative Visual Assessment in Children with Cortical/Cerebral Visual Impairment (CVI) Using Eye Tracking

Melinda Chang¹, Mark Borchert¹

¹*Children's Hospital Los Angeles, Los Angeles, California, USA*

Introduction:

Cortical/cerebral visual impairment (CVI) is the most common cause of visual impairment among children in developed countries. Currently, there is no standardized, objective, and quantitative assessment tool to evaluate the multiple aspects of vision affected in CVI. Eye tracking is a novel technology that could be used for this purpose.

Methods:

We prospectively recruited five children with CVI and six age-matched controls (age range 2-12 years). All children underwent complete ophthalmologic exam. In children with CVI, visual acuity was graded clinically on a previously published 6-level scale. The EyeLink® system tracked eye position remotely at 500 Hz while subjects viewed stimuli on a computer monitor. Grating acuity, contrast sensitivity, and color saturation threshold were assessed using forced preferential looking. Characteristics of saccades (latency and velocity) and fixations (duration) were calculated by the EyeLink® software.

Results:

Among children with CVI, grating acuity threshold by eye tracking strongly correlated with clinical visual acuity ($r=0.87$, $p=0.05$). Compared to controls, children with CVI had significantly worse grating acuity threshold (mean 8.6 ± 7.6 vs. 20 ± 0 cycles per degree, $p=0.01$) and contrast sensitivity threshold ($31 \pm 19\%$ vs. $7.0 \pm 3.5\%$, $p=0.05$). Color saturation threshold was not significantly different between groups ($22 \pm 16\%$ [CVI] vs. $12 \pm 4.1\%$ [controls], $p=0.30$). Latency to first saccade was longer in CVI patients (392 ± 84 vs. 279 ± 40 ms, $p=0.01$), but average and peak saccade velocity did not differ ($p>0.80$). Children with CVI had longer fixation duration (492 ± 93 vs. 351 ± 45 ms, $p=0.05$) and fewer fixations (3.7 ± 0.83 vs. 6.9 ± 0.74 , $p=0.0043$) and saccades (4.8 ± 0.44 vs. 7.1 ± 0.65 , $p=0.0043$) per trial.

Conclusions:

Eye tracking shows promise as a quantitative measure of vision in children with CVI. Visual function and oculomotor findings are consistent with previously published qualitative data. Further research is necessary to establish the reliability and validity of this technique, which could potentially serve as an outcome measure in clinical trials of treatments for CVI.

References: None.

Keywords: Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

Grant Support: Children's Eye Foundation of AAPOS (CEF/FAAPOS) Research Grant Research to Prevent Blindness

Contact Information: Melinda Chang, MD, melinda.y.wu@gmail.com

Tuesday, March 10th from 8:45 - 9:00 am

Anterograde Axonal Degeneration in Children with Vision Loss Secondary to NF1 Associated Optic Pathway Glioma

Robert Avery¹, Ritobrato Datta¹, Aditya Rao¹, Michael Fisher¹, Grant Liu¹

¹*Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA*

Introduction:

The presence and evolution of anterograde axonal degeneration from an acquired optic neuropathy is an important feature to consider when designing treatment and neuroprotection strategies. We studied the association between measures of striate cortex volume and vision loss in children with optic pathway gliomas secondary to Neurofibromatosis type 1 (NF1-OPG).

Methods:

Children with and without visual acuity loss from a NF1-OPGs were eligible if they underwent SD-OCT measures of circumpapillary retinal nerve fiber layer (cpRNFL) thickness and brain MRI isotropic T1-weighted sequences on a 3T Siemen's scanner. Using FreeSurfer toolkit, grey and white matter boundaries were segmented after processing and registration to a spherical atlas. Retinotopic visual areas (V1, V2 and V3) were confirmed using a standardized anatomic pediatric template and morphometric measures of volume (mm³) from both hemispheres were averaged. The global cpRNFL thickness from both eyes was averaged and compared to individual retinotopic and whole striate cortex volumes using linear regression. Whole brain volume was also measured.

Results:

Twenty-seven children (mean age: 7.3 years, range: 4.1 – 11.9) were included. Ten subjects had vision loss (≥ 0.2 logMAR in at least one eye). cpRNFL thickness in the vision loss group was lower than the normal vision group (65 vs. 97 microns respectively, $p < 0.01$). Average cpRNFL thickness demonstrated a significant positive association with whole striate cortex volume ($p < 0.01$) even when controlling for whole brain volume ($p < 0.02$). Individual V1 dorsal/ventral along with V2/V3 dorsal regions demonstrated a significant positive association with average cpRNFL ($p < 0.05$).

Conclusions:

Optic neuropathy and vision loss secondary to NF1-OPGs results in anterograde axonal degeneration to the striate cortex. It is conceivable that striate cortex volume loss may decrease the probability of a favorable treatment response as well as the potential success of neuroprotection and visual restoration strategies.

References: None.

Keywords: Neuroimaging, Genetic disease, Pediatric neuro-ophthalmology, Tumors, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: NIH EY029687

Contact Information: averyr@email.chop.edu

Tuesday, March 10th from 9:00 - 9:15 am

Is Visual Snow a thalamo-cortical dysrhythmia of the visual processing system – a magnetoencephalogram study

Jenny Hepschke¹, Andrew Etchell², Robert Seymour², Paul Sowman², Clare Fraser³

¹Save Sight Institute, Sydney NSW, Australia, ²Department of Cognitive Science, Macquarie University, Sydney NSW, Australia, ³Save Sight Institute, Faculty of Health and Medicine, The University of Sydney, Sydney NSW, Australia

Introduction:

Visual snow (VS) has been described as a unique clinical entity, which may occur with increased neuronal excitability. (1) Sensory information processing relies on the interactions between the thalamus and cortex. When hyperexcitability affects cortical networks, it can lead to thalamocortical dysrhythmias, resulting in tinnitus. (2) We hypothesize that VS is the visual manifestation of thalamocortical dysrhythmia. Visual cortex gamma oscillations reflect cognitive processing and alpha oscillations are associated with thalamically generated pulses of cortical inhibition, altering information processing. (3) This oscillatory network activity is a characteristic property of the thalamocortical system. Therefore, we used Magnetoencephalography (MEG) to record the visual cortex oscillatory dynamics, as a measure of possible thalamocortical dysrhythmia in VS patients and controls.

Methods:

20 patients diagnosed with VS and age-matched controls underwent MEG testing (MEG160 Model PQ1160R-N2, KIT). Results were recorded during resting state and while subjects were visually engaged with a static grating presented for 1.5s. Alterations in MEG signals were assessed between the task types, and participant groups. Neuronal synchronisation in the gamma band (30–100Hz) and oscillatory activity in the alpha band (8–13Hz), were measured in the V1 primary visual cortex.

Results:

The resting state power spectral density in V1 was similar between VS and controls. During the visual gratings, the increase in gamma power and peak frequency in V1 was similar for the two groups. However, there was a lower alpha peak frequency and greater reduction in alpha power in the controls compared with the VS group at ~11Hz. Alpha-gamma phase-amplitude coupling in V1 is shifted towards lower alpha frequencies for VS patients.

Conclusions:

The observed changes in visual cortex alpha oscillations provide evidence that neuronal activity is less able to be inhibited through the thalamic pathways in VS patients. This supports the hypothesis that VS is associated with a thalamocortical dysrhythmia.

References: 1. Bou Ghannam A, Pelak VS. Visual Snow: a Potential Cortical Hyperexcitability Syndrome. *Curr Treat Options Neurol*. 2017 Mar;19(3):9. 2. De Ridder D, Vanneste S, Langguth B, Llinas R. Thalamocortical Dysrhythmia: A Theoretical Update in Tinnitus *Front Neurol*. 2015; 6: 124. 3. Bonnefond, M., S. Kastner, and O. Jensen, Communication between Brain Areas Based on Nested Oscillations. *eNeuro*, 2017. 4(2).

Keywords: Higher visual cortical functions, Higher visual functions

Financial Disclosures: The authors had no disclosures.

Grant Support: This study was kindly supported by the NANOS Pilot Grant scheme.

Contact Information: Dr Jenny Hepschke drjennyhepschke@gmail.com

Tuesday, March 10th from 9:15 - 9:30 am

Gender distribution of speakers at the North American Neuro-Ophthalmology Society annual meetings.

Obadah Moushmoush¹, William Weirich¹, David Weirich², John Nguyen¹, Jamie Schaefer³, Brian Ellis¹

¹West Virginia University, Morgantown, West Virginia, USA, ²Root Insurance Co, Columbus, Ohio, USA, ³The Warren Alpert Medical School at Brown University, Providence, Rhode Island, USA

Introduction:

Presentation at conferences serves as an important evidence of external recognition. As more women entered the field of ophthalmology, little is known about women representation at neuro-ophthalmology conferences. We investigated gender representation over a 10-year period among presenters at North American Neuro-Ophthalmology Society (NANOS) conferences.

Methods:

A retrospective audit of annual NANOS meeting programs from 2010-2019 was performed. Accrued gender data was stratified by podium presentations, posters, moderators, Frank Walsh presenters, and information speakers and by symposium year. Gender data was determined through an online search of each name.

Results:

Here was a total of 3062 presentations across the 10 years, of which 1434 (46.8%) were delivered by females. Of the 188 Frank Walsh presentations, 94 (50.0%) were delivered by females. There were 289 moderators, with 120 of them female (41.5%). There was a total of 2070 posters with 1061 first-authored by females (51.3%). Representation in all categories was rather consistent from year to year with no significant trend upward or downward from 2010 to 2019 ($p>0.05$). There were a total of 578 informational speakers, 189 of which were female (32.7%).

Conclusions:

Overall, female authorship across presenters, moderators, and first-authored posters of the annual NANOS conference has remained relatively balanced over the past 10 years. However, informational speakers have shown consistently lower female representation. A study of female speakers at surgical specialty conferences showed female representation to span between 20.1 and 28.4% between 2007 and 2017. It is encouraging to see female representation at NANOS much higher than the average of other surgical subspecialties.

References: 1. Ruzyski SM, Fletcher S, Earp M, Bharwani A, Lithgow KC. Trends in the Proportion of Female Speakers at Medical Conferences in the United States and in Canada, 2007 to 2017. *JAMA Netw Open*. 2019;2(4):e192103. 2. Davids, Jennifer S., et al. "Female Representation and Implicit Gender Bias at the 2017 American Society of Colon and Rectal Surgeons' Annual Scientific and Tripartite Meeting." *Diseases of the Colon & Rectum*, vol. 62, no. 3, 2019, pp. 357–362., doi:10.1097/dcr.0000000000001274. 3. Klein, Robyn S, et al. "Speaking out about Gender Imbalance in Invited Speakers Improves Diversity." *Nature Immunology*, vol. 18, no. 5, 2017, pp. 475–478., doi:10.1038/ni.3707.

Keywords: Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.



North American Neuro-Ophthalmology Society

46th Annual Meeting

March 7 – March 12, 2020

Omni Amelia Island Plantation Resort • Amelia Island, FL

SCIENTIFIC PLATFORM SESSION III

Tuesday, March 10 - 10:00 – 12:00 pm

Amelia Ballroom

Moderators: Ruth Huna-Baron, MD and Kenneth Shindler, MD, PhD

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Tuesday, March 10th from 10:00 - 10:15 am

Static And Abduction Versus Adduction Dynamic Ocular Motor Abnormalities In Spinocerebellar Ataxia Type 3

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Introduction:

Static [esotropia] and dynamic [gaze-evoked and optokinetic nystagmus (GEN; OKN), hypometric/hypermetric saccades, low gain pursuit and head impulse (HI)] ocular motor abnormalities (OMA) have all been described in spinocerebellar ataxia type 3 (SCA3). Importantly, dynamic ocular motor abnormalities during eye abduction and adduction are often asymmetric in ataxia. We sought to evaluate the role of static OMA, and abduction vs. adduction dynamic OMA as potential biomarkers in SCA3.

Methods:

We prospectively accessed in SCA3 patients, CAG repeat number, disease duration, scale for the assessment and rating of ataxia (SARA) score, ocular alignment at near and distance, abduction and adduction GEN, OKN, pursuit, saccades, and HI. An adjusted p value <0.003 and <0.001 were considered significant for between- and within-groups, and correlation analysis, respectively.

Results:

We recruited 38 SCA3 patients (mean age, 49.8±12.2; 24 females) and 22 healthy controls (mean age, 50.7±12.5; 12 females) (p=0.651; p=0.589). Patients were significantly or near significantly more esotropic at far than controls (3.3±8.4 vs. 0.1±1.8 prism diopters) and showed GEN, faster adduction saccades (512±117 vs. 429±53°/s), smaller abduction saccades (84.9±/-12.4 vs. 91.6±/-6.0) and lower abduction and adduction pursuit and HI gain, and OKN slow phase velocity (SPV) (0.79±0.11 and 0.78±0.13 vs. 0.90±0.03 and 0.90±0.04; 0.67±0.28 and 0.70±0.28 vs. 0.96±0.12 and 1.0±0.1; 11.1±4.9 and 10.7±5.8 vs. 17.3±2.6 and 16.6±2.4°/s). Abduction and adduction OKN and HI significantly correlated with CAG repeat number and SARA score, and abduction OKN only, with disease duration (R range, -427, -718). Abduction and adduction GEN and ocular alignment at near, significantly and near significantly correlated, respectively, with SARA score (R range, -461, -716).

Conclusions:

Abduction and adduction dynamic eye movements not only correlate with disease markers of progression in SCA3, but importantly, these seem to be distinctively affected, perhaps reflecting an adaptive reorganization of the central ocular motor network in response to progressive esotropia at far.

References: 1. Kim, J. S., Kim, J. S., Youn, J. , Seo, D. ,et al. (2013), Ocular motor characteristics of different subtypes of spinocerebellar ataxia: Distinguishing features. *Mov Disord.*, 28: 1271-1277. 2. Versino M, Hurko O, Zee DS. Disorders of binocular control of eye movements in patients with cerebellar dysfunction. *Brain.* 1996 Dec;119 (Pt 6):1933-50. 3. Luis L, Costa J, Muñoz E, de Carvalho M, Carmona S, et al. Vestibulo-ocular reflex dynamics with head-impulses discriminates spinocerebellar ataxias types 1, 2 and 3 and Friedreich ataxia. *J Vestib Res.* 2016 Jul 2;26(3):327-34. 4. Lemos J, Novo A, Duque C, Castelhana J, Eggenberger E, et al. "Pinball" intrusions in spinocerebellar ataxia type 3. *Neurology.* 2018 Jan 2;90(1):36-37.

Keywords: Ocular manifestations of vestibular disorders, Adult strabismus with a focus on diplopia, Nystagmus, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Tuesday, March 10th from 10:15 - 10:30 am

The 100,000 Genomes Project – Uncovering Pathogenic Variants in inherited Optic Neuropathies with Whole-Genome Sequencing

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Introduction:

Inherited optic neuropathies (ION) are a genetically heterogeneous group of disorders characterised by progressive and irreversible loss of retinal ganglion cells. Reaching a confirmed molecular diagnosis can be challenging given the number of disease-associated genes that have been identified within both the nuclear and mitochondrial genomes. In addition, routine genetic testing will also not identify novel causes of optic atrophy. In this study, we applied whole-genome sequencing (WGS) to investigate a cohort of patients with a clinical diagnosis of ION.

Methods:

As part of the 100,000 Genomes project, we have so far analysed 61 probands with ION. Variant calling was conducted using an automated bioinformatics pipeline. In the first instance, variant prioritisation in a curated virtual gene panel (<https://panelapp.genomicsengland.co.uk/panels/186/>) was performed, followed by clinical variant interpretation and a discussion at a multidisciplinary meeting. For unsolved cases, we looked specifically for non-coding and structural variants in the gene panel and new gene/disease associations. Potential pathogenic variants were selected for functional analysis by applying an integrated analysis pipeline incorporating deep clinical phenotyping, variant filtering and interpretation tools.

Results:

To date, 61/137 (44.5%) probands with optic atrophy have been analysed. Using our integrated bioinformatics approach, we have identified likely pathogenic variants in 34/61 (56%) probands. Of these, 29 (85%) cases harbor variants in known optic atrophy genes whereas 5 (15%) cases harboured likely pathogenic variants outside of the gene panel. 24/61 (39%) undiagnosed cases currently undergoing expanded variant discovery analysis, where we expect to identify novel optic atrophy genes.

Conclusions:

Implementation of WGS as part of a clinical genomic pipeline is a powerful strategy leading to a molecular diagnosis in over half of all cases investigated. Furthermore, we identified novel optic atrophy genes and new gene/disease associations in the undiagnosed cases.

References: None.

Keywords: Genetic disease, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Tuesday, March 10th from 10:30 - 10:45 am

Progressive Optic Atrophy in a Retinal Ganglion Cell-Specific Mouse Model of Complex I Deficiency

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Introduction:

Optic atrophy resulting from retinal ganglion cell (RGC) degeneration is the most prominent ocular manifestation of mitochondrial dysfunction. Efforts to develop effective pharmacotherapies for mitochondrial optic neuropathies have been hampered, in part, by the lack of an ideal preclinical animal model. Although mutant mice lacking the mitochondrial complex I accessory subunit NADH:ubiquinone oxidoreductase (NDUFS4) develop early-onset optic atrophy, severe systemic mitochondrial dysfunction leads to very early death, making this mouse line impractical for studying the pathobiology of mitochondrial optic neuropathy.

Methods:

A transgenic mouse line expressing Cre recombinase under transcriptional control of the promoter for the vesicular glutamate transporter Vglut2 (*Vglut2-Cre*) was crossed with a Cre-dependent tdTomato reporter line and the expression of Cre assessed in retinal cross sections and flat mounts. The *Vglut2-Cre;ndufs4loxP/loxP* transgenic mouse line was generated to delete *ndufs4* within most RGCs. Optic nerve NDUFS4 protein content was assessed via Western blot, and the retinal phenotype was assessed via electroretinography and histological quantification of RGC somas in retinal flat mounts and RGC axon density within optic nerve cross sections at multiple time points.

Results:

Vglut2-driven Cre expression was achieved in 96% of RGCs, but also in a small fraction of cones and horizontal cells. Inactivation of *ndufs4* in RGCs resulted in reduced expression of NDUFS4 protein within the optic nerves of *Vglut2-Cre;ndufs4loxP/loxP* mice. No significant outer retinal electrophysiological abnormalities were detected, whereas degeneration of RGCs in *Vglut2-Cre;ndufs4loxP/loxP* retinas commenced around postnatal day 45 (P45) and progressed to loss of two-thirds of RGCs by P90.

Conclusions:

Complex I deficiency within RGCs achieved via tissue-specific deletion of *ndufs4* induces rapid and profound optic atrophy in a cell-autonomous manner. Compared to the germline *ndufs4*^{-/-} knockout mouse, the longer lifespan of the *Vglut2-Cre;ndufs4loxP/loxP* mouse makes this line a promising preclinical model for testing therapies for mitochondrial optic neuropathies such as Leber Hereditary Optic Neuropathy.

References: None.

Keywords: Optic neuropathy, Genetic disease

Financial Disclosures: The authors had no disclosures.

Grant Support: This work was funded by the National Eye Institute via grants EY028610 (S.M.G.), EY022959 (V.Y.A.), and Core Grant EY005722 (Duke University), as well as a Duke University School of Medicine Strong Start Award (S.M.G.), and an Unrestricted Research to Prevent Blindness Grant (Duke Eye Center).

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Tuesday, March 10th from 10:45 - 11:00 am

Development of a Retinal Ganglion Cell Specific Gene Therapy Using SIRT1 Signaling for Neuro-Protection

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Introduction:

Loss of retinal ganglion cells (RGC) can occur by trauma, inflammatory, and ischemia leading to irreversible effects upon vision. Sirtuin 1 (SIRT1) deacetylase has demonstrated therapeutic value in multiple models of optic neuropathy with small molecule biologics. The initial use of gene therapy modestly improved visual outcomes in the EAE-induced mouse model of optic neuritis but with limited effects due to a low transduction rate and lack of cell specificity. Here we investigated the therapeutic potential of RGC specific SIRT1 gene augmentation in a mouse model of optic nerve crush (ONC).

Methods:

AAV7m8 vectors were designed to express green fluorescent protein or human SIRT1 driven by the RGC-specific gamma-synuclein (SNCG) promoter. Vectors were delivered by intravitreal injections and the RGC transduction profile was examined post injection using immunohistochemistry techniques. Efficiency and specificity was compared to previously described AAV2 vectors driving SIRT1 expression with the non-cell specific CAG promoter. The new AAV7m8 vector was then tested for efficacy using ONC with visual function and retina evaluated for RGC numbers.

Results:

The improved AAV7m8 vector expressing SIRT1 driven by the SNCG promoter demonstrated enhanced expression of SIRT1 compared with its AAV2 predecessor using the CAG promoter. The AAV7m8-SIRT1 vector showed a 40% transduction efficiency compared with only 21% by AAV2-SIRT1, and AAV7m8-SIRT1 drove expression exclusively in RGCs. Intravitreal delivery of AAV7m8-SIRT1 in ONC mediated significant preservation of vision and RGC numbers compared to vehicle and GFP controls.

Conclusions:

RGC specific expression of SIRT1 offers targeted therapy for a animal models with significant RGC loss. Over-expression of SIRT1 through gene transduction within RGCs specifically delays vision loss and RGC loss, indicating a RGC specific component of neuro-protection in ONC. This may be a strong therapeutic candidate for testing in models of other optic neuropathies.

References: 1) Hathiram, Bachi T., K. S. Khattar, and Supriya Rode. "Traumatic optic neuropathy." *Int J Otorhinolaryngol Clin* 3: 188-196 (2011) 2) Levin, Leonard A., et al. "The treatment of traumatic optic neuropathy: the International Optic Nerve Trauma Study." *Ophthalmology* 106.7: 1268-1277(1999) 3) Sengillo, Jesse D., et al. "Gene and cell-based therapies for inherited retinal disorders: An update." *American Journal of Medical Genetics Part C: Seminars in Medical Genetics*. Vol. 172. No. 4. 2016. 4) Jia, Yu, et al. "Next-generation CRISPR/Cas9 transcriptional activation in Drosophila using flySAM." *Proceedings of the National Academy of Sciences* 115.18: 4719-4724 (2018). 5) McDougald, Devin S., et al. "SIRT1 and NRF2 gene transfer mediate distinct neuroprotective effects upon retinal ganglion cell survival and function in experimental optic neuritis." *Investigative ophthalmology & visual science* 59.3: 1212-1220 (2018) 6) Khan, Reas S., et al. "Intranasal delivery of a novel amnion cell secretome prevents neuronal damage and preserves function in a mouse multiple sclerosis model." *Scientific reports* 7 : 41768 (2017)

Keywords: Optic neuropathy, Optic nerve trauma and treatment, Orbit/ocular pathology, Miscellaneous

Financial Disclosures: NIH K08 Funding; Robert Wood Johnson Foundation Grant

Grant Support: 1) NIH Mentored Clinical Scientist Award: K08 EY030163-01, 2) Robert Wood Johnson Harold Amos Faculty Development Award

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Tuesday, March 10th from 11:00 - 11:15 am

Bilateral Visual Improvement with Unilateral Gene Therapy for Leber Hereditary Optic Neuropathy (LHON)

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Introduction:

LHON is a mitochondrially-inherited disease causing severe bilateral optic neuropathies. A point mutation in the mitochondrial ND4-gene accounts for 75% of LHON cases. rAAV2/2-ND4 is a gene therapy enabling allotropic expression and delivery of the wildtype ND4 protein to mitochondria of retinal ganglion cells. We assessed the clinical efficacy of a single intravitreal injection of rAAV2/2-ND4 (GS010), an investigational gene therapy for ND4-LHON.

Methods:

RESCUE (NCT02652767) and REVERSE (NCT02652780) are Phase III, randomized, double-masked, sham-controlled trials in which LHON subjects with the G11778A ND4 mutation received a single unilateral intravitreal injection of rAAV2/2-ND4. Visual functions, retinal anatomy, and quality of life were monitored for 96 weeks following administration. A concurrent study on 3 non-human primates with an equivalent unilateral injection was performed.

Results:

At Week 96, rAAV2/2-ND4-treated eyes of REVERSE subjects gained on average +15 ETDRS letters equivalent compared to baseline. Sham-treated eyes showed a similar improvement (+13 ETDRS letters), counter to expected natural history of the disease. In RESCUE, mean BCVA worsened to a nadir in both eyes, followed by a parallel improvement from Week 48 to Week 96. On average, rAAV2/2-ND4-treated eyes of RESCUE subjects gained +26 ETDRS letters equivalent compared to their nadir BCVA. A clinically relevant response (CRR) from nadir was observed in at least one eye of 78% of REVERSE subjects, and 63% of RESCUE subjects. By comparison, a natural history study reported only 28% of LHON subjects with the G11778A mutation had a spontaneous CRR from nadir in at least one eye. The presence of rAAV2/2-ND4 in the fellow non-injected eye was demonstrated in the non-human primates.

Conclusions:

Final results of RESCUE and REVERSE showed clinically meaningful improvements of visual functions. Improvement in the contralateral eye may be explained by the transfer of rAAV2/2-ND4 to the sham-treated eye, as supported experimentally by the concurrent non-human primate study.

References: None.

Keywords: Genetic disease, Optic neuropathy

Financial Disclosures: Consultant for GenSight, Santhera and Stealth; research support from GenSight and Santhera

Grant Support: GenSight Biologics

Contact Information: None provided.

Tuesday, March 10th from 11:15 - 11:30 am

Expanded access program (EAP) in Leber's hereditary optic neuropathy (LHON) patients treated for 24 months

Thomas Klopstock¹, Xavier Llòria², Magda Silva², Rudolph Guenther³, Felice Lob³, Bettina Von Livonius³, Claudia Catarino³

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Introduction:

LHON is a mitochondrial genetic disorder resulting in severe bilateral central VA loss. Three primary mitochondrial DNA mutations cause over 90% of cases. Data from idebenone EAP for patients with LHON receiving treatment for at least 24 months were analyzed to assess rate of clinically-relevant recovery (CRR)

Methods:

EAP patients were treated with idebenone (900 mg/day) in routine practice. The Long-Term LHON Cohort (LT-LHON) was defined as patients treated for at least 24 months and with at least one post-baseline VA assessment. The Long-Term Efficacy Cohort (LT-EC) included only LT-LHON patients with any of the three major mutations and onset of vision loss in the most recently affected eye less within 12 months. CRR was defined as an improvement from off-chart to on-chart vision by the equivalent of at least 1 full line in the ETDRS chart or an improvement in on-chart vision by at least 2 lines

Results:

Among 111 patients included in the EAP, 51 (102 eyes) fulfilled the LT-LHON criteria and 42 (84 eyes) the LT-EC. In LT-LHON 58 eyes (56.9%) in 33 patients (64.7%) had CRR from Nadir and 25 of these (75.8%) responded in both eyes. In LT-EC 46 eyes (54.8%) in 26 patients (61.9%) had CRR from Nadir and 20 of these (76.9%) responded in both eyes. The last recorded CRR was observed after 34.6 months of treatment. At the time of CRR the median magnitude of improvement was 19 ETDRS letters in LT-LHON and 20 in LT-EC, with a maximum gain of 60. At last visit median magnitude of improvement was 38 and 39 letters with a maximum of 90

Conclusions:

Recovery rate and VA improvement observed in EAP patients receiving at least 24 months of treatment are greater than those previously reported in literature. Benefit of treatment was not limited to patients with recent onset

References: None.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Tuesday, March 10th from 11:30 - 11:45 am

Proof of Concept for Levodopa Treatment in Rescuing Retinal Morphology and Visual Function in Albinism

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Introduction:

There is a paucity of treatments for oculocutaneous albinism (OCA), a condition characterised by pigment deficiency, abnormal retinal development, and significant visual disability. L-DOPA, a signalling molecule which is essential for normal retinal development, is deficient in OCA. Residual plasticity of the developing retina in young children with albinism has been demonstrated, suggesting a post-natal window for therapeutic rescue. In this study, we investigate if post-natal retinal morphology and visual function in OCA can be improved through oral Levodopa supplementation, if administered during the critical period of neuroplasticity.

Methods:

The effects of a 28-day course of oral L-DOPA treatment administered to OCA mice from birth (n=11) and 28 days (n=10) of age on retinal morphology and function were investigated using optical coherence tomography (OCT) and electroretinography (ERG), respectively. 336 examinations were obtained at 4, 5, 6, 8, 12 and 16 weeks of age. Generalised linear mixed regression modelling was used to analyse group differences.

Results:

We observed significant increases in retinal nerve fibre layer ($z=2.01$, $p=0.044$), outer nuclear layer ($z=1.97$, $p=0.049$) and photoreceptor end tips ($z=3.43$, $p=0.001$) OCT thickness measurements, significant increases in ERG A-wave (χ^2 (9, N=420) = 91.97, $p<0.0001$) and B-wave (χ^2 (9, N=420) = 121.24, $p<0.0001$) amplitudes and significant reductions in A-wave latencies (χ^2 (9, N=420) = 47.92, $p=0.01$) recorded from OCA mice treated with L-DOPA from birth, compared to untreated mice. Interestingly, we did not observe any significant effects on ERG amplitudes or latencies in OCA mice treated with L-DOPA from 28 days of age.

Conclusions:

We have demonstrated that abnormal retinal development, morphology and visual function can be rescued post-natally using oral L-DOPA supplementation, but only if administered during the critical period of neuroplasticity.

References: None.

Keywords: Pediatric neuro-ophthalmology, Nystagmus, Genetic disease

Financial Disclosures: The authors had no disclosures.

Grant Support: Medical Research Council (MRC), London, UK (grant number: MR/R007640/1), Academy of Medical Sciences (AMS) (grant number: SGL014\1009), Gift of Sight, University of Southampton Research Management committee and the National Institute for Health Research (NIHR).

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Tuesday, March 10th from 11:45 am - 12:00 pm

Ectopic Melanopsin For Visual Restoration: Comparisons With Alternative Optogenetic Tools

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Introduction:

Background: Melanopsin is an optogenetic tool - it renders neural cells sensitive to light when exogenously expressed - and is emerging as a prime candidate for clinical optogenetic approaches to visual restoration. A model for this approach lies in the neuroretinal tissue surviving in the inherited retinal degenerations (IRD). However, a diversity of neural light responses naturally exists in the healthy retinae and it remains unclear which optogenetic tool is best suited to fully replicate natural neuroretinal responses. Purpose: To compare melanopsin with leading optogenetic tools exogenously targeted to ON-bipolar cells without the “noise” of intrinsic responses by using retinae devoid of both canonical and pRGC photoreception.

Methods:

Retina-degenerate mice lacking native melanopsin and expressing Cre recombinase in retinal ON-bipolar cells (*L7.Cre, Opn4^{-/-}, Pde6b^{rd1/rd1}*) were used. At P45, intravitreal injections of saline (N=8) or adeno-associated virus containing the melanopsin(*OPN4*)(N=8), rhodopsin(*RHO*)(N=8) or channelrhodopsin(*ReaChR*)(N=8) genes driven by a “floxed” promoter were administered. Eight weeks later, ex-vivo multiple electrode array recordings of retinal ganglion cell (RGC) light responses were made.

Results:

Melanopsin treated retinae demonstrated slow onset, but long-lived RGC light responses, persisting beyond the end of the light stimulus. ReaChR responses were fast onset and ‘sustained’ - terminating on stimulus removal. Rhodopsin responses were fast onset but transient “ON” type (terminated before light offset). Melanopsin driven responses were the most ($EC_{50}=13.63\log_{10}\text{photons}\text{cm}^{-2}\text{s}^{-1}$) and ReaChR responses the least sensitive ($EC_{50}=14.21\log_{10}\text{photons}\text{cm}^{-2}\text{s}^{-1}$)($p=0.021$).

Conclusions:

This direct comparison of optogenetic tools is the first in the literature and shows three tools to produce markedly different RGC light responses. Each is evocative of a different type of wild type RGC response and therefore presents ON-bipolar targeting of multiple tools as a powerful approach to restore naturalistic neuro-retinal responses, central to translating optogenetics as a clinical vision restoration therapy.

References: None.

Keywords: Genetic disease, Pupils retina

Financial Disclosures: The authors had no disclosures.

Grant Support: MJG is supported by a Wellcome Trust Clinical Research Training Fellowship (grant number 205151/Z/16/Z) ML is supported by a German Research Foundation Fellowship (grant number LI2846/1-1)

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North American Neuro-Ophthalmology Society

46th Annual Meeting

March 7 – March 12, 2020

Omni Amelia Island Plantation Resort • Amelia Island, FL

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196	Are koniocellular pathways involved in visual snow pathophysiology?	Jenny L. Hepschke
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199	Pupil abnormalities in patients with Neuromyelitis Optic Spectrum	Emely Z. Karam Aguilar
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Poster 171**Factors Associated with Increased Emergency Department Utilization in Patients with Acute Optic Neuritis.**

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Introduction:

Symptoms of acute vision loss and eye pain may lead patients with optic neuritis to seek care in the emergency department(ED). Given availability of lower cost alternatives for providing medical care for optic neuritis, this study aimed to identify factors associated with higher ED utilization.

Methods:

Subjects with acute optic neuritis were identified through chart review of adult patients with ICD-9 or ICD-10 codes for optic neuritis with corresponding acute MRI findings (n=30) in the medical record research repository of a tertiary care institution. Subjects were grouped based on number of ED visits(0-1, 2-3) within two months of either ICD code or positive MRI. Demographics, characteristics of disease presentation, type and location of medical care, testing, treatment, type of follow-up visits and duration of care were extracted from the medical record.

Results:

Of 30 acute optic neuritis cases(age 41 +/- 16), 53%(16/30) female), 19 had 0-1 ED visit and 11 had 2-3 ED visits. Fewer ED visits was associated with an initial clinical encounter in an outpatient setting(p=.0197, chi-square), but not residential distance from the hospital or insurance type. Fewer ED visits was associated with an increased incidence of lumbar puncture(p=.0444, chi-square), but not with neuro-imaging or laboratory testing. Both groups presented in a similar time frame with similar symptoms and clinical signs. Treatment was similar in both groups. Number of ED visits was not associated with the duration or type of follow up(opthalmology, neurology, or both).

Conclusions:

Patients with their first clinical encounter for optic neuritis in the ED had more visits to the ED overall when compared to those first seen in an outpatient setting. Number of ED visits was not associated with demographics, disease presentation, treatment or follow up care type and duration. Established outpatient care may be a role in limiting ED care for acute optic neuritis.

References: None.

Keywords: Optic neuritis

Financial Disclosures: The authors had no disclosures.

Grant Support: Research to Prevent Blindness, NIH P30 026877

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Poster 172**Ganglion Cell Layer Complex and Retinal Nerve Fibre Layer measurements in Pituitary Adenoma cases.**

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Introduction:

Axonal and neuronal degeneration are important features of optic chiasm compression in cases of pituitary adenoma. The study was carried out to evaluate and compare the regional relationships between GCL-IPL (Ganglion cell layer- Inner Plexiform Layer) and Retinal Nerve Fiber Layer (RNFL) thickness as measured by spectral domain Optical Coherence Tomography (SD-OCT) in pituitary adenoma cases and its correlation with visual field (VF).

Methods:

Detailed Neuro-ophthalmic examination including Perimetry, RNFL and GCL-IPL thickness were measured pre operatively in 24 cases of pituitary adenoma with chiasmal compression. These parameters were repeated one year after the surgery.

Results:

Patterns of GCL-IPL thinning corresponded to visual field defects and significantly correlated with the MD (Mean Deviation) of VF. The average GCC-IPL thickness was $63.10 \pm 16.1 \mu$ in patients and $81 \pm 5.2 \mu$ in controls ($P < 0.001\%$). Effect size to assess the magnitude of difference between cases and control is 1.51. ROC curve values to compare GCL-IPL and RNFL thickness shows that GCL-IPL (85.9%) is a better diagnostic tool than RNFL analysis (73.1%). Postoperatively, VF MD improved in 11 out of 14 patients with persistent GCL-IPL nasal thinning.

Conclusions:

GCL-IPL measurements on OCT is a sensitive tool to detect early anterior visual pathway changes in chiasmal compression. It correlates well with visual field changes and may help to prognosticate visual outcome following treatment. Thinning of GCL-IPL may be detected before loss of RNFL in some patients. After surgical removal of tumor there was improvement in visual acuity and visual fields despite persistent GCL-IPL loss, but lesser GCL-IPL loss prior to surgery had better post operative visual fields.

References: 1. G Cennamo, RS Auriemma², D Cardone¹, LFS Grasso³, N Velotti¹, C Simeoli³, C Di Somma³, R Pivonello³, A Colao³ and G de Crecchio¹. Evaluation of the retinal nerve fibre layer and ganglion cell complex thickness in pituitary macroadenomas without optic chiasmal compression. *Eye* (2015) 29, 797–802. 2. Jing Zhang,^{#1} Sunfu Zhang,^{#1} Yanlin Song,^{#2} Chenjing Zhu,^{#2} Min He,¹ Qingqing Ren,¹ Baoyin Shan,¹ Ziqiong Wang,¹ Yunhui Zeng,¹ and Jianguo Xu Predictive value of preoperative retinal nerve fiber layer thickness for postoperative visual recovery in patients with chiasmal compression *Oncotarget*. 2017 Aug 29; 8(35): 59148–59155. Published online 2017 Jul 18. Phal PM, Steward C, Nichols AD, Kokkinos C, Desmond PM, Danesh-Meyer H, Sufaro YZ, Kaye AH, Moffat BA. Assessment of Optic Pathway Structure and Function in Patients with Compression of the Optic Chiasm: A Correlation with Optical Coherence Tomography. *Invest Ophthalmol Vis Sci*. 2016;57:3884–3890

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Visual fields, Tumors, Optic neuropathy, Perimetry

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 173**OCT Angiography quantification of the capillary peripapillary plexus in non-arteritic anterior ischemic neuropathy**

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Introduction:

OCT angiography is an imaging method allowing the visualization of the retinal peripapillary and optic nerve head (ONH) vessels. With specific algorithms it is also possible to quantify the vascular density and the flux index of these areas. Quantification is based on an automatic segmentation which includes both RNFL and GCL layers, each of them being vascularized by two different plexus. At the acute phase of non-arteritic anterior ischemic optic neuropathies (NAION) previous studies have shown controversial results concerning the peripapillary blood flow and vessel density. The aim of our study is to perform a vascular quantification of the top-most retinal layer including exclusively the RNFL using a new algorithm.

Methods:

Retrospective analysis of 15 eyes with acute NAION in 15 patients. ONH was imaged using a swept-source OCT-A (PLEX® Elite 9000 device - Carl Zeiss Meditec, Inc., Dublin, USA). Scan centered on the disc, and measuring 6mm x 6mm were acquired. The capillary flux index (CFI) and the capillary perfusion density (CPD) were quantified. The CFI is defined as the total weighted area of perfused vasculature per unit area in a region of measurement. The CPD is defined as the total area of perfused microvasculature per unit area in a region of measurement. Each NAION eye was compared with the unaffected fellow eye. The Wilcoxon test for matched samples was used. A *p*-value less than 0.05 was considered statistically significant.

Results:

In NAION eyes, the CFI was statistically higher on average ($p=0.0002$) and in the 4 quadrants when compared to the healthy eye. The CPD was lower in NAION eyes on average ($p=0.03$) and in the inferior quadrant ($p=0.0054$).

Conclusions:

Even if there is a lower CPD in NAION eyes, increased CFI suggest an autoregulatory phenomenon to compensate the ischemic process at the level of the ciliary vasculature.

References: None.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 174**Homonymous Macular Ganglion Cell Complex Atrophy on Optical Coherence Tomography without Significant Visual Field Changes**

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Introduction:

Neuro-ophthalmologists may discover homonymous thinning of the optical coherence tomography (OCT) macular-ganglion cell complex (GCC) without significant visual field defects in the workup of patients with suspected optic neuropathies or visual field defects. The differential diagnosis for this finding remains unknown. The goal of this study was to determine the causes of homonymous thinning of the OCT macular-GCC without significant visual field changes.

Methods:

A retrospective chart review was performed on consecutive patients that underwent OCT retinal nerve fiber layer-(RNFL) and macular-GCC. Patients were included in the study if they had high quality OCT scans, MRI brain, Humphrey visual fields and homonymous macular-GCC atrophy without significant visual field changes. A normalized asymmetry score (NAS)¹ and the degree of bow-tie atrophy was quantified.

Results:

A total of 6 patients, 3 females and 3 males, with a mean age of 40.3 (range 27 to 57) years were included in the study. Homonymous OCT macular-GCC thinning was secondary to demyelination of the optic tract in 4 patients (3 with multiple sclerosis and 1 with clinically isolated syndrome) and traumatic brain injury (TBI) in 2 patients. Three patients with demyelinating disease had a documented prior homonymous visual field defect that resolved. One TBI patient experienced a subjective visual field defect, but did not have this documented. There was a higher mean NAS among TBI patients (0.33) compared to those with demyelination (0.20, $p=0.07$). No significant difference in the degree of bow-tie atrophy was observed between groups (TBI 0.49, demyelination 0.50, $p=0.55$).

Conclusions:

Homonymous thinning of the OCT macular-GCC with essentially normal visual fields is mainly a result of previous demyelination involving the optic tract and TBI. OCT macular-GCC represents a novel method for establishing previous optic tract involvement in multiple sclerosis, which can help in establishing dissemination in time and space.

References: 1. Mitchell JR, Oliveira C, Tsiouris AJ, Dinkin MJ. Corresponding Ganglion Cell Atrophy in Patients With Postgeniculate Homonymous Visual Field Loss. *J Neuroophthalmol* 2015;35:353–359.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: This study was supported by a research grant from Kensington Vision and Research Centre, Toronto, Ontario, Canada

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Poster 175**Comparison Between inter-GCIPL, RNFL, VEP latency in Patients with Optic Neuritis.**

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Introduction:

Optic neuritis is a common manifestation of multiple sclerosis. The diagnosis of MS is heavily based on MRI findings but the latter is relatively insensitive in detecting optic nerve lesions. Identification of optic nerve lesion using ancillary tools such as spectral-domain optical coherence tomography (SDOCT) by measuring the retinal nerve fiber layer (RNFL) and ganglion cell-inner plexiform layer (GCIPL), and visual-evoked potentials latencies (VEP) may facilitate early diagnosis and treatment of multiple sclerosis.

Methods:

Thirty patients with diagnosed clinically with optic neuritis and fifty healthy control subjects were tested with SDOCT and VEP and the sensitivity, specificity, negative and positive predictive values of optimal values from healthy controls and optic neuritis patients were determined for the identification of unilateral optic nerve lesion.

Results:

The inter-eye GCIPL difference of 3.5 microns is highly sensitive (100%) and specific (98%) in identifying unilateral optic nerve lesion, while the lowest 5th percentile normal GCIPL threshold value of 71 microns was highly sensitive (100%) but less specific (83.3%). The inter-eye RNFL difference of 5.5 microns had a sensitivity of 70% and specificity of 90% in identifying optic nerve lesion while the lower 5th percentile normal RNFL value of 92.3 microns was poorly sensitive (40%). Finally, the 95th percentile normal VEP latency of 104.50 milliseconds had a sensitivity of 80% and specificity of 76% in identifying optic nerve lesion.

Conclusions:

The inter-eye GCIPL difference is a powerful index for identifying unilateral optic nerve lesion, while the inter-eye RNFL difference and 95th percentile normal VEP latency had very good sensitivity and specificity. These measures can be useful in the evaluation of the first demyelinating event of MS and therefore can facilitate early diagnosis and therapy.

References: None.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 176**The relationship between sleep disorders and non-arteritic anterior ischemic optic neuropathy**

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Introduction:

Previous research has strongly suggested a link between sleep disturbances and non-arteritic anterior ischemic optic neuropathy (NAION), the most common form of acute optic neuropathy among adults. While there is a significant body of literature suggesting an association between NAION and OSA, the relationship between NAION and non-OSA sleep disturbances remains elusive. We hypothesized that NAION would be associated not only with OSA, but also with non-OSA sleep disorders.

Methods:

We performed a retrospective analysis of the in-laboratory polysomnography and clinical data of 21 NAION patients (mean age 63.6 ± 9.7 years, 33.3% male, and mean BMI 29.4 ± 5.4 kg/m²). We also analyzed subjective NAION symptoms and sleep quality features. Furthermore, we compared the polysomnographic and clinical data of the NAION patients to 21 control patients free of neurological disease and 21 lacunar ischemic stroke patients, with all three groups matched for age, sex, and BMI.

Results:

We found no significant differences in the apnea-hypopnea index (AHI), mean apnea length, and minimum oxygen saturation between groups, despite the significantly higher vascular risk burden in the lacunar stroke group. We also found no significant differences among the three groups in the total sleep time, sleep efficiency, number of awakenings, percentage of TST spent in each sleep stage (N1, N2, N3, and REM), arousal index, and the periodic limb movement index.

Conclusions:

Our research did not reveal any significant relationship between NAION and both OSA and non-OSA sleep disorders, when comparing NAION patients to age, sex and BMI-matched controls who were free of neurological disease or had sustained a lacunar stroke. The pathophysiological connection between NAION and sleep disturbances remains unclear, and a larger prospective study is required for future investigations. The negative results of our study bring into question the referral of all NAION patients for sleep assessment.

References: None.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 177**Cerebrospinal fluid in a compartmented optic nerve sheath.**

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Introduction:

Cerebrospinal fluid has three main functions, 1: mechanical protection of brain and spinal cord tissue from trauma, 2: distribution of nutrients to CNS tissue, and 3: removal of waste products from cerebral metabolism. . CSF also helps maintain the correct ionic and protein composition of the environment surrounding nervous tissue cells. Given the multiple biologically relevant functions of CSF, impaired CSF dynamics and altered content would be expected to exercise a negative influence on tissue that depends on a homeostatic CSF environment. fluid is an important medium for maintaining the healthy of neurons and axons. Reduced CSF turnover is discussed in the pathophysiology of normal tension glaucoma (NTG) papilledema and SANS. One reason for a disturbed CSF turnover is the optic nerve sheath compartment syndrome. It has been described in patients with normal tension glaucoma and in some patients with papilledema.

Methods:

Case reports of six patients with optic nerve sheath compartment syndrome due to different etiologies.

Results:

Compartmentation of the ON sheath demonstrated by CT cisternography was the consistent finding in six patients who demonstrated findings of ON dysfunction. The etiologies in the cases varied and included meningitis, papilledema, sphenoid wing meningioma, disc herniation and normal-tension glaucoma.

Optic disc findings included low grade papilledema, disc pallor, disc cupping. Optic nerve sheath diameters were enlarged in all patients.

Conclusions:

ON damage was caused by a number of apparently disparate disorders, such as meningitis, papilloedema, disc herniation and NTG, in fact share a common aetiology: ONS compartmentation. This pathological entity may also be responsible, at least in part, for the neural damage that occurs in patients with AD and even for patients with isolated olfactory dysfunction. The management implications of this hypothesis are significant. In the setting of an ONSCS, an ONS fenestration might be an effective method for treating stagnation of CSF.

References:

- Pircher A, Montali M, Pircher J, Berberat J, Remonda L, Killer HE. Perioptic cerebrospinal fluid dynamics in idiopathic intercranial hypertension. *Front Neurol.* 2018; 28;9:506
- Pircher A, Montali M, Wostyn P, Pircher J, Berberat J, Remonda L, Killer HE. Impaired cerebrospinal fluid dynamics along the entire optic nerve in normal-tension glaucoma. *Acta Ophthalmol.* 2018 Mar 12.
- Boye D, Montali M, Miller NR, Pircher A, Gruber P, Killer HE, Remonda L, Berberat J. Flow dynamics of cerebrospinal fluid between the intracranial cavity and the subarachnoid space of the optic nerve measured with a diffusion magnetic resonance imaging sequence in patients with normal tension glaucoma. *Clin Exp Ophthalmol.* 2017 Nov 25.
- Killer HE, Pircher A. Reduced Free Communication of the Subarachnoid Space Within the Optic Canal in the Human. *Am J Ophthalmol.* 2017 Nov; 183: 164-165

Keywords: Optic neuropathy, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 178**Visual Outcomes in Pituitary Apoplexy**

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Introduction:

The aim of the study was to review the visual outcomes of patients undergoing either conservative or surgical management of pituitary apoplexy at a tertiary referral centre.

Methods:

A retrospective case analysis, of patients with pituitary apoplexy presenting between 2008 to 2018, was performed. Data on visual function and the presence of ocular motility deficits was recorded. A novel scoring system was used to quantify Goldmann visual field (GVF) defects.

Results:

Forty-one patients were identified. Headache and visual disturbance were presenting symptoms in 63% and nausea or vomiting in 39%. Cranial neuropathy was found in 58% (22/38), reduced best corrected visual acuity (BCVA) in 53% (18/34), abnormal visual field in 50% (16/34), relative afferent pupillary defect in 21% (8/38) and reduced colour vision in 71% (22/31).

Twenty-two patients (54%) were managed surgically. Of these, 14 (63%) had reduced BCVA at presentation and of the 12 with follow-up data, 11 recovered to normal BCVA and 1 did not. Eleven patients (50%) had reduced visual fields, of which 6 improved with an overall mean GVF score improvement of 1.7. Fifteen (68%) had abnormal motility; 12 recovered fully, 2 partially and 1 did not recover. Seven (32%) had RAPD and 2 recovered. Fifteen patients (68%) had reduced colour vision, of which 14 recovered.

Nineteen patients (46%) were managed conservatively. Four (21%) had reduced vision; 2 had follow-up data, of which 1 recovered fully and 1 did not. Four (21%) had reduced visual fields and 2 had follow-up data, 1 of which recovered fully with an overall mean GVF score improvement of 1.3. Seven (37%) had abnormal motility and reduced colour vision, all of which recovered fully.

Conclusions:

Although visual function is commonly affected in pituitary apoplexy, there is often substantial improvement following either surgical or conservative management.

References: None.

Keywords: Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 179**Prediction of Visual Field loss in Optic Disc Drusen Using Peripapillary and Macular Microvasculature**

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Introduction:

Optic disc drusen (ODD) is characterized by semi-translucent deposits on the optic nerve head. ODD causes vision loss and increased risk of nonarteritic anterior ischemic optic neuropathy. In this study, we quantified structural and blood flow changes in ODD and used principal component analysis, hierarchical clustering and correlation matrix to identify measurements that predict vision loss.

Methods:

We studied optical coherence tomography and angiography (OCT/OCTA) in 29 ODD and 53 age-matched control eyes. We used MATLAB scripts to measure vessel area density (VAD), vessel skeleton density (VSD), vessel perimeter index (VPI), vessel complexity index (VCI), flux and vessel diameter (VD). Statistical analysis was performed using custom R scripts and SPSS.

Results:

Principal component analysis revealed 5 key measurements that predicted vision loss in ODD: retinal nerve fiber layer (RNFL) thickness, macular ganglion cell complex (GCC) thickness, peripapillary VAD, macular VD and macular flux. Peripapillary and macular VAD was highly correlated with VSD, VPI, VCI. Hierarchical clustering of the 5 key measurements vs. all eye clinical characteristics revealed 3 patterns. ODD with no visual field (VF) loss (static perimetry mean deviation (MD) >-2 dB) had normal RNFL, GCC, and peripapillary VAD and *low* macular VD and flux. ODD eyes with mild VF loss (MD -2 dB to -5 dB) had normal RNFL, GCC, peripapillary VAD and *high* macular VD and flux. ODD eyes with moderate/severe VF loss (MD <-5 dB) had low RNFL, GCC, Disc VAD and *high* macular VD and flux.

Conclusions:

OCT/OCTA provided objective structural and blood flow measurements that can help predict visual field loss in ODD. Our data predict a model of altered microcirculation in ODD where visual field loss is associated with a compensatory increase in macular blood flow before structural thinning of the RNFL and GCC.

References: None.

Keywords: Optic neuropathy, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 180**Optic Disc Drusen Prevalence in Young Patients with NA-AION: a 10-year Retrospective Study**

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Introduction:

Non-arteritic anterior ischemic optic neuropathy (NA-AION) in young patients (age ≤50) accounts for a minority of all cases of NA-AION. Optic disc drusen (ODD) are associated with crowded optic nerves, and are located in the prelaminar optic nerve head where they could contribute to NA-AION pathogenesis. The purpose of this study was to determine the prevalence of ODD in the eyes of young NA-AION patients and to compare it to the baseline 1.8-2.0% prevalence of ODD in the general population.

Methods:

In this retrospective study, all young NA-AION patients (ages 18-50 years, inclusive) seen in two tertiary care neuro-ophthalmology clinics in the ten-year interval between April 1, 2009, and March 31, 2019, were identified and their medical charts reviewed. Patients were included in the study if ODD were diagnosed by any method (including ophthalmoscopy, ultrasound (US), fundus autofluorescence (FAF), computed tomography (CT), or any optical coherence tomography (OCT) method), or if ODD were excluded by enhanced-depth imaging OCT (EDI-OCT). The presence or absence of ODD was recorded for each eye.

Results:

There were 37 eligible patients (74 eyes). Mean age of NA-AION onset was 38.5 ±10.0 years. 23 patients (62%) were men. 36 patients had undergone EDI-OCT. We found an ODD prevalence of 56.7% in NA-AION-affected patients (53.3% in NA-AION-affected eyes). Only 35.9% of ODD were visible on ophthalmoscopy. 20 of 21 ODD patients (95.2%) had bilateral ODD. Age of onset and sex did not differ significantly between the ODD-positive group and the ODD-negative group. EDI-OCT outperformed any combination of ophthalmoscopy, US, FAF, CT at detecting ODD.

Conclusions:

ODD had much higher prevalence in young patients with NA-AION than in the general population, and were usually bilateral and buried. ODD may contribute to NA-AION pathogenesis by exacerbating an underlying compartment syndrome in the crowded “disc at risk”.

References: None.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Optic neuropathy, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: The project was supported in part by The Velux Foundations (Grant number: 00018408)

Contact Information: None provided.

Poster 181**Optic Neuritis Relapse Rate In Different Anatomical Locations Of The Optic Nerve.**

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Introduction:

Optic neuritis (ON) often relapses. A description about the frequency of recurrence in different anatomical portions of the optic nerve has not been assessed. The main objective is to describe the frequency at which the anatomical portions of the optic nerve are affected in cases of ON relapse. The secondary objective is to describe the relative frequency of affection of the different portions of the optic nerve by ON etiology.

Methods:

This study is an observational, retrospective chart review. We looked at patients with a history of ON relapses. The initial MRI-Orbit images of the optic nerve and subsequent images after relapse were compared. The determination of whether the position is the same as the previous attack was made on a patient-by-patient basis. Patients under 18 years of age, with prior history of other eye disease or prior orbit or brain surgery, were excluded.

Results:

We looked at 18 patients. 7 patients had multiple sclerosis, 3 had AQP4+ NMOSD, 5 had Anti-MOG+ (AQP-4-) NMOSD, 2 patients were diagnosed as recurrent optic neuritis, and 1 patient had IgG4 associated disease. 52.8% of the cases were intraorbital, 30.5% retrobulbar, 13.9% were pre-chiasmatic, and 2.7% were intracranial. Patients with AQP-4+ disease had more posterior lesions by a statistically significant margin versus the other groups. Patients with Anti-MOG+ disease had more anterior and more extensive lesions. Recurrence in the same portion of the optic nerve occurred 27,8% of the time. The patients that recurred in the same anatomical location had all different etiologies.

Conclusions:

The frequency of relapse by location is similar to that reported in the literature. This finding is particularly true for AQP-4+ NMOSD and MOG+ NMOSD patients, in which more posterior and longer lesions have been previously described. Only 5 patients (27,8%) had a recurrence in the same anatomical location. [AJMV1] [AJMV1]

References: Waschbisch A, Atiya M, Schaub C, Derfuss T, Schwab S, Aquaporin-4 antibody-negative recurrent isolated optic neuritis: clinical evidence for disease heterogeneity. *J Neurol Sci* 331:72–75. (2013) <https://doi.org/10.1016/j.jns.2013.05.01> Park KA, Oh SY, Min JH, Kim BJ. Incidence and timing of recurrence of optic neuritis. *Graefes Arch Clin Exp Ophthalmol*. 2019;257(3):651-655. DOI:10.1007/s00417-018-04217-7 Lotan I, Hellmann MA, Benninger F, Stiebel-Kalish H, Steiner I. Recurrent optic neuritis – Different patterns in multiple sclerosis, neuromyelitis optica spectrum disorders and MOG-antibody disease. *J Neuroimmunol*. 2018;324(August):115-118. DOI:10.1016/j.jneuroim.2018.09.010 Chen JJ, Flanagan EP, Jitprapaikulsan J, et al. Myelin Oligodendrocyte Glycoprotein Antibody–Positive Optic Neuritis: Clinical Characteristics, Radiologic Clues, and Outcome. *Am J Ophthalmol*. 2018;195(1):8-15. DOI:10.1016/j.ajo.2018.07.020

Keywords: Demyelinating disease, Neuroimaging, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: PAAO stipend

Grant Support: None.

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Poster 182**Reduced Blood Flow in the Choroidal Watershed Zone and Relation to Optic Disc Blood Flow**

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Introduction:

The choroidal watershed zone is a region of reduced blood flow due to its distal location at the interface between the major posterior ciliary arteries supplying the choroid and may be vulnerable to decreases in perfusion pressure in NAION and glaucoma. We sought to establish the degree of reduced blood flow in this region and corresponding sectors of the optic nerve head lying with it using laser speckle flowgraphy (LSFG).

Methods:

A case-control study of 48 patients with NAION and 28 control subjects were studied using LSFG. In a subset of eyes, fluorescein angiography was used to spatially correlate the location of the choroidal watershed zone with LSFG. Blood flow was compared between the areas within and outside of the choroidal watershed zone and its relation to blood flow in different sectors of the optic nerve head.

Results:

Blood flow within the watershed zone was reduced to $50.6 \pm 16.5\%$ (mean \pm SD) of blood flow in the adjacent choroid, outside of the watershed zone. Besides a highly significant correlation between blood flow in sectors of the optic nerve rim tissue and adjacent peripapillary choroid, blood flow was significantly lower in rim sectors on the temporal side of the nerve compared to the nasal side ($p=0.0001$), especially when the watershed zone was located more temporal to the center of the optic nerve.

Conclusions:

Blood flow is significantly lower in the choroidal watershed zone, making its vascular bed more vulnerable to dips in ocular perfusion pressure. The spatial location of the choroidal watershed zone relative to the optic nerve head and its shared blood supply with the prelaminar optic nerve may impart additional risk to those nerve sectors lying within it in ischemic disorders of the optic nerve.

References: None.

Keywords: Vascular disorders, Optic neuropathy, Neuroimaging, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: Iowa City VA Center for the Prevention and Treatment of Visual Loss. Funded by the VA Rehabilitation Research and Development (RR&D) Division I5ORX003002-01 Alcon Scholarship for visiting professor (Dr. Hashimoto)

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Poster 183**MACULAR GANGLION CELLS AND 10-2 VISUAL FIELD (SIZES I,II,III STIMULI) RELATIONSHIP IN CHIASM COMPRESSION**

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Introduction:

Structure-function relationship studies are important in the anterior optic pathway diseases. For structural measurement, macular ganglion cell layer (mGCL) has recently gained great importance in assessing retinal neural loss and is generally correlated with standard automated perimetry (SAP) using either the 30-2, 24-2 or 10-2 strategies with the Goldmann size III stimulus. Here, we compare the relationship between mGCL thickness and the 10-2 VF sensitivity evaluated using targets of Goldmann sizes III, II and I in eyes with band atrophy(BA) from chiasm compression.

Methods:

Twenty-three eyes (21 patients) with BA and temporal VF defect on the 24-2 strategy and 14 eyes of 7 normal controls underwent Spectralis[®] OCT. mGCL was determined as average, in 4 quadrants and 2 horizontal hemifields. Subjects underwent 10-2 strategy VF on a Haag-Streit Octopus-900[®] perimeter (Dynamic strategy), and target sizes: I, II and III. VF sensitivity(VFS) loss was estimated in a global average, in 4 quadrants and in two horizontal hemifields. Spearman correlation coefficients were used to evaluate associations between OCT and VF parameters.

Results:

Mean age was 56±16.5 for BA patients, and 42.4±13.3 for controls. Eleven eyes had VF defect of less than one quadrant, and 12 eyes had complete temporal hemianopia. Correlation between mGCL parameters and VFS loss ranged from 0.47-0.89 (size III), 0.52-0.91 (size II) and 0.32-0.89 (size I) (Table). For all target sizes, the strongest correlation coefficients were between the temporal hemifield VFS and the nasal hemiretina mGCL thickness, followed by the inferior-temporal VFS and the superior-nasal mGCL or the superior-temporal VF and the inferior-nasal mGCL.

Conclusions:

VFS assessed on 10-2 strategy with size II stimulus showed the strongest correlation with OCT-measured mGCL. Our findings suggest that using size II target on the central VF testing may be more sensitive at detecting VF abnormalities in patients with chiasmal compression.

References: None.

Keywords: Visual fields, Perimetry, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 184**Towards a Greater Understanding of Visual Snow**

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Introduction:

Visual Snow (VS) is a persistent, visual disturbance that affects the entire visual field, often described as similar to the static of a poorly tuned analogue television. Despite recent reports of neuronal changes within visual processing areas of cortex, little is known about the underlying causes of VS or the functional impact of these changes. As the first in a series of studies integrating behavioural, neuroimaging and electrophysiological techniques we report results from a suite of ocular motor assessments, designed to provide insight into how impairments in the way visual signals are propagated, organised, processed and transformed, manifest in this often debilitating phenomena.

Methods:

63 patients with VS and 25 age-matched healthy controls participated. Three ocular motor paradigms were included: prosaccades, antisaccades, interleaved pro- and anti-saccades, the latter evaluating the impact of increased complexity on task performance.

Results:

Compared to healthy controls, VS patients generated shorter latency prosaccades, and made significantly more antisaccade errors across both antisaccade and interleaved paradigms. In VS, performance costs normally associated with switching between pro- and antisaccades, were comparable to controls. That is, task complexity did not influence performance. These changes were found in VS patients both with and without migraine, eliminating the presence of migraine as a potential contributor.

Conclusions:

Given the absence of executive, prosaccade/antisaccade switching deficits in VS, we propose that these changes are consistent with disruption to lower order thalamo-cortical connections, rather than more frontally driven processes. This is the first evidence of aberrant sensory-motor transformation deficits in VS, and we propose that these measures provide sensitive, objective markers that may be used to explore functional changes using a multimodal approach, and ultimately track the effects of any therapeutic intervention.

References: None.

Keywords: Ocular motility, Higher visual cortical functions, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: This work is partially funded by the Visual Snow Initiative

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Poster 185**VEP in eyes affected by optic neuritis from multiple sclerosis or neuromyelitis spectrum disorder**

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Introduction:

ON may frequently occur in patients with MS or NMOSD. 1-4 Visual evoked potentials (VEP) has been extensively studied in multiple sclerosis (MS) patients showing normal amplitude and P100 latency reduction⁵. However, previous studies are scarce and controversial in neuromyelitis optica spectrum disorder (NMOSD)^{5,6}. We compared VEP data in eyes with optic neuritis (ON) in the recovery state, in patients with MS or NMOSD. We also evaluated the relationship between VEP, OCT, contrast sensitivity (CS) and visual field (VF) in both groups of patients.

Methods:

A total of 55 eyes with ON from 29 patients (14 with MS and 15 with NMOSD) and 57 eyes from 29 controls were submitted to a complete ophthalmologic evaluation including automated perimetry, CS, OCT and VEP. Amplitude and peak time were assessed on VEP in 3 groups of eyes: 1. Eyes with history of ON from MS (ON-MS), 2. Eyes with history of ON and NMOSD (ON-NMOSD) and 3. controls.

Results:

Compared to controls, ON-MS eyes showed delayed N75 ($p=0.008$) and P100 ($p<0.001$) latencies when testing with the small stimulus, and delayed P100 latency with the greater stimulus ($p=0.001$) (Table 1). No significant difference was found with regard to amplitude measurements. ON-NMOSD group presented lower N75/P100 amplitude at the smaller ($p=0.017$) and largest ($p=0.004$) stimuli, lower P100/N135 amplitude ($p=0.02$) and delayed P100 latency ($P=0.045$) with the small stimulus. The average pRNFL as well as inner retinal layer measurements were significantly reduced in eyes with history of ON. Both groups of patients had a lower average CS mean sensitivity when compared to controls. In ON-NMOSD, a strong positive correlation was found between the VEP data and OCT-measured inner retinal layer measurements (Table 2).

Conclusions:

While eyes with ON from MS have normal amplitude and delayed latency, eyes with ON from NMOSD show reduced amplitude and delayed latency. VEP may help differentiate EM from NMOSD.

References: 1. Fernandes DB, et al. Comparison of visual acuity and automated perimetry findings in patients with neuromyelitis optica or multiple sclerosis after single or multiple attacks of optic neuritis J Neuroophthalmol. 2012;32:102-6. 2. Monteiro ML, et al. Quantification of retinal neural loss in patients with neuromyelitis optica and multiple sclerosis with or without optic neuritis using Fourier-domain optical coherence tomography. Invest Ophthalmol Vis Sci. 2012; 53:3959-66. 3. Weinstock-Guttman, B., et al. Pattern reversal visual evoked potentials as a measure of visual pathway pathology in multiple sclerosis. Mult Scler 2003; 9: 529-534. 4. Wingerchuk, D. M., et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology 2015; 85: 177-189. 5. Neto S P, et al. Evaluation of pattern-reversal visual evoked potential in patients with neuromyelitis optica. Mult Scler 2013; 19: 173-178. 6. Ringelstein M, et al. Visual evoked potentials in neuromyelitis optica and its spectrum disorders. Mult Scler 2014; 20: 617-620.

Keywords: Demyelinating disease, Optic neuropathy, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Perimetry

Financial Disclosures: The authors had no disclosures.

Grant Support: Supported by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), grant number 308172/2018-3

Contact Information: None provided.

Poster 186**Racial Differences in Clinical Characteristics and Visual Outcomes of Myelin Oligodendrocyte Glycoprotein Antibody-Associated Optic Neuritis**

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Introduction:

Race is known to be a factor associated with clinical features and outcomes in demyelinating optic neuritis. However, its role in myelin oligodendrocyte glycoprotein antibody-associated optic neuritis (MOG-ON) has yet to be established.

Methods:

A combined retrospective cohort study of adult-onset MOG-ON from 2 unpublished cohorts (USA, Thailand), 2 published cohorts provided through collaboration (USA, Japan) and 7 cohorts from the literature. Inclusion criteria were case level data including race (asian, white), age, gender and visual acuity (VA) outcome in subjects with one or more episodes of acute optic neuritis and MOG+/NMO- serum testing. White and asian subjects were compared according to clinical presentation features and outcomes.

Results:

157 patients with optic neuritis (ON) and MOG-IgG1 positive serum testing were included: 84 (53.5%) white and 73 (46.5%) asian. Average age of onset (39.02+/-15.67 years), gender (97(61.78%) female) and follow up duration (ranged 1-432 months) did not differ by race. Although isolated ON was the most common initial presentation regardless of race, white subjects were more likely to have bilateral involvement (79.76% VS. 45.20%, $p<0.0005$, chi-square), ocular pain (90.67% VS 81.82%, $p=0.036$, Fisher's Exact test) and recurrent ON (annualized relapse rate 1.98 VS 1.03, $p=0.004$, t-test). Asian subjects were more likely to have isolated ON as the final disease phenotype (58.3% VS 80.9%, $p=0.009$, t-test). Neither optic disc swelling, nadir and final VA, nor neuroimaging characteristics differed between races.

Conclusions:

Acute MOG-ON differed between white and asian subjects according to binocular involvement and pain. Long-term outcomes differed by phenotype and relapse rate. Prospective and population-based studies are warranted to confirm these findings as well as investigate across other races, determine incidence according to race and evaluate the effect of geographical location.

References: 1. Moss HE, Gao W, Balcer LJ, Joslin CE. Association of race/ethnicity with visual outcomes following acute optic neuritis: an analysis of the Optic Neuritis Treatment Trial. *JAMA Ophthalmol.* 2014;132(4):421-7. 2. Chen JJ, Flanagan EP, Jitprapaikulsan J, Lopez-Chiriboga ASS, Fryer JP, Leavitt JA, et al. Myelin Oligodendrocyte Glycoprotein Antibody-Positive Optic Neuritis: Clinical Characteristics, Radiologic Clues, and Outcome. *Am J Ophthalmol.* 2018;195:8-15. 3. Akaishi T, Nakashima I, Takeshita T, Kaneko K, Mugikura S, Sato DK, et al. Different etiologies and prognoses of optic neuritis in demyelinating diseases. *J Neuroimmunol.* 2016;299:152-7.

Keywords: Optic neuritis, Demyelinating disease, Neuro-ophth & systemic disease (g. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: Research to Prevent Blindness, NIH P30 026877

Contact Information: None provided.

Poster 188**New, diagnostic flicker test for optic neuritis shows dynamic pattern following disease onset.**

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Introduction:

Optic neuritis (ON) is primarily diagnosed clinically, but diagnosis may be complicated especially in the case of recurrent disease. We present here the results of a new, digitalized version of the Aulhorn flicker test, the digital flicker test (DFT). The aim of this study was to examine the sensitivity of the DFT in ON and the pattern of DFT response during the course of ON and how this compared to standard visual evoked potentials (VEP).

Methods:

The DFT is a psychophysical test of the subjective brightness of a flickering field (0-60 Hz). In normal subjects, brightness enhancement occurs at medial frequencies, whereas in acute ON the pathological response is a darkness enhancement (DE) at these frequencies. DE was expressed as a quantitative covariate. VEPs were recorded using pattern reversal of 9 mm checkers.

Results:

122 consecutively referred, untreated ON patients and 27 age-matched, healthy controls were examined. Patients were examined within 31 days and followed up at 3 and 6 months. In acute ON 113 of 122 patients showed abnormal DFT (sensitivity 93%). The flicker test was performed 17.0 days (SD:10.5) following ON onset. During follow up the mean flicker test variable had improved by 43 % at 3 months and by 60 % at 6 months following ON onset. Abnormal flicker test response was shown in 67 % at 3 months and in 55 % at 6 months. VEP showed abnormal latency prolongation in 91% at first visit, 82% by 3 months and 78 % by 6 months.

Conclusions:

We present a sensitive and easy-to-use test for acute ON. Due to a more pronounced dynamic response than VEP following ON onset, and a higher sensitivity in the acute phase than OCT measurements, the flicker test may be of diagnostic value including in the case of recurrent ON.

References: None.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Demyelinating disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: This study was funded by the Danish Multiple Sclerosis Society.

Contact Information: None provided.

Poster 189**A Comparative Study of Bruch's Membrane Opening-Minimum Rim Width in Glaucoma, Chiasm Compression and Controls**

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Introduction:

Pathologic optic disc cupping is often related to glaucoma, but can also be caused by compressive optic pathway diseases. The differentiation between these conditions in some cases may be challenging. We compared the ability of Bruch's Membrane Opening – Minimum Rim Width (BMO-MRW) measurements in detecting structural abnormalities in patients with band atrophy (BA) of the optic nerve from compressive chiasmal lesions, glaucoma and controls.

Methods:

Cross-sectional, observational, prospective study with 31 eyes of 22 patients with BA and temporal hemianopia from chiasmal compression, 20 eyes (18 patients) with perimetric glaucoma and 18 eyes of 9 normal age-matched controls were examined including Humphrey 24-2 visual field(VF) testing and Spectralis[®]OCT for BMO-MRW measurement. Glaucoma and BA eyes were matched for severity of field loss based on VF Mean Deviation. BMO-MRW was averaged in superior(S), inferior(I), nasal(N), temporal(T), horizontal (N+T average) and vertical (S+I average) sectors. Data were compared using GEE models. Area under the ROC Curves(AUC) were used to evaluate the discrimination ability of each parameter.

Results:

BMO-MRW mean values were significantly thinner in glaucoma and BA when compared to controls in all parameters with AUC ranging from 0.953 to 1.000 for glaucoma and from 0.835 to 0.934 for chiasmal lesions. Glaucoma eyes differed significantly from BA eyes in all but the temporal sector, with AUC ranging from 0.748 to 0.929. Measurements from the vertical and inferior sectors showed the best discriminatory between BA and glaucoma eyes (AUC 0.929 and 0.927, respectively) (Table).

Conclusions:

BMO-MRW parameters provide comparable diagnostic performance to differentiate glaucoma and BA eyes from healthy subjects, with larger AUCs for glaucoma patients. Our results show that while BMO-MRW reduction is more pronounced in glaucoma eyes, compressive lesions of the anterior optic pathway may also lead to significant cupping and may to some extent mimic glaucomatous optic disc abnormalities.

References: 1. Monteiro ML, Leal BC, Rosa AA, Bronstein MD. "Optical coherence tomography analysis of axonal loss in band atrophy of the optic nerve." *Br J Ophthalmol* 88 (7):896-9. 2004 2. Monteiro ML, Moura FC, Medeiros FA. "Diagnostic ability of optical coherence tomography with a normative database to detect band atrophy of the optic nerve." *Am J Ophthalmol* 143 (5):896-9. 2007 3. Danthurebandara VM, Vianna JR, Sharpe GP et al. "Diagnostic accuracy of glaucoma with sector-based and a new total profile based analysis of neuroretinal rim and retinal nerve fiber layer thickness." *Investigative Ophthalmology and Visual Science* 57 (1):181-187. 2016 4. Reis ASC, Zangalli CES, Abe RY et al. "Intra- and interobserver reproducibility of Bruch's membrane opening minimum rim width measurements with spectral domain optical coherence tomography." *Acta ophthalmologica*:1-8. 2017 5. Danesh-Meyer, HV, Yap J, Frampton C, Savino PJ. "Differentiation of Compressive from Glaucomatous Optic Neuropathy with Spectral-Domain Optical Coherence Tomography." *Ophthalmology* 121 (8):1516-1523. 2014

Keywords: Optic neuropathy, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 190**Incidence and Risk Factors of Retro-Orbital Embolic Central Retinal Artery Occlusions**

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Introduction:

This retrospective study describes the incidence of retro-orbital emboli as a source of central retinal artery occlusion (CRAO) as detected by orbital color Doppler imaging (OCDI) in an eye emergency department. We additionally report association of retro-orbital embolic (ROE) events with vasculopathic risk factors and rates of co-incident cerebral vascular ischemia as assessed by MRI imaging.

Methods:

638 records of patients examined with OCDI through the Wills Eye Hospital Emergency Department from May 2017 to June 2019 were reviewed retrospectively. Records were reviewed for patient demographics, indications for OCDI, ophthalmic exam findings, vasculopathic risks factors, MRI results, and OCDI results. The database was analyzed for incident rates and odds ratio associated with risk factors for retro-orbital embolus positive (ROE+) cases compared to embolus negative (ROE-) cases.

Results:

156/638 (24.4%) cases were examined with OCDI due to concern for CRAO, embolus, or plaque. 135/156 (86.5%) cases were negative for visible emboli on fundoscopy. 34/135 (25.2%) cases were found to have hyperechoic retrobulbar plaques on OCDI. ROE+ cases were older (OR =1.007, CI=1.002-1.012, p=0.0110*) and presented with worse vision (OR=1.768, CI=1.207-1.701, p=<0.0001*). ROE+ cases were more likely to present with smoking history (OR =1.195, CI=1.032-1.383, p=0.0187*) and atrial fibrillation (OR=1.862, CI=1.471-2.358, p=<0.0001*). CRAO cases that were ROE- were at a higher risk of co-incident sub-acute infarction compared to ROE+ cases (OR=1.191, CI=1.027-1.381, p=0.0232*).

Conclusions:

ROE are a source of CRAO in a sizeable portion of cases presenting emergently for retinal ischemic events where no visible plaques are detectable on fundoscopy. OCDI is a clinically necessary technology to establish a diagnosis of embolic CRAO when clinical exam is unrevealing or equivocal. Rapid detection of emboli with OCDI allows for differentiation of cases from giant cell arteritis, urgent cardiovascular workup for embolic source, and initiation of anti-coagulation to mitigate risk of hemispheric stroke.

References: None.

Keywords: Vascular disorders, Stroke trauma

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 191**Autoregulation of Blood Flow in Human Retina, Optic Nerve, and Choroid Using Novel Vacuum Goggles**

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Introduction:

Autoregulation of human ocular vascular beds in response to ocular perfusion pressure change (OPP) is not fully understood in healthy and diseased eyes. The purpose of this study was to investigate the dynamics of blood flow in the retina, choroid and optic nerve vascular beds in normal and eyes with optic neuropathy using a novel vacuum goggle device (Equinox Ophthalmic, Newport Beach, CA) which can induce an abrupt lowering of intraocular pressure (IOP).

Methods:

In this cohort study, eleven healthy subjects (mean age 39 years; range 26-65), two patients with non-arteritic anterior ischemic optic neuropathy (NAION) and 2 patients with glaucoma were studied using laser speckle flowgraphy (LSFG-NAVI, Softcare, Japan). Blood flow was measured at baseline, during acute reduction of IOP by 7.5mmHg for five minutes and after termination of the goggle vacuum for 3 minutes. We quantified the blood flow in the retinal arterioles, optic nerve head tissue and choroid in normal regions and in locations of atrophy from optic neuropathy.

Results:

In 22 normal eyes, blood flow in the optic nerve, retina and choroid showed an initial transient increase during IOP drop, followed by a return to baseline flow during sustained goggle vacuum, followed by a transient decrease in blood flow at termination of vacuum when IOP increased (Friedman test and Dunn's multiple comparison test; $P < 0.05$), indicating autoregulation. Conversely, in NAION and glaucomatous eyes, a sustained increase in retinal and optic nerve blood flow occurred in both atrophic and intact regions during IOP decrease from goggle vacuum, indicating poor autoregulation.

Conclusions:

We demonstrated strong autoregulation of blood flow in normal eyes but not in eyes with NAION and glaucoma. Vacuum goggles may provide a novel means to predict how much increase in ocular blood flow will result from lowering of IOP in individual eyes.

References: None.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Vascular disorders, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: Ryuya Hashimoto MD, PhD: International scholar for visiting professor

Randy H Kardon MD. Ph.D :Iowa City VA Center for the Prevention and Treatment of Visual Loss, funded by the VA Rehabilitation Research and Development (RR&D) Division I50RX003002-01

Zaidoon Al-Share MD; Nitsan Dudevan-Strier MD ;Jan Full RN; Julie Nellis RN; none

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Poster 193**The effect of image post-processing on the detection of optic neuritis on routine brain MRI**

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Introduction:

Patients with optic neuritis presenting initially to general practitioners are often imaged with a routine brain MRI, which is suboptimal for optic nerve assessment. Because of the reduced sensitivity of MRI in detecting this typically self-limiting disease beyond 30 days after symptom onset, neuro-ophthalmologists often rely upon the initial brain MRI to confirm the diagnosis.(1-3)Our aim was to assess if image post-processing could facilitate the detection of optic neuritis on routine brain MRI.

Methods:

In this retrospective case control study of 60 patients (30 clinically confirmed optic neuritis, 30 controls; 47.2 ± 17.9 years; 23M, 37F), FLAIR and contrast-enhanced images were processed using an image-processing algorithm that aimed to selectively accentuate the signal intensity of diseased optic nerves.(4-5)We assessed the quantitative effect of processing on the contrast-to-noise ratio (CNR) between optic nerves and normal-appearing white matter. Qualitatively, diagnostic performance was evaluated through masked review of both baseline and processed images by two expert neuro-radiologists.

Results:

Image processing increased signal intensity of 17/30 (56.7%), 8/30 (26.7%), and 14/23 (60.9%) diseased optic nerves on FLAIR, contrast-enhanced axial, and contrast-enhanced coronal images, respectively, with a corresponding increase in CNR (p<0.001, 0.03, and <0.001). CNR for controls was not significantly affected (p=0.25, 0.27, and 0.50). The average sensitivities (and specificities) of our readers in detecting optic nerve abnormalities on FLAIR, post-contrast axial, and post-contrast coronal images were 54.2% (86.2%), 16.7% (87.1%), and 52.2% (86.3%) before processing, and 55% (95.7%), 30% (100%), and 56.5% (100%) after processing. Positive predictive values increased by 24.2%, 134.5%, and 25.2% from baseline values. Inter-observer agreement (kappa range 0.08-0.29) improved substantially after processing (kappa range 0.67-1).

Conclusions:

Image processing selectively increased the CNR of diseased nerves, translating into improved diagnostic performance by neuroradiologists as demonstrated by substantial increases in positive predictive values and inter-observer reliability.

References: Rizzo JF 3rd, Andreoli CM, Rabinov JD. Use of magnetic resonance imaging to differentiate optic neuritis and nonarteritic anterior ischemic optic neuropathy. *Ophthalmology*. 2002;109(9):1679. Kupersmith MJ, Alban T, Zeiffer B, Lefton D. Contrast-enhanced MRI in acute optic neuritis: relationship to visual performance. *Brain*. 2002;125(Pt 4):812. Hickman SJ, Toosy AT, Miszkiel KA, Jones SJ, Altmann DR, MacManus DG, Plant GT, Thompson AJ, Miller DH. Visual recovery following acute optic neuritis--a clinical, electrophysiological and magnetic resonance imaging study. *J Neurol*. 2004;251(8):996. Sharma A, Sharma A. Method for medical image analysis and manipulation. US patent 9, December 18, 2017; 846-937 Stunkel L, Kung NH, Wilson B, et al. Incidence and causes of over- diagnosis of optic neuritis. *JAMA Ophthalmol*. 2018;136:76–81.

Keywords: Neuroimaging, Magnetic resonance imaging, Demyelinating disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 194**Dry Eye Syndrome in Patients with Pituitary Tumors with and without Transsphenoidal Tumor Resection**

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Introduction:

Dry eye syndrome (DES) is a multifactorial disease which can contribute significant morbidity. Some hormonal disturbances have been associated with DES, and animal studies have shown hypophysectomy can cause regression of lacrimal glands; this relationship has not been studied in humans. We hypothesized transsphenoidal pituitary tumor resection would be associated with DES.

Methods:

Retrospective analysis of 203 patients with pituitary tumors who received eye exams within the last 7 years found 77 patients with transsphenoidal surgery. Patients with history of ocular surface disease, eye surgery, glaucoma medication, head radiation, or autoimmune disease associated with dry eye were excluded. We compared 43 patients with documented eye exams. Suspicion for dry eye was based on suggestive physical exam findings (tear film debris, tear lake deficiency, corneal punctate epithelial erosions) and Schirmer testing. The primary outcome was percentage of patients with dry eye after transsphenoidal pituitary tumor resection. Secondary outcomes included percentage of patients with dry eye on hormone replacement therapy. Analysis used chi-square independence tests.

Results:

Dry eye was present in 50% of patients after transsphenoidal surgery but 88% of nonsurgical patients ($\chi^2(1, N=14) = 2.36, p = 0.124$). Hormone replacement therapy was used in 37% of post-surgical patients and was associated with lower suspicion for dry eye when compared with patients not on hormones (31% vs 41%), though this was not statistically significant ($\chi^2(2, N=35) = 2.51, p = 0.285$).

Conclusions:

Patients with transsphenoidal tumor resection may be at lower risk for DES. In patients with resected tumors, hormone replacement may be protective against DES. Prospective studies might better evaluate these relationships.

References: Azzarolo AM, Bjerrum K, Maves CA, et al. Hypophysectomy-induced regression of female rat lacrimal glands: Partial restoration and maintenance by dihydrotestosterone and prolactin. *Investig Ophthalmol Vis Sci.* 1995; 36(1): 216-226. McClellan KA, Robertson FG, Kindblom J, et al. Investigation of the role of prolactin in the development and function of the lacrimal and Harderian glands using genetically modified mice. *Investig Ophthalmol Vis Sci.* 2001; 42(1): 23-30. Peck T, Olsakovsky L, Aggarwal S. Dry eye syndrome in menopause and perimenopausal age group. *J Midlife Health.* 2017; 8(2): 51.

Keywords: Tumors, Skull base, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 195**OCT-based Interpretation of the Optic Nerve Head Anatomy in Young Adults with Vascular Optic Neuropathies**

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Introduction:

Vascular disease affecting the optic nerve head (ONH) is occasionally seen in young adults with no or few systemic risk factors. The aim of this study was to examine the anatomy of the ONH using optical coherence tomography (OCT) in young adults diagnosed with central retinal vein occlusion (CRVO), branch retinal vein occlusion (BRVO), central retinal artery occlusion (CRAO), branch retinal artery occlusion (BRAO), and anterior ischemic optic neuropathy (AION), in order to look for inherent and potentially predisposing anatomic anomalies.

Methods:

This cross-sectional study included 56 patients (ages 16-50 years) seen between January 2009 and December 2018 with a diagnosis of CRVO (26), BRVO (14), CRAO (1), BRAO (5), and AION (10). The presence of optic disc drusen (ODD), prelaminar hyperreflective lines and peripapillary hyperreflective ovoid mass-like structures (PHOMS), and the determination of scleral canal size, retinal nerve fiber layer thickness (RNFLT), and macular ganglion cell layer thickness (GCLT) was obtained using enhanced depth imaging OCT.

Results:

ODD were found in 12.5% of all patients, 2.2% of patients with retinal vascular occlusions, and 60% of AION patients ($p = 0.042$). Prelaminar hyperreflective lines were found in 33.9% of all patients, 23.9% of patients with retinal vascular occlusions, and 80% of AION patients ($p = 0.0015$). PHOMS were evenly distributed between AION, BRVO and CRVO patients. RNFLT was decreased in ODD patients compared to patients without ODD ($p = 0.01$). No differences in scleral canal diameter or GCLT were observed when comparing patients with and without ODD, prelaminar hyperreflective lines or PHOMS.

Conclusions:

Underlying ODD and prelaminar hyperreflective lines were more often present in AION patients compared to patients with retinal vascular occlusions. This corresponds to a suggested close pathophysiological relationship between ODD and hyperreflective lines and underlines the provoking nature of these structures to the densely packed ONH.

References: None.

Keywords: Optic neuropathy, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 196**Are koniocellular pathways involved in visual snow pathophysiology?**

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Introduction:

Visual Snow (VS) is a disorder characterised by the subjective perception of black-and-white visual static with at least one associated symptom of palinopsia, photopsia, nyctalopia and entoptic phenomena. The aetiology of this condition is not known. We have hypothesised that VS results from a thalamocortical dysrhythmia of the visual system associated with the koniocellular pathways, which include cells that transmit short-wave (S-cone) signals for blue-yellow colour vision. This study aims to characterise the colour preferences of VS patients in order to pursue this hypothesis further.

Methods:

Patients (n=22) with classic VS based on the diagnostic criteria, underwent Intuitive Colorimetry (IC) testing (Cerium Visual Technologies). Twelve hue directions (expressed as angle in CIE 1976 LUV space relative to D65) were rated on a five-point scale from preferred (relieving, positive score) to non-preferred (exacerbating, negative score), and overall preferred and non-preferred angles were chosen.

Results:

Patients showed preference for one of two spectral regions which relieved VS symptoms: orange-yellow (range 50–110 deg., mean 79 +/- 24, n = 14) and turquoise-blue (range 210–250 deg., mean 234 +/- 27, n = 8).

A non-preferred violet region near the tritanopic confusion line / S-cone axis (267 deg.), was strongly associated with exacerbation of VS symptoms (range 250–310 deg, mean 276 +/- 16, n = 20, 2 outliers, Rayleigh p < 0.001). Median rank at hue angle 270 deg was significantly lower than at angle 90 (-1.5 vs 0.0, p < 0.001, Wilcoxon non-parametric rank-sum test).

Conclusions:

Our results show that specific colour hues activating koniocellular S-cone pathways are involved in mediation and exacerbation of VS. Our specific hypothesis now is that S-cone activation and processing plays a crucial role in the pathogenesis of this disorder.

References: None.

Keywords: Higher Visual Cortical functions, Higher visual functions

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 197**Predicting visual outcomes in acute demyelinating optic neuritis**

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Introduction:

The purpose of our study was to develop prediction models of corticosteroid treatment benefit over time at the individual level for patients with acute demyelinating optic neuritis (ON).

Methods:

Using data from the Optic Neuritis Treatment Trial (ONTT), multivariable linear regression models were built to predict visual acuity (VA) at one year. Secondary outcomes were one-year contrast sensitivity (CS), and VA and CS at 15 and 30 days. Independent variables included age, sex, race, multiple sclerosis history, fellow eye ON episodes, vision symptoms (days), pain, optic disc swelling, viral illness, treatment group (intravenous [IV] corticosteroid, oral corticosteroid, placebo) and baseline VA or CS.

Results:

410 (90.1%) subjects had 1-year outcomes. Median VA improved from 20/66 at enrollment to 20/17 at 1-year. Of the 11 predictors assessed, only baseline VA was associated with VA at 1 year. At 15 days, both baseline VA and treatment status predicted VA. However, the difference of medians between treatment status was small for the average subject (20/18 [95% CI: 20/17, 20/19] IV corticosteroids versus 20/23 [95% CI: 20/21, 20/26] placebo) and there was no evidence of treatment benefit for subjects with light perception or no light perception VA at baseline.

Conclusions:

The only predictor of long-term VA was severity of baseline vision loss. Early benefits with IV corticosteroid treatment were limited to patients with baseline vision better than light perception. However, the early and temporary benefit of IV corticosteroids is of questionable clinical significance and should be weighed against the potential harms.

References: None.

Keywords: Optic neuritis, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: NIH EY027849

Contact Information: None provided.

Poster 198**Frequency of Acquired, Non-glaucomatous Optic Neuropathy in a Population-based Cohort**

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Introduction:

The relative frequency and demographics of optic neuropathies is not known. Prior studies have been from tertiary centers that may skew the representation of presenting diseases due to referral bias. This study uses a population-based dataset to report the true frequency of acquired, non-glaucomatous optic neuropathies.

Methods:

This study used a population-based medical records linkage system that catalogs patients in a given county in the United States. The database was queried from 2001-2016 to identify all patients with any diagnosis code that could indicate an optic neuropathy. Patient charts were manually reviewed to confirm an accurate diagnosis. Congenital disorders and glaucomatous optic neuropathy were excluded from this study.

Results:

We identified 391 patients with an acquired, non-glaucomatous optic neuropathy for an overall annual incidence of 17.4/100,000 (95% CI 15.8-19.2). The median age at diagnosis was 46 years (range 0-98 years) and 58.6% were female. The most common etiologies were non-arteritic anterior ischemic optic neuropathy (NAION) (24.6%), optic neuritis (24%), papilledema (24%), compressive (7.9%), and traumatic (5.1%). The following conditions had less than 10 events: arteritic anterior ischemic optic neuropathy (2.3%), diabetic papillitis (1.5%), posterior ischemic optic neuropathy (1.3%), dominant optic atrophy (0.5%), sarcoidosis-related optic neuropathy (0.5%), autoimmune optic neuropathy (0.26%), Leber hereditary optic neuropathy (0.26%), infiltrative optic neuropathy (0.26%), radiation optic neuropathy (0.26%), encephalitis-related optic neuropathy (0.26%), and medication-induced optic neuropathy (0.26%). Twenty-six (6.6%) patients had optic neuropathy without an identifiable cause. In patients under age 50, papilledema and optic neuritis accounted for 87.8% of cases. In patients over age 50 years, NAION was most common (60.6%). Papilledema and optic neuritis occurred more commonly in women (72.3% and 70.2%, respectively), compared to NAION (43.8%) ($P < 0.0001$).

Conclusions:

In this population-based cohort, NAION, optic neuritis, and papilledema account for nearly 75% of patients who present with an acute, acquired optic neuropathy.

References: None.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 199**Pupil abnormalities in patients with Neuromyelitis Optic Spectrum**

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Introduction:

Neuromyelitis Optic Spectrum (NMOS) is a recurrent autoimmune inflammatory disease of the CNS with high predilection to the optic nerve, brainstem and medulla. The more common neuroophthalmological manifestation is bilateral optic neuritis which can cause relative afferent pupillary defect (RAPD) if there is asymmetry in the optic nerve damage. We observed that most of our patients with NMS have light-near dissociation pupil (LND).

Methods:

To review the pupils abnormalities in patients with NMOS.

Results:

We evaluated 14 patients whom meet the international consensus diagnostic criteria for NMOS. One of the patients was excluded because he had retinal detachment in one eye. Of 13 patients studied with bilateral optic neuritis; 9 (69%) cases presented LND; 3 (23%) RAPD and 1(8%) patient with slow reaction pupil without RAPD and/or LND. One a case with LND also presented RAPD.

Conclusions:

The more common pupillary defect in our group of patients with NMOS was the LND. LND may be caused by a defect in the afferent or the efferent system subserving pupillary function as Argyll Robertson pupils, aberrant regeneration, mesencephalic and afferent pathway lesions. In our cases, the patients had long pupils with poor response to light and more active response to accommodation or convergence. This is probably due to the afferent visual system lesions due to optic neuritis or eventually to the efferent visual system due to brainstem disease (midbrain) involvement. Many of them do not presented RAPD probably because they had bilateral optic neuritis with symmetric damage. We reviewed the literature and no descriptions were found of the predominant pupil defect in this entity, so the pupil could be an important marker when this demyelinating disease is suspected.

References: 1. Tan CT, MaoZ,Qiu W, Hu. X, Wingerchichuk DM, Weinshenker BI: International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. *Neurology* 2;86(5):491-2,2016 2. Borisow N, Mori M, Kuwabara S, Scheel M, Paul F: Diagnosis and Treatment of NMO Spectrum Disorder and MOG Encephalomyelitis. *Front Neurol.* 23;9:888:1-15,2018

Keywords: Optic neuritis, Demyelinating disease, Neuro-opth & systemic disease (eg. MS, MG, thyroid), Miscellaneous,

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 200

Functional Correlates of Luxury Perfusion in NAION

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Introduction:

Luxury perfusion refers to vascular autoregulation during anterior ischemic optic neuropathy, diverting blood to adjacent regions of the infarcted disc (1). Disc hemorrhage is found in approximately 3/4 of patients with Non-Arteritic Ischemic Optic Neuropathy (NAION) (2). The functional and prognostic significance of disc hemorrhages in NAION have not been formally studied to our knowledge. We hypothesized that concordance and discordance between sectoral disc hemorrhage and visual field loss in acute NAION predicts the severity of visual loss.

Methods:

In this IRB-approved retrospective chart review of patients diagnosed with acute NAION, we examined the location of disc hemorrhages and grouped patients according to whether the hemorrhage location corresponded with the more severely affected hemifield. Only patients with fundus photographs and interpretable visual fields were included.

Results:

Our initial dataset included 10 patients with acute NAION and disc hemorrhage; 6 with concordance of their disc hemorrhage and field loss, and 4 with discordance. The mean difference in mean deviation (Concordant: -15.3 +/- 2.9 dB, Discordant: -11.9 +/- 5.9 dB), pattern standard deviation (Concordant: -12.4 +/- 2.0 dB, Discordant: 11.9 +/- 3.7 dB), and visual acuity (Concordant: 0.2 +/- 0.2 LogMAR, Discordant: -0.3 +/- 0.5 LogMAR) were not statistically significant between these two groups (p values > 0.35).

Conclusions:

In this pilot study, we examined the location of optic disc hemorrhage in acute NAION with regard with visual field loss. Our preliminary data suggest no statistical differences between those whose hemorrhages are concordant and discordant. Further study will include adding more patients by expanding the scope of our data set and examining the location of prominent sectoral swelling as an additional dependent variable.

References: 1. Friedland, S, et. al. Luxury Perfusion Following Anterior Ischemic Optic Neuropathy. *Journal of Neuro-Ophthalmology*. 16(3): 163-171, 1996. 2. Characteristics of patients with non-arteritic anterior ischemic optic neuropathy eligible for the Ischemic Optic Neuropathy Decompression Trial. *Arch Ophthalmol*. Nov 1996;114(11):1366-1374

Keywords: Optic neuropathy, Visual fields, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 201**Understanding physician prescribing of corticosteroids for acute demyelinating optic neuritis**

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Introduction:

Survey data suggests that most neurologists and ophthalmologists are aware of the Optic Neuritis Treatment Trial and believe it was important study, but continue to recommend high-dose corticosteroids for typical optic neuritis based on the severity of vision loss, pain and desire to improve long-term visual outcomes, none of which are evidence-based. Other important reasons for why physicians choose to use corticosteroids are uncertain, but likely include behavioral determinants. We aim to use a theory-based approach to explore behavioral determinants of corticosteroid prescribing for typical optic neuritis.

Methods:

We used the Theoretical Domain Framework (TDF) to develop topics for semi-structured, in-depth interviews of neuro-ophthalmologists and neurologists. Exploration of TDF construct domains using qualitative research techniques can uncover the breadth of factors that underlie physicians' optic neuritis treatment decisions, as well as specific barriers or facilitators to delivering evidence-based care. They can also be mapped to a matrix of behavioral change techniques. Interviews are transcribed verbatim and entered into a qualitative data analysis program. Two investigators (LBD, CR) independently read the transcripts and initial codes and memos were generated. Using a constant comparison method, a codebook is developed iteratively and organized into emerging themes. Sampling is adjusted until thematic saturation is reached.

Results:

Based on preliminary interviews, beliefs about consequences (minimizing potential treatment harms), knowledge application, and social influences (eg. corticosteroids were already recommended by another physician) are the primary drivers of corticosteroid treatment decisions. Concerns about personal or patient-level decisional regret (emotion) also appears to be a driver of corticosteroid use.

Conclusions:

Although knowledge of the ONTT results is a pre-requisite for evidence-based decision making for ON, it is unlikely to be sufficient to change decision making. Efforts to change decision making must additionally address beliefs about consequences, and respect social influences and emotion. Further interviews will refine important behavioral determinants.

References: None.

Keywords: Optic neuritis

Financial Disclosures: The authors had no disclosures.

Grant Support: NIH EY027849

Contact Information: None provided.

Poster 202**Developing prediction models of typical and atypical optic neuritis**

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Introduction:

It is increasingly important for clinicians to distinguish typical optic neuritis (tON) from atypical (aON), immune-mediated causes, to direct appropriate diagnostic testing and institute potentially sight-saving therapies. Numerous clinical, laboratory, and imaging characteristics have been associated with tON and specific aON diagnoses, but no studies have investigated associations of these characteristics within a heterogeneous population or how these characteristics interact to predict tON versus aON in a mixed cohort.

Methods:

We are performing a retrospective, longitudinal analysis of patients 18 years or older with acute optic neuropathy presenting to the University of Calgary Neuro-Ophthalmology Clinic between 2010-2018. All patients were examined by a fellowship-trained, neuro-ophthalmologist. Data abstracted from clinical charts includes: date of birth, race/ethnicity, pain, optic disc edema, severity of optic disc edema, prior episodes of optic neuritis, medications, other medical diagnoses, symptoms onset, high/low contrast visual acuity, Humphrey visual fields mean deviation, brain imaging, optical coherence tomography imaging, pertinent reactive serologies. Descriptive statistics will be used to describe the cohort. Bivariate associations between clinical, serological, and radiographic data and optic neuritis type will be explored using two tailed t-tests for continuous variables and chi squares for categorical variables. Multiple logistic regression will be used to explore associations between independent variables and optic neuritis type.

Results:

We have developed a database of 200 patients with acute optic neuropathy. The strength of our cohort is the continuous neuro-ophthalmic surveillance within the Canadian health care system. We will report estimated incidence of tON versus aON, demographics for the cohort and demographics by optic neuritis subtype, and results of bivariate and multivariate models.

Conclusions:

Exploring the associations between clinical, laboratory, and imaging characteristics, and specific optic neuritis diagnoses will guide the development of a robust clinical prediction tool that can be used by neuro-ophthalmologists to deliver cost effective, evidence-based care for patients with optic neuritis.

References: None.

Keywords: Optic neuritis, Demyelinating disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 203

Visual outcome following plasma exchange for optic neuritis

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Introduction:

Plasma exchange (PLEX) is routinely utilized in the setting of optic neuritis (ON) from neuromyelitis optica spectrum disorders (NMOSD), however there are few studies evaluating PLEX in other forms of ON. This study retrospectively evaluated the visual outcomes of PLEX for ON from various etiologies and investigated variables that influenced those outcomes.

Methods:

Multicenter retrospective review of ON patients treated with PLEX from 2001 to 2019.

Results:

Sixty-eight patients with ON were treated with PLEX. The median age was 46.5 (range 21-73) and 72% were female. Etiologies were: aquaporin-4 (AQP4)-IgG+ NMOSD (20), myelin oligodendrocyte glycoprotein (MOG)-IgG+ (11), multiple sclerosis (MS) (22), seronegative NMOSD (3), idiopathic (10), and other (2). Median time to treatment was 3 weeks. Median VA at time of PLEX was count fingers with no difference among the various etiologies. Median final VA was 20/40. Twenty (29%) patients had a final VA of $\leq 20/200$. Among those with poor outcomes, 9 were AQP4-IgG+, 8 were MS, 1 was seronegative NMOSD, 2 were idiopathic and none were MOG-IgG+. Patients with poor outcomes had a worse VA at time of PLEX ($p < 0.001$) and lower frequency of MOG-IgG+ than the rest of the cohort ($p = 0.03$). Among the 25 patients with VA $\leq 20/200$ treated with PLEX within 3 weeks, 23 (92%) had ≥ 3 lines improvement in VA. Seven (28%) had a final outcome of $\leq 20/200$. Among the 21 patients with VA $\leq 20/200$ treated later than 3 weeks, 12 (57%) had ≥ 3 lines improvement. Twelve (57%) had a final outcome of $\leq 20/200$.

Conclusions:

The majority of patients with ON treated with PLEX showed some improvement. Severity of vision loss, etiology of ON, and timing of PLEX all influenced final VA outcome. Future randomized clinical trials will be required to determine the efficacy of PLEX for ON based on specific etiologies.

References: None.

Keywords: Optic neuropathy, Demyelinating disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: John Chen- chen.john@mayo.edu, 507-284-4946

Poster 204**Ischemic Optic Neuropathy Secondary to Central Retinal Artery (CRA) Embolism**

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Introduction:

To describe cases of embolic ischemic optic neuropathy (ION) detected by Orbital Color Doppler Imaging (OCDI).

Methods:

A computerized search was performed to identify all patients with ION seen at the Neuro-ophthalmology Service, Wills Eye Hospital, Philadelphia between 2010 and present. It is our practice to perform OCDI in patients with ION with atypical features including absence of disc edema in the affected eye or 'disc at risk' in the contralateral eye. We identified 38 patients who underwent OCDI and reviewed their clinical records.

Results:

Twelve patients had positive finding of embolus on CDI. The average age was 69.3 years (median 70, range 44-92). All patients presented with sudden onset, unilateral vision loss except for one patient who had sudden realization of a preexisting visual loss. There was prior history of transient vision loss in the same eye (17%) and nonarteritic anterior ischemic optic neuropathy (NAION) in the contralateral eye (8%). Optic disc edema typical for NAION was noted at presentation (83%), but only one patient had disc at risk in the contralateral eye. Five patients were evaluated for giant cell arteritis prior to OCDI and had negative temporal artery biopsies. OCDI revealed retrobulbar embolus in the central retinal artery (CRA) (92%) and embolus anterior to the optic disc (8%). All patients were referred for stroke work up following diagnosis. Atrial fibrillation was detected in one patient, requiring long term anticoagulation.

Conclusions:

Contrary to conventional wisdom, we have found CRA embolus in patients with IONs. OCDI is an important imaging modality that can help detect embolus in the retrobulbar course of the artery. The detection of embolus should be followed by evaluation of the the embolic source to reduce the risk of subsequent hemispheric stroke.

References: None.

Keywords: Optic neuropathy, Stroke trauma, Orbit/ocular pathology, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 205**Histological changes in inferior oblique muscle with fourth cranial nerve palsy : A stereological study**

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Introduction:

Purpose: To compare morphological structures of inferior oblique muscles from patients with fourth cranial nerve palsy and human controls.

Methods:

Samples from five cases were obtained after inferior oblique myectomy in patients with fourth cranial nerve palsy and secondary inferior oblique overaction defined clinically as overelevation in adduction plus excyclotortion in the eye fundus exam. Five inferior oblique muscles from cadaveric non-strabismic humans were used as controls. The number of muscle fibers in 5000µm² and volume densities (Vv) of muscle and collagen were measured using stereology. Independent samples t-test and Wilcoxon rank-sum test were used to compare morphological structures between cases and controls.

Results:

Four females and one male between 4 and 48 years with fourth cranial nerve palsy were selected as cases. All controls were Caucasian males between 35-45 years.

Volume density of collagen was significantly higher in the overacting inferior oblique muscles from cases compared to controls. Samples from cases had a smaller number of muscle fibers in 5000µm² and volume density of muscle.

Conclusions:

Secondary overacting inferior oblique muscles showed fibrotic and atrophic changes. Thus, muscle overaction seen in patients with fourth cranial nerve palsy is related to the expansion of the connective tissue rather than to an increase in the number of muscle fibers or volume density of muscle. Our study provides new insights into morphological changes in strabismus, and opens new avenues for research.

References: 1, Kushner BJ. Multiple mechanisms of extraocular muscle "overaction". Arch Ophthalmol. 2006;124(5):680-8 2. Kono R, Demer JL. Magnetic Resonance Imaging of the Functional Anatomy of the Inferior Oblique Muscle in Superior Oblique Palsy. Ophthalmology. 2003;110(6):1219-29. 3. Stager D, McLoon LK, Feliuss J. Postulating a role for connective tissue elements in inferior oblique muscle overaction (an American Ophthalmological Society thesis). Trans Am Ophthalmol Soc. 2013;111:119-32

Keywords: Ocular motility, Adult strabismus with a focus on diplopia, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 206**The Accuracy of Clinician Detection of Ocular Motor Abnormalities: A Corroboration with Eye Movement Recordings**

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Introduction:

Saccades are rapid eye movements with which the visual world is explored. Saccadic slowing is pathologic, key to neurological diagnosis, and often correlated with disease severity. There is currently no universally accepted standard for the definition of saccadic slowing, and inter- and intra-rater reliability is unknown.

Methods:

Patients with slow saccades and control participants with eye movement videos and quantified eye tracking (Eyelink) were identified. Quantified saccade data were categorized as normal versus mildly/moderately/severely slow by blinded expert review (3 authors) of main sequence relationships (peak velocity to amplitude). We compiled 24 de-identified, brief looped clips showing horizontal or vertical saccades. Videos were randomized and placed in a slideshow. Subsequently, clinicians, stratified by expertise level, reviewed the videos for saccadic slowing and, if present, graded the degree as mild, moderate, or severe. Clinician responses were compared to main sequence analysis categorization.

Results:

Nine patients (7 PSP, 1 genetic parkinsonism, 1 SCA2) and 3 control participants were included. Ten clinicians were recruited; five senior neurology residents (PGY-3-4) and five general neurology attending physicians. For saccades deemed normal as per recordings, 51% of general neurology attendings and 58% of senior residents judged saccadic velocities as normal. Horizontal and vertical saccades were, respectively, accurately judged as normal 60% versus 40-50% of the time. For saccades deemed abnormal as per recordings, 81% of general neurology attendings and 87% of senior neurology residents judged saccadic velocities as slow. Horizontal and vertical saccades were, respectively, accurately judged as slow 68-77% versus 94-97% of the time.

Conclusions:

Clinicians showed greater capacity to identify saccadic slowing, especially vertically, than to confirm normal saccadic speed. Horizontal saccades were more easily identified as normal than vertical saccades. Identification of normal and abnormal saccades was largely unaffected by experience level.

References: Stephen CD and JD Schmammann. *Cerebellum*. 2019 Jun 7. Doi: 10.1007/s12311-019-01044

Keywords: Ocular Motility, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Nystagmus, Vestibular

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 207

Evaluating Accuracy of Orbital Tumor Volume Measurements Using 3D Printed Orbital Models and MRI Imaging

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Introduction:

This study uses 3-dimensional printed orbit and tumor models of known volume to evaluate the accuracy of various imaging techniques to detect tumor volume and change over time.

Methods:

A 3D printed orbit “phantom” was made. Water-based starch was modeled into “tumors” of known volume in three common tumor shapes: spherical, ovoid, or diffuse. To test the accuracy and threshold of measurable volume change on MRI, each “tumor” was 1 ml of base volume and additional volume was added to represent 10%, 20%, 30% and 40% change.

Three observers obtained standard volume measurements, semi-automated, and manual segmentation measurements on software Vital and TeraRecon. Correlation coefficients were calculated comparing measurements to the true volumes. A student T-test, Cohen’s kappa test for inter-rater and intra-rater reliability, and the intra-class co-efficient (ICC) were also used.

Results:

The ICC for semi-automated segmentation on Vital was 0.7389 ($p=0.0016$), 0.9082 ($p<0.00001$) and 0.7145 ($p=0.0004$) for spherical, ovoid, and diffuse tumors which demonstrates a strong positive linear relationship between true volume and semi-automated volumes.

The CCs for manual segmentation were $R=0.8808$ ($p<0.0001$), $R=0.9372$ ($p<0.0001$), and $R=0.3563$ ($p=0.0533$) for spherical, ovoid, and diffuse tumors which demonstrates excellent relationship between true volume and manually segmented volumes for spherical and ovoid tumors, but poor correlation for diffuse tumors.

Manual planar volumes demonstrated excellent inter-reader correlation ($ICC=0.814$). Semi-automated volumetric software Vital demonstrated good intra-reader correlation ($ICC=0.5792$) and excellent inter-reader correlation ($ICC=0.8986$). Manual volumetric software TeraRecon demonstrated fair intra-rater correlation ($ICC=0.4670$) and fair inter-rater correlation (0.5792).

Conclusions:

Our study demonstrates the value of in-vitro semi-automated volumetric measurements of orbital tumors and the reliability of measurements according to tumor shape. Semi-automated measurements best correlate to true volumes and yield excellent inter-rater correlation. While manual segmentation volumetric measurements correlated well for spherical and ovoid tumors, diffuse tumors were not able to be accurately measured.

References: None.

Keywords: Neuroimaging, Orbit, Orbit/ocular pathology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 208**Central Positional Nystagmus And Hyperactive Anterior Head Impulses In Anti-GAD Syndrome: A Case Series**

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Introduction:

Video-oculography (VOG) analysis in anti-glutamic acid decarboxylase (GAD) antibody syndrome has been anecdotally reported and mostly focuses on the presence of spontaneous downbeat (DBN) or upbeat nystagmus (UBN) in upright position. Importantly, video-head impulse test (VHIT) data and VOG data on positional nystagmus in anti-GAD syndrome is largely unknown.

Methods:

We provide retrospective VOG data in upright and supine position and VHIT data of patients with anti-GAD syndrome followed in our clinic.

Results:

We included 3 patients. All were diabetic and anti-GAD antibody levels ranged from 56 to 239 U/ml. Patient 3 had no ataxia, while patients 1 and 2 showed mild gait and limb ataxia. Patient 1: A 68-year old female presented with 2-year positional vertigo. VOG showed spontaneous DBN (mean slow phase velocity, 4.3°/s), gaze-evoked nystagmus (GEN), and positional transient UBN (25°/s) in head hanging. VHIT showed anterior and horizontal hyperactive responses (gain ~1.5). Patient 2: A 57-year old female presented with 12-year positional vertigo. VOG revealed spontaneous DBN (2.8°/s), GEN and positional transient DBN (21,7°/s) followed by persistent DBN (4.1°/s) in head hanging. VHIT showed hyperactive anterior (gain ~1.7), horizontal (gain ~1.3) and posterior (gain ~1.2) responses. Patient 3: A 69-year old female presented with 8-year positional vertigo. VOG showed GEN, positional transient DBN (18°/s) in head hanging and positional transient UBN (28°/s) when returning to upright position. VHIT showed anterior hyperactive (gain ~1.4) and horizontal hypoactive (gain ~0.5) responses. Intravenous immunoglobulin abated spontaneous and positional nystagmus in patient 1 but not in patient 2, while patient 3 awaits post-treatment assessment.

Conclusions:

The presence of positional transient UBN or DBN and predominantly anterior canal-related hyperactive VHIT responses, with or without spontaneous DBN/UBN and/or GEN, should raise the suspicion for the presence of anti-GAD-related nystagmus, particularly in diabetics, even in the absence of ataxia.

References: 1. Antonini G, Nemni R, Giubilei F, Gragnani F, Ceschin V, et al. Autoantibodies to glutamic acid decarboxylase in downbeat nystagmus. *J Neurol Neurosurg Psychiatry*. 2003;74:998–999. 2. Tilikete C, Vighetto A, Trouillas P, Honnorat J. Potential role of anti-GAD antibodies in abnormal eye movements. *Ann N Y Acad Sci*. 2005;1039:446–454. 3. Chen Y, Morgan ML, Palau AE, Mudd JA, Lee AG, et al. Downbeat down south. *Surv Ophthalmol*. 2015;60:177–181. 4. Tilikete C, Vighetto A, Trouillas P, Honnorat J. Anti-GAD antibodies and periodic alternating nystagmus. *Arch Neurol*. 2005;62:1300–1303. 5. Pierrot-Deseilligny C, Milea D. Vertical nystagmus: clinical facts and hypotheses. *Brain*. 2005;128:1237–1246

Keywords: Nystagmus, Ocular manifestations of vestibular disorders, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 209

A 6-Month Trial Of Oral Memantine For Pendular Nystagmus And Related Phenomena In Oculopalatal Tremor

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Introduction:

Acquired oculopalatal tremor (OPT) is characterized by pendular nystagmus (PN) and continuous movements of the soft palate. There is anecdotal evidence showing that memantine may improve PN in OPT. We sought to test memantine treatment for PN and related phenomena in OPT during a 6-month period.

Methods:

Adult OPT patients were assessed at baseline (visit 1), 2 (visit 2) and 6 months (visit 3) post-treatment with video-oculography, best-corrected visual acuity (BCVA), visual function questionnaire (VFQ25), orbicularis oris electromyography (EMG) and subjective visual vertical test (SVV). Memantine was titrated to 20mg/day and stopped after 6 months. The study was approved by the Ethics Committee of ARS-Centro, IP.

Results:

We included 8 patients (7 females; median age was 66 [interquartile range (IQR), 60-72]). At visit 1, PN median velocity and amplitude was 11.76 (1.175-11.5)°/s and 1.78 (1.04-4.25)°, respectively, while median BCVA, VFQ25, and SVV was 0.5 (0.3-0.7), 67.4 (56.4-78.8) and -6.46 (-10.25 to -1.165), respectively. At visit 2, 3 (50%) patients showed a >50% improvement in PN horizontal velocity and/or amplitude in at least one eye, while 1 (16%) showed worsening. 2 (33%) patients showed >50% worsening in PN vertical velocity and/or amplitude in at least one eye. At visit 3, PN improvement along the horizontal plane was not sustained in 2/3 of patients, and median BCVA was 0.8 (0.4-1.0) (p=0.02 vs visit1). There was no correlation between PN parameters and BCVA. No significant differences were observed for VFQ25, SVV, and soft palate tremor frequency, between visits.

Conclusions:

In OPT patients, memantine produced distinct effects in horizontal and vertical PN parameters, which were nevertheless modest and not sustained over time. BCVA improvement over time was not accompanied by VFQ25 improvement or correlation with PN behavior, raising questions about a possible placebo effect.

References: 1. Kim JS, Moon SY, Choi K-D, Kim J-H, Sharpe JA. Patterns of ocular oscillation in oculopalatal tremor: Imaging correlations. *Neurology*. 2007 Apr;68(14):1128–35. 2. Ehrhardt D, Eggenberger E. Medical treatment of acquired nystagmus. *Curr Opin Ophthalmol*. 2012;23(6):510–6. 3. Thurtell MJ, Joshi AC, Leone AC, Tomsak RL, Kosmorsky GS, et al. Crossover trial of gabapentin and memantine as treatment for acquired nystagmus. *Ann Neurol*. 2010;67(5):676–80.

Keywords: Nystagmus, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 210**Ocular Torsion and its variation according to types of photographic methods**

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Introduction:

Abnormal torsion could be associated with cyclovertical strabismus. We examined the torsional changes using different photographic methods

Methods:

We took fundus photographs of exotropia patients without vertical strabismus or oblique dysfunction (Group 1, $n=47$), superior oblique palsy patients (Group 2, $n=10$), and normal subjects (Group 3, $n=86$) from March 2018 to October 2019 using a fundus camera with internal fixation target (CcF) and without fixation (CsF) and Optical coherent tomography (OCT). In fundus photography, we examined the torsional angle (θ) between a horizontal line drawn through optic disc center and a line connecting optic disc center with the fovea using the Image J Program®. For optical coherence tomography, the fovea-to-disc alignment function in the computer program was used to automatically calculate the angle. We then compared the torsional changes according to types of photographic methods.

Results:

For Group 1, θ was 5.29° with CcF, 8.55° with CsF, 5.32° with OCT in right eye, 6.17° with CcF, 8.61° with CsF, 6.07° with OCT in left eye 6.67°. For Group 2, θ was 12.78° with CcF, 14.20° with CsF, 12.73° with OCT in paretic eye, 7.05° with CcF, 9.36° with CsF, 7.28° with OCT in sound eye. For Group 3, θ was 4.83° with CcF, 8.71° with CsF, 4.79° with OCT in right eye, 5.19° with CcF, 8.80° with CsF, 5.19° with OCT in left eye. There was no statistically significant difference between the results of the two different methods (CcF vs. OCT) in three groups. However, significant difference was observed between the CsF and other two methods (CcF and OCT) in three groups (all $P<0.05$).

Conclusions:

When comparing the conventional method of measuring ocular torsion with fundus photographs to OCT, the fovea-to-disc alignment of the OCT may be useful to automatically calculate the cyclotorsion. However, torsional angle measured by CsF could be overestimated.

References: None.

Keywords: Ocular Motility, Adult strabismus with a focus on diplopia

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: shineye@kuh.ac.kr

Poster 211**Presence of fatty infiltration in extraocular muscles of patients undergoing strabismus surgery.**

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Introduction:

Histopathology of extra-ocular muscles (EOMs) of both healthy and strabismic eyes reveal presence of lipid-like droplets, collagen proliferation, and abnormal arrangements and sizes of contractile elements. The significance of these changes and phenotypic correlation has not been previously studied. Our objective was to study the significance of fatty infiltration in resected muscles of patients with strabismus.

Methods:

Histopathology of resected muscles in those with esotropia and exotropia were examined from adult patients. Those with prior surgery on the muscle of interest and those with scleral buckle and glaucoma device placement were excluded. Three hematoxylin and eosin slides per specimen were examined for presence of adipose infiltration. Disease phenotype and clinical history were obtained by chart review.

Results:

Of the 90 patients there were 40 with exotropia and 50 with esotropia who underwent surgery. Exotropic subjects had an average misalignment of 41 prism diopters (PDs) (SD, 15.4) compared to 26 PDs (SD, 11.2) for those with esotropia. In 88% (35/40) of subjects with exotropia and 30% (15/50) of subjects with esotropia, some degree of fatty infiltration in the resected medial rectus muscle and lateral rectus muscle was identified (OR=10.88, 95% CI: 3.25 to 36.4, p<0.001). There was no correlation between extent of fatty infiltration and age, gender, race, etiology of strabismus or degree of misalignment.

Conclusions:

A higher percentage of subjects with exotropia were found to have fatty infiltration compared to esotropia with no correlation seen with age, gender, race, etiology of strabismus or degree of misalignment. Larger studies are necessary to explore the significance of histopathological changes in the extra ocular muscles in those with strabismus.

References: 1. Agarwal AB, Feng C-Y, Altick AL, et al. Altered Protein Composition and Gene Expression in Strabismic Human Extraocular Muscles and Tendons. *Investigative Ophthalmology & Visual Science*. 2016;57(13):5576. 2. Altick AL, Feng C-Y, Schlauch K, Johnson LA, Bartheld CSV. Differences in Gene Expression between Strabismic and Normal Human Extraocular Muscles. *Investigative Ophthalmology & Visual Science*. 2012;53(9):5168. 3. Domenici-Lombardo L, Corsi M, Mencucci R, Scrivanti M, Faussonne-Pellegrini M, Salvi G. Extraocular Muscles in Congenital Strabismus: Muscle Fiber and Nerve Ending Ultrastructure according to Different Regions. *Ophthalmologica*. 1992;205(1):29-39. 4. Kim S-H, Cho YA, Park C-H, Uhm C-S. The ultrastructural changes of tendon axonal profiles of medial rectus muscles according to duration in patients with intermittent exotropia. *Eye*. 2008;22(8):1076-1081. 5. Martinez AJ, Hay S, Mcneer KW. Extraocular muscles light microscopy and ultrastructural features. *Acta Neuropathologica*. 1976;34(3):237-253.

Keywords: Ocular motility, Adult strabismus with a focus on diplopia

Financial Disclosures: The authors had no disclosures.

Grant Support: Research to Prevent Blindness

Contact Information: None provided.

Poster 212**Measuring ocular torsion using a virtual reality double Maddox rod**

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Introduction:

Ocular torsion is tilting of the eyes, which can cause double vision. Accurate & precise detection is important for diagnosis of the underlying cause and treatment planning. Ocular torsion is traditionally measured using specialized prism lenses, a trial frame and penlight. The goal of this project is to create a stand-alone double Maddox test suitable for use by non-expert examiners.

Methods:

We Implemented the double Maddox rod test on a mobile device (iPhone, Apple) via a custom application in conjunction with a virtual reality (VR) viewer. Normal adult subject (n=3) ability to neutralize starting angles of 5, 10, 45, 90, 135, 170 and 175 degrees was compared between traditional double Maddox (TdM) rod and VR double Maddox (VRdM) rod techniques.

Results:

Similar to the traditional test, the VR double Maddox rod test presents a white bar to the right eye and a red bar to the left eye. The user rotates the bar using a single button or touch input to align the bars to the horizontal. The device outputs a digital measurement of the relative angle between the bars. All subjects neutralized all starting angles to 0-3 degrees of neutral with both TdM and VRdM. VRdM was easier to use and could be used for self testing.

Conclusions:

VRdM is a mobile application that replicates the double Maddox rod test via a smartphone and VR headset. Validation in normals shows similar precision and accuracy as traditional testing. This testing paradigm provides a streamlined test for physicians within clinic, and had potential as a home monitoring tool. Further study is needed to validate VRdM in patients with ocular torsion.

References: None.

Keywords: Adult strabismus with a focus on diplopia, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: Stanford Predictive and Diagnostics Accelerator, Research to Prevent Blindness, NIH P30 -26877

Contact Information: None provided.

Poster 213**'Inverse' calibration of eye movement recordings: a technique tailored to patients**

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Introduction:

It is often difficult to capture quantitative eye movement data from neurologically impaired patients due to intractable difficulties with calibrating infrared eyetrackers. Thus, patients are excluded from ocular motor research. Here we introduce a new method of calibrating eyetracking equipment, designed to foster inclusion of neurological patients by easing the normal difficulties encountered during calibration.

Methods:

We demonstrate the accuracy obtainable with a novel method of calibration that inverts the usual calibration sequence. Instead of requiring prolonged fixation of a pre-set sequence of targets, subjects are instructed to make natural fixations on a computer monitor. As the eye begins each fixation, a grid of characters is flashed on the screen, and subjects report the character nearest the center of fixation. A calibration mapping is constructed from the combination of multiple character-fixation pairs.

Results:

We demonstrate that the error distribution describing the separation between fixation and the reported characters over multiple character-fixation pairs is Gaussian. We further demonstrate that this is true even when there are errors in the reported character (i.e., the reported character is not nearest to the center of fixation). Finally, we show that this level of error, combined with a rate of data acquisition of between 0.2 and 1 Hz, yields calibration accuracy that surpasses traditional calibration for the same amount of data.

Conclusions:

Objective eye movement studies of patients are critical to fully characterize ocular motor dysfunction in neurological disease. Here, we demonstrate a new method of eyetracker calibration that is designed to foster inclusion of patients that would normally be excluded due to an inability to maintain prolonged fixation.

References: None.

Keywords: Higher visual functions, Ocular motility, Nystagmus

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 214**Strabismus video goggles versus prism cover testing for the measurement of ocular deviation**

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Introduction:

With our prototype strabismus video goggles, ocular deviation can be measured by means of alternate occlusion of the eyes with LCD shutters and a head-fixed target display. Previously, the goggles have been successfully validated against the conventional Hess screen test (1). The goal of the current study is to compare the strabismus angle measurements measured by the video goggles with alternate prism cover testing (aPCT) in primary position.

Methods:

We measured 55 subjects (39 strabismus patients, 16 healthy volunteers). Diagnoses included cranial nerve palsies (n=25), comitant esotropia (n=10), and others (n=4). All subjects underwent complete orthoptic examination including aPCT at near and distance, as well as video oculography with the strabismus video goggles. Binocular eye position was recorded while fixating the head-mounted laser target on a 0±15° 9-point grid at 0.5m distance. Eyes were dissociated with alternate occlusion by the built-in LCD shutters. For the current analysis, only the center fixation point was considered. We compared the deviation in angles of rotation (°) between the two testing methods.

Results:

The median difference between measurements with the video goggles and aPCT was 0.3±4.2° for horizontal deviations and 0.6±1.8° for vertical deviations. In the Bland-Altman plots, we observed no systematic bias between the two methods for horizontal deviations, whereas the video goggles slightly overestimated vertical deviations compared to aPCT.

Conclusions:

Strabismus angle measurements with our video strabismus goggles were in good agreement with routinely employed aPCT. The goggles therefore offer a simple, fast and accurate method to assess the amount of ocular deviation. Their clinical applications will be explored in further clinical studies in order to facilitate a comprehensive ocular motor examination.

References: 1. Weber KP, Rappoport D, Dysli M, Schmückle Meier T, Marks GB, Bockisch CJ, et al. Strabismus Measurements with Novel Video Goggles. *Ophthalmology*. 2017;124(12):1849–56.

Keywords: Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: Albert Bruppacher Foundation for Eye Research, University Hospital Zurich, Switzerland; the OPOS Foundation, St. Gallen, Switzerland; the Dr Dabbous Foundation, University of Zurich, Switzerland; the Betty and David Koetser Foundation for Brain Research, Zurich, Switzerland; and the Garnett Passe and Rodney Williams Memorial Foundation, Melbourne, Australia.

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Poster 215**Assessment of Levator Muscle Strength Using External Eyelid Weights**

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Introduction:

Levator muscle strength is currently inferred from eyelid excursion, commonly referred to as levator function (LF). However, eyelid excursion is influenced by a number of factors, highly variable, and a very imprecise measure of muscle strength. In this pilot study, we investigated the use of graded eyelid weights as an objective measure of levator muscle strength.

Methods:

We prospectively evaluated the response of marginal reflex distance (MRD) 1 to various eyelid weights in patients without pre-existing involutional blepharoptosis. Patients were photographed at baseline and after serial placement of eyelid weights (Tantalum Weight Sizing Set, MedDev Corp. Sunnyvale, CA) along the right eyelid margin. Weights varied from 0.6 g to 2.0 g in 0.2 g increments. The change in MRD1 from baseline with weight placement was compared for different eyelid weights.

Results:

Data was collected and analyzed for 26 eyes of 13 patients (6 female), aged 52-85 years. Baseline MRD1 was 2.56 ± 1.03 mm, and there was no difference in average MRD1 between patients above and below age 65 ($P = 0.39$). Overall, change in average MRD1 increased with increasing value of eyelid weight. This increase was steepest between 0.6 g and 1.6 g (CC 0.98, R^2 0.96) and plateaued between 1.6 g and 2.0 g (CC 0.60, R^2 0.93).

Conclusions:

Placement of pre-fabricated eyelid weights represents a new method of measurement of levator muscle strength, with a weight of 1.6 g possibly representing an optimal weight for testing. With increasing evidence that abnormalities of the levator muscle itself play a role in the pathogenesis of blepharoptosis, [1, 2] such new methods for evaluation of levator strength warrant further study.

References: 1. Cahill KV, Buerger GF, Johnson BL. Ptosis associated with fatty infiltration of Muller's muscle and levator muscle. *Ophthal Plast Reconstr Surg* 1986;2:213– 217. 2. Pereira LS, Hwang TN, Kersten RC, Ray K, McCulley TJ. Levator superioris muscle function in involutional blepharoptosis. *Am J Ophthalmol* 2008;145(6):1095-98.

Keywords: Orbit/ocular pathology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 216**SSBP1 missense variants cause dominant optic atrophy with variable retinal degeneration**

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Introduction:

Autosomal dominant optic atrophy (DOA) is the most common inherited optic neuropathy with a minimum prevalence of 1 in 25,000. About 60% of cases are due to pathogenic variants in the OPA1 gene. DOA is genetically heterogeneous, however in majority of cases the pathology seems to be limited to the retinal ganglion cells (RGC).

Methods:

Linkage analysis and candidate gene sequencing were performed in multigeneration families and sporadic cases with suspected DOA to identify disease-causing genes. Two probands from two independent families were subsequently recruited and analyzed by whole-genome sequencing (WGS) as part of the Genomics England 100,000 Genomes project. The functional consequences of putative mutations were investigated *in silico* and confirmed experimentally using the zebrafish model. Patients underwent deep phenotyping with a comprehensive neuro-ophthalmological examination, imaging and electrophysiology. In selected cases, retrospective data was analysed to define the chronology of the progressive retinal degeneration.

Results:

Three missense variants in *SSBP1* c.113G>A (p.(Arg38Gln)), c.320G>A (p.(Arg107Gln)) and c.422G>A (p.(Ser141Asn)) were identified in affected individuals from four unrelated families by a combination of linkage analysis, direct sequencing and WGS. Patients presented with optic atrophy, followed by retinal vascular attenuation and retinal pigmentary changes that was seen to be progressive. In addition to ocular manifestations, four patients were diagnosed with hypothyroidism and three patients with renal disorders. Both knockdown zebrafish model as well as administrated with exogenous mRNAs carrying the identified human mutations led to compromised development of RGC, proving that *SSBP1* is essential in retina development.

Conclusions:

Heterozygous missense variants in *SSBP1* causing DOA and retinal degeneration were identified. Detailed clinical and electrophysiological characterisation of affected individuals showed the chronology of the observed outer and inner retinal degenerative process. Further studies are needed to investigate the underlying pathophysiological pathways whether there is a causal relationship with renal and thyroid dysfunction in some *SSBP1* mutation carriers.

References: None.

Keywords: Genetic disease, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 217**Clinical, laboratory, and histopathological findings in patients with suspected temporal arteritis**

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Introduction:

Temporal arteritis, also known as giant cell arteritis (GCA), is an idiopathic systemic inflammatory syndrome that typically affects patients over the age of 60 and can cause catastrophic irreversible vision loss from ocular ischemia. Temporal artery biopsies (TABs) frequently show changes that can be diagnostically challenging, in particular healed or treated GCA and those with less robust CD68 staining. We aim to identify predictive variables for the clinical diagnosis of GCA using clinical examination findings, laboratory tests, and histopathologic features.

Methods:

A retrospective study was performed on patients who underwent TAB. Clinical and demographic characteristics, laboratory features, and biopsy results were recorded. Wilcoxon test and logistic regression analysis were performed to identify features that predict GCA status.

Results:

Of 101 patients who underwent TAB, 34 (34%) were diagnosed with GCA. Patients with GCA were significantly older (74.1 ± 8.0 years) than those without GCA (68.7 ± 10.2 years) ($P = 0.010$). There were 15 positive TABs (15%), 68 negative TABs (67%), 5 healed or treated TABs (5%), and 13 suggested healed or treated TABs (13%). Anterior arteritic ischemic optic neuropathy (AAION), ophthalmic artery occlusion (OAO), and amaurosis fugax were diagnoses seen only with GCA and were observed in 3, 2, and 3 patients, respectively. Age, biopsy result of healed temporal arteritis (HTA), and suggested HTA were able to predict GCA status with area under characteristic operating curve of 0.85. CD68 staining had a true positive rate of 67% and false positive rate of 21%.

Conclusions:

Age at time of biopsy, HTA, and suggested HTA biopsy results were found to be predictive for the diagnosis of GCA. AAION, OAO, and amaurosis fugax may be important ophthalmic manifestations of GCA. CD68 staining is neither a sensitive nor specific feature for the diagnosis of GCA.

References: None.

Keywords: Optic neuropathy, Orbit/ocular pathology, Vascular disorders, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: Funded in part by National Eye Institute Vision Core Grant P30EY028102

Contact Information: None provided.

Poster 218**New Insight into Correlation Among Convergence Insufficiency, Vestibular Abnormalities and Depression in Post-Concussion Syndrome**

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Introduction:

Concussion and post-concussion syndrome (PCS) cause visual symptoms, including blurred- and double-vision those are partly caused by convergence insufficiency (CI). Depression is also a common complication in PCS. Several studies have suggested that depression recovery in concussion is in tandem with other symptoms. Depressed patients are less motivated and have a tendency to exaggerate their physical and cognitive deficiencies. We studied the correlation between CI and depression, in concussion and vestibular system for the first time. Our findings are interesting and in contrast to the current findings in the literature.

Methods:

We tested the vestibular system in 48 patients with EVestG. All patients filled Montgomery-Asberg-Depression-Rating-Scale (MADRS) and 20 patients filled Rivermead-post-concussion-questionnaire (RPQ). An EVestG feature (Field Potential (FP)-area) was extracted from the stationary part of the EVestG signals. A neuro-ophthalmologist examined all patients with prism bar to measure CI at near-vision (cross-cover examination).

Results:

We found that: 1) FP-area and CI values were significantly correlated in PCS ($R=0.68$, $p<0.01$). 2) correlations between RPQ3 and CI ($R=0.70$, $p<0.01$), RPQ3 and FP-area were significant ($R=-0.56$, $p<0.02$). On a sub-group analysis based on MADRS score, CI was highest in the PCS group without depression ($CI=7.5(PD)\pm 1.2(SE)$), moderate ($CI=5.2(PD)\pm 1.0$) with mild-depression, and lowest with moderate/severe depression ($CI=1.6(PD)\pm 0.7$).

Conclusions:

We demonstrated a negative correlation between CI and depression and motivation did not play any role in our results as more depressed patients showed less CI. Depression is likely localized to supratentorial centers, whereas CI is likely an infratentorial/brainstem disorder. Our findings indicate that PCS generates a mixed heterogeneous population with supra- and infratentorial damages. These findings are important in localizing the pathology of PCS.

References: None.

Keywords: Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 219**Saccadic Latencies in Progressive Supranuclear Palsy**

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Introduction:

The study objective is to assess saccadic latencies (reaction time) in Progressive Supranuclear Palsy (PSP). Saccadic latency to novel stimuli is typically 180-200 msec. With a gap paradigm (introduction of a temporal gap between extinguishing the fixation target and saccade target appearance), some individuals generate express saccades (ES) with shorter latencies (85-130 msec). The superior colliculus (SC) rostral pole plays a role in fixation release and, thus, in ES generation. In monkeys, SC lesions eliminate ES. Given SC involvement in PSP, we hypothesized that latencies will be longer in PSP patients and ES less frequent than in healthy individuals.

Methods:

Participants performed pro- and gap- saccade sequences. Eye movements were recorded with EyeLink 1000+ video-oculography.

Results:

Eleven participants with PSP (mean age 68+/-8 years) and eleven healthy controls (mean age 66+/-6 years) were included. Pro- and gap- vertical saccadic latencies were longer in PSP than control participants (pro:314.8+/-121.5 versus 216.7+/-69.1 msec, p=0.0001; gap:300.6+/-108.1 versus 193.4+/-65.2, p=0.003). There were no clear differences in ES generation between the two groups (horizontal: 28% and 29% of saccades in control and PSP; vertical: 16% and 17% of saccades in control and PSP), although PSP patients generated saccades with overall longer latency distributions than controls in both the horizontal and vertical dimensions. Latencies were substantially longer in the vertical than horizontal dimension in controls (difference of: 16 msec, p=0.06), and this difference was exaggerated in PSP (difference of: 100 msec, p=0.003).

Conclusions:

Saccadic latency prolongation is seen in PSP compared to healthy controls, especially for vertical saccades. This may reflect SC or frontal lobe involvement. However, reduced generation of ES was not seen, suggesting retained albeit impaired SC function in this PSP cohort. Future studies with correlation of saccadic latency to disease severity will determine if ES generation, along with impairment in timing, is lost with disease progression.

References: None.

Keywords: Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 220
Optic Nerve OCT Parameters As A Surrogate Marker Of Brain Volume

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Introduction:

It has been established that the normal human retinal nerve fiber layer (RNFL) thickness decreases with age. Meanwhile, brain volume and weight decline by around 5% per decade after age 40. While the relationship between the ganglion cell layer complex and temporal lobe size has been described, the relationship between brain volume and RNFL thickness has not been established. The present study aims to study the relationship between anatomical structures measured by optical coherence tomography (OCT) and the normal brain volume calculated utilizing specialized software based on magnetic resonance imaging (MRI).

Methods:

This is a retrospective, chart review study of normal patients seen in our clinic between 2014 and 2019. Both OCT and brain MRIs were collected and reviewed. All patients were older than 18 years; patients with brain tumors, hemorrhagic or ischemic lesions or any neurological pathology were excluded. For all subjects, the best eye was analyzed, and retinal nerve fiber layer (RNFL) and ganglion cell-inner plexiform layer (GC-INL) examinations were performed (HD-OCT). Nineteen patients were reviewed for a confidence interval of 5% and statistical significance was met at 0.05. All relationships were calculated with a multivariable linear regression model.

Results:

11 females and 8 males patients' charts were reviewed with a mean age of 51.6 +/- 13.5 years. The mean adjusted brain volume was 1520.2 CC. The mean RNFL was 95+/-10 mm and the GC layer was 80+/-7 mm. Brain volumes were weighted by gender to account for known disparities. The relationship with RNFL / age, and brain volume / age were confirmed.

Conclusions:

Total brain volume and RNFL thickness decreases with age in a 21:1 (ml/mm) relationship. This corroborates previous studies for each individual relationship and establishes a correlation with normal data from MRI to normal OCT imaging.

References: 1. Casaleto KB, Ward ME, Baker NS, Green, A. Retinal thinning is uniquely associated with medial temporal lobe atrophy in neurologically normal older adults. *Neurobiol Aging*. 2017;51:141-147. doi:10.1016/j.neurobiolaging.2016.12.011 2. Alasil T, Wang K, Keane PA, et al. Analysis of normal retinal nerve fiber layer thickness by age, sex, and race using spectral domain optical coherence tomography. *J Glaucoma*. 2013 Sep;22(7):532-41. 3. Peters R. Ageing and the brain. *Postgrad Med J*. 2006 Feb;82(964):84-88. 4. Pueyo V, Perez T, Gonzales I, et al. Retinal structure assessed by OCT as a biomarker of brain development in children born small for gestational age. *British Journal of Ophthalmology*. 2017;101:1168-1173. 5. Shi Z, Zheng H, Hu Jingxiao, et al. Retinal Nerve Fiber Layer Thinning Is Associated With Brain Atrophy: A Longitudinal Study in Nondemented Older Adults. *Frontiers in Aging Neuroscience*. 2019 Apr; <https://doi.org/10.3389/fnagi.2019.00069>

Keywords: Neuroimaging, Magnetic resonance imaging

Financial Disclosures: Alvaro Mejia-Vergara has a scholarship stipend by the PAAO

Grant Support: None.

Contact Information: Alvaro Mejia-Vergara, MD- amejiavergara@mednet.ucla.edu

Poster 221**Visual Improvement following Visual Rehabilitation In Patients with Visual Field Defect after Stroke (Retrospective Study)**

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Introduction:

Homonymous hemianopia (HH) is a significant consequence of stroke where patients lose vision on one side of their visual field (VF). HH has devastating effects on patients' quality of life (e.g. loss of ability to drive and independence). Evidence suggests visual rehabilitation (VR) may improve visual function in HH patients but a considerable lack of high-quality research impedes VR treatments from being broadly administered. The criticism to VR has been partly raised from the lack of strict control of compensatory eye movements when VFs were tested in previous studies*. Our objective was to analyze the effectiveness of VR in improving VF defects and overall visual function in HH, retrospectively.

Methods:

20 HH patients went through VR with Sanet Vision Integrator (SVI) system which included computerized visual exercises involving numbers, letters, and circles performed on a 50" touchscreen TV. Perimetry was performed to measure VF improvement on Compass (Centervue, Italy), and Octopus 900 (Haag-Streit International, Switzerland), which use state-of-art technologies (scanning laser ophthalmoscopy and eye-tracking systems) to account for potential eye movements during VF testing.

Results:

We showed that VR may improve visual function in HH by comparing mean deviation (MD), pattern standard deviation (PSD), mean sensitivity (MS), square root of Loss Variance (sLV) and Fundus Perimetry Deviation Index (FDPI) values in VFs, pre- and post- VR. Using the Compass machine, there were overall 0.93dB ($p<0.001$), 0.37dB ($p=0.0094$) and 2.1% ($p<0.001$) improvement in MD, PSD, and FDPI after training, respectively. The Octopus machine data showed 0.85dB ($p=0.004$), 0.90dB ($p=0.005$) and 0.69dB ($p=0.002$) improvement in MD, MS and sLV, respectively.

Conclusions:

Standardized treatments and rehabilitation programs for HH are needed*. There is great potential in meeting this need by visual restoration methods. We derived results that demonstrate the positive effect of VR on visual function.

References: *Mansouri, Roznik, Rizzo, Prasad, Rehabilitation of visual loss, where we are and where we need to be, J Neuroophthalmol, 38, 223–229, 2018

Keywords: Stroke trauma, Visual fields, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 222**Optic Nerve Crush Causes Increased Nerve Damage in Diabetic Mice**

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Introduction:

Optic nerve crush (ONC) is a common model simulating optic neuropathy and was used in this study to evaluate its effect in diabetic mice (DM). The aim of the study was to characterize the vulnerability of DM to ischemic optic neuropathy.

Methods:

ONC was induced in 7 NOD (NOD/ShiLtJ) and 8 homozygous db/db (C57BLKS/J-leprdb/leprdb) DM, type I and II diabetes respectively, and to 6 wild type (WT) mice. The right optic nerve was crushed and the left served as control. The retinae were extracted for mRNA on day 3 and the optic nerves were gelatin fixated for histological analysis. Optic nerves were stained for Luxol fast blue and retinae for gliosis and inflammation (GFAP and CD45). The expression levels of HO-1 and SOD, stress related genes, were measured using RTPCR.

Results:

Four of the 7 (57%) NOD and 6 of 7 (84%) db/db DM survived the ONC procedure. All WT mice survived. HO-1 levels significantly increased (4.3 folds) in the WT, remained baseline in db/db and decreased to 0.5 fold in the NOD mice. SOD levels did not change from baseline in WT, mildly increased in NOD and decreased in the db/db mice. Optic nerve staining with luxol fast blue showed severe axonal loss in the diabetic nerves as compared with the WT.

Conclusions:

DM, especially type I (NOD), are more sensitive to ONC damage with increased morbidity and mortality. HO-1 is an important regulator of the Muller cells in the retina, which are affected in diabetes. While the levels of HO-1 were elevated in WT mice we detected baseline (db/db) or decreased (NOD) levels in the DM. SOD levels remained at baseline. This model can help to explore the pathophysiology underlying optic neuropathy in diabetic patients, and the differences between type I and II.

References: None.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic nerve trauma and treatment, Optic neuropathy, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: This study was partially supported by the Zanyvl and Isabelle Krieger Fund, Baltimore, Maryland, USA (NGC).

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Poster 223**Ophthalmic Manifestations of Mitochondrial Disease**

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Introduction:

The high metabolic demand of the afferent and efferent visual systems makes them particularly susceptible to mitochondrial dysfunction. Over a third of patients with mitochondrial disease harbor eye conditions that can cause significant morbidity. Herein we describe the most common ophthalmic manifestations that should raise suspicion of mitochondrial disease and briefly describe management principles.

Methods:

We combine a survey of current literature with our personal experience in diagnosing and managing patients with neuro-ophthalmic signs of mitochondrial disease.

Results:

The most common ophthalmic manifestations include:

- 1) Blepharoptosis due to weakness of levator palpebrae superioris
- 2) Lagophthalmos due to weakness of orbicularis oculi
- 3) Exposure keratopathy secondary to orbicularis oculi weakness or ptosis surgery
- 4) Ocular dysmotility and convergence insufficiency due to extraocular muscle weakness
- 5) Pigmentary retinopathy and macular pattern dystrophy secondary to RPE dysfunction
- 6) Optic neuropathy most commonly associated with Leber hereditary optic neuropathy and dominant optic atrophy
- 7) Retrochiasmal disease causing homonymous hemianopia or cerebral visual impairment

Mitochondrial dysfunction tends to cause bilateral, mostly symmetric disease. The majority of manifestations progress insidiously; however, optic neuropathy and retrochiasmal disease may occur acutely.

Currently, there are few treatment options for mitochondrial dysfunction, therefore management of ophthalmic associations is largely symptomatic. Conservative measures such as artificial tears, ptosis crutches and low vision aids are preferable due to the progressive nature of most diseases. When this becomes impractical, then surgical intervention can be pursued with caution. Genetic testing and genetic counseling have ever-increasing importance in the holistic management of patients with mitochondrial disease.

Conclusions:

Recognition of these ophthalmic manifestations may prompt consideration and further investigation for an underlying mitochondrial disorder, some of which have life-threatening systemic associations. Symptomatic treatment may facilitate improved visual function and better quality of life.

References: None.

Keywords: Genetic disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 224**Effect of Initial Prednisone Dosing on Ocular Myasthenia Control at 1 Month**

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Introduction:

Ocular myasthenia gravis (OMG) is an autoimmune condition responsive to corticosteroids. Experts recommend corticosteroids as first line immunosuppressive treatment (1); however, no guidelines exist for initial dosing. Prior retrospective reports have suggested initial doses of 40-80 mg daily (2) but also have demonstrated success at doses as low as 10 mg daily (3). The goal of this study is to determine whether initial prednisone dosing has any effect on symptoms control at 1 month.

Methods:

Charts were identified retrospectively among patients with OMG seen by two neuro-ophthalmologists with different prescribing practices. Patients were separated into 2 groups based on maximum equivalent daily dose in first month of treatment: ≤ 20 mg versus >20 mg. The primary outcome was control rate at 1 month.

Results:

42 patients met inclusion and exclusion criteria, 19 in the low dose group and 23 in the high dose group. At 1 month: 37% in the low dose group and 30% in the high dose group were controlled; 37% in the low dose group and 43% in the high dose group were improved but uncontrolled; and 26% in both groups had no significant improvement, Fisher exact $p = 0.9$.

Of the 42 patients, 17 were antibody negative, and 25 were acetylcholine receptor antibody positive. At 1 month: 12% in the antibody negative group and 48% in the antibody positive group were controlled; 41% in the antibody negative group and 36% in the antibody positive group were improved but not controlled; and 41% in the antibody negative and 16% in the antibody positive group were uncontrolled, Fisher exact $p = 0.03$.

Conclusions:

Patients with OMG on low and high dose prednisone did not show a significant difference in 1-month control status, suggesting low dose prednisone may be appropriate for initial dosing. Antibody negative patients may have a more protracted course.

References: 1. Kerty E, Elsas A, Argov Z, Evoli A, Gilhus NE, EFNS/ENS Guidelines for the treatment of ocular myasthenia, Eur J Neurol, 21(5), 687-93, 2014. 2. Kupersmith MJ, Moster M, Bhuiyan S, Warren F, Weinberg H, Beneficial effects of corticosteroids on ocular myasthenia gravis, Arch Neurol, 53(8), 802-4, 1996. 3. Miano MA, Bosley TM, Heiman-Patterson TD, Reed J, Sergott RC, Savino PJ, Schatz NJ, Factors influencing outcome of prednisone dose reduction in myasthenia gravis, Neurology, 41(6), 919-21, 1991.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Myasthenia

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 225**The association between retinal vasculopathy and retinal amyloid-beta accumulation**

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Introduction:

Patients with Alzheimer's disease (AD)-related cognitive disorders exhibit retinal and choroidal vascular abnormalities and intraretinal accumulation of A β plaque. Modern retinal imaging modalities to quantify retinal vasculopathy and amyloid-beta (A β) burden have advanced the field. We analyze the relationship between retinal microvascular abnormalities and retinal amyloid-beta (A β) burden on autofluorescence retinal fundus photographs, in a cohort of subjects with cognitive decline.

Methods:

33 subjects underwent neuropsychometric evaluation, brain MRI, and curcumin-enhanced retinal fluorescent imaging. The left eye supero-temporal quadrants were used to quantify A β plaque count (APC) and area (APA) in the posterior pole (PP), proximal mid-periphery (PMP), and distal mid-periphery (DMP). Vessel inflection index (VII) and branching angle (VBA) were computed in a predefined region of interest between 1.5 and 5 optic disc diameters. The diagnostic groups were compared for demographic, retinal and brain imaging parameters using Student's t-test. Linear regression models assessed the correlations between retinal vascular and A β parameters.

Results:

Our cohort included 8 subjects with normal cognition (NC), 22 amnesic MCI (aMCI) and 3 probable AD (pAD). The groups did not appreciably differ in VII or VBA, but significantly greater APC in the PP and PMP was noted in AD and aMCI patients as compared to NC. VII correlated with APC and APA in the PP, and BA and VII were associated with APC in the DMP. Older patients had significantly larger APA in PMP (p=0.04).

Conclusions:

We found that certain retinal vascular changes correlate with A β count in the retinal posterior pole and distal mid-periphery. Future studies should be conducted in larger cohorts in order to determine the temporal and topographic relationship between retinal vasculopathy and retinal A β deposition in subjects with cognitive disorders.

References: None.

Keywords: Higher visual cortical functions, Neuroimaging, Miscellaneous, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 226**Assessment of Visual Function in Patients with Acute Ischaemic Stroke**

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Introduction:

Visual field loss, inattention, and ocular motor disturbance are not uncommon in stroke. However, several reports have suggested that disturbance of higher visual function is under-recognised. Visual disturbance can impact on patients' disability, impairment and quality of life and may impair rehabilitation. The extent to which vision is routinely assessed in stroke patients is unclear. This study aimed to determine how often stroke patients' vision was assessed, to what extent, and by whom.

Methods:

A retrospective chart review of the 50 most recently-admitted ischaemic stroke patients. Notes were rated against a standard template by two independent assessors. Any disagreement was resolved by discussion. For standardisation purposes it was assumed that, if visual assessment was not documented, no assessment had been performed. Data acquired included demographic information, whether assessment had been performed for vision, neglect and ocular motor function by day 3 of admission and at time of discharge, if so, to what extent and by whom.

Results:

The mean age of the 50 patients was 69 years (male:female ratio 2:1). Where documented, patients' NIHSS scores ranged from 1 to 23 (median 4). 42 (90%) patients had some form of visual assessment by day 3 and 43 (92%) by discharge. However, assessment was variable: only 17% were assessed for vision, neglect and ocular motor function by day 3, 34% by discharge. There was no evidence of fundoscopy or assessment of higher visual function in any patient.

Conclusions:

Most stroke patients had some form of visual assessment. However, assessments were, in general, variable. 8% of stroke patients had no documented visual assessment by the time of discharge. More detailed and directed assessment of visual function in stroke patients has the potential to detect problems not hitherto identified with potentially beneficial implications for rehabilitation and patients' quality of life.

References: None.

Keywords: Stroke trauma, Higher visual functions, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 227**Self-reported vision and hallucinations in older adults: results from two longitudinal U.S. health surveys**

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Introduction:

Vision loss may be a risk factor for hallucinations, but this has not been studied at the population level.

Methods:

To determine the association between self-reported vision loss and hallucinations in a large community-based sample of older adults, we performed a cross-sectional and longitudinal analysis of two large, nationally representative U.S. health surveys: the National Health and Aging Trends Study (NHATS) and the Health and Retirement Study (HRS). Visual impairment and hallucinations were self- or proxy-reported. Multivariate single and mixed effects logistic regression models were built to examine whether visual impairment and history of cataract surgery were associated with hallucinations.

Results:

In NHATS (n=1,520), hallucinations were more prevalent in those who reported difficulty reading newspaper print (OR 1.77, 95% CI: 1.32-2.39) or recognizing someone across the street (OR 2.48, 95% CI: 1.86-3.31) after adjusting for confounders. In HRS (n=3,682), a similar association was observed for overall (OR 1.32, 95% CI: 1.08-1.60), distance (OR 1.61, 95% CI: 1.32-1.96), and near eyesight difficulties (OR 1.52, 95% CI: 1.25-1.85). In neither sample was there a significant association between cataract surgery and hallucinations after adjusting for covariates.

Conclusions:

Visual dysfunction is associated with increased odds of hallucinations in the older U.S. adult population. This suggests that the prevention and treatment of vision loss may potentially reduce the prevalence of hallucinations in older adults.

References: None.

Keywords: Higher visual cortical functions, Higher visual functions

Financial Disclosures: The authors had no disclosures.

Grant Support: This work was supported by the National Institute of Neurological Disorders and Stroke (grant number T32 NS061779-10 to AGH, grant number R01 NS099129-01A1 to AWW).

Contact Information: None provided.

Poster 228**Ocular Myasthenia Gravis – How Effective is Low Dose Prednisone Long Term?**

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Introduction:

Ocular myasthenia gravis (OMG) therapy should address three issues – restoration of normal binocular vision, prevention of deterioration to generalized MG (GMG), and avoiding significant adverse effects of treatment. Prior studies suggest that moderate dose followed by low dose daily prednisone can accomplish this for at least two years. Long term issues however, have not been addressed. We hypothesize that OMG patients who had been treated or required daily low dose prednisone (< 7.5 mg daily) would maintain control of OMG and continue with a low rate of conversion to GMG.

Methods:

Chart review of OMG patients managed in one Neuro-Ophthalmology service who did not develop GMG within 2 years (previously reported) with longer than 3 years follow up were evaluated. We evaluated the average daily prednisone dose, additional immunomodulatory therapies, whether diplopia in primary and downgaze remained, ocular motility exam (at the last visit), and whether GMG developed after 2 years.

Results:

106 patients (30 women, 76 men, age 56.6 ± 19.3) were followed for 8.4 ± 5.2 years. 87 (83%) required chronic prednisone, approximately 5.2 ± 8.4 mg daily dose. 41 (39%) had prednisone failure requiring additional therapy (azathioprine, mycophenolate, plasmapheresis, IVIG, rituximab, cyclosporine). GMG developed in 13/106 (12.3%) of patients at average 7.7 ± 8.2 years (yearly incidence 2.4%). At the last evaluation, 84% had no or limited diplopia or vision blocking ptosis.

Conclusions:

Low dose prednisone remains an adequate therapy to control OMG in the majority of patients, but a significant minority have underlying medical issues or fail therapy, requiring additional immunosuppressive therapies. Conversion to GMG remains low on low dose prednisone and / or other immunosuppressive agents. Prednisone remains the main therapy for OMG but it is not a cure or ultimate panacea.

References: None.

Keywords: Myasthenia, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 229**Pattern Electroretinogram in patients with multiple sclerosis: 2-Year Follow-up**

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Introduction:

Impaired ganglion cell function occurred in multiple sclerosis (MS) regardless of optic neuritis, indicating generalized subclinical ganglion cell dysfunction in cross-sectional studies (Jiang, et al. NANOS 2019, JNO in press). The goal was to determine retinal ganglion cell function in patients with MS in the two-year follow-up.

Methods:

Nineteen RRMS patients (2 males and 17 females, age 41.0 ± 9.0 years at baseline) with disease duration of 6.4 ± 8.4 years were recruited and tested using the new generation of pattern electroretinogram (PERG) (Monsalve P. et al. 2018, Jiang et al. 2019). There were 5 eyes with optic neuritis (MSON), 5 non-ON fellow eyes (MSFE) and 28 non-ON MS eyes (MSNON). A steady-state PERG was concurrently recorded from each eye in response to black-white horizontal grating lines. Fourier analysis was performed to retrieve amplitude and latency at baseline and 2-year follow-up visits (24.3 ± 2.3 months).

Results:

No significant changes of expanded disability status scale and low contrast sensitive between baseline and follow-up visits. The average PERG amplitude (1099 ± 421 nV at baseline vs. 1108 ± 420 nV at follow-up) and phase (73 ± 18 degrees at baseline vs. 74 ± 14 degrees at follow-up) in MS eyes were not significantly different between the baseline and follow-up (post hoc, $P > 0.05$). Further more, there were no significant PERG adaptation of amplitude and phase adaptation between baseline and follow up. There were not significant differences between the baseline and follow-up in subgroups of the MSON, MSFE and MSNON eyes (post hoc, $P > 0.05$).

Conclusions:

This is the first study to follow the ganglion cell function over a period of 2 years using the new generation PERG. The sustained ganglion cell function in the retina may indicate the stable status in patients with RRMS.

References: None.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Demyelinating disease.

Financial Disclosures: The authors had no disclosures.

Grant Support: The work has been supported by the National Multiple Sclerosis Society, NIH Center Grant P30 EY014801, and a grant from Research to Prevent Blindness (RPB)

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Poster 230**The Timing of Cataract Surgery in Giant Cell Arteritis Patients**

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Introduction:

To our knowledge, there are currently no recommendations or guidelines in the literature regarding the safety and timing of cataract surgery in giant cell arteritis (GCA) patients. The purpose of our study is to determine a safe time frame and parameters for performing cataract surgery following diagnosis and treatment of GCA.

Methods:

This retrospective study used ICD9/10 and CPT codes to identify all patients with biopsy-proven GCA who underwent cataract surgery from 2005 to 2019 at a single institution. Excluded from the study were patients whose date of biopsy diagnosis or dose of corticosteroids at the time of cataract surgery was unknown.

Results:

Chart review identified 10 patients and 15 eyes that met the inclusion criteria. 80% of the patients were female, and the mean age was 74.4 years. Two patients had a history of arteritic ischemic optic neuropathy. There were no peri-operative or post-operative complications in the 15 eyes that underwent cataract surgery with varying doses of prednisone at the time of surgery (1 to 25 mg daily prednisone +/- 10 to 25 mcg weekly methotrexate; median prednisone dose of 10.75 mg) and varying time from biopsy diagnosis of GCA to surgery of at least 7 months (median 13.75 months).

Conclusions:

Cataract surgery appears to be safe for GCA patients on varying doses of prednisone at time of surgery at least 7 months from time of biopsy diagnosis. There is a need for a systematic review with a larger cohort of data from neuro-ophthalmologists and cataract surgeons nationally to establish guidelines for safe cataract surgery in GCA patients.

References: None.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 231**Critical Flicker Fusion as a Novel Measure of Remyelination in Multiple Sclerosis**

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Introduction:

Visual dysfunction is ubiquitous in multiple sclerosis (MS). Demyelination of the optic nerve is common, and visual impairment is a leading cause of disability in people with MS (pwMS). The eye provides an easily accessible window into the central nervous system, making the visual system an ideal model to evaluate remyelination therapies in MS. However, there are currently no fast, validated tests which reliably measure myelination status in the visual pathway. Visual evoked potential (VEP) is the current gold-standard measure of optic nerve function, however it is resource and time intensive, limiting its use. Critical flicker fusion (CFF) is a low-cost, efficient measure of optic nerve function. Participants view a rapidly flashing light that increases in frequency until it is perceived as a continuous light, the CFF threshold. While prior studies have demonstrated altered CFF thresholds in pwMS after optic neuritis, this is the first to establish intra-subject reliability and efficacy of CFF in pwMS with stable disease in comparison to VEP.

Methods:

Twenty adult pwMS will be recruited for this cross-sectional pilot study. Subjects will undergo CFF, VEP, and standard visual outcome measures: visual acuity, fields, color vision, optical coherence tomography, and visual function questionnaires (NEI-VFQ-25).

Results:

Mixed-effects linear regression analysis will compare VEP latency and CFF thresholds, accounting for demographic and MS disease history. CFF test-retest reliability will be assessed using correlation analysis. Exploratory correlative analyses will compare CFF to additional visual outcome measures.

Conclusions:

This study will determine whether CFF is a reliable, effective, clinically useful alternative to VEP in evaluating demyelinating disease in pwMS. This will support the use of CFF as a practical validation tool in future studies of remyelination therapies.

References: None.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Demyelinating disease, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 232**Visual function and retinal structure differences between relapsing remitting and secondary progressive multiple sclerosis**

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Introduction:

Visual impairment contributes to disability in multiple sclerosis (MS). Though relapsing remitting (RRMS) and secondary progressive MS (SPMS) are considered phases along a continuum, prior reports suggest better vision in SPMS. Previous structural and angiographic retina studies have not compared between RRMS and SPMS. The aim of this study is to compare visual function and retinal structure between RRMS and SPMS.

Methods:

Adult MS subjects with inactive RRMS and SPMS were recruited prospectively. Eyes with history of optic neuritis (ON) were excluded. Best corrected low contrast (LCVA) and high contrast (ETDRS) visual acuity were measured. Macula OCT and OCT angiography (OCTA, Avanti, Optovue Inc, Fremont, CA) were obtained. Generalized estimating equation (GEE) models, accounting for within subject correlation and age, were used to compare visual function, retina structure and vessel density (VD) between RRMS and SPMS eyes.

Results:

32 eyes without ON (20 RRMS, 12 SPMS) in 20 subjects (age 28-74 years, 92% female) were studied. SPMS subjects were older. ETDRS and LCVA were lower in SPMS eyes but did not reach statistical significance ($p=0.25$, $p=0.09$ GEE accounting for age). Superficial macular thickness was decreased in SPMS eyes compared to RRMS eyes ($p=0.067$, $p=0.002$ and $p=0.005$ for central 1mm, 2mm and 3 mm regions), as was superficial macular VD, though this was not significant ($p=0.412$, $p=0.114$ and $p=0.448$ for 1mm, 2mm, 3mm regions). OCT and OCTA measures showed very strong correlation within each region ($R=0.87, 0.85$ and 0.84 , one eye per subject, for 1mm, 2mm, 3mm). Superficial macular OCT and OCTA measures appear useful for discriminating SPMS from RRMS eyes.

Conclusions:

Our results suggest that SPMS eyes have reduced visual function, superficial macular thinning on OCT and reduced superficial macular VD on OCTA compared to RRMS eyes. Macular OCT and OCTA were tightly correlated and may aid in classifying eyes from different MS phases. Further study is needed to assess its clinical utility.

References: 1. Baier et al. Low-contrast letter acuity testing captures visual dysfunction in patients with multiple sclerosis. *NEUROLOGY*, 64, 992–995, 2005 2. Balcer et al. Contrast letter acuity as a visual component for the Multiple Sclerosis Functional Composite. *NEUROLOGY*, 61, 1367–1373, 2003 3. Jiang et al. Impaired retinal microcirculation in multiple sclerosis. *Multiple Sclerosis Journal* Vol. 22(14) 1812–1820, 2016 4. Lanzillo et al. Optical coherence tomography angiography retinal vascular network assessment in multiple sclerosis. *Multiple Sclerosis Journal*. 24(13), 1706–1714, 2018 5. Lublin et al. Defining the clinical course of multiple Sclerosis. *Neurology*, 83:278–286, 2014 6. Spain et al. Optical coherence tomography angiography enhances the detection of optic nerve damage in multiple sclerosis. *British journal of ophthalmology*, 102(4):520–524, 2018

Keywords: Demyelinating disease, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Higher visual functions, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: Research to Prevent Blindness, Myelin Repair Foundation, NIH P30 026877

Contact Information: None provided.

Poster 233**Characteristics Of Retinal Microvascular Abnormalities in ED Patients Presenting for Suspected TIA: FOTO-ED TIA Study**

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Introduction:

Up to 20% of patients affected with transient ischemic attacks (TIAs) or minor strokes will have a new cerebrovascular event (CVE) within 90 days. Ocular fundus abnormalities are common (13%) and associated with cerebrovascular disease among patients with focal neurologic deficits, independent of ABCD2 and DWI. Our goal was to ascertain the patient demographics and prevalence of specific retinal findings among those with microvascular abnormalities in the FOTO-ED TIA study.

Methods:

FOTO-ED TIA is a prospective cohort study of adult patients with NIH stroke scale ≤ 3 who were admitted to the ED observation unit for accelerated diagnostic protocol for suspected TIA or admitted to the hospital with a diagnosis of TIA or stroke. Nonmydriatic fundus photos of both eyes were obtained from study patients and reviewed for microvascular and non-microvascular findings.

Results:

395 patients were enrolled in the FOTO-ED TIA study, with 34 (9%) having retinal microvascular findings (median age; 61 years (interquartile range [IQR]: 54-70) women; 17 (50%) black; 23 (68%), Hispanic; 2 (6%). Only 22 patients (65%) with microvascular findings were diagnosed with a CVE. Of the 68 eyes studied, findings of nonmydriatic fundus photography included retinal hemorrhages (40%), cotton wool spots (32%), microaneurysms (13%), inferotemporal arteriovenous nicking (13%), hard exudates (10%), optic pallor (10%), supratemporal arteriovenous nicking (15%), focal arteriolar narrowing (9%), retinal occlusion (6%), and retinal embolism (4%). Among all patients with microvascular findings, hard exudates and optic disc pallor were only observed in those diagnosed with a CVE ($p=0.046$, $p=0.046$).

Conclusions:

In the FOTO-ED TIA study, patients with microvascular findings on nonmydriatic fundus photography were most often found to have retinal hemorrhages and cotton wool spots. Not all patients with microvascular findings were determined to have a CVE. Of note, only patients with a definitive CVE demonstrated findings of hard exudates and optic disc pallor.

References: Bruce BB et al, Nonmydriatic Ocular Fundus Photography in the Emergency Department, N Engl J Med, 364(4), 387-389, 2012.

Keywords: Stroke trauma, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: NIH R01-NS089694

Contact Information: None provided.

Poster 234**Therapeutic Effect of Botulinum Toxin in Vestibular Migraine**

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Introduction:

Vestibular migraine (VM) has been increasingly recognized as a distinct clinical entity, implying vestibular symptoms during migraine without objectively demonstrated interictal vestibulopathy. Recently, both the Bárány Society and the Migraine Classification Subcommittee of the International Headache Society have proposed original diagnostic criteria for VM, which have been included in the recent edition of the International Classification of Headache Disorders (ICHD-3). The migraine prophylactic medications significantly improved the headache profiles as well as the parameters of dizziness. However, in many patients, VM attacks are severe and long-lasting, and frequent even though the prophylactic treatments.

Methods:

To evaluate the effect of Botulinum toxin type A (BOTOX®) which is approved treatment with proven preventive effects against chronic migraine, for the patients with VM refractory to the conventional migraine prophylactic therapies. Twenty patients suffering from headache and vestibular symptoms who were satisfied the diagnostic criteria of VM based on ICHD-3 beta version, were treated with BOTOX® injection. Headache and vestibular symptoms were compared using visual analogue scale, headache impact score-6, migraine disability assessment, migraine-specific quality of life, vertigo symptom scale, dizziness handicap inventory, Beck depression inventory, Beck's anxiety inventory before and 12 weeks after the injection therapy.

Results:

The evaluation scales showed a marked improvement in the vestibular parameters as well as headache ones after BOTOX® injection treatment ($p < 0.05$, paired t-test). The degree of disability of daily life caused by these uncomfortable symptoms was also reduced, and it was confirmed that the quality of life of patients was remarkably improved, which lasted for at least 12 weeks.

Conclusions:

This current study suggests that BOTOX® injections have therapeutic effects on not only chronic migraine but also VM.

References: None.

Keywords: Vestibular, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 236**Retinal Layers and Choroid Thickness in Patients with Parkinson's Disease with or Without Pramipexole Treatment**

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Introduction:

Parkinson's disease (PD) is characterized by accumulation of alfa-synuclein and degeneration of dopaminergic neurons in the brain and presumably in the retina. Preclinical studies demonstrated neuroprotective effects of the dopamine agonist pramipexole, but clinical evidence remains unclear. OCT is an important biomarker in PD, but few studies have evaluated segmented retinal layers and choroid. We compared structural changes in retinal layers and choroid in PD patients and healthy controls. We also compared PD patients receiving (PD+P) with patients not receiving (PD-P) pramipexole treatment.

Methods:

Thirty-eight eyes of 19 patients (9 PD+P, 10 PD-P), and 40 eyes of 20 controls were examined using SD-OCT (Cirrus, v5.0, Carl Zeiss Meditec, Inc., Dublin, CA). Measurements included full-thickness retina and choroid and the following segmented retinal layers: macular retinal nerve fiber layer (mRNFL), ganglion cell layer+inner plexiform layer (GCL+IPL), inner nuclear layer (INL), outer plexiform layer (OPL), outer nuclear layer (ONL) and photoreceptor layer (PRL). Global average and sectoral parameters were determined. At each sector, measurements were grouped in inner retinal layers (IRL, including RNFL+GCL+IPL+INL) and the remaining outer retinal layers (ORL). For comparisons a $p \leq 0.01$ was considered significant.

Results:

Full-thickness measurements revealed significant thinning of the fovea in PD patients. The following segmented sectors were also significantly thinner: inferior inner mRNFL; foveal GCL+IPL; foveal and inferior inner ganglion cell complex (GCC, including GCL+IPL+RNFL); foveal IRL and ORL. Compared to PD+P, eyes of PD-P patients showed significant thinning of the inferior inner mRNFL, superior outer ONL, inner annulus GCC, inferior inner GCC, and inferior inner IRL. There was no significant difference in choroidal thickness.

Conclusions:

Fovea and inner sectors of IRL and ORL are thinner in PD than controls. Segmented OCT layers seem a better biomarker of retinal degeneration in PD than full-thickness retinal analysis. Abnormalities were significantly less prominent in patients receiving Pramipexole treatment suggesting that it may help to prevent retinal thinning in patients with PD.

References: 1. Bartels AL, Leenders KL. Parkinson's disease: the syndrome, the pathogenesis and pathophysiology. *Cortex*. 2009;45(8):915-21. 2. Ekker MS, Janssen S, Seppi K, Poewe W, de Vries NM, Theelen T, et al. Ocular and visual disorders in Parkinson's disease: Common but frequently overlooked. *Parkinsonism Relat Disord*. 2017;40:1-10. 3. Albrecht S, Buerger E. Potential neuroprotection mechanisms in PD: focus on dopamine agonist pramipexole. *Curr Med Res Opin*. 2009;25(12):2977-87. 4. Chrysou A, Jansonius NM, van Laar T. Retinal layers in Parkinson's disease: A meta-analysis of spectral-domain optical coherence tomography studies. *Parkinsonism Relat Disord*. 2019;64:40-9. 5. Firsov M, Astakhova L. The role of dopamine in controlling retinal photoreceptor function in vertebrates. *Neuroscience and Behavioral Physiology*. 2016;46(2):138-45.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Neuro-opth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 237**Yield of Frozen Section versus Permanent Pathology in Temporal Artery Biopsy for Giant Cell Arteritis**

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Introduction:

There is significant debate as to whether bilateral temporal artery biopsies (TABs) are required for the diagnosis of giant cell arteritis (GCA). Discordance rates have varied in the literature and the utility of TAB frozen sections are unclear. We set out to evaluate the discordance rate of TABs and determine the sensitivity and specificity of TAB frozen versus permanent section pathology results for GCA.

Methods:

Retrospective chart review of 795 patients, ≥ 40 years of age, who underwent TAB with both frozen and permanent sectioning performed at our institution from January 1, 2010 to December 1, 2018.

Results:

GCA was confirmed in 120 of 795 (15.1%) cases; 65% were female with a median age of 73 years. Frozen section was positive in 103 (85.8%) cases with 4 false positives (0.6%) and 21 false negatives (17.5%). There was a 5.5% discordance rate among bilateral TABs. However, among positive cases that underwent bilateral TABs, 40.8% were discordant between the two sides. Of the TAB positive cases, the median biopsy length was 2.475 cm, median sedimentation rate was 56 mm/hr, C-reactive protein 53.9 mg/L, and platelet count 341.5 K/ μ L. Variables correlated with a positive TAB were biopsy length, CRP, and jaw claudication.

Conclusions:

The overall discordance rates between sides was low, but was fairly high among positive TABs (40.8%), which suggests that it may be beneficial to do bilateral TABs in patients with a high pretest probability of GCA. TAB frozen sections have 82.5% sensitivity and 99.4% specificity for detecting vascular inflammation consistent with GCA. Based on these results, a negative frozen section result should not be relied upon to refute the diagnosis of GCA. However, if the frozen section is positive on the first TAB, a contralateral TAB is not required given the very low false positive rate.

References: Boyev et al., Efficacy of unilateral versus bilateral temporal artery biopsies for the diagnosis of giant cell arteritis, *Am J Ophthalmol*, 128, 211-5, 1999. Breuer et al., Association between histological features in temporal artery biopsies and clinical features of patients with giant cell arteritis, *Isr Med Assoc J*, 15, 271- 4, 2013. Frohman et al., New developments in giant cell arteritis, *Surv Ophthalmol*, 61, 400–421, 2016.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 238**Prognostic Value of the Neurological Pupil Index in Subarachnoid Hemorrhage (SAH) Patients: The FOTO-ICU Study**

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Introduction:

The neurological pupil index (NPI) provides a quantitative assessment of pupil reactivity and may have value as an early prognostic marker in patients with increased intracranial pressure (ICP), including those with SAH. This study aimed to explore associations between NPI and outcomes in SAH patients.

Methods:

This prospective study included 81 consecutive patients admitted to our neurosurgical ICU with acute SAH between 09/2014-07/2015. Age, sex, APACHE score, and respiratory failure were recorded at admission and NPI in each eye. Primary outcomes included death and poor clinical outcome (defined as inpatient death, care withdrawal or discharge Glasgow Outcome Score <4). Groups were compared using Fisher's exact test and predictive models developed with fast-and-frugal trees (FFT).

Results:

Fifty-three patients for whom all variables were available were included: 21 (40%) had poor clinical outcomes and 2 (4%) died. Univariate analysis found that only APACHE score ($p < 0.001$) and respiratory failure ($p = 0.04$) were significantly associated with poor clinical outcome. NPI in both eyes were lower among patients with poor clinical outcomes (mean 4.3 OD, 4.2 OS) versus those without (mean 4.5 OD, 4.5 OS), but neither was significant. However, the most accurate FFTs for death and poor clinical outcome included NPI after accounting for age in the death FFT and APACHE score in the poor outcome FFT (sensitivity (sn) = 100%, specificity (sp) = 94%, accuracy (ac) = 94% in a model for death using age of 39, NPI OS of 4.5 and NPI OD of 4.5; sn = 100%, sp = 50%, ac = 70% in a model for poor clinical outcome using APACHE score of 6, NPI OS 4.1 and NPI OD 4.2).

Conclusions:

Our study supports the NPI as a useful prognostic marker for poor outcomes in acute SAH after accounting for other common markers of poor outcome such as age and APACHE score.

References: 1. Natzedder et al. Portable Infrared Pupillometer in Patients with Subarachnoid Hemorrhage: Prognostic Value and Circadian Rhythm of the Neurological Pupil Index (NPI). J Neurosurg Anesthesiol. 2019 Oct;31(3):428-433. 2. Knaus WA, Draper EA, Wagner DP, et al. APACHE II: a severity of disease classification system. Crit Care Med. 1985;13(10):818-829.

Keywords: High intracranial pressure/headache, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 239**Diagnostic Agreement of Video Oculography and MRI for Internuclear Ophthalmoplegia in Multiple Sclerosis Patients**

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Introduction:

Internuclear ophthalmoplegia (INO) affects 20-30% of patients with multiple sclerosis (MS). There is no established gold-standard for diagnosing INO. Magnetic resonance imaging (MRI) is a widely used ancillary test for detecting lesions in the medial longitudinal fasciculus (MLF), yet not all patients with INO show such lesions. Early INO detection is important for disease subtyping, treatment and prognosis of MS. In one study(1), 71% of clinicians missed the diagnosis of subtle INO, that was otherwise detected using video oculography (VOG).

Methods:

We prospectively compared MRI (with a 3T scanner) and VOG in 66 MS patients and 28 healthy volunteers to evaluate their diagnostic agreement. The saccadic versional disconjugacy index (VDI, peak velocity ratio of abducting to adducting eye) was calculated for each patient and a cutoff (upper 95th percentile of normal) was defined for INO diagnosis(2). For each patient a concurrent MRI was reviewed by three experienced neuro-radiologists independently for findings suggestive of INO to calculate the inter-rater agreement. The consensus MRI score for INO was compared to the VDI for each patient.

Results:

Of the 66 patients, 35 tested negative for INO both on MRI and VOG. 14 patients tested positive on both tests. 17 cases had contradicting test results: 11 patients were INO-positive on VOG and INO-negative on MRI, and 6 patients were INO-positive on MRI and INO-negative on VOG. Compared to VOG, MRI had a positive percent agreement (PPA) of 56% and a negative percent agreement (NPA) of 85%. Conversely, VOG had a PPA of 70% and NPA of 76% compared to MRI.

Conclusions:

VOG was more sensitive for detecting INO than MRI. Consequently, a normal VOG is suitable to rule out INO, while a positive MRI is suitable to rule in INO with certainty. VOG is a simple, quick and non-invasive test to help diagnose INO.

References: 1) Frohman TC, Frohman EM, O'Suilleabhain P, Salter A, Dewey RB Jr. Accuracy of clinical detection of INO in MS: corroboration with quantitative infrared oculography. *Neurology*. 2003 Sep 23;61(6):848-50 2) Nij Bijvank JA, van Rijn LJ, Balk LJ, Tan HS, Uitdehaag BMJ. Diagnosing and quantifying a common deficit in multiple sclerosis: Internuclear ophthalmoplegia. *Neurology*. 2019 May 14;92(20):e2299-e2308

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Ocular motility, Demyelinating disease

Financial Disclosures: The authors had no disclosures.

Grant Support: This study was supported by the Frieda Magdalena Cattaruzza Foundation, Switzerland, the Albert Bruppacher foundation, Switzerland, the Swiss National Science Foundation [320030_166346] and the Uniscientia Stiftung, Liechtenstein.

Contact Information: None provided.

Poster 240**Role for OCT in detecting homonymous ganglion cell layer thinning in patients with demyelinating disease**

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Introduction:

Thinning in the ganglion cell layer + the inner plexiform layer (GCIPL) on optical coherence tomography (OCT) can be quantified and used as a proxy for neurodegeneration. Additionally, studies have demonstrated that lesions in the optic radiations can lead to a characteristic homonymous pattern of degeneration in the retina. It is unknown whether lesions in demyelinating diseases including multiple sclerosis (MS), neuro-myelitis optica (NMO) and anti-myelin oligodendrocyte glycoprotein syndrome (anti-MOG) lead to these patterns on OCT. This study's purpose was to identify homonymous patterns of GCIPL thinning in a demyelinating disease cohort.

Methods:

Participants in an ongoing collaborative study of visual outcomes underwent GCIPL analysis on OCT. Results from each eye were assessed by one rater qualitatively for pattern of loss (superior/inferior, nasal/temporal, or right/left upper/lower quadrant) and size of lesion (small/medium/large). Patterns across both eyes were assessed. Those with OCT thinning on same field in each eye consistent with homonymous hemianopia (HH), were noted and confirmed by another rater. In these patients brain MRI and medical record were examined to determine whether chiasmal or post-chiasmal lesions might account for the OCT findings. Healthy control subjects (n=42) were reviewed for comparison.

Results:

Five of 136 patients with demyelinating disease (age 41.9±12.2 years, median disease duration 5 (0-30) years, 72% female, and 121 MS, 14 NMO and 1 anti-MOG) had homonymous pattern of GCIPL thinning and lesions on MRI that could correlate with HH. One patient had a noted history of HH on visual field testing, one had an exam consistent with optic neuritis, two had no history of visual complaints or findings on exam, and one had subjective visual complaints, but no clear pattern of findings on exam. None of the healthy controls had a homonymous pattern of thinning.

Conclusions:

Posterior visual pathway lesions contribute minimally to visual dysfunction in demyelinating diseases.

References: None.

Keywords: Demyelinating disease, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 241**Calcification on Temporal Artery Biopsy: What to make of it?**

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Introduction:

Temporal artery calcification is an uncommon finding of unclear significance with respect to ocular ischemia (1,2). It may be reported as Mönckeberg's sclerosis, an age-related form of dystrophic calcification characterized by deposits in the tunica media, or as advanced atherosclerosis, particularly in patients with chronic kidney disease. There are case reports of vision loss attributed to calciphylaxis on temporal artery biopsy (TAB), and is a rare phenomenon in end stage renal disease (ESRD) characterized by precipitous arteriole calcium deposition typically presenting as skin necrosis (3). Our goals are to: 1) examine incidence of calcification in our cohort of TABs, 2) describe the characteristics of the calcifications and clinical presentation of these cases and 3) review the literature.

Methods:

We performed a retrospective chart review of all TABs performed at a single institution over 10 years (with available eye exams) and noted 10% (7/73) incidence of reported calcifications. We reviewed the pathology description of the calcifications and clinical presentations of these 7 cases and 5 additional cases shared by other authors.

Results:

Calcification was focal in 7 (mean/SD age: 81.5/6.6 years) and prominent/diffuse in 5 patients (mean/SD age: 72/10.9 years). 60 % with prominent calcifications had ESRD while only 1 patient with focal calcification had stage 3 renal disease. While 2 of the patients with focal calcifications had biopsy-positive giant cell arteritis (GCA), none of the patients with more extensive calcification showed biopsy evidence of GCA though one patient presented with pallid disc edema and ESRD similar to some cases in literature (4-6).

Conclusions:

Based upon our case series and review of literature, we conclude that in the absence of TAB positive for GCA and presence of extensive calcifications, presence of pallid disc edema in patients with ESRD can be a manifestation of calciphylaxis.

References: 1. BV Castillo, E Torczynski, DP Edward. Monckeberg's sclerosis in temporal artery biopsy specimens. British Journal of Ophthalmology. Volume 83, Issue 9. 2. Aznwar, E Zan, M Carone, A Ozturk, SM Sozio et al. Superficial temporal artery calcification in patients with end-stage renal disease: Association with vascular risk factors and ischemic cerebrovascular disease. Indian Journal of Radiology and Imaging. Vol 3, Pg 215-220. 3. Budisavljevic MN, Cheek D, Ploth DW. Calciphylaxis in chronic renal failure. Journal of the American Society of Nephrology. 1996;7(7):978-982. 4. S Farooqui, ASY Chan, JF Cullen, D Milea. Too Young to Undergo Temporal Artery Biopsy? Calciphylaxis-Related Anterior Ischemic Optic Neuropathy. Neuro-Ophthalmology. Vol 43, No. 4, 252-255, 2019. 5. Awwad ST, Ghosn S, Hogan RN. Calciphylaxis of the temporal artery masquerading as temporal arteritis. Clin Exp Ophthalmol. 2010;38:511-513. 6. Sivertsen MS, Strom EH, Endre KMA, Jorstad OK. Anterior ischemic optic neuropathy due to calciphylaxis. J Neuroophthalmol. 2018;38:54-56.

Keywords: Vascular disorders, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 242**Could the Nerve Fiber Layer Serve as a Biomarker of Gulf War Illness?**

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Introduction:

Gulf War Illness (GWI) is a multisystem disease with neurologic dysfunction affecting hundreds of thousands of veterans, but lacks readily available, non-invasive biomarkers to assist diagnosis. We explored optical coherence tomography (OCT) measurements as potential biomarkers for GWI without overt eye disease.

Methods:

We performed a retrospective case-control study consisting of patients who were active duty during the Gulf War Era (GWE; 1990-91) and were seen between November 18th, 2018 and April 18th, 2019 in an optometry clinic. Individuals were split into two groups: those with a diagnosis of GWI and those who served during the GWE who did not meet the Kansas criteria for GWI via phone interview (controls). Of 145 GWE veterans identified, 60 met criteria for GWI and 85 were controls. 66 individuals (28 GWI and 38 controls) with available OCT data and without retinal or optic nerve disease were included in the final OCT analysis. OCT imaging included macular, ganglion cell layer (GCL), retinal nerve fiber layer (RNFL), and optic nerve head measurements. Differences in means were analyzed using Student's t-test or Mann-Whitney U test, as appropriate. Predictors of GWI were analyzed using forward stepwise binary logistic regression and receiver operating characteristic (ROC). All reported p-values are two-tailed, and p<0.05 was considered statistically significant.

Results:

GWI had thinner RNFL and macular layers, except for GCL, which was thicker compared to controls. Average RNFL thickness (odds ratio; OR=0.95), average cup-to-disc ratio (OR=0.005), age (OR=0.822), and post-traumatic stress disorder (OR=20.5) were significant predictors of a GWI diagnosis and these parameters explained 80% of the variability of a GWI diagnosis (area under the curve=0.8).

Conclusions:

Veterans with GWI tended to have thinner RNFL and macular layers, but a thicker GCL compared to controls. RNFL thinning was predictive of a GWI diagnosis and may serve as a biomarker for disease.

References: None.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Neuro-opth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: Supported by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Clinical Sciences Research EPID-006-15S (Dr. Galor), R01EY026174 (Dr. Galor), NIH Center Core Grant P30EY014801 and Research to Prevent Blindness Unrestricted Grant.

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Poster 243**Baseline Near Point of Convergence and Concussion Test Scores in a Cohort of Athletes**

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Introduction:

Sports-related concussions can impair many brain functions, including vision, cognition, and memory. Concussion has also been associated with an abnormal near point of convergence (NPC). The SCAT-3 (Sport Concussion Assessment Tool, 3rd edition) and MULES (Mobile Universal Lexicon Evaluation System), a picture-based rapid automatized naming (RAN) test, are effective in detecting sports-related concussions. However, less is known about the role of the SUN (Staggered Uneven Number) test, a number-based RAN test, and NPC in concussion diagnosis as well as the relationship between concussion tests and NPC. Our aim was to establish baseline NPC and concussion test scores for collegiate and professional athletes and to compare these test values with each other.

Methods:

We performed a cross-sectional study where we measured NPC and administered the SCAT 3, MULES, and SUN to 69 collegiate/professional athletes without concussion. The tests within the SCAT-3 include the SAC (Standardized Assessment of Concussion), mBESS (Modified Balance Error Scoring System), and the TTG (Timed Tandem Gait). Baseline scores were recorded and associations between scores and NPC were evaluated.

Results:

Among 69 athletes aged 18-24, on average, total SAC score was 26.1 ± 2.3 s, best trial time for the TTG was 12.6 ± 2.3 s, total mBESS was 11.1 ± 4.482 s, best MULES time and errors were 38.0 s and 0.77, respectively, and best SUN time and errors were 49.5 s and 1.7, respectively. Average NPC was found to be 1.4 ± 1.5 cm. Further, increased NPC distance was associated with a lower MULES time ($p=0.03$, linear regression).

Conclusions:

This study establishes baseline values of NPC, SCAT3, and RAN test scores for collegiate and professional athletes without concussion. NPC was found to only correlate with MULES test scores. Future studies comparing baseline with post-concussion values will help determine if NPC and newer tests such as the SUN can facilitate concussion evaluation.

References: None.

Keywords: Ocular motility, Vestibular, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 244**Analysis of Rapid Sideline Tests and Mechanism of Injury from a Multidisciplinary Concussion Center Registry**

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Introduction:

According to the CDC, TBI-related injuries contributed to approximately 2.5 million emergency department visits, hospitalizations, and deaths in the United States. Although TBIs are associated with sports, many cases result from motor vehicle accidents (MVA), suicide attempts, and falls. Currently the SCAT-3 (Sport Concussion Assessment Tool) is used to assess sports-related concussions on the sideline. Not a lot is known, however, regarding the validity of SCAT-3 in the context of non-sports concussions. We aim to determine the most common cause of concussion seen at the center; if test scores correlate; and if the cause of concussion affects scores.

Methods:

We performed a cross-sectional observational study and administered the SCAT-3 to 754 patients (6-86 years old) with a concussion who received care at the center. The tests within the SCAT-3 include the SAC (Standardized Assessment of Concussion); mBESS (Modified Balance Error Scoring System); and the TTG (Timed Tandem Gait). Patient age, accident etiology, MULES test performance, and consequences from TBI were evaluated in relation to SCAT-3 outcome measures.

Results:

Participants sustained concussions due to sports (24.9%); falls (26.7%); MVA (20.0%); and trauma (31.6%).

Trauma and assault were associated with a lower SAC total score when controlling for age. Fall, trauma, MVA, and helmeted sports demonstrated higher mBESS scores. Only falls show association with longer tandem gait times.

One of the most common referrals generated at the center was vision/occupational therapy, representing 22% of all referrals.

Longer MULES times and errors were associated with lower (worse) SAC total scores; higher (worse) mBESS scores; and longer (worse) TTG times.

Conclusions:

This study demonstrates that falls and trauma-related concussions are seen more commonly than sports related concussions at the center. In addition, it shows the importance of visual referrals for a concussed patient, and the relationship between our visual concussion tests, MULES, and parts of SCAT-3.

References: None.

Keywords: Miscellaneous, Vestibular, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 245**Neuro-Ophthalmic Manifestations of Acute Leukemia**

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Introduction:

Ophthalmic involvement in acute leukemia is common, with 36% of patients having ophthalmic involvement at the time of diagnosis. However, neuro-ophthalmic involvement is relatively rare. We present a comprehensive characterization of neuro-ophthalmic findings in patients with acute leukemia.

Methods:

This is a retrospective review of cases of acute leukemia with central nervous system involvement and neuro-ophthalmic manifestations that presented from January 2013 to September 2019 to a tertiary care facility. Data collected included demographic information; leukemia details; diagnostic testing; and details regarding associated neuro-ophthalmic manifestations.

Results:

Twelve patients with mean age 42 years (range 12-65, median 39) were included. 7 (58%) patients were male, and 5 (42%) were female. Eight (67%) were diagnosed with AML, and 4 (33%) with ALL. Neuro-ophthalmic findings included 4 patients with isolated sixth nerve palsies, 2 with multiple cranial nerve palsies, 2 with orbital lesions with proptosis, 4 with optic disc swelling, and 1 with isolated fourth nerve palsy. Five (42%) neuro-ophthalmic presentations were associated with known CNS disease, 3 (25%) were associated with active disease but heralded the discovery of CNS involvement, 3 (25%) were the presenting features of relapse, and 1 (8%) led to the original leukemia diagnosis. Neuroimaging showed 4 with leptomeningeal enhancement, 4 with cranial nerve enhancement/thickening, 3 with optic nerve/sheath enhancement, 1 with bony lytic lesion, 1 with soft tissue mass, and 1 with cytotoxic brain edema. One case had normal neuroimaging. Overall, patients had a poor prognosis, with 6 passing away from leukemia or its complications and only 1 obtaining a sustained remission.

Conclusions:

Neuro-ophthalmic manifestations of leukemia may occur as presenting features of diagnosis, relapse, or CNS involvement, and portend a poor prognosis. Neuro-ophthalmologists should be familiar with potential neuro-ophthalmic presentations of acute leukemia to avoid delayed diagnosis of primary disease, relapse, or CNS involvement.

References: None.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 246**Do Unrecognized Neurodegenerative Diseases Impact Age-Related Eye Disease Research Outcome Measures?**

Yosbelkys Martin Paez¹, Anne Lynch¹, Tara Churney¹, Jennifer Patnaik¹, Maria Jasso¹, Prem Subramanian¹, Naresh Mandava¹, Samantha Holden², Victoria Pelak¹

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Introduction:

Age-related neurodegenerative diseases (NDDs) that lead to dementia, such as Alzheimer's disease, Parkinson's disease, and Lewy Body Dementia, result in retinal degeneration and brain-related visual dysfunction. Given that recognition of dementia-related NDDs, a significant portion of participants in age-related eye disease studies could harbor an undiagnosed NDD that impacts retinal OCT and visual quality of life measures. Our long-term goal is to determine whether screening for NDDs and controlling for NDD-associated retinal and visual quality of life changes is necessary in age-related eye disease research. The objective of this pilot study is to investigate the relationship between NDD screening measures and retinal OCT and visual quality of life measures in a control cohort within an age-related macular degeneration (AMD) registry.

Methods:

In this ongoing cross-sectional study, up to 50 controls enrolled in the Colorado AMD Registry are being screened for NDDs with a neurologic examination, the Montreal Cognitive Assessment (MoCA), the Colorado Parkinsonian Checklist (CPC), and the Lewy Body Composite Risk Score (LBCRS). Inner retinal macular OCT thickness and Visual Function Questionnaire-25 scores will be correlated to MoCA, CPC, and LBCRS results using Spearman rank-order correlation.

Results:

To date, we have enrolled 8 subjects (6 women) with a mean age of 70.6 and the following average scores: MoCA 26.4 (max of 30), CPC 0.125 (max of 11), LBCRS 0.125 (max of 10), and VFQ-25 96.8 (max of 100). Preliminary correlation analysis will occur after 25 patients are enrolled. Two subjects (25%) screened positive for previously unrecognized and significant cognitive impairment.

Conclusions:

Estimates of dementia-related NDDs are consistent with our preliminary screening results. This study has the potential to provide important insights into the impact of undiagnosed NDDs on outcome measures in age-related eye disease research, as well as provide an embedded method for earlier detection of dementia in aging research participants.

References: 1. Pelak VS. Visual disturbances in cortical degenerative disorders. *Expert Review Ophthalmol.* 2009;4(3):283-297. 2. Pelak VS, Hills W. Vision in Alzheimer's disease: a focus on the anterior afferent pathway. *Neurodegener Dis Manag.* 2018;8(1):49-67. 3. Blanks JC, Hinton DR, Sadun AA, Miller CA. Retinal ganglion cell degeneration in Alzheimer's disease. *Brain Res.* 1989;501(2):364-372. 4. den Haan J, Verbraak FD, Visser PJ, Bouwman FH. Retinal thickness in Alzheimer's disease: A systematic review and meta-analysis. *Alzheimers Dement (Amst).* 2017;6:162-170. 5. Prince M, Bryce R, Ferri C. World Alzheimer's Report 2011: The Benefits of Early Diagnosis and Intervention. *Alzheimer's Disease International.* 2011.

Keywords: Miscellaneous

Financial Disclosures: Funded by Fight For Sight - NANOS Research Award.

Grant Support: Funded by Fight For Sight/NANOS research grant.

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Poster 247**Neuro-ophthalmic Manifestations of Checkpoint Inhibitors**

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Introduction:

Checkpoint inhibitors, such as ipilimumab, nivolumab, and pembrolizumab, have been reported to cause ophthalmic adverse events. While myasthenia gravis induced by these medications has been previously documented, other neuro-ophthalmic manifestations have been rarely reported. This study aims to identify those rarer manifestations.

Methods:

A retrospective chart review of patients on checkpoint inhibitors who developed neuro-ophthalmic adverse events was undertaken. Visual acuity, color vision, pupillary reactivity, slit lamp and fundus examination, as well as ophthalmic imaging modalities (visual fields, optical coherence tomography, etc) were analyzed.

Results:

Five patients were identified with neuro-ophthalmic manifestations, three of which carried a melanoma diagnosis. Four patients were treated with combination therapy of ipilimumab and nivolumab. Optic neuritis was present in 3 patients, ocular myasthenia in 2 patients, and giant cell like vasculitis in 1 patient. One optic neuritis patient and one ocular myasthenia gravis patient had been previously reported.¹ Treatment modalities included intravenous immunoglobulins, topical and oral steroids and resulted in resolution in all patients.

Conclusions:

Neuro-ophthalmic manifestations including optic neuritis and giant cell like vasculitis can occur following use of checkpoint inhibitors.

References: 1. Kim, J., Materin, M., Sznol, M., et al. Ophthalmic Immune-Related Adverse Events of Immunotherapy: A Single Site Case Series. *Ophthalmology*. 2019; 126: 1058-1062.

Keywords: Chemotherapy and radiation injury, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 248**Validity of Forced eyelid closure test (FECT) in Africans- a pilot study**

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Introduction:

The validity of forced eyelid closure test (FECT) as a clinical screening test to aid in the diagnosis of myasthenia gravis has never been documented in Africans. We plan to evaluate the sensitivity and specificity of FECT compared with Cogan's Lid Twitch (CLT) and benchmark them to clinical and serologic diagnosis.

Methods:

All patients presenting with ptosis and/or diplopia at the University of Abuja Teaching Hospital Gwagwalada, Nigeria will be evaluated with FECT and CLT. Their final diagnosis, based on clinical and serologic findings, will be recorded. To perform FECT, the patient is asked to squeeze the eyelids shut for 5-10 seconds, then open quickly and fixate in primary position. The excessive upward overshoot of eyelids movement indicates a positive FECT. A Neuro-ophthalmologist will be performing the tests and evaluating the patient with regards to the eventual diagnosis.

Results:

We present the preliminary data of 3 patients, seen between September 2019 and October 2019, who had a final clinical diagnosis of ocular myasthenia gravis. All 3 were seropositive for anti- acetylcholine receptor antibodies. All three had positive FECT as well as CLT.

Conclusions:

FECT is a simple clinical screening test that appears to perform at least as well as CLT in the diagnosis of myasthenia gravis. We will continue to recruit more patients to establish its sensitivity and specificity for ocular and generalized myasthenia gravis; and its utility in differentiating from other conditions that present with ptosis and diplopia.

References: Apinyawasisuk, Supanut MD; Zhou, Xinkai MS; Tian, Jack J.; Garcia; Karanjia, Rustum MD, PhD; Sadun, Alfredo A. MD, PhD, Validity of Forced Eyelid Closure Test A Novel Clinical Screening Test for Ocular Myasthenia Gravis, Journal of Neuro-Ophthalmology, Volume 37, p253-257, 2017

Keywords: Myasthenia, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 249**Altered resting-state functional connectivity in Wernicke's encephalopathy with vestibular impairment**

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Introduction:

To reveal the neural basis of Wernicke's encephalopathy (WE) with impaired vestibulo-ocular reflex (VOR), we evaluated resting-state functional connectivity (rs-fc) in the vestibular processing brain regions.

Methods:

Rs-fc between the vestibular regions and the rest of the brain were compared with neurotological features including the head-impulse tests (vHIT) and caloric responses in patients with WE (n=5, mean age 53.4 ± 10 years) and healthy controls (n=20, mean age 55.0 ± 9.2 years). Rs-fc analyses employed a region of interest (ROI)-based approach using regions selected a priori that participate in vestibular processing including the cerebellar vermis, insula, parietal operculum, and calcarine cortex.

Results:

The main neurologic findings for patients with WE were mental changes; gait ataxia; spontaneous and gaze-evoked nystagmus (GEN); and bilaterally positive HIT for the horizontal canals. Video HIT documented bilateral horizontal canal dysfunction with decreased gain and corrective saccades. Caloric irrigation and rotation chair testing revealed prominent bilateral horizontal canal paresis. Patients with WE also had decreased spatial memory, which substantially recovered after treatments. Functional connections at the predefined seed regions, including the insular cortex and parietal operculum, were attenuated in the WE group compared to healthy controls.

Conclusions:

WE is related to impaired VOR and visuospatial dysfunction, and fMRI documented changes in the rs-fc of multisensory vestibular processing regions including the insula, parietal operculum, and superior temporal gyrus, which participate in integration of vestibular perception.

References: None.

Keywords: Vestibular, Magnetic resonance imaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 250**Neuro-anatomical correlates of post-stroke positive perceptual phenomena**

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Introduction:

Stroke and other brain lesions produce not only deficits but through the disconnection of various cerebral structures also positive phenomena like hallucinosis or dysmorphopsia. Herein, we studied the neuroanatomical correlate of brain hallucinosis or dysmorphopsia in patients with ischaemic brain lesion.

Methods:

7 patients with acute stroke that experienced hallucinosis or dysmorphopsia were clinically assessed. DWI sequence of the clinical MRI was used to manually extract masks of the brain lesions. Scans were registered on the ICBM152 template of the Montreal Neurological Institute, available with the MRICron software. Disconnectome maps were computed with the 'disconnectome map' tool of the BCBToolkit software.

Results:

Using advanced structural neuroimaging methods, we identified different neural systems that are likely involved in the development of hallucinosis and dysmorphopsia when disconnected or directly damaged.

Conclusions:

Identification of neural networks involved in the pathogenesis of hallucinosis and dysmorphopsia developed in patients with acute stroke represents a step forward in the global comprehensions of these phenomena.

References: 1. Moro, V., Pernigo, S., Tsakiris, M., Avesani, R., Edelstyn, N. M., Jenkinson, P. M., & Fotopoulou, A. (2016). Motor versus body awareness: voxel-based lesion analysis in anosognosia for hemiplegia and somatoparaphrenia following right hemisphere stroke. *Cortex*, 83, 62-77. 2. Foulon, C., Cerliani, L., Kinkingnehun, S., Levy, R., Rosso, C., Urbanski, M., ... & Thiebaut de Schotten, M. (2018). Advanced lesion symptom mapping analyses and implementation as BCBtoolkit. *GigaScience*, 7(3), giy004.

Keywords: Higher visual cortical functions, Neuroimaging, Stroke trauma, Higher visual functions

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 251**The Clinical Utility of Optical Coherence Tomography in a Multiple Sclerosis Practice: A Retrospective Analysis**

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Introduction:

Optical Coherence Tomography (OCT) is becoming an increasingly utilized technology to assist in the diagnosis of demyelinating disorders, and offers a reliable way to quantify retinal tissue. While it is increasingly being advocated for as a component for the diagnostic criteria of demyelinating disease, the prevalence of incidentally found co-morbid ophthalmological disease seems underreported.

Methods:

A retrospective analysis was performed on new patients who had OCT performed as part of the evaluation at a tertiary referral center in the last year. Patients whose OCT did not fulfill at least 5 of the 7 OSCAR-IB criteria were excluded, and each patient's clinical diagnosis, reported history, and OCT results were reviewed. Optic neuropathy was defined as previously indicated the literature or as a structural abnormality with supporting clinical history, such as history of bilateral optic neuritis with greater than expected retinal nerve fiber layer thinning compared to an age-matched control.

Results:

In our cohort of patients, nearly 50% of patients with a reported history of unilateral optic neuritis (ON) fit criteria for bilateral optic neuritis. At the same time, of the entire cohort reporting unilateral optic neuritis, roughly 30% did not fit structural criteria for optic neuropathy. Nearly 20% of the patients reporting no history of optic neuritis fit structural criteria for optic neuropathy. Of the patients reporting a history of ON, 20% offered a different diagnosis, with virtually 20% of these patients having a separate, intervenable diagnosis.

Conclusions:

OCT not only offers data in corroborating the history in the diagnosis of demyelinating disorders but also can provide an alternative diagnosis in many patients. Independent of this OCT detects separate ophthalmological disease in a significant portion of patients and offers other avenues to preserve vision. OCT can be considered an effective tool in the evaluation of the patient with demyelinating disease.

References: None.

Keywords: Optic neuropathy, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Demyelinating disease, Orbit/ocular pathology, Pupils retina

Financial Disclosures: The authors had no disclosures.

Grant Support: National Multiple Sclerosis Society; Physician Scientist Training Program

Contact Information: None provided.

Poster 252**Neuro-Ophthalmic Manifestations of Sarcoidosis**

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Introduction:

Sarcoidosis is an idiopathic, multisystem disease, characterized pathologically by noncaseating granulomatous inflammation. Clinically, central nervous system involvement is present in 5-15% of sarcoidosis cases, with about one-third of these having neuro-ophthalmic manifestations.

Methods:

We performed a retrospective chart review of cases of biopsy-proven sarcoidosis with neuro-ophthalmic manifestations seen at our tertiary care facility from January 2013 to September 2019.

Results:

22 cases were included. 15 patients identified as black and 7 as white. 15 were female, and 7 male. Mean age at sarcoidosis diagnosis was 46 years (range 26-66). Neuro-ophthalmic findings included optic neuropathy in 11; proptosis/orbital inflammation in 5; abducens nerve palsy in 5; trochlear nerve palsy, trigeminal distribution numbness, and bitemporal hemianopia in 2 each; and oculomotor nerve palsy, facial palsy, optic perineuritis, dorsal midbrain syndrome, central vestibular nystagmus, and papilledema in 1 each. Neuroimaging was abnormal in all but 1 case. In 8 cases (36%), the diagnosis of sarcoidosis already was established at the time of presentation with a neuro-ophthalmic finding; however, in 14 cases (64%), the neuro-ophthalmic manifestation was the presenting feature that led to further evaluation and the sarcoidosis diagnosis. Diagnostic work up in patients without known sarcoidosis at the time of neuro-ophthalmic presentation demonstrated that all 7 tested for ACE were negative, 75% of the 12 who had CT chest had findings suggestive of sarcoidosis (86% of black patients versus 50% of white patients), and 50% of the 10 who had lumbar puncture had elevated monocytes and 60% had high protein.

Conclusions:

Patients with neurosarcoidosis may present initially with a neuro-ophthalmic manifestation. Serum testing for ACE is not helpful in the evaluation of a neuro-ophthalmic presentation of sarcoidosis. CT chest may be more helpful for diagnosis in black than in white patients.

References: None.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 253**Clinical and radiological findings in patients with traumatic optic neuropathy: a case series**

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Introduction:

Traumatic optic neuropathy is a well-recognised consequence of head trauma and frequently results in significant irreversible loss of vision. Previous reports have suggested that up to 10% of patients with craniofacial fractures have traumatic optic neuropathy. Corticosteroids and orbital decompression have previously been advocated as treatment options, although studies have previously shown no significant improvement in visual outcome with steroids and some studies have suggested that steroids may result in increased mortality. There is limited understanding of the exact pathophysiology of traumatic optic neuropathy and of the correlation between injury mechanism, anatomical location and final visual outcome.

Methods:

We present results of a recent case series of traumatic optic neuropathy in 14 eyes in 13 adult patients who presented to our institution between October 2016 and May 2019. Mean patient age at presentation was 40 years (17-65 years). All patients were seen in a subspecialty neuro-ophthalmology clinic following referral from trauma services. We present results of the visual assessment and looked for any association with the mechanism of injury and anatomical location.

Results:

In keeping with previous findings final visual outcome was frequently poor with limited improvement from time of first presentation. Final logmar visual acuity ranged from 0.00 to NPL. 4 of the 13 eyes (30.8%) had a final visual acuity of CF or worse. Mean logmar visual acuity in those with better than CF VA was 0.61. Patients with better visual acuity typically had altitudinal field defects only. RAPD and disc pallor correlated with poor final visual acuity. OCT demonstrated reduced RNFL thickness on follow up with mean thickness of 66.4µm (±29.6).

Conclusions:

Our case series demonstrates that traumatic optic neuropathy is primarily a condition which affects a working age population. Visual outcomes vary significantly between patients and more investigation is needed to stratify patients more likely to have poorer outcomes.

References: Kanamori A, Nakamura M, Yamada Y, Negi A. Longitudinal Study of Retinal Nerve Fiber Layer Thickness and Ganglion Cell Complex in Traumatic Optic Neuropathy. Arch Ophthalmol. 2012;130(8):1067–1069. Lee JY, Cho K, Park KA, Oh SY. Analysis of Retinal Layer Thicknesses and Their Clinical Correlation in Patients with Traumatic Optic Neuropathy. PLoS One. 2016;11(6):e0157388. Yan W, Chen Y, Qian Z, Selva D, Pelaez D, Tu Y, Wu W. Incidence of optic canal fracture in the traumatic optic neuropathy and its effect on the visual outcome. Br J Ophthalmol. 2017 Mar;101(3):261-267. Sosin M, De La Cruz C, Munding GS, Saadat SY, Nam AJ, Manson PN, Christy MR, Bojovic B, Rodriguez ED. Treatment Outcomes following Traumatic Optic Neuropathy. Plast Reconstr Surg. 2016 Jan;137(1):231-8.

Keywords: Optic nerve trauma and treatment, Neuroimaging, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: Clinical and radiological findings in patients with traumatic optic neuropathy: a case series

Contact Information: gabriella.guevara@nhs.net

Poster 254**Ocular Myasthenia Gravis: AChR seropositivity and generalization.**

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Introduction:

Ocular Myasthenia Gravis (OMG) is an autoimmune disorder of the neuromuscular junction characterized by fatigable weakness of extraocular muscles, levator palpebrae, and orbicularis oculi resulting in fatigable ptosis and binocular diplopia. The predominant auto-antibodies in Myasthenia Gravis are, among others, those against acetylcholine receptors. Multiple studies reported a seropositivity between 40% and 60% for OMG. Some patients may develop weakness in their limbs, bulbar or respiratory muscles, that is, Generalized Myasthenia Gravis (GMG). The purpose of this study is to report the frequency of Acetylcholine Receptor Antibody (AChR) seropositivity in patients with clinical suspicion of OMG and the percentage of these patients who developed GMG during the follow up.

Methods:

Retrospective, observational study of all patients diagnosed with OMG at the Neuro-Ophthalmology Section of two Public Hospital from Buenos Aires, Argentina.

Results:

A total of 79 medical records of patients with OMG were review. Twenty patients were excluded due to insufficient data. Fifty-nine patients were included: 31 (53%) were women. The mean age at onset was $52 \pm 16,78$ years. Seven (12%) patients had concomitant thyroid disease, another 12% had other autoimmune diseases.

ACRA was found positive in 24 patients (40,68%), 20% of them converted to GMG, only one ACRA seronegative patient developed GMG. Among 59 patients, 6 (10%) developed GMG, ACRA was positive in 83% of them, against 35% of those who did not develop GMG. There was no positive correlation between autoimmune comorbidities, thymic abnormalities, treatment and GMG development. Males were more likely to convert to GMG. The mean conversion time was 12 months.

Conclusions:

Our study reveals a lower AChR seropositivity in OMG as well as a lower conversion rate to GMG, compared with the consulted literature. In our review, males developed GMG more often than women, and there was no association between generalization and comorbidities.

References: 1. Wong SH, Huda S, vicent A, Plant GT. Ocular myasthenia gravis: controversies and updates. Curr Neurol Neurosci Rep. 2014;14:421. 2. Wong SH, Plant GT. Ocular myasthenia gravis: Toward a risk of generalization score and sample size calculation for a randomized controlled trial of disease modification. J Neuro-Ophthalmology 2016;36:252-258. 3. Huang Gz, Lo YL. Correlation between acetylcholine receptor antibody levels and thymic pathology in myasthenia gravis: a review. J Clin Neuromuscul Dis. 2013;14:209-217. 4. Kerty E, Elsaia A, Argov Z, Evoli A, Gihus NE. EFNS/ENS Guidelines for the treatment of ocular myasthenia gravis. J Am Me Assoc. 1953;153:529-532. 5. Nagappa M, et al. Autoantibodies in acquired myasthenia gravis: Clinical phenotype and immunological correlation. Acta Neurol Scand, 2019. 139(5):855-90

Keywords: Myasthenia, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 255**Comparing SS-OCT-A and FA in detection of choroidal perfusion defects in GCA**

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Introduction:

Peripapillary choroidal filling delay demonstrated by dye-based angiography is well recognized as a non-specific but suggestive finding of giant cell arteritis (GCA). Optical coherence tomographic angiography (OCT-A) has been studied as a non-invasive alternative for vasculature imaging in GCA. We previously reported cases in which spectral domain OCT-A was unable to detect the choroidal nonperfusion seen on fluorescein angiography (FA). Herein, we aimed to determine whether swept source OCT-A (SS-OCT-A), with improved resolution of deeper retinal and choroidal vessels, is capable of demonstrating choroidal perfusion abnormalities.

Methods:

This is an observational case series in which patients with visual loss secondary to GCA were enrolled at a single tertiary care neuro-ophthalmology practice at the time of initial presentation. En face SS-OCT-A (DRI OCT Triton, Topcon, Tokyo, Japan) and FA centered on the macula were obtained at presentation. SS-OCT-A was segmented in slabs corresponding to the superficial and deep retinal capillary plexuses and the choriocapillaris. All images were then qualitatively analyzed for perfusion abnormalities and compared with FA. Scans with severe artifacts or poor signal were discarded.

Results:

Six eyes of 3 patients with bilateral AAION from GCA had SS-OCT-A of adequate quality for inclusion and analysis. Four eyes demonstrated macular choroidal perfusion defects on FA, with decrease in choriocapillaris flow on SS-OCT-A in an identical geographic distribution. In 2 of these cases, we observed dilation of the corresponding overlying area of deep retinal capillary plexus, which may represent a compensatory change to deeper ischemia. In the 2 eyes with no perfusion defects on FA, no abnormalities were seen on SS-OCT-A.

Conclusions:

This case series suggests comparability between FA and SS-OCT-A in visualization of choroidal perfusion defects from GCA, and highlights the utility of SS-OCT-A as a noninvasive adjunctive study and potential alternative to FA in diagnostic evaluation of the disease.

References: None.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Vascular disorders, Pupils retina

Financial Disclosures: The authors had no disclosures.

Grant Support: EDG: NIH K08 EY030164

Contact Information: None provided.

Poster 256**Microvascular Changes in Wolfram syndrome**

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Introduction:

Wolfram syndrome (WS) is a rare autosomal recessive progressive neurodegenerative disease. The purpose of this work is to evaluate systemic, genetic and ophthalmic characteristics, including optical coherence tomography angiography (OCTA) measurements of capillary network vessel density (VD), in patients with WS.

Methods:

In total, 9 patients with WS underwent systemic, ophthalmic and genetic analyses and compared with healthy controls.

Results:

Three families were included. The mean age of the subjects was 31.4 ± 7.7 years, of which 2 (22.2%) were male. All patients who underwent genetic analysis had mutations in the WFS1 gene. The best-corrected visual acuity (BCVA) ranged from light perception to 0.1 logMar, with a mean of 1.22 logMar. There was a severe decrease in the average retinal nerve fiber layer and macular ganglion cell-inner plexiform layer (GCIPL) thicknesses (49.9 and 57.5 μm , respectively). OCTA analysis of the optic nerve showed significantly lower whole-image, inside disk, and peripapillary VD in the patients with Wolfram syndrome than in the healthy controls ($p < 0.001$ for all). In the parafoveal region, the vessel length density was significantly lower at WS patients ($p < 0.001$). In the sectorial analysis, vascular changes remained significant in the parafoveal nasal, inferior and superior regions. A comparison of ophthalmic characteristics highlighted the significant decrease in the mean macular GCIPL thickness in patients with BCVA more than 1 logMar compared to those with BCVA less than 1 logMar ($p = 0.001$). However, there were no statistically significant differences in others variables in the OCTA parameter densities between these groups.

Conclusions:

OCTA is a novel imaging tool that provides critical vascular information despite being a non-invasive technique. Significant microvascular changes in the optic nerve head, peripapillary retinal blood supply and vessel length density in the parafoveal region can occur in the patients with WS.

References: Ustaoglu, M., Onder, F., Karapapak, M., Taslidere, H. and Guven, D. Ophthalmic, systemic, and genetic characteristics of patients with Wolfram syndrome. *European Journal of Ophthalmology*, (2019).

Keywords: Genetic Disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 257**Self-paced Saccades in Patients with Concussion**

Neda Anssari¹, Behzad Mansouri², Alexandra Santos¹, Jonathan Chung³, Kailin Hong⁴, Runjie Shi⁴, Foad Taghdiri⁴, Tharshini Chandra¹, Mark Bayley¹, Danielle Porplycia¹, Steven Friedman¹, Moshe Eizenman⁵, Maria Tartaglia¹

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Introduction:

Currently there are no diagnostic measures that can predict which patients with concussion will develop post-concussion syndrome (PCS). In a previous study we showed that higher symptom burden and alterations in white-matter integrity are associated with impairment in the control of self-paced saccades in patients with PCS. Previous studies suggest that this impairment will improve over a short time period in some PCS patients but some will continue to demonstrate eye movement abnormalities. Identifying patients with sustained impairment to their eye movements including self-paced control system can help predict those patients that will develop PCS.

Methods:

We investigate several attributes of a variety of eye movements with an Visual Attention Scanning technology (VAST, EL-MAR Inc.) and obtain Rivermead scores in concussion patients within seven, thirty, ninety and one hundred eighty days after concussion.

Results:

The study is ongoing. To date, the preliminary results in four patients, showed a significant increase in the number of self-paced saccades ($\pm 10^\circ$) in 60 seconds between first seven and thirty days after concussion (paired t-test, $p=0.0024$). When the results from each patient was analyzed separately, there were significant increases in the number of self-paced saccades in three out of four patients. All four patients had some improvement in Rivermead score.

Conclusions:

Our preliminary results are consistent with the hypothesis that control of self-paced saccades improves in most patients within 1 month after concussion. This study includes measurements of a variety of other eye-movement parameters (VOR, smooth-pursuit). We will repeat the tests at 3 and 6 months after concussion to determine the utility of a self-paced saccade measure (or other measures) as a prognostic test for PCS.

References: None.**Keywords:** Ocular motility, Miscellaneous**Financial Disclosures:** The authors had no disclosures.**Grant Support:** None.**Contact Information:** neda.anssari@uhn.ca, 2048915371, 50 Southvale drive, East York, ON

Poster 258**Systemic Treatment of Herpes Zoster Ophthalmoplegia: A Case Report and Case-based Meta-Analysis**

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Introduction:

The role of systemic steroids in the treatment of herpes zoster (HZ) ophthalmoplegia is controversial. We present a case of HZ ophthalmoplegia with close follow-up examination during extended treatment course with oral prednisone taper and valacyclovir. We then provide a meta-analysis on published cases of HZ ophthalmoplegia, reviewing outcomes with systemic antiviral and steroid therapy.

Methods:

An 88-year-old female developed HZ ophthalmicus and two days later developed blepharoptosis and ophthalmoplegia consistent with a third nerve palsy. We collected follow up data regarding her efferent exam during treatment with systemic steroids and antiviral therapy over 4 months.

We performed a literature review of published cases of HZ ophthalmoplegia by searching Pubmed and Google-Scholar, which elicited 51 cases (11 cases were excluded due to incomplete follow up data). The association between systemic steroid duration and ophthalmoplegia recovery was analyzed using Fisher's exact test. Other findings such as visual acuity, pupillary defects, and optic neuropathy were presented as descriptive results due to limited available information in cases reviewed.

Results:

40 reported cases and the present case were divided into short-term treatment groups (≤ 2 weeks; $n=19$) and long-term treatment groups (≥ 3 weeks; $n=22$) with a binary, primary outcome of complete resolution of ophthalmoplegia. Fisher's exact test comparing treatment length (short vs. long) and resolution rate showed longer treatment is associated with better resolution rate. Similarly, a 3-way split of treatment length with Chi-square test showed a significant difference in resolution rate based on treatment length, $\chi^2(2, N=41) = 7.107, p=0.0286$. Finally, it was noted that the recovery rate for patients who received any systemic steroid was 37% (11/30), whereas recovery rate for patients without steroid treatment was 9% (1/11).

Conclusions:

Our meta-analysis suggests that extended steroid taper is effective in aiding the recovery for ophthalmoplegia secondary to HZ and should be considered early on in the management of these cases.

References: 1. Liesegang TJ. Herpes Zoster Ophthalmicus. Natural History, Risk Factors, Clinical Presentation, and Morbidity. *Ophthalmology*. 2008;115(2 SUPPL.):3-12. doi:10.1016/j.ophtha.2007.10.009 2. Sanjay S, Chan EWE, Gopal L, Hegde SR, Chang BCM. Complete unilateral ophthalmoplegia in herpes zoster ophthalmicus. *J Neuro-Ophthalmology*. 2009;29(4):325-337. doi:10.1097/WNO.0b013e3181c2d07e 3. Im M, Kim BJ, Seo YJ, Park JK, Lee JH. Complete ophthalmoplegia after herpes zoster. *Clin Exp Dermatol*. 2007;32(2):162-164. doi:10.1111/j.1365-2230.2006.02296.x 4. Rapuano C, Heng W. Cornea. In: *Color Atlas & Synopsis of Clinical Ophthalmology (Wills Eye Hospital)*: McGraw-Hill. ; 2003:171-174. 5. Al-Abdulla NA, Kelley JS, Green WR, Miller NR. Herpes Zoster Vasculitis Presenting As Giant Cell Arteritis With Bilateral Internuclear Ophthalmoplegia. *Am J Ophthalmol*. 2002;134(6):912-914. doi:10.1097/00006982-200308000-00027

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 259**The Prevalence and Diagnostic Utility of Binding, Blocking, and Modulating Antibodies in Ocular Myasthenia**

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Introduction:

Myasthenia gravis (MG) is characterized by the presence of auto-antibodies against the acetylcholine receptor (AChR). One can test for several types of AChR antibodies to make a successful MG diagnosis. This study aimed to examine whether antibody testing can be streamlined to what is crucial for diagnosis and whether prednisone and/or pyridostigmine were correlated with conversion from ocular to systemic MG.

Methods:

A retrospective chart analysis was performed on 79 patients from 2007-2017. Age, gender, year of MG diagnosis, antibody test results, treatment with prednisone and/or pyridostigmine, eye exam results, conversion from ocular to systemic MG, and use of neurologic secondary treatments were collected.

Results:

Of the 79 ocular myasthenia patients, 36 (45.6%) tested positive for at least one subtype of the AChR antibodies. Of these 36 patients, 36 (100%) tested positive for the binding antibody, while 26 (72.2%) tested positive for the blocking antibody and 25 (69.4%) tested positive for the modulating antibody. 23 patients (63.9%) tested positive for all three antibodies. Two-sample T-testing demonstrated a correlation between older mean age (70.6 years) and a positive test for one AChR antibody ($p < 0.05$). Presence of ptosis and patients who received a medical treatment for MG were more likely to have a positive AChR antibody test. With respect to conversion from ocular to systemic MG, a correlation was found with female gender, and the use of pyridostigmine, compared to prednisone which appeared to be more protective ($p = 0.01$ Fisher exact test).

Conclusions:

Of the patients who tested positive for at least one AChR antibody, 100% tested positive for the binding subtype, while only 72.2% and 69.4% tested positive for the blocking and modulating subtypes, respectively, thus we believe it is reasonable to limit AChR antibody testing to the binding subtype alone. This measure would improve cost-effectiveness of testing, saving an average of \$40 per patient.

References: None.

Keywords: Myasthenia, Ocular Motility, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 260**Treatment Outcome in Ocular Myasthenia Gravis**

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Introduction:

Ocular Myasthenia Gravis (OMG) is an autoimmune disease that affects the neuro-muscular junction resulting in ptosis and/or diplopia without general or bulbar symptoms. OMG patients can suffer from disabling ocular symptoms. The outcome of treatment with OMG is poorly understood. Our aim is to assess outcome over time.

Methods:

Retrospective chart review of patients diagnosed with OMG are followed for at least 1 year after IRB approval. Patients younger than 18 or with concomitant thyroid eye disease were excluded. We recorded age, gender, presenting symptoms, method of diagnosis (acetylcholine receptor antibody or single-fiber electromyography (SFEMG)), treatments, and outcomes. Treatment at onset, one year, and final visit were recorded.

Results:

We reviewed charts of 51 patients. Twenty were female and 31 male. Mean age at diagnosis was 66. At presentation, 29% had diplopia, 12% had ptosis, and 59% had both. 71% were positive for the acetylcholine receptor antibody, while 29% of patients were diagnosed by SFEMG. At onset 78% were treated with pyridostigmine. 14% were not treated due to intermittent or minimal symptoms. 8% were treated with prisms. Of patients treated with pyridostigmine, 51% had symptom resolution. 49% who failed pyridostigmine started immunosuppressive therapy, 68% had resolution at one year. 26% had resolution by their last follow up. 6% required a third therapy or had incomplete relief of symptoms. These patients had an average follow up duration of 7.5 years.

Conclusions:

About half of patients with OMG who started therapy with pyridostigmine had symptom resolution. Those who failed pyridostigmine and transitioned to a second therapy had 94% resolution. A small percent of patients required no therapy, or could be treated with prism. With this information, we can inform patients of treatment outcomes and can provide a treatment algorithm for providers.

References: None.

Keywords: Myasthenia, Ocular motility, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Adult strabismus with a focus on diplopia

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 261

Results of an Experimental Model of Traumatic Optic Neuropathy

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Introduction:

The mechanism of indirect traumatic optic neuropathy, based on laser interferometer study of cadaver crania, is presumed to occur by force transmission through bone.¹ We propose an alternate mechanism, i.e., the amplification of a soft tissue shock wave within the orbit. When travelling through the conical orbital space in an anterior to posterior direction, amplification theoretically occurs with a magnitude inversely proportional to cross sectional area. This study investigates the mechanism and location of tissue damage in indirect traumatic optic neuropathy.

Methods:

Accelerometers placed on the optic nerve in the intracranial space adjacent to the optic chiasm and on the optic nerve adjacent to the orbital apex recorded movement during a series of impacts directed at 0, 45, 90 and 180 degrees relative to the forehead. The velocity of the impactor was 2 m/s for all impacts, with a calculated impact energy around 5 Joules Waveforms from the first 100 milliseconds following impact were generated from 1 test at the stated angles.

Results:

The two most notable findings were as follows. 1) At the orbit apex, the magnitude of acceleration was highest with a frontal impact, with a progressive decrease as point of impact moved posteriorly. 2) The difference in absolute velocity at the orbital apex versus the intracranial location (1.1 vs 0.2 meters/second) was higher than any other comparison suggesting tethering of the nerve at the optic canal.

Conclusions:

Our findings are consistent with orbital soft tissue shock wave amplification with frontal impact, related to the conical shape of the orbit, and may explain why indirect traumatic optic neuropathies are seen almost exclusively with frontal impact. The marked difference seen between measures at the orbit apex and the intracranial optic nerve also support the hypothesis that the optic canal is the most common site of damage.

References: 1. Gross CE, DeKock JR, Panje WR, et al. Evidence for orbital deformation that may contribute to monocular blindness following minor frontal head trauma. J Neurosurg 1981;55:963-6.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 262**Retinal Imaging in Neurodegenerative Diseases of Brain**

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Introduction:

Recent research suggests that Tau is the culprit lesion along with neuroinflammation in the etiology of Alzheimer' s Disease (AD). Retina is the extention of the brain and is the most easily approachable part of the central nervous system. Detection of the pathological protein accumulations may be possible by using spectral domain optical coherescent tomography (SD-OCT) and fundus autofluorescein (FAF). There is evidence showing that retinal plaques start accumulating even earlier than the ones in the brain. Most recent Tau protein images in the brain consist of normal or reverse C-shaped paired hellical filaments.

Methods:

30 patients with PET proven AD were examined by SD-OCT and FAF. Mean age was 72. Hypo or hyperfluorescent retinal lesions on FAF were scanned by SD-OCT and neurofibrillary tangles (NFT) and other accumulations were observed in a masked fashion. The researchers agreed on the shape of the lesions. Both C-shaped (normal or reverse) NFTs and thinner fibrillary structures were taken into consideration. Also 10 age-matched healthy controls were examined.

Results:

In all the patients, NFTs that exactly corresponded with the histopathologic and cryo-EM images of Tau in terms of shape and dimension were detected along with thin fibrils and lesions similar to amyloid beta. The number of the retinal filaments and other abnormal proteins was in concordance with the severity of the disease process. The advanced NFT lesions had normal or reverse paired C shapes and thin fibrils had the shape of histopathologic images seen in early developmental stages of the disease. Healthy patients did not have NFTs, but only had rare thin filamentous shapes.

Conclusions:

Retinal images of Tau were disclosed for the first time in live AD patients. Retinal neuroimaging is a trustable biomarker and tool for monitoring the disease.

References: None.

Keywords: Neuroimaging, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Neuro-opth & systemic disease (eg. MS, MG, thyroid), Pupils retina, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 263**Features distinguishing abnormal retinal ganglion cell physiology from optic pathway glioma formation in neurofibromatosis mice**

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Introduction:

We report additional features of a mouse model that elucidate electrophysiologic mechanisms that may better explain visual loss among children with neurofibromatosis type 1 (NF1) and optic pathway gliomas (OPGs). These features are separated in time and space from anatomic pathology in the retina, optic nerve and chiasm, and from OPG formation per se.

Methods:

In retinas from mutant and littermate transgenic mice (NF1-OPG) with neurofibromin (Nf1) knocked out in glial precursor cells, we mapped the retinotopic locations of RGCs recordable by in vitro multielectrode methods and their activity under differing light stimulation conditions, comparing these with the anatomic distribution of RGCs. We also searched for within-subject correlations among visual behavior measures (optomotor responses, OMR), in vivo anatomy (OCT), and histologic parameters of RGCs, optic nerves and chiasm (number and distribution of surviving RGCs, structural integrity of their axons and glia).

Results:

Retinotopic maps confirm that in NF1-OPG mice 1) very few RGCs are active in regions with severe RGC loss; 2) despite surviving, fewer RGCs are active in retinas with diffuse, mild loss; and 3) within regions of evenly distributed cells, activity localizes to irregular patches. Second, among active RGCs, discrete light pulses evoke normal responses, whereas longer stimuli elicit weaker responses above background. This suggests impaired light or contrast adaptation – characteristics not routinely tested in patients. Third, we identify no strong correlation between specific abnormalities of retinal/optic nerve anatomy, behavioral or electrophysiologic deficits, and OPG measurements in these mice.

Conclusions:

Our findings further support the hypothesis suggested by our previous findings: vision loss in many young NF1-OPG patients may result directly from aberrant early glial development and consequent RGC dysfunction, rather than later OPG formation and direct neural injury. This understanding may improve identification of patients at higher risk for visual loss and identify additional treatment targets.

References: None.

Keywords: Pediatric neuro-ophthalmology, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Genetic disease, Chemotherapy and radiation injury, Higher visual functions

Financial Disclosures: The authors had no disclosures.

Grant Support: Gilbert Family Neurofibromatosis Institute; Department of Defense (Investigator-Initiated Research Award)

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Poster 264

A National Neuro-Ophthalmology Consensus Statement on the Terminology for Automated Visual Field Abnormalities

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Introduction:

A multitude of terms have been used to describe automated visual field abnormalities. To date, there is no universally accepted system of definitions. Variability among clinicians creates the risk of miscommunication and the compromise of patient care. The purposes of this study were to 1) assess the degree of consistency among the nation's neuro-ophthalmologists in the description of visual field abnormalities, and 2) to create a national consensus statement with standardized terminology and definitions.

Methods:

In phase one of the study, the country's neuro-ophthalmologists were asked to complete a survey requiring free text descriptions of the abnormalities in 10 randomly selected automated visual fields. In phase two of the study, the authors created a national consensus statement on the terminology and definitions for visual field abnormalities using a modified Delphi method. In phase three of the study, the country's neuro-ophthalmologists were asked to repeat the initial survey of the 10 visual fields using the consensus statement to formulate their answers.

Results:

Twenty-six neuro-ophthalmologists participated in the initial survey. An average of 7.6 distinct terms were used to describe each of the visual field abnormalities (SD 3.5). Twenty-two neuro-ophthalmologists participated in the creation of a consensus statement which included 24 types of abnormalities with specific definitions. Twenty-three neuro-ophthalmologists repeated the survey using the consensus statement. There was a significant decrease in the variability with an average of 5.0 distinct terms per visual field abnormality (SD 1.3, paired *t* test = 0.02).

Conclusions:

The study confirmed a great degree of variability in the use of terminology to describe automated visual field abnormalities. The creation of our consensus statement was associated with improved consistency. Further efforts are warranted to standardize terminology and definitions.

References: None.

Keywords: Visual fields, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 265**Correlation of Intracranial Elastance with Venous Sinus Stenosis(VSS) in Idiopathic Intracranial Hypertension(IIH)**

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Introduction:

Intracranial elastance(E), a measure of the rebound capacity of the cerebrospinal fluid (CSF) compartment, was recently shown to be increased in IIH and has been theorized to play a role in its pathophysiology, however the relationship between E and venous sinus stenosis(VSS) has never been evaluated. We hypothesized that E would be increased in IIH with VSS compared to those without and also sought to confirm the lack of correlation between VSS and opening pressure(OP.)

Methods:

Retrospective study of IIH patients seen in neuro-ophthalmology clinic between September 2015 and September 2017, who underwent computed tomography or magnetic resonance venogram and diagnostic lumbar puncture with documentation of OP. Patients were categorized into three groups: bilateral VSS, unilateral VSS or no VSS. E and pressure-volume index(PVI) were calculated with closing pressure(CP) and volume(V) of CSF removed, using established equations: $E = (OP - CP)/V$ and $PVI = V/\log_{10}(OP/CP)$, respectively. Statistical analysis was performed using a one-way analysis of variance(ANOVA) for the three-group comparison, and a two-sample t-test for the two-group comparison of the no VSS group with a combined VSS(unilateral and bilateral VSS) group, with $p < 0.05$ considered statistically significant.

Results:

Ninety patients were included, 49 had bilateral VSS(54.4%), 10 had unilateral VSS(11.1%) and 31 had no VSS(34.4%). E and PVI were determined for 61 patients (67.8%). 35 had bilateral VSS(57.4%), 5 had unilateral VSS(8.2%) and 21 had no VSS(34.4%). There was no significant difference in OP($p = 0.61, 0.60$), E ($p = 0.80, 0.92$) or PVI($p = 0.84, 0.89$) among the three-group or the two-group comparison, with p-values listed respectively.

Conclusions:

In our cohort of IIH, there was no correlation between VSS and opening pressure or intracranial elastance. To our knowledge, this is the first study to examine the relationship between VSS and intracranial elastance in IIH patients.

References: 1. Riggeal BD, Bruce BB, Saindane AM, et al. Clinical course of idiopathic intracranial hypertension with transvers sinus stenosis. *Neurology* 2013;80:289-295. 2. Chisholm JT, Sudhakar P, Alhajeri AN, Smith JH. Intracranial elastance is increased in idiopathic intracranial hypertension. *European Journal of Neurology* 2017;24:1457-1463. 3. Marmarou A. A theoretical model and experimental evaluation of the cerebrospinal fluid system. PhD thesis, Drexel University, 1973. 4. Friedman DI, Liu GT, Digre KB. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. *Neurology* 2013;81(13):1159-65.

Keywords: High intracranial pressure/headache, Neuroimaging, Pseudotumor cerebri, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 266**Relationship Between Optic Nerve Angle, Intracranial Pressure, and Visual Outcomes in Idiopathic Intracranial Hypertension (IIH)**

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Introduction:

The tortuosity of the optic nerve can be quantified radiologically by measuring the angle of optic nerve deformation (ONA). In IIH patients, lowering the intracranial pressure (ICP) to a normal range by lumbar puncture (LP) leads to straightening of the optic nerve and an increase in the measured ONA on MRI. It is uncertain if ONA can be used as a marker of ICP or if a relationship between ONA and visual function exists. The objective of this study was to determine the ONA in patients with and without IIH, and to explore the relationship between ONA, CSF-opening pressure (CSF-OP) on LP, and visual function.

Methods:

Retrospective study of patients with/without IIH, who had neuro-ophthalmologic assessment (visual acuity, Humphrey visual field [HVF], fundus photography) and MRI brain immediately followed by LP with CSF-OP. Sagittal ONA was measured on multiplanar T2-SPACE images on a DICOM viewer by two masked reviewers. Papilledema was also graded on fundus photographs (Frisén scale) by two masked reviewers.

Results:

Fifty-four IIH patients and 30 unmatched controls were included. The IIH group was six years younger (95%CI 2-10, $p=0.002$), had 8.7 kg/m² heavier body-mass-index (4.9-12.5, $p<0.001$), and 26% more women ($p=0.01$) compared to controls. In both eyes, ONA was significantly smaller in IIH patients by 12° compared to controls (7°-17°, $p<0.001$). In the IIH group, there was no significant correlation between ONA and CSF-OP in either eye (right [OD] $r=0.19$; left [OS] $r=0.18$; $p>0.15$). ONA had no significant correlation with logMAR visual acuity (OD $r=0.26$, $p=0.06$; OS $r=0.15$; $p=0.27$), HVF mean deviation (OD $r=0.0059$; OS $r=-0.069$; $p>0.63$), or Frisén grade (OD Spearman's $\rho=0.058$; OS $\rho=0.14$; $p>0.30$).

Conclusions:

The ONA is a sign of raised ICP and is significantly smaller in IIH patients compared to controls, but does not correlate with CSF-OP, severity of papilledema, or visual function.

References: Hu R, Holbrook J, Newman NJ, et al. Cerebrospinal Fluid Pressure Reduction Results in Dynamic Changes in Optic Nerve Angle on Magnetic Resonance Imaging. *J Neuroophthalmol* 39(1): 35-40, 2019

Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 267**Optical Coherence Tomography and Ultrasonographical Biomarkers in Papilledema— A Retrospective Study on 267 Patients.**

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Introduction:

The differentiation between papilledema and pseudopapilledema is an essential, non-trivial diagnostic task in neuroophthalmological routine. Retrobulbar optic nerve sheath diameter (NSD) measured by standardized A-scan ultrasound and a widened nerve void (WNV) in B-scan ultrasound provide useful information when differentiating the two conditions and proved to yield a high predictive value for intracranial hypertension. Spectral domain optical coherence (SD-OCT) tomography yields objective morphometric data on peripapillary retinal nerve fiber layer (RNFL). The aim of this study was to evaluate the association of peripapillary RNFL thickness and NSD in papilledema.

Methods:

Retrospective analysis of paired ultrasonography and SD-OCT peripapillary RNFL examinations. The assessed parameters were the presence of WNV, the retrobulbar nerve sheath diameter (NSD), the mean SD-OCT RNFL thickness, and the best-corrected visual acuity (BCVA).

Results:

864 examinations of 267 patients (165 female, 102 male; mean age at examination 28.6 ± 18.5 years) between June 2014 and April 2019 were included. In 674 cases, WNV was evident on ultrasonography. NSD difference between eyes with and without WNV was statistically significant (5.37 ± 0.7 vs. 4.13 ± 0.93 mm, $p < 0.001$). Mean peripapillary RNFL thickness differed statistically significantly between eyes with and without WNV (131.08 ± 68.12 vs. 105.22 ± 31.58 μm , $p < 0.001$). In the entire cohort as well as amongst the WNV and the non-WNV eyes, NSD and mean peripapillary RNFL thickness showed no correlation ($R = 0.099$, $R = 0.009$, and $R = 0.197$, respectively). Amongst the non-WNV eyes, BCVA and RNFL thickness showed a moderate inverse correlation ($R = -0.37$).

Conclusions:

In our retrospective analysis of eyes with papilledema, peripapillary RNFL swelling showed not to be quantitatively correlated with NSD, although it was statistically significantly higher in eyes with papilledema. SD-OCT is a useful tool for the continuous assessment of RNFL swelling, but for the differentiation of pseudopapilledema and papilledema, ultrasonography is recommended.

References: None.

Keywords: High intracranial pressure/headache, Pseudotumor cerebri, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 268**A "Brain Stethoscope" for Measurement of Brain Compliance: A Non-Invasive Tool for Intracranial Pressure Assessment**

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Introduction:

Determination of intracranial pressure (ICP) is essential for the diagnosis and management of papilledema due to pseudotumor cerebri or other causes. Currently, monitoring of ICP requires invasive procedures including lumbar puncture or an intra-cranial monitor. A non-invasive method to measure raised ICP is needed. It is known that alteration of brain compliance (dP/dV) is present in patients with raised ICP. The ICP waveform can be derived from tympanic membrane (TM) pulsation. Abnormal compliance is associated with faster rise time of the waveform. A modified stethoscope which "hears" the infrasonic movement of the TM can be used to detect this change. Previous data has shown waveforms identical to an implanted ICP sensor.

Methods:

A standard stethoscope was modified for airtight external ear canal fit; the dome was exchanged for an ultrasensitive magnetic reluctance sensor, allowing detection of the ICP pulse. Analog TM pulsations are analyzed in real time by measuring slope ratio of the pulse. 9 normal subjects (age 18-32) underwent hyperventilation and tilt table testing to induce incremental ICP. The raw data was then processed by a trained algorithm which predicted if the patient had raised ICP.

Results:

The slope ratio method of quantification showed consistent and stable changes to represent abnormal increased ICP and abnormal brain compliance. Additionally, the classification algorithm was able to correctly identify subjects with elevated ICP in 36 of 36 independent recordings on 9 subjects.

Conclusions:

1) The "brain stethoscope" can correctly derive the ICP waveform from TM pulsation. 2) Analysis of the waveform by slope ratio can indicate normal vs abnormal brain compliance. 3) The classification algorithm was able to correctly determine a subject's ICP status with high accuracy. 4) The "Brain Stethoscope" may function as a non-invasive, practical and inexpensive tool to diagnose and monitor increased ICP by measuring brain compliance.

References: None.

Keywords: High intracranial pressure/headache, Pseudotumor cerebri, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: University of Central Florida; Focused Inquiry Research Experience Grant

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Poster 269**Brain MRV predicts the postoperative risk of recurrence of spontaneous cerebro-spinal fluid (CSF) leaks**

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Introduction:

A relationship between idiopathic intracranial hypertension (IIH) and spontaneous skull base CSF leaks has been proposed by which the CSF leak acts as a release valve, improving symptoms/signs (papilledema) of elevated increased intracranial pressure (ICP), but making the diagnosis of IIH challenging. Patients with undiagnosed IIH have an increased risk of raised ICP with papilledema and recurrent CSF leak after leak repair, making treatment challenging. Our goal was to assess whether radiographic signs of ICP predict postoperative recurrence of spontaneous CSF leaks.

Methods:

Retrospective review of demographics, fundus examination and pre-surgical brain MRI/MRV findings in patients seen at our institution from 10/2013-09/2019 for spontaneous CSF leak repair.

Results:

72 spontaneous CSF leak patients (median [IQR]: 51 [46-63] years; BMI:36 [22-63] kg/m²; 94% women; 58% black; 11% with known preexistent IIH) with brain MRI/MRV were included. Bilateral transverse venous sinus stenoses (TVSS) were more frequent (83% versus 49%, p=0.02) and degree of stenosis was higher (median: 65% versus 10%, p=0.01) in patients with either papilledema or recurrent CSF leak. Of these 72 patients, 60 had a CSF leak repair without prior or simultaneous CSF diversion procedure, of which 11 had a recurrence; patients with TVSS were 8.2 times (95% CI: 1.35-157.8) more likely to develop a recurrence (p=0.05) after a median follow-up of 7.7 [2.0-16.2] months. Other radiographic signs of raised ICP were similar in both groups: [cephaloceles, osseous defects: 89%/75%; empty sella: 89%/81%; enlarged Meckle's cave: 67%/67%; globe flattening: 29%/35%; prominent perioptic CSF space: 44%/50%, of patients with recurrent CSF leak/papilledema versus non-recurrence/no papilledema].

Conclusions:

Spontaneous CSF leak patients who develop papilledema or a recurrent CSF leak following repair of spontaneous CSF leak have a higher prevalence of bilateral TVSS and a higher degree of stenosis. Brain MRV is warranted preoperatively, as bilateral TVSS is a risk factor for postoperative CSF leak recurrence.

References: 1. Friedman DI, Liu GT, Digre KB. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. *Neurology*2013;81:1159-65 2. Bidot S, Levy J, Saindane A, Oyesiku N, Newman N, Biousse V. Do most patients with a spontaneous cerebrospinal fluid leak have idiopathic intracranial hypertension? *J Neuro-ophthalmol*2019 (In press). 3. Peker E, Oz D, Kul M, Erdogan M, Oztuna D, Erden M. Neuro-ophthalmologic MRI Findings in the detection of rhinorrhoea aetiology. *Neuro-ophthalmology*2019; 43: 244-249 4. Nelson R, Gantz B, Hansen M. The rising incidence of spontaneous cerebrospinal fluid leaks in the United States and the association with obesity and obstructive sleep apnea. *Otol Neurotol* 2015;36:476-80 5. Bidot S, Saindane AM, Peragallo JH, et al. Brain imaging in idiopathic intracranial hypertension. *J Neuroophthalmol*2015;35:400-11.

Keywords: High intracranial pressure/headache, Neuroimaging, Pseudotumor cerebri, Skull base

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 270**Variability Within Individual Optic Nerve Optical Coherence Tomography Measures Distinguishes Papilledema from Pseudopapilledema.**

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Introduction:

A longstanding dilemma for the ophthalmologist is determining if an elevated optic nerve represents papilledema or pseudopapilledema. Previous studies looking at OCT have compared quadrant measurements, features of the subretinal fluid space and Bruch's membrane opening. Very little have utilized the clock hour data. We hypothesized that variability and magnitude of the RNFL thickness could differentiate papilledema from pseudopapilledema.

Methods:

Patients presenting to a single neuro-ophthalmologist with clinically elevated optic nerves were included for retrospective review. Further inclusion criteria were age over 18 years, confirmed diagnosis, reliable OCT measurements, and bilateral pathology. Both eyes were included. Exclusion criteria included other optic nerve, retinal or intracranial pathology and grade 5 papilledema. The absolute consecutive difference and magnitude of clock-hours 1-12 were compared between the two groups using mixed-effect models adjusting for age and clock-hour with random intercept for subjects and eyes (nested within subject). The area under the curve (AUC) of receiver operating characteristics (ROC) curve and calibration curve were used to evaluate potential clinical usage.

Results:

Forty-four patients with papilledema and 72 pseudopapilledema (34 of whom had optic nerve drusen) were identified. The papilledema group had a higher absolute consecutive difference (papilledema = 57 ± 20 μ m, pseudopapilledema = 26 ± 11 μ m, $p < 0.001$). The same effect was seen for magnitude (papilledema = 163 ± 68 μ m, pseudopapilledema = 82 ± 22 μ m, $p < 0.001$). When the linear combination of their average values were used to classify the two groups, we achieved AUC of 96% (95% CI 92.4%-98.8%) with optimized sensitivity of 90.3% and specificity of 90.9% as well as good calibration (mean absolute error=0.016).

Conclusions:

Patients with papilledema have higher intrinsic variability and magnitude within their OCT, and this finding reliably distinguishes them from those with pseudopapilledema.

References: None.

Keywords: Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 271**Magnetic Resonance or Computed Tomography Venography in the Evaluation of Overweight Women with Papilledema**

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Introduction:

Magnetic Resonance Venography (MRV) or Computer Tomography Venography (CTV) is routinely obtained to rule-out dural venous sinus thrombosis (DVST) in patients with papilledema, but the urgency/necessity of these tests is still debated. Our goal was to determine the utility of MRV/CTV in overweight women with incidentally discovered papilledema and patients presenting due to symptomatic intracranial hypertension (IC-HTN) to neuro-ophthalmology.

Methods:

Retrospective study of consecutive female patients meeting inclusion criteria: i) age 16-50 years ii) papilledema iii) Optical coherence tomography (OCT)-Retinal Nerve Fibre Layer (RNFL) thickness >100mm iv) BMI >25kg/m² based on self-reported weight/height v) MRV/CTV head. Exclusion criteria: personal/family history of venous thrombosis, rheumatological disease, cancer or pregnancy. Patients were divided into Group-1 (incidentally discovered papilledema) and Group-2 (sought medical attention due to symptoms of IC-HTN).

Results:

103 patients (n=45 Group-1, n=58 Group-2) were included with a final diagnosis of idiopathic intracranial hypertension (IIH; n=94), drug-induced IC-HTN (n=4), DVST (n=2), intracranial mass (n=2) and POEMS (n=1). Group-2 patients were significantly more likely to have pulsatile tinnitus (p=0.017), TVOs (p=0.007) and showed a trend for increasing headache (p=0.058). Group-2 patients had a higher lumbar puncture opening pressure (38.5 vs. 33.0, p=0.013), but there was no difference in age, BMI, OCT-RNFL thickness or mean deviation between groups. MRV/CTV revealed distal transverse sinus stenosis in 100/104 (96%) of patients and DVST in 4 patients; however, a false positive result was determined in 2 patients and the 2 DVST patients had significant neurological symptoms.

Conclusions:

DVST is rare among overweight women with papilledema without risk factors. No patient with incidentally discovered papilledema was ultimately diagnosed with DVST and MRV/CTV may be interpreted incorrectly leading to false positive results. Therefore, there is room for clinical judgment when deciding to perform MRV/CTV in the workup in overweight women with incidentally discovered papilledema without risk factors.

References: None.

Keywords: Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: This study was supported by a Kensington Vision and Research Centre research grant.

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Poster 272**Idiopathic Intracranial Hypertension in patients aged 50+**

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Introduction:

Idiopathic Intracranial Hypertension (IIH) classically affects obese women of childbearing age. Few studies have investigated the clinical features of patients diagnosed with IIH later in life. Further characterization of this patient population would advance understanding of this rare disorder, and therefore we examined a large cohort of IIH patients ≥ 50 years old at time of diagnosis.

Methods:

We reviewed the medical records of 65 consecutive patients who met the Modified Dandy Criteria for IIH and were diagnosed at an age of 50 or older from four academic centers. Additionally, each center provided a randomly selected IIH patient under 50 years old as a control for each study patient identified at their location. We recorded patient demographics, presenting symptoms, medications, coexisting medical conditions, treatments, and data from initial and final neuro-ophthalmic visits. At time of this abstract submission 54 of the anticipated 65 controls were available for analysis.

Results:

Preliminary results demonstrate older patients with IIH had lower cerebrospinal fluid (CSF) opening pressures (median 33.0 vs 34.9 cmH₂O, $p = 0.016$), were less likely to present with headaches (51 vs 78%, $p = 0.004$), and more likely to be asymptomatic with an incidental finding of papilledema on examination (29 vs 7%, $p = 0.006$). Older patients had worse visual acuity at final follow-up (upper quartile LogMAR 0.2 vs 0.05, $p = 0.002$). Older and younger patients had similar BMIs and similar severity of papilledema at presentation.

Conclusions:

This study suggests that patients with idiopathic intracranial hypertension diagnosed after age 50 present with lower CSF opening pressures, fewer headaches, and may have worse visual outcomes than typical younger patients with IIH.

References: None.

Keywords: Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 273**Corneal Hysteresis: A New Risk Factor in Idiopathic Intracranial Hypertension?**

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Introduction:

Corneal hysteresis (CH) is a biomechanical property measured by the Ocular Response Analyzer (ORA) associated with glaucoma disease risk and severity. This factor is postulated to approximate the tissue properties at the lamina cribrosa, a structure also implicated in idiopathic intracranial hypertension (IIH). We conducted a study to investigate the association of CH with disease severity in IIH.

Methods:

All adult patients between 18 and 50 with IIH presenting to a neuro-ophthalmology practice over a 4 month period were recruited. Those with glaucoma, corneal, and retinal diseases were excluded. A historical survey, measures of axial length (AL), central corneal thickness (CCT), and CH were conducted. Those with Logmar visual acuity (VA) ≥ 0.30 (Snellen $\leq 20/40$), mean deviation on visual fields ≤ -3.00 , or optic nerve pallor on exam were considered moderate-severe, while all others were considered mild and groups thus divided.

Results:

Twenty-two mild and 19 moderate-severe cases were then analyzed. All participants were female. There were no differences in age, race, family history of glaucoma, or years since diagnosis. Body mass index was significantly different at 38.19 and 43.86 in the mild and moderate-severe groups respectively ($p < 0.05$). Corneal hysteresis was 10.95 and 10.91 in the mild and moderate-severe groups ($p = 0.45$). Pearson correlation analyses did not show significant correlation with either visual field mean deviation or LogMAR VA. There were no significant differences in AL, CCT, opening pressure, or translaminal pressure gradients. However, disc edema grade on diagnosis was grade 2 in the mild group and grade 3 in the moderate-severe group ($p = 0.01$).

Conclusions:

There were no differences in CH when comparing IIH patients with moderate-severe visual dysfunction to those with milder disease ($p = 0.45$) There was no notable correlation between CH and either visual acuity or visual field changes.

References: None.

Keywords: High intracranial pressure/headache, Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 274**Differentiating Papilledema from Pseudopapilledema Using RNFL OCT**

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Introduction:

The difficulty in distinguishing optic discs with true pathology (i.e papilledema) from pseudopapilledema is a frequently encountered one in neuro-ophthalmology clinics. Observation of optic discs alone may over- or under-diagnose papilledema. The addition of RNFL OCT provides quantitative information on RNFL thickness and can identify other causes of elevated optic discs such as drusen. We have instituted a formal protocol for all cases of anomalous optic discs. Baseline disc photos and RNFL OCT are obtained. Patients return to clinic at 4-6 weeks with repeat imaging and measurements. If stable, diagnosis of anomalous optic discs is made. If there is any change in RNFL thickness and/or disc appearance, presumed papilledema is diagnosed and further work-up is obtained.

Methods:

A retrospective chart review will be performed identifying all cases of anomalous optic discs that presented to neuro-ophthalmology clinic from 2005 to 6/2019. Cases will be identified using search of the electronic medical record system and ICD10 codes. Information (ex: chief complaint, visual acuity, RNFL thickness) will be collected from presentation and follow-up visits. We will use descriptive statistics to characterize this population of patients and their outcomes.

Results:

We anticipate analysis of approximately 100 patients with both baseline and follow-up disc photos and RNFL OCT. We aim to better characterize this patient population and help quantify the outcomes of our protocol (i.e. how many patients were ultimately classified as papilledema and underwent further work-up).

Conclusions:

The question of papilledema versus anomalous optic discs is a frequently encountered one and has important implications for patient care as well as health care in general (cost of testing, etc.). We hope to establish the utility of easy to obtain RNFL OCT measurements in helping to make this determination and the validity of our standardized approach.

References: 1) McCafferty B, McClelland C, Lee M. The diagnostic challenge of evaluating papilledema in the pediatric patient. Taiwan J Ophthalmol. 2017;7:15-21. 2) Lee KM, Woo SJ, Hwang JM. Differentiation of optic nerve head drusen and optic disc edema with spectral-domain optical coherence tomography. Ophthalmology. 2011;118:971-7. 3) Rebolledo G, Kawasaki A, de Juan V, Oblanca N, Munoz-Negrete JF. Optic coherence tomography to differential papilledema from pseudopapilledema. Curr Neurol Neurosci Rep. 2017;17:74.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 275**Sleep disturbances and Idiopathic Intracranial Hypertension in Men**

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Introduction:

Idiopathic intracranial hypertension (IIH) is characterized by increased intracranial pressure of unknown etiology. The consensus is that IIH predominantly affects obese women of childbearing age, with the male to female ratio ranging from 1:4 to 1:8 of IIH patients in the 14 to 60 age group. Males with IIH are reported to be four times more likely to be at high risk for obstructive sleep apnea (OSA) compared to age and BMI matched controls.

Methods:

Our research group investigated the relationship between sleep disturbances and the characteristics of IIH in males and females. We performed a review of 54 clinical charts and in-laboratory polysomnography test results; 27 of these were IIH patients (9 males and 18 females), and 27 were patients free of neurological disease who served as a control group matched for age, sex and BMI.

Results:

Our preliminary results did not reveal any significant differences between the male and female IIH patients in terms of age and BMI. However, there was a trend for male IIH patients to have significantly more severe OSA compared to female IIH patients (mean respiratory disturbance index (RDI) 31.7 vs. 9.0 events/hr, $p=0.07$; mean apnea length 19.1 vs. 12.6 seconds, $p<0.05$; mean minimum oxygen saturation 84.8% vs. 91.1%, $p=0.14$). We plan to report on a larger sample of male IIH patients at the time of the conference, as well as ascertain gender differences in terms of whether the burden of IIH symptoms correlates with OSA severity.

Conclusions:

There appears to be a significant sex difference in terms of OSA severity among male and female IIH patients. Given the notable sex differences and the paucity of outcome data in males, it is unknown as to what extent, if any, management strategies for IIH may need to differ in males and females.

References: None.

Keywords: High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 277**Idiopathic intracranial hypertension disproportionately affects minority and low-income communities**

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Introduction:

Idiopathic intracranial hypertension (IIH) has been reported to be more common among black women relative to general demographic data^{1,2}, but this has not been evaluated in the context of other socioeconomic determinants of health within metropolitan environments such as low-income status and access to healthy food.

Methods:

We performed a case-control study of female neuro-ophthalmology patients seen at the University of Pennsylvania and reviewed medical records to confirm IIH diagnostic criteria and obtain basic demographic information. Street addresses were geocoded and merged with U.S. census data to obtain census tract-level information on median income and food access. Choropleth maps visualized IIH clusters within certain neighborhoods. Conditional logistic regression compared the proportion of IIH patients from racial minority backgrounds, low-income census tracts, and low food access census tracts to age- and sex-matched non-IIH controls.

Results:

We identified 184 women with IIH and 10,049 women without IIH from a tertiary neuro-ophthalmology clinic in a major northeastern US city. In our cohort, when matched for age, women with IIH were more likely to be black (OR 4.34; 95% CI 3.15-5.99) or Hispanic (OR 2.47; 95% CI 1.20-5.28) and live in low-income census tracts (OR 2.41; 95% CI 1.79-3.25). There was no difference in the proportion of IIH vs. non-IIH patients belonging to low food access census tracts after adjusting for covariates (OR 0.9; 95% CI 0.61-1.47). Among IIH patients in our cohort, higher baseline weight and BMI were associated with low-income census tracts (adjusted difference in weight 11.22 kg, 95% CI: 1.60-20.85) but not with race or food desert census tract.

Conclusions:

IIH is more common among black and Hispanic women than expected even when accounting for the demographics of a metropolitan city, and at least some of this relationship is driven by the association of obesity and IIH incidence with low income.

References: 1) Galvin JA, Van stavern GP. Clinical characterization of idiopathic intracranial hypertension at the Detroit Medical Center. J Neurol Sci. 2004;223(2):157-60. 2) Bruce BB, Preechawat P, Newman NJ, Lynn MJ, Biousse V. Racial differences in idiopathic intracranial hypertension. Neurology. 2008;70(11):861-7.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 278**Quantification of Peripapillary Venous Tortuosity in Idiopathic Intracranial Hypertension using Optos Fundus Imaging**

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Introduction:

Tortuosity of the retinal veins, due to pressure that is transmitted from the peri-optic neural sheath to the base of the globe, is an important clinical finding in patients with IIH (1). Given this, we used a validated algorithm to quantify peripapillary retinal venous tortuosity in patients with IIH to assess whether tortuosity correlates with improvement in clinical disease (2). The authors also postulate that peripapillary venous tortuosity may be a more sensitive measure of changing ICP than Frisen grade or optical coherence tomography.

Methods:

This prospective longitudinal study followed patients with a new diagnosis of IIH to assess venous tortuosity measured from Optos fundus photography. Baseline measurements were compared to measurements at follow-up examinations. These measurements were compared with Frisen grade and OCT RNFL and BMI-matched controls.

Results:

Preliminary results include peripapillary venous tortuosity of 10 IIH patients (5 patients with follow-up) and 1 control. Although there was a trend towards increased tortuosity in patients with IIH compared to control, this did not reach statistical significance ($p=0.19$). Two patients had significant improvement in Frisen grade at follow-up visit. Patient A improved from Frisen grade 4 to 1, with 51.5% improvement in OCT RNFL and 14.5% decrease in vessel tortuosity index (VTI) ($p=0.014$). Patient B improved from Frisen grade 3 to 1, with 53.8% improvement in OCT RNFL and 10.2% decrease in VTI ($p=0.043$).

Conclusions:

To our knowledge, venous tortuosity has not previously been quantified in IIH patients. We show that peripapillary venous tortuosity decreases as the severity of disc edema in IIH decreases. Venous tortuosity, however, did not appear to outperform Frisen grade or OCT measurements as a sign of improving papilledema. More IIH and control patients are needed. Future directions include comparing venous tortuosity measured using different imaging modalities, including OCT-A, and expanding assessment of venous tortuosity beyond the peripapillary region.

References: 1. Miller NR, Subramanian PS, Patel VR. Walsh & Hoyt's Clinical Neuro-Ophthalmology: The Essentials, 3rd Edition. Baltimore: Wolters Kluwer, 2015. 2. Khansari MM, O'Neill W, Lim J, Shahidi M. Method for quantitative assessment of retinal vessel tortuosity in optical coherence tomography angiography applied to sickle cell retinopathy. Biomedical Optics Express. 2017;8:8.

Keywords: Pseudotumor Cerebri, High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 279**Experimental measurement of optic nerve sheath material properties**

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Introduction:

Changes in the optic nerve sheath (ONS) have been described in several ophthalmologic disorders, such as idiopathic intracranial hypertension (IIH) and space-flight associated neuro-ocular syndrome (SANS). Additionally, ONS traction on the optic nerve (ON) head may play a role in glaucoma pathophysiology. Despite the ONS changes reported in SANS and IIH, and its potential role in glaucoma, ONS biomechanical material properties remain poorly understood, particularly in humans. Knowledge of ONS material properties is required for finite element analysis of ONS biomechanics, and may provide insights into the pathophysiology of IIH, SANS4, and glaucoma.

Methods:

In preparation for testing human tissue, porcine ONSs (pONSs) were dissected from the ONs and placed in 1X PBS. A cylindrical sample of pONS (1 mm diameter), obtained using a biopsy punch, was placed on a MicroTester platform (CellScale, Ontario, Canada) in a temperature-controlled fluid bath (PBS at 37°C). Samples were pre-loaded with a compressive tare load of 100 uN, allowed to equilibrate, and then subjected to a 6-step stress relaxation protocol (5-30% compressive strain). Data from each step were analyzed independently using poroelastic theory to determine the pONS through-plane compressive modulus, the in-plane tensile modulus, and tissue permeability.

Results:

pONS compressive modulus was 1.44 ± 0.77 kPa at 5% compressive strain and increased to 7.58 ± 3.17 kPa at 30% strain (mean \pm standard deviation). pONS tensile modulus was 8.83 ± 1.70 kPa at 5 % compression and increased to 107.2 ± 23.8 kPa at 30% compression. pONS permeability was $2.49\text{E-}16 \pm 2.67\text{E-}16$ m² at 5% compression, decreasing to $3.21\text{E-}18 \pm 2.68\text{E-}18$ m² at 30% compression.

Conclusions:

The pONS showed increased compressive and tensile moduli and decreased permeability under increasing strain, consistent with properties of a biphasic tissue. We will compare the material properties of pONS to those of other species, specifically non-human primates and humans.

References: 1. Bidot S, Bruce BB. Update on the Diagnosis and Treatment of Idiopathic Intracranial Hypertension. *Semin Neurol* 2015;35:527-38. 2. Bidot S, Saindane AM, Peragallo JH, Bruce BB, Newman NJ, Biousse V. Brain Imaging in Idiopathic Intracranial Hypertension. *J Neuroophthalmol* 2015;35:400-11. 3. Mader TH, Gibson CR, Pass AF, et al. Optic disc edema, globe flattening, choroidal folds, and hyperopic shifts observed in astronauts after long-duration space flight. *Ophthalmology* 2011;118:2058-69. 4. Raykin J, Forte TE, Wang R, et al. Characterization of the mechanical behavior of the optic nerve sheath and its role in spaceflight-induced ophthalmic changes. *Biomech Model Mechanobiol* 2017;16:33-43. 5. Demer JL. Optic Nerve Sheath as a Novel Mechanical Load on the Globe in Ocular Duction. *Invest Ophthalmol Vis Sci* 2016;57:1826-38. 6. Shin A, Yoo L, Park J, Demer JL. Finite Element Biomechanics of Optic Nerve Sheath Traction in Adduction. *J Biomech Eng* 2017;139.

Keywords: Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 280**FLAIR Hyperintensity of the Optic Nerve/Optic Nerve Head and Visual Parameters in Idiopathic Intracranial Hypertension**

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Introduction:

FLAIR hyperintensity of the optic nerve/optic nerve head (ON/ONH) has been described as a sensitive imaging finding for the detection of papilledema in patients with idiopathic intracranial hypertension (IIH), but no imaging findings have been correlated with long-term visual outcomes.^{1,2,3} The purpose of this study is to confirm that ON/ONH FLAIR signal hyperintensity is associated with IIH as well as to evaluate the relationship between aberrant ON/ONH FLAIR signal and visual parameters.

Methods:

We performed a retrospective case-control study of 36 subjects (24 IIH, 12 controls) with dedicated orbital MRI performed within one month of clinical exam. Three neuroradiologists independently performed a masked review of the FLAIR images, evaluating for the presence of hyperintense signal within the ON/ONH. Clinical parameters of papilledema grade, visual acuity (VA), visual field mean deviation (VFMD), retinal nerve fiber layer (RNFL) thickness, and ganglion cell layer (GCL) thickness were extracted for all cases. We compared signal hyperintensity in cases and controls and examined the correlation between FLAIR hyperintensity and clinical parameters.

Results:

FLAIR signal within both the ON and ONH was significantly higher in cases of IIH versus controls ($p=0.04$ and $p=0.0007$ respectively). Papilledema grade was significantly correlated with ONH ($r=0.467$, $p=0.021$) but not ON ($r=-0.082$, $p=0.704$) FLAIR signal hyperintensity within the IIH group. RNFL thickness was also significantly correlated with ONH ($r=0.498$, $p=0.018$) but not ON ($r=0.051$, $p=0.821$) FLAIR hyperintensity. Correlation of the other clinical parameters did not reach significance. Further analysis will be presented at the meeting.

Conclusions:

FLAIR hyperintensity within the ON/ONH is again found to be associated with IIH. Aberrant ONH FLAIR signal is significantly correlated with papilledema grade and RNFL thickness, and has the potential to provide meaningful clinical information for patients with IIH.

References: 1Golden E, Krivochenitser R, Mathews N, Longhurst C, Chen Y, Yu J, Kennedy T. Contrast Enhanced 3D FLAIR Imaging of the Optic Nerve and Optic Nerve Head: Novel Neuroimaging Findings of Idiopathic Intracranial Hypertension. *Am J Neuroradiol.* 40(2):334–339. 2019. 2Padhye LV, Van Stavern GP, Sharma A, Viets R, Huecker JB, Gordon MO. Association between visual parameters and neuroimaging features of idiopathic intracranial hypertension. *J Neurol Sci.* Sep 15 2013;332(1-2):80-85. 3Salvay DM, Padhye LV, Huecker JB, et al. Correlation between papilledema grade and diffusion-weighted magnetic resonance imaging in idiopathic intracranial hypertension. *J Neuroophthalmol.* Dec 2014;34(4):331-335.

Keywords: Neuroimaging, Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 281**Venous Sinus Stenting for Idiopathic Intracranial Hypertension: Impact on Headache-Specific Quality of Life Scores**

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Introduction:

Venous sinus stenting (VSS) for treatment of idiopathic intracranial hypertension (IIH) has emerged as a viable alternative treatment to traditional surgical interventions. Headache, the most common symptom in IIH, may persist after the resolution of papilledema consistent with successful treatment response. Formal assessment of headache impact on quality of life (QOL) by questionnaire provides valuable information and better understanding for patients and doctors regarding treatment progress and outcome. We assessed headache-specific QOL (HQOL) scores and CSF opening pressure (OP) before and after VSS. We hypothesized that postoperative improvement in HQOL scores would correlate with improvement in CSF-OP.

Methods:

A previously validated HQOL questionnaire was distributed to IIH patients before and ³3 months after VSS. Retrospective chart review was conducted to obtain CSF-OP before and after procedure.

Results:

Mean QOL score improved from 48.5 to 20.6 after surgery ($n = 38$, range 3-48 months postoperatively), ($P < .001$). CSF-OP was reduced from 32.8 to 18.1 cm H₂O ($n = 25$) ($P < .001$). Linear regression of Δ CSF-OP vs. Δ QOL was conducted with available data, with correlation coefficients of 0.02 ($P = .91$). Twelve patients (32%) did not repeat lumbar puncture after VSS.

Conclusions:

As expected, HQOL scores along with CSF-OP improved after VSS, however we did not observe a significant correlation between changes in score and CSF-OP. In part this could be explained by the multifactorial nature of the headache presentation of IIH patients given cases of persistent headache even after CSF-OP normalization. The limited number of patients in our sample and variable interval of time for the posttreatment HQOL questionnaire assessment remain as other potential explanations. Nonetheless, we believe our findings reinforce the importance of a systematic and formal assessment of the headache in IIH patients utilizing HQOL questionnaires.

References: None.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Interventional neuroradiology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 282

Prediction of ONSF Based on Ophthalmological Examination in Patients with Intracranial Hypertensive Papilledema

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Introduction:

Papilledema is one of the most common complications of intracranial hypertension (IH). The purpose of this study is to stratify the degree of visual impairment caused by IH in order to predict the time of optic nerve sheath fenestration and to prevent irreversible visual impairment in high-risk patients.

Methods:

From January 1, 2014 to December 31, 2018 the optic nerve sheath fenestration has been performed in Department of Ophthalmology at Xuanwu Hospital. 78 patients who underwent optic nerve sheath fenestration were eligible for this study. According to the ophthalmological examination at admission, the patients were divided into two groups and examined for 3 months.

Results:

In the retrospective cohort, 24(54.55%) patients underwent ONSF bilaterally, while 20 (45.45%) underwent unilateral ONSF. Best corrected visual acuity (BCVA) improved or remained stable in 54(80.60%), and deteriorated in 13(19.40%) patients. The cutoff for predicting the time of optic nerve sheath fenestration was 101.75um.

Conclusions:

RNFL(T)≥101.75um may be a cut-off value to predict the deterioration of visual damage in Chinese papilledema patients. ONSF should be considered promptly in this condition, particularly when the IH cannot be solved within a short period. It is reasonable for papilledema patients to keep the RNFL(T) below 101.75um to improve or stable BCVA.

References: None.

Keywords: High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 283**Aetiology of acute sixth nerve palsies in children**

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Introduction:

Existing literature on the aetiology of acute sixth cranial nerve palsies in children is variable with limited generalisability given that many studies originate from tertiary neuro-ophthalmic centres. An acute sixth nerve palsy may be the presenting feature of a brain tumour, but the spectrum of underlying aetiology in children is wide including many more benign causes. Given the potential for serious underlying pathology, and as assessment of children with acute esotropia may be difficult, many proceed to neuroimaging often requiring general anaesthesia. We aimed to determine the incidence, underlying aetiology and further management of acute sixth nerve palsy in our dedicated eye hospital.

Methods:

A retrospective study of children under the age of 16 years diagnosed with acquired sixth nerve palsy was performed using the electronic clinical database and paper notes, between 2001 and 2018. Demographic details, presenting symptoms, examination findings, further investigations, diagnosis and outcome were recorded.

Results:

Sixty-four cases were identified with a mean age at presentation of 6.6 years. There was predominance for right sixth nerve palsies (54% right, 38% left, 8% bilateral). The underlying aetiologies were: idiopathic (39%), post-viral (27%), inflammatory (8%), infective (11%), tumours (8%), trauma (3%), non-tumour raised intracranial pressure (3%), and cavernous sinus pathology (1%). Neuroimaging was performed in the majority - more children had an MRI scan (90%) compared to a CT scan (25%).

Conclusions:

This study identified a lower incidence of serious underlying pathology compared to previous studies, many of which were based in institutions where serious pathologies may be over-represented. The majority of children had a benign aetiology; two thirds had idiopathic or post-viral 6th nerve palsies. However, tumours were identified in 8% of children and accordingly the majority of children underwent neuroimaging.

References: None.

Keywords: Ocular motility, Pediatric neuro-ophthalmology, Tumors, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 284**Predictors of Visual Outcomes in Pediatric Idiopathic Intracranial Hypertension**

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Introduction:

Pediatric idiopathic intracranial hypertension (IIH) may be associated with significant visual morbidity in a subset of patients but the risk factors for poor visual outcome have not been well delineated. (1) Informed by the adult IIH Treatment Trial, we sought to investigate what factors at presentation including OCT optic nerve head volume, disk findings (hemorrhages, cotton wool spots, retinal folds) (2-4), and opening pressure were predictive of poor visual outcome.

Methods:

We performed a retrospective review of pediatric patients Idiopathic Intracranial Hypertension at Boston Children's Hospital from 2010 through of 2018 using current diagnostic criteria. (5) limited the cohort to patients with OCT Optic Nerve Head Volume and reliable Humphrey Visual Fields within 4 weeks of initiation of therapy and at recent follow up.

Results:

33 patients (5 male and 29 female) met inclusion criteria. The average age was 14.3 years (+/- 4.7) and opening pressure 38.1 cm H₂O (+/-8.1). Lumbar puncture opening pressure was moderately correlated with the initial optic nerve head volume (OD Rho =0.57, p<0.001, OS Rho = 0.67, P<0.001) but not initial RNFL measures. Opening pressure was weakly correlated with the mean deviation on follow up Humphrey visual fields. The amount of change between first and final OCT optic nerve head volumes was not correlated with the final Humphrey visual field mean deviation (OD Rho = -0.24, p=0.26, OS Rho = -0.26 , P= 0.21). Visual outcomes were not found to be significantly different between those with retinal hemorrhages, retinal folds or cotton wool spots.

Conclusions:

In this cohort, visual outcomes were positive in the majority of patients. Structural changes at presentation did not provide predictive information regarding visual outcome. Prospective studies powered to evaluate these relationships in greater detail are warranted.

References: 1.Cinciripini GS, Donahue S, Borchert MS. Idiopathic intracranial hypertension in prepubertal pediatric patients: characteristics, treatment, and outcome. Am J Ophthalmol 1999;127:178-82. 2. Sheils et al. The Relationship Between Optic Disc Volume Area, and Frisen Score in Patients with Idiopathic Intracranial Hypertension, Am J Ophthalmol 2018;195:101-109. 3. Smith SV and Friedman DI, The Idiopathic Intracranial Hypertension Treatment Trial:A Review of the Outcomes, Headache 2017; 57 (8):1303-1310. 4. Wall et al. Optic Disc Haemorrhages at Baseline as a Risk Factor For Poor Outcome In the Idiopathic Intracranial Hypertension Treatment Trial, BR J Ophthalmol 2017; 101: 1256-1260 5. Friedman DI et al. Revised Diagnostic Criteria for the Pseudotumor Cerebri Syndrome in Adults and Children. Neurology 2013; 81:1159-1165.

Keywords: Pediatric neuro-ophthalmology, Pseudotumor cerebri, High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 285**Absent Vestibulo-Ocular Reflexes in Children with Cortical Visual Impairment**

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Introduction:

Children with cortical visual impairment often have ocular motor abnormalities such as exotropia and conjugate gaze deviation. These problems are generally assumed to be cortical in origin, however, neuroimaging can show injury to subcortical regions involved in ocular motor control as well. We therefore sought to determine whether the subcortical vestibulo-ocular reflexes (VORs) can be compromised in children with CVI.

Methods:

Records of children with CVI presenting to a pediatric ophthalmology practice between September of 2016 and April 2018 were retrospectively reviewed. VORs were assessed clinically by a pediatric neuro-ophthalmologist. Corresponding magnetic resonance (MR) images were assessed by a pediatric neuroradiologist in a masked fashion. The main outcome measures were the integrity of the VORs and the presence of brainstem abnormalities on MR imaging.

Results:

We found 20 children who met the classic definitions of pre-or-perinatal CVI. The most common etiologies for CVI were hypoxic ischemic encephalopathy (25%), followed by intraventricular hemorrhage of prematurity (15%), congenital brain anomalies (15%), and traumatic brain injury (15%). VORs were found to be absent or severely impaired in 13/20 (65%) of children. More surprisingly, the Doll's head maneuver failed to substantially overcome the deviated eye position in (8/13) (62%) of children with conjugate gaze deviations. Reduced brainstem size and brainstem signal abnormalities on MR imaging were found in 4/7 (57%) of children with normal VORs and in 9/13 (69%) of children with abnormal VORs, showing no correlation with the integrity of the VOR.

Conclusions:

Absence of VORs is a common accompaniment of CVI that may further complicate visual fixation. This novel finding probably signifies associated injury to the subcortical ocular motor system, which is known to be involved in severe cases of CVI. These children may lack an important visual compensatory mechanism to stabilize gaze during head movements. This knowledge may prove useful in planning visual rehabilitation.

References: None.

Keywords: Ocular motility, Pediatric neuro-ophthalmology, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 286**Idiopathic Cranial Nerve Six Palsies in Pediatric Patients**

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Introduction:

Idiopathic cranial nerve 6 (CN6) palsy in pediatric patients is a well-recognized yet rare phenomenon. (1) Etiology includes tumor, elevated ICP, trauma, congenital, inflammatory, and idiopathic. (1,2) In the absence of any other findings upon workup, children can be diagnosed as idiopathic CN6 palsy, typically resolving a few months after onset. (3) The literature is quite mixed as to the description, expected workup, and rate of spontaneous vs. incomplete recovery for these patients.

Methods:

This study collected a case series of all diagnosed pediatric CN6 palsies at a single institution over a 1-year period from October 2018-2019. In total, 5 subjects were identified and reviewed for characteristics related to their presentation, workup, and recovery.

Results:

Four males and 1 female, ranging from 9 months to 12 years of age, were identified. All had follow-up with neuro-ophthalmology, with 60% partial and 40% complete recovery (range: 1-2 months). No preference for laterality was observed. All subjects had lack of preceding trauma, normal intraocular exam, and unremarkable neuroimaging. 80% had a reported preceding viral illness by history. None of the subjects received any form of treatment.

Conclusions:

This case series describes the clinical entity of idiopathic CN6 palsies in pediatric patients. Current literature is quite sparse; one single center retrospective 14-year review identified 2 idiopathic cases. (3) The largest literature review to date identified only 126 total patients over a 40-year timespan, which included >40 studies globally. (1) This data being collected over a 1-year period, demonstrates either a significantly underreported phenomena or a significant increase in regional frequency. Given 80% of reported cases had a viral prodrome, we suggest a common viral etiology may have been contributory to recent increase. In addition this study aims to further guide the clinician in appropriate workup and expected time course of idiopathic CN6 palsies.

References: 1. Yousuf, Salman, Khan, Presenting features suggestive for later recurrence of idiopathic sixth nerve paresis in children, *Journal of American Association for Pediatric Ophthalmology and Strabismus* 11, no. 5, 452-455, 2007 2. Lee, Galetta, Volpe, Liu, Sixth nerve palsies in children, *Pediatric neurology* 20, no. 1, 49-52, 1999 3. Merino, Gómez, Villalobo, Franco, Gómez, Etiology and treatment of pediatric sixth nerve palsy, *Journal of American Association for Pediatric Ophthalmology and Strabismus* 14, no. 6, 502-505, 2010

Keywords: Ocular motility, Pediatric neuro-ophthalmology, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 287**Ophthalmologic Findings and Clinical Characteristics of Pediatric Miller-Fisher Syndrome in Korea**

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Introduction:

Miller-Fisher Syndrome (MFS) is a rare condition, especially in the pediatric population. We aimed to investigate the neuro-ophthalmologic manifestations, presence of anti-GQ1b antibody, and disease course of pediatric MFS.

Methods:

We retrospectively reviewed medical records of fourteen pediatric MFS who had acute ophthalmoplegia with ataxia.

Results:

The median age of onset was 11 years (range 4-17 years), and there were seven male and seven female patients. All the patients had a preceding infection; 6 had gastrointestinal symptoms, 7 had upper respiratory symptoms, and 1 had otitis media with fever. Eight patients had classic MFS, and 6 had atypical MFS. Neuro-ophthalmologic examination revealed that five patients had horizontal strabismus only, and four showed horizontal and vertical strabismus both. Moreover, four patients had internal ophthalmoplegia. In terms of laboratory results, three patients had anti-GQ1b antibody, and eight patients had albumin-cytologic dissociation in cerebrospinal fluid study. In addition, nerve conduction study demonstrated that 7 patients among 12 patients had prolonged terminal latency, and decreased nerve conduction velocity. Twelve patients were treated with intravenous immunoglobulin, and two patients received intravenous methylprednisolone. Within one month, nine patients showed partial regression of symptoms and signs, and 11 patients fully recovered within 3 months.

Conclusions:

Neuro-ophthalmic manifestations and disease course of pediatric MFS were similar to adult MFS in literature. However, prevalence of anti-GQ1b antibody was lower in pediatric MFS than adult MFS.

References: Buompadre, Ganez, Miranda, Arroyo, Unusual variants of GuillainBarre syndrome in infancy, Rev. Neurol, 42, 85–90, 2006 Nishimoto, Odaka, Hirata, Yuki, Usefulness of anti-GQ1b IgG antibody testing in Fisher syndrome compared with cerebrospinal fluid examination, J. Neuroimmunol, 148, 200–205, 2004

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 288**Risk of Physical Injuries in Children with Neuro-Ophthalmic Diseases in the OptumLabs Data Warehouse**

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Introduction:

There is a strong association between the risk of physical injuries and the presence of binocular vision disorders in aged Medicare-beneficiaries. The association of eye diseases, particularly neuro-ophthalmic disorders, with the risk of injuries in children is unknown.

Methods:

We used the OptumLabs® Data Warehouse, a longitudinal, real-world data asset with de-identified administrative claims and electronic health record data between 2007-2018, to calculate the incidence of physical injuries in children aged <18 years with and without more common eye diseases, based on ICD-9/10 codes. Analyses were performed using Kaplan Meier analyses, log-rank tests, and hazard ratio (HR) estimates. 95% confidence intervals (CI) were obtained using a Cox regression model.

Results:

There were 331,678 children with any eye disease and 13,540,473 without eye disease (controls). The incidence of any physical injury in children was 12% for children with ophthalmic disease and 10% in controls ($p < 0.001$). The HR for risk of injury was 1.86 (95%CI 1.61-2.16) for children with history of pseudotumor cerebri (PTC), 1.85 (95%CI 1.5-2.29) for pediatric optic neuritis (ON), 1.00 (95%CI 0.98-1.02) for amblyopia, and 1.1 (95%CI 1.08-1.11) for strabismus compared with controls. When comparing children with PTC to children with amblyopia and strabismus, the HR for injury was 1.85 (95%CI 1.59-2.15) and 1.69 (95%CI 1.46-1.96). For ON, the HR for injury risk compared to children with amblyopia and strabismus was 1.85 (95%CI 1.50-2.29) and 1.68 (95%CI 1.35-2.08), respectively.

Conclusions:

There was an increased incidence of physical injuries in children with eye disease. The risk was highest among children with neuro-ophthalmic diseases (PTC=86% higher risk and ON=85% higher risk than controls). Parents of children with eye and neuro-ophthalmic disease should be informed of the increased risk of physical injury; the risk for children with PTC and ON is increased compared with strabismus and amblyopia.

References: 1. Pineles SL, Repka MX, Yu F, Lum F, Coleman AL. Risk of musculoskeletal injuries, fractures, and falls in medicare beneficiaries with disorders of binocular vision. JAMA Ophthalmol. 2015;133(1):60-5. PubMed PMID: 25340322; PMCID: 4507425. 2. OptumLabs. OptumLabs and OptumLabs Data Warehouse (OLDW) Descriptions and Citation. Cambridge, MA: n.p., May 2019. PDF.

Keywords: Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

Grant Support: R21EY029655 Research to Prevent Blindness Disney Award for Amblyopia Research

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Poster 289**Comparison of Radiographic Findings in Papilledema and Pseudopapilledema in the Pediatric Population**

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Introduction:

Differentiating between papilledema and pseudopapilledema in the pediatric population is challenging for neuro-ophthalmologists. Prevalence of well characterized signs of intracranial hypertension (IIH)^{1,2} has not been specifically tested in children with pseudopapilledema. We aimed to study if imaging differences in children with papilledema and pseudopapilledema could help differentiate the two, thereby avoiding lumbar puncture.

Methods:

We performed a retrospective chart and imaging review of patients <18 years old with a diagnosis of papilledema and pseudopapilledema who were seen at our institution from June 2012 through September 2018. The determination of pseudopapilledema was decided upon clinical judgment including a normal intracranial pressure (ICP) and/or stability of exam on serial testing. There were 17 patients with pseudopapilledema [age (SD) 11.56 (4.32) years; 9 females] and 29 patients [mean (SD) age 12.37 (4.28) years; 23 females] with papilledema and opening pressure greater than 28 cm H₂O. Presence of signs of IIH on brain MRI, as determined by a masked neuro-radiologist, were compared between the two groups.

Results:

In our IIH cohort, flattening of the posterior poles was seen in 41% (12/29), distention of the optic nerve sheath in 41% (12/29), tortuosity of the optic nerve in 21% (6/29), sellar changes in 34% (10/29), and tonsillar descent in 17% (5/29). Flattening of the globe was seen statistically significantly less often (5.9% versus 41%) in pseudopapilledema group ($p=0.007$). Prevalence of distention of the optic nerve sheath, tortuosity of the optic nerve, sellar changes, and tonsillar descent was not found to be significantly different between the two groups ($p=0.087, 0.575, 0.195, \text{ and } 0.270$ respectively).

Conclusions:

Presence of flattening of the globe on MRI should suggest raised ICP and consideration for workup for IIH when clinical differentiation between pseudo-papilledema and papilledema is difficult.

References: 1) Bidot, Samuel, et al. "Brain imaging in idiopathic intracranial hypertension." *Journal of neuro-ophthalmology* 35.4 (2015): 400-411. 2) Hartmann, Alexander JPW, et al. "Imaging features of idiopathic intracranial hypertension in children." *Journal of child neurology* 32.1 (2017): 120-126.

Keywords: High intracranial pressure/headache, Neuroimaging, Pediatric neuro-ophthalmology, Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 290**Final Diagnosis of Pediatric Patients referred for Pseudotumor Syndrome**

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Introduction:

Pediatric pseudotumor syndrome (PTS) is a rare condition and can be associated with visually devastating outcomes. While prompt diagnosis is instrumental in management of this condition, misdiagnosis can lead to unnecessary tests, invasive procedures and delayed treatment and management of other conditions. In this study, we sought to analyze data from patients who were referred with a diagnosis of pediatric PTC and review their final diagnosis and identify key presenting symptoms, afferent and efferent exam findings, and neuro-imaging results associated with their diagnosis.

Methods:

This is a retrospective chart review of pediatric patients referred with a diagnosis of likely PTC from January 2008-June 2018. The primary objective of this study is to identify the final diagnosis of patients referred for suspected pediatric PTC. We present the initial review of 25 patients.

Results:

An review of twenty-five subjects was performed. (14 male patients; age range of 3 years to 17 years, with mean of 11.95 years). Of these twenty-five subjects referred for PTC, fourteen were confirmed to have this diagnosis (group 1). In this cohort, 6 patients were male. Two developed PTC in the setting of minocycline therapy and one was found to have venous sinus thrombosis. . The remaining eleven patients (group 2) were found to have optic disc drusen, pseudopapilledema (in the setting of high hyperopia), crowded optic nerves or disc edema related to retinitis pigmentosa. These patients were more likely to be asymptomatic. (eleven patients in group one had symptoms, most commonly headache, compared to only three patients with symptoms in group two). There was no difference in presenting visual acuities between the two groups.

Conclusions:

In this initial retrospective chart review of twenty-five patients referred for pediatric PTC, only 14 patients had this as their final diagnosis. In the remaining 11 patients the most common diagnosis was optic disc drusen.

References: •Phillips PH, Repka MX, Lambert SR. Pseudotumor cerebri in children. JAAPOS. 1998 Feb;2(1):33-8 •Cinciripini GS, Donahue S, Borchert MS. Idiopathic intracranial hypertension in prepubertal pediatric patients: characteristics, treatment, and outcome. Am J Ophthalmol. 1999 Feb; 127(2):178-82 •Heidary G. Pediatric papilledema: review and a clinical care algorithm. Int Ophthalmol Clin. 2018 Fall;58(4):1-9 •Sheldon CA, Paley GL, Xiao R, Kesler A, Eyal O, KoMW et al. Pediatric Idiopathic Intracranial Hypertension: Age, Gender, and Anthropometric Features at Diagnosis in a Large, Retrospective, Multisite Cohort. Ophthalmology. 2016 Nov;123(11):2424-2431. •Gilbert AL, Heidary G. Update on the evaluation of pediatric idiopathic intracranial hypertension. Curr Opin Ophthalmol. 2016 Nov;27(6):493-497

Keywords: Pediatric neuro-ophthalmology, Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 291**Non-mydratric Fundus Photograph (NMFP) Regional Quality in Patients Evaluated Acutely for Transient Ischemic Attack (TIA)**

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Introduction:

Approximately 10% of patients presenting with a TIA will have a new stroke or cardiovascular event within 90 days. Our study investigates the role of NMFP in patients evaluated acutely for TIA in the emergency department (ED). Here we provide data regarding the quality of four regions within the fundus photographs obtained in the study.

Methods:

NMFP were obtained from patients evaluated for TIA in three EDs in a large metropolitan area. Demographics and overall quality of the photographs (1-5; 5 optimal) were collected. The best quality photograph was assessed for quality in four separate regions: optic disc, macula, and superior and inferior arcades. Quality grades were assigned as follows: A (able to see region and determine normality with certainty), B (able to see region, but unable to determine normality with certainty), or C (unable to see region).

Results:

395 patients (mean age: 57 years [SD ±13]; 219 [55%] women; 250 [63%] black) had NMFP obtained in at least one eye. Mean best overall photograph quality was 3.9±1.0 (1-5; 5 optimal). Based on a McNemar chi square with Bonferroni correction, regional quality assessment determined the optic disc quality was better than other regions ($p<0.001$ for all regions) in both right and left eyes. The optic disc was also able to be assessed well on photographs of poorer quality. In the right eye (similar results in left eye not shown), mean overall quality rating of photographs with an “A” rating was 3.96 for the optic disc and 4.39 for the macula. The mean general quality rating of photographs with a “B” rating was 2.26 for the optic disc, and 2.80 for the macula.

Conclusions:

The study confirms our previous findings that regional quality of the optic disc is superior to the regional quality of the macula and superior and inferior arcades on NMFP.

References: Lamirel C, Bruce BB, Wright DW, Delaney KP, Newman NJ, Biousse V. Quality of non-mydratric digital fundus photographgraphy obtained by nurse practitioners in the emergency department: the FOTO-ED study. *Am J Ophthalmol* 2012;119:617–624.

Keywords: Vascular disorders, Stroke trauma

Financial Disclosures: The authors had no disclosures.

Grant Support: NIH R01-NS089694

Contact Information: None provided.

Poster 292

Brain and Optic Nerve Study with Artificial Intelligence (BONSAI): The Final Outcomes

Dan Milea¹, Raymond Najjar², Caroline Vasseneix², Shweta Singhal³, Zubo Jiang⁴, Daniel Ting², Masoud Aghasaei Fard⁵, Pedro Fonseca⁶, Steffen Hamann⁷, Luis Mejico⁸, Jing Liang Loo³, Nicolae Sanda⁹, Catherine Vignal-Clermont¹⁰, Sharon Tow³, Chiara LaMorgia¹¹, Marie-Bénédicte Rougier¹², Kavin Vanikieti¹³, Carmen Chan¹⁴, Jost Jonas¹⁵, Selvakumar Ambika¹⁶, Patrick Yu Wai Man¹⁷, Wolfgang Lagreze¹⁸, Richard Kho¹⁹, Clare Fraser²⁰, Neil Miller²¹, Yong Liu²², John Chen²³, Nancy Newman²⁴, Tien Yin Wong¹, Valerie Biousse²⁵

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Introduction:

The timely and accurate detection of optic disc abnormalities, in particular papilledema, is a key part of the clinical examination; however, few physicians confidently perform ophthalmoscopy. Our goal was to develop an artificial intelligence deep learning system (AI-DLS) capable of distinguishing “normal optic nerves”, “papilledema” (optic disc edema from proven intracranial hypertension), and “other optic nerve abnormalities” on standard digital fundus photographs from a large, multiethnic, worldwide, patient population. This classification was chosen to provide a low-cost, non-invasive test that facilitates identification of patients less (those with normal optic nerves) or more (those with papilledema) likely to have neurologic disorders associated with high morbidity/mortality in emergency settings.

Methods:

We developed and validated an AI-DLS to automatically classify optic discs as “normal” or “abnormal”, and specifically detect “papilledema”, using 15,846 digital ocular fundus photographs (14,341 images for DLS training and validation; 1,505 for external testing) from adult patients as part of an international consortium. The DLS performance to classify the optic disc appearance was evaluated by calculating the area under the receiver operating curve (AUC), sensitivity and specificity, with reference to expert neuro-ophthalmologists.

Results:

We included 9,156 images of “normal” discs, 2,148 images with “papilledema”, and 3,037 images with “other” optic disc abnormalities. In the primary validation dataset, the DLS successfully discriminated “normal” from “abnormal” optic discs (AUC 0.99 [0.99-0.99]), and “papilledema” from “other” (AUC 0.98 [0.98-0.98]). Similar performance was observed on external datasets, with AUC 0.98 (0.97-0.98), sensitivity 95.3 (93.8-96.6) and specificity 86.6 (83.8-89.3) for the detection of “normal”, and AUC 0.96 (0.95-0.97), sensitivity 96.4 (94.2-98.1) and specificity 84.7 (82.6-86.7) for the detection of “papilledema.”

Conclusions:

A fundus photograph-based DLS can automatically discriminate normal optic discs, papilledema and other optic disc abnormalities in a multi-country, multi-ethnic patient population, with potential applications for the management of headache and neurologic patients in various clinical settings.

References:

None.

Keywords: Optic neuropathy, Pseudotumor cerebri, High intracranial pressure/headache, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: NMRC, CS-IRG Grant and ACP Grant, Singapore (Dan Milea)

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Poster 293**Red Desaturation Prevalence And Severity In Healthy Patients**

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Introduction:

Clinicians often use red desaturation to grossly determine a perceived color difference between eyes to quickly determine if a patient may have an optic neuropathy. We sought to determine the percentage of the healthy population that responded asymmetrically to the red desaturation test, and to approximate the degree of red desaturation in those individuals. We also studied the correlation between demographic variables and red desaturation prevalence and severity.

Methods:

Adults aged 18+ with a normal eye exam including confrontation fields and best-corrected visual acuity of $\geq 20/25$ OU were eligible for this prevalence study. Those with any objective or subjective afferent visual dysfunction were excluded. 77 participants (28.6% male; 71.4% white race; mean [SD] age: 42.8 [15.6] years), without pre-existing knowledge of the study question, were queried whether monocular perception of redness of a standardized tropicamide bottle cap was the same. Participants noting a difference were then asked to estimate in percentage terms, with one eye perceiving the bottle cap at "100% redness."

Results:

20/77 participants (26.0%) experienced some degree of red desaturation. For these individuals with red desaturation, the average interocular difference was 9.2% (range 2-25%, 95% CI: 5.65-12.75%). There was no statistical evidence for a relationship between red desaturation and variables such as race, gender, or age.

Conclusions:

This study shows that approximately a quarter of healthy patients without apparent asymmetric optic nerve or macular function may recognize red desaturation. This clinical knowledge might be useful when interpreting the results of red desaturation tests for patients suspect for optic nerve abnormalities. Further research should be conducted with larger sample sizes to identify predictors of red desaturation in healthy patients, establish the threshold at which red desaturation is more likely to represent pathology than physiologic phenomena, and assess the stability of red desaturation over time in affected individuals.

References: None.

Keywords: Optic neuritis, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 294**How to Diagnose Optic Neuropathy in a Blink!**

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Introduction:

In response to a light stimulus, a reflex orbicularis contraction of the upper and lower eyelid occurs. Our purpose was to determine if the photic blink reflex can be used as an objective clinical measure of afferent visual pathology, in a similar manner to Relative Afferent Pupillary Defect (RAPD). We compared the orbicularis and pupillary responses to increasing light in subjects with and without unilateral optic neuropathy. We hypothesized that the orbicularis contraction correlates with pupil contraction for the same light stimulus and would produce a relative afferent eyelid defect (RAED) in optic neuropathy.

Methods:

The eyelid response increased as a function of light intensity and was significantly decreased in the optic neuropathy eyes compared to the fellow, unaffected eyes (Wilcoxon test $P < 0.0001$), but not between the two eyes of the healthy subjects (Wilcoxon test, $p = 0.547$). The eyelid response in optic neuropathy eyes correlated with the pupil response ($r = 0.66$, $P = 0.012$), ganglion cell layer ($r = 0.543$, $P = 0.0479$) and retinal nerve fiber layer thickness ($r = 0.622$, $P = 0.347$).

Results:

The eyelid response increased as a function of light intensity and was significantly decreased in the optic neuropathy eyes compared to the fellow, unaffected eyes ($P < 0.0001$), but not between the two eyes of the healthy subjects ($p = 0.547$). The eyelid response in optic neuropathy eyes correlated with the pupil response ($r = 0.66$, $P = 0.012$), ganglion cell layer ($r = 0.543$, $P = 0.0479$) and retinal nerve fiber layer thickness ($r = 0.622$, $P = 0.347$).

Conclusions:

Patients with unilateral optic neuropathy display a relative afferent eyelid defect (RAED) in addition to RAPD. The eyelid response correlated with the pupil response and provides a novel, additional method for evaluating optic neuropathies, even after pupil dilation.

References: None.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Optic neuropathy, Orbit/ocular pathology, Miscellaneous, Non-organic visual disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: Randy Kardon: Iowa City VA Center for the Prevention and Treatment of Visual Loss, the Busse Family Foundation, and the Mintzer Family

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Poster 295**Evolution of fundus photography. Lessons for neuro-ophthalmology as well as the retina service**

Steven Newman¹

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Introduction:

In 1850, Helmholtz developed the ophthalmoscope which for the first time allowed practitioners to see the back of a living eye. Prior to this, the only studies of the retina were post mortem. Photography had started in the 1830s, but at adapting it to allow pictures of the fundus was limited. It was not until Nordonsen working with Zeiss in the 1920s was able to reduce reflections off the cornea and lens surface with a dot that a practical camera was invented. There were still limitations, including the amount of light, leading to attempts at improving lightening, especially with something like Xenon photocoagulator and later with incandescent bulbs. Significant limitations remained including in most cases the need to dilate the patient, limited illumination, and limited field to the posterior pole (initial studies on diabetes were done with multiple overlapping shots of the posterior pole).

Methods:

In a consecutive series of 130 patients Recent work developed an improved visual reading system, expanded the image size, and allowed for a non-contact photography often through a non-mydrated pupil. Through this pilot study at the University of Virginia, we have been utilizing this camera to take pictures of patients to demonstrate its effectiveness.

Results:

A small light, inexpensive, hand-held camera has improved the lighting allowed for a non-mydratic photographs, improved the amount of retina seen on individual photographs, and allowed for non-contact photography. This has been adapted in several situations. We are optimistic that this will be a significant advance in allowing us to record details of the fundus and may be adapted to the neonatal intensive care unit and the emergency room.

Conclusions:

A new fundus camera has permitted more extensive photographs of the eye in vivo, non-contact often non-mydratic pictures.

References: None.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Neuro-opth & systemic disease (eg. MS, MG, thyroid), Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 296**Hue: A Quantitative Measure of Optic Nerve Color**

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Introduction:

Optic nerve color is one of the three cardinal features used to evaluate the optic nerve. Quantitative measures have been used to aid in evaluating each feature; however, most methods for evaluating optic nerve color require specialized non-commercially available equipment (microdensitometry and fundus reflectometry). Hue is a quantitative measurement of color that has been separated from an image's intensity and can be easily obtained from routine fundus photography without significant image manipulation. We hypothesize that hue can be easily used to differentiate between glaucomatous optic neuropathy (GOA) versus non-glaucomatous optic neuropathy (NGOA).

Methods:

In this retrospective study, fundus photos of twenty eyes of twenty subjects (ten with GOA and ten with NGOA) had hue calculated from the RGB color space using ImageJ (Bethesda, Maryland). The extracted hue was normalized with reference to the hue of inferior retinal vein at the border of the neuro-retinal rim in each image. A paired T-test was used to evaluate the results from each group. Bonferroni correction was applied.

Results:

Mean hue values were statistically significantly lower in GOA compared to NGOA: Superior $3.6^{\circ} \pm 1.7$ vs. $24.6^{\circ} \pm 12.8$, p-value= 0.003079; Nasal $4.8^{\circ} \pm 1.8$ vs $21.8^{\circ} \pm 9.0$, p-value= 0.001025; Inferior $3.8^{\circ} \pm 2.6$ vs $32.4^{\circ} \pm 18.1$, p-value= 0.00399; Temporal $4.2^{\circ} \pm 2.5$ vs $41.4^{\circ} \pm 20.0$, p-value= 0.001299.

Conclusions:

In this pilot study, we showed a statistically significant difference between the mean hue values of GOA vs. NGOA. Hue measurements are easy to perform on fundus photographs. Further studies with a larger sample size are needed to validate this method which has potential to be used to aid in the evaluation of optic neuropathies.

References: Miller JM, Caprioli J. Videographic quantification of optic disc pallor. Invest Ophthalmol Vis Sci. 1988;29:320-323. Schwartz B, Kern J. Scanning microdensitometry of optic disc pallor in glaucoma. Arch Ophthalmol. 1977;95:2159-2165.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 297**The SUN Test of Vision: Investigation in Healthy Volunteers and Comparison to the MULES**

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Introduction:

Rapid automatized naming (RAN) tests have been widely used in evaluating various neurological conditions. These tests require quick and accurate identification of numbers and pictures, thus assessing brain pathways involved in vision, memory, language, and attention. The MULES (Mobile Universal Lexicon Evaluation System), an established picture-naming RAN test, has been effective in identifying concussion, multiple sclerosis, and Parkinson's disease. To complement the MULES, we have developed a novel number-based RAN test called the SUN (Staggered Uneven Number) test. This study introduces and determines baseline values for the SUN and compares the SUN to the MULES.

Methods:

We obtained a convenience sample of 54 adult volunteers from clinical and research offices who had no history of visual or neurological conditions. Participants were asked to perform two trials of the SUN and MULES and total time in seconds and number of errors for each trial were recorded.

Results:

Among 54 participants, aged 20-66 years old, the SUN took a greater time (45.2 ± 8.3 s) compared to the MULES (37.4 ± 9.9 s), although on average it took a shorter time to identify a number (0.31 s) compared to a picture (0.69 s). SUN and MULES times did not differ by gender. However, older age was associated with greater (worse) MULES ($r=0.43$, $p=0.001$), but not SUN times. Primary language also affected MULES times (44 s for non-primary English speakers vs. 36 s for primary English speakers, $p=0.03$), but not SUN times. Further, MULES had a greater learning effect between trials, with a 16% improvement compared to 5% for the SUN ($p=0.0001$).

Conclusions:

The SUN is a new vision-based test that complements RAN tests involving picture naming. Differences in content and learning effect suggest these test types involve different pathways for visual processing/memory, language, attention, and eye movements. Use of both may better capture changes in neurological function.

References: None.

Keywords: Optic nerve trauma and treatment

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 298**Augmented Optic Nerve Head Blood Flow Depends on Stimulus Wavelength and Duration**

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Introduction:

The neurovascular coupling mechanism has been examined by presenting repeated flashes of light, termed flicker stimulation, to stimulate optic nerve head blood flow (ONHBF). The current study investigated how stimulus features (i.e., wavelength and duration) from two common visual electrophysiology tests (i.e., photopic negative response, PhNR; visual evoked potentials, VEP) may alter ONHBF.

Methods:

Healthy non-smoking adult subjects without hypertension, diabetes or optic neuropathy were recruited. After mydriasis, baseline ONHBF was acquired using the NAVI-Lite laser speckle flowgraphy (LSFG) device. Monocular flicker stimulation was then performed in 10 and 60 second epochs using a handheld Ganzfeld stimulator. Immediately after cessation of the PhNR stimulus (640nm red light, 465nm blue background at 10 Hz) or flash VEP stimulus (diffuse white light at 10 Hz), ONHBF was measured every 30 seconds. Percent change in ONHBF (global as well as individual artery/vein) between baseline and following stimulus cessation was calculated.

Results:

Five subjects (median age: 37 years, range 34-48) met inclusion criteria and completed both protocols (ten subjects will be presented in the final analysis). Total ONHBF increased after both the 10 second stimuli (PhNR = 10.5%; VEP = 9.7%) and 60 second stimuli (PhNR = 15.4%; VEP = 15.0%) when compared to baseline. For individual vessels along the superior/inferior arcade, increased blood flow to both arteries and veins was most pronounced for the 60 second (18.8% and 23.2%, respectively) compared to the 10 second (10.7% and 9.4%, respectively) VEP stimuli. Changes in individual arteries/veins were less robust using the PhNR stimulus.

Conclusions:

Our preliminary data demonstrates that PhNR and flash VEP flicker stimulation induces a demonstrable increase in ONHBF—the most robust response produced by longer duration stimuli. Our testing paradigm permits interrogation of neurovascular coupling and may serve as a model to evaluate changes in vascular reactivity due to optic neuropathies or vascular diseases.

References: None.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: The Foerderer Foundation of Children's Hospital of Philadelphia.

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Poster 299**Assessing Patient Educational Needs in Neuro-Ophthalmology**

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Introduction:

Effective patient education has therapeutic value for improving adherence to medical regimens. One strategy for personalizing patient education used by pharmaceutical industries utilizes psychographic segmentation paradigms to identify individual educational needs. Drug treatment education strategies are then marketed according to patient cognitive-behavioural subtypes with the aim of increasing medication compliance. Patient segmentation in neuro-ophthalmology, with the goal of targeting education to increase compliance with medical recommendations, has not been studied. The objective of this project is to characterize the educational needs of neuro-ophthalmology patients at a tertiary-care academic center using a validated patient segmentation tool, and glaucoma patients in the same center as control.

Methods:

Using the 7-question Better Conversations[®] survey (Novartis Pharmaceutical Corporation), adult subjects with scheduled outpatient appointments were divided into four segments based on an established algorithm for educational needs. Segments were collapsed into categories for high and low educational needs (HEN/LEN). Distribution of patients was compared between neuro-ophthalmology and glaucoma. Subject age, gender, distance travelled, number of medications (as a proxy for health) and new vs. follow-up appointment status were considered as covariates.

Results:

Among 152 respondents (97% response rate (152/157), ages 19-97, 58% female, 72 glaucoma, 80 neuro-ophthalmology), 55 were HEN and 97 LEN. Though both neuro-ophthalmology and glaucoma clinics had a majority of LEN subjects, the proportion of HEN was greater in neuro-ophthalmology (44% vs. 28%, $p=0.04$, chi-square). HEN and LEN subjects did not differ with respect to age, gender, distance traveled, number of medications or new vs. follow-up status.

Conclusions:

The field of neuro-ophthalmology has a large proportion of HEN patients compared to glaucoma, and is thus particularly suited for implementation of targeted educational interventions. Further research is required to understand personality and illness perception characteristics among neuro-ophthalmology patients in order to tailor educational interventions accordingly, with the goal of improving health outcomes through increased compliance.

References: None.

Keywords: Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: Unrestricted Grant for Research to Prevent Blindness NIH P30 EY026877 Novartis Pharmaceutical Corporation provided access to the Better Conversations survey tool, but did not have influence over the study design, analysis and interpretation.

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Poster 300**The effect of blue-enriched light on medical error rates in a university hospital ICU**

Yanjun (Judy) Chen¹, Aimee Broaman¹, Reginald Bruskevitz¹, Geoffrey Priest², Steven Lockley³

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Introduction:

Medical error that occurred during patient care has imposed a tremendous socioeconomic impact on the health care system. Short-wavelength, blue-enriched light has been shown to promote alertness and attention. The present study sought to investigate if blue-enriched light installed in the nurse working area in an intensive care unit (ICU) helps to reduce medical error.

Methods:

We conducted a prospective interventional study where we replaced traditional fluorescent light with interventional blue-enriched light-emitting diode (LED) light at the nurse workstation and common areas in a university hospital ICU in winter months from January to May. We identified medical errors by manual chart review using the Institute for Healthcare Improvement (IHI) Global Trigger Tool (GTT). Poisson regression and descriptive analysis were used to compare the medical error rate between the interventional LED lighting (Jan-May 2017, post-intervention) and traditional fluorescent lighting in the preceding year (Jan-May 2016, pre-intervention).

Results:

The study included a total of 1073 ICU admissions, 522 from the traditional fluorescent, and 551 from the interventional LED lighting. There was a modest trend of error reduction (harmful and non-harmful) in the post- vs. pre-intervention (39.9 and 45.5 per 1000 person-days, respectively) (rate ratio=0.94, $p>0.05$). There appeared to be a prominent reduction of level F error in the post-compared to pre-intervention (12.4 and 21.1 per 1000 person-days, respectively).

Conclusions:

In this prospective interventional study of medical error rate in a university ICU, we found a modest trend of overall error reduction and a prominent reduction of level F error, when the traditional fluorescent light was replaced by interventional blue-enriched light in the nurse working area. Future studies are needed to replicate the findings in diverse inpatient care settings and be powered to assess the impact of interventional lighting on harm level.

References: 1. Kohn LC, JM; Donaldson MS. To err is human: building a safer health system. . Washington, DC: National Academics Press; 1999. 2. Landrigan CP, Parry GJ, Bones CB, Hackbarth AD, Goldmann DA, Sharek PJ. Temporal trends in rates of patient harm resulting from medical care. N. Engl. J. Med. 2010;363(22):2124-2134. 3. Viola AU, James LM, Schlangen LJ, Dijk DJ. Blue-enriched white light in the workplace improves self-reported alertness, performance and sleep quality. Scand. J. Work. Environ. Health. 2008;34(4):297-306. 4. Lockley SW, Evans EE, Scheer FA, Brainard GC, Czeisler CA, Aeschbach D. Short-wavelength sensitivity for the direct effects of light on alertness, vigilance, and the waking electroencephalogram in humans. Sleep. 2006;29(2):161-168. 5. Hattar S, Liao HW, Takao M, Berson DM, Yau KW. Melanopsin-containing retinal ganglion cells: architecture, projections, and intrinsic photosensitivity. Science. 2002;295(5557):1065-1070.

Keywords: Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: The project was supported by Midwest Lighting Institute, the Clinical and Translational Science Award (CTSA) program, through the NIH National Center for Advancing Translational Sciences (NCATS), grant 1UL1TR002373, and an unrestricted research grant from Research to Prevent Blindness, Inc. to the Department of Ophthalmology and Visual Sciences at the University of Wisconsin

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Poster 301**Impact of visual abstracts and social media on neuro-ophthalmology publication viewership**

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Introduction:

Visual abstracts portray information from a scientific paper in an easy to understand pictogram that can be easily posted on social media. Social media platforms have 300 million to 3 billion users and can be utilized to help distribute knowledge as well as drive traffic and readers to medical journals. The purpose of this study is to see if visual abstracts can aid in distribution of newly created neuro-ophthalmic knowledge.

Methods:

Journal of Neuro-Ophthalmology (JNO) Twitter and Facebook posts along with associated articles were analyzed from 4/29/2019 to 9/5/2019. Posts were divided into two categories: standard automated posts (SAP) generated by the publisher and visual abstract posts (VA) designed by two young neuro-ophthalmologists. Social media metrics tracked on the platforms and article metrics tracked on the JNO website were compared. P values were calculated by t-test.

Results:

Mean twitter engagements for SAP were 9 +/- 12 and for VA were 34 +/- 24, $p < 0.001$ and for Facebook 18 +/- 7 vs 96 +/- 70, $p = 0.003$ respectively. Twitter impressions for SAP were 252 +/- 294 and for VA were 1360 +/- 1264, $p = 0.006$ and for Facebook 117 +/- 17 & 823 +/- 580, $p = 0.002$ respectively. Twitter VA led to more citations by individual social media accounts and number of posts linking to JNO articles compared to SAP, $p = 0.04$ and $p < 0.001$ respectively. There were no statistically significant differences across article metrics including Full Text or Abstract views, and PDF downloads between SAP and VA.

Conclusions:

Visual abstracts in social media increase multiple social media metrics but failed to increase Full Text and Abstract views / downloads on the JNO website which may be limited by social media use among target viewership. Further research is needed to determine the best way to utilize these new resources to distribute neuro-ophthalmic knowledge.

References: None.

Keywords: Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 302**Sleep-Deprived Residents and Rapid Picture Naming Performance Using the Mobile Universal Lexicon Evaluation System (MULES)**

Jenna Conway¹, Luke Moretti¹, Omar Akhand¹, Binu Joseph¹, Liliana Serrano¹, Arielle Kurzweil¹, Steven Galetta¹, Laura Balcer¹

¹NYU School of Medicine, New York, New York, USA

Introduction:

The Mobile Universal Lexicon Evaluation System (MULES) is a rapid picture naming task that captures extensive brain networks involving afferent/efferent visual, cognitive, and language pathways. MULES performance is impaired in concussion and multiple sclerosis. Many of the factors captured by MULES may also be abnormal in sleep-deprived post-call residents. The objective of this study was to investigate the effect of sleep deprivation in post-call residents on MULES performance.

Methods:

MULES, which consists of 54 color photographs of various items (fruits, animals, and random objects) was administered to a cohort of neurology residents on 24-hour in-hospital call (n=20) and a group of similar-aged controls not taking call (n=20). Differences in times and errors between baseline and follow-up MULES scores were compared between the two groups.

Results:

MULES time in post-call residents was significantly worse (slower) from baseline (average 1.5 seconds, range -6.3 to 11.5) compared to controls not taking call (average -11 seconds, range -0.4 to -28.4) ($p<0.0001$, Wilcoxon rank sum test). For all participants, the change in MULES time from baseline was significantly correlated to the change in subjective level of sleepiness ($r_s=0.63$, $p<0.0001$) and to number of MULES errors ($r_s=0.32$, $p=0.048$). For both groups, there was no significant correlation between MULES time and amount of sleep obtained ($r_s=0.08$, $p=0.62$), time since last caffeine consumption ($r_s=0.35$, $p=0.07$), or sleep quality questionnaire score ($r_s=0.22$, $p=0.17$). For post-call residents, the duration of sleep obtained during call did not significantly correlate with change in MULES scores ($r_s=-0.1$, $p=0.69$).

Conclusions:

The MULES is a novel test for effects of sleep deprivation on visual processing, rapid eye movements, attention, and language. Sleep deprivation significantly worsens MULES performance. Worsened MULES performance is associated with increased subjective sleepiness and number of errors. MULES may serve as a useful performance assessment tool for sleep deprivation in residents.

References: Cobbs L, Hasanaj L, Amorapanth P, et al. Mobile Universal Lexicon Evaluation System (MULES) test: A new measure of rapid picture naming for concussion. *J Neurol Sci.* 2017;372:393-398. Akhand O, Galetta MS, Cobbs L, et al. The new Mobile Universal Lexicon Evaluation System (MULES): A test of rapid picture naming for concussion sized for the sidelines. *J Neurol Sci.* 2018;387:199-204. Seay M, Akhand O, Galetta MS, et al. Mobile Universal Lexicon Evaluation System (MULES) in MS: Evaluation of a new visual test of rapid picture naming. *J Neurol Sci.* 2018;394:1-5.

Keywords: Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 303**NANOS-NOVEL committee members find their work rewarding.**

Sachin Kedar¹, Kathleen Digre², M. Tariq Bhatti³, Nancy Lombardo⁴

¹University of Nebraska Medical Center, Omaha, Nebraska, USA, ²Moran Eye Center, University of Utah, Salt Lake City, Utah, USA, ³Mayo Clinic College Of Medicine, Rochester, Minnesota, USA, ⁴Eccles Health Sciences Library, University of Utah, Salt Lake City, Utah, USA

Introduction:

The Neuro-Ophthalmology Virtual Education Library (NOVEL) Committee, the NOVEL Editorial Board, and the NANOS Curriculum Committee, work together to develop, maintain, and improve NOVEL and the licensed products, the NANOS Illustrated Curriculum (IC) and the North American Neuro-Ophthalmology Society (NANOS) Neuro-ophthalmology Examination Techniques (NExT). The objective of this survey is to determine the value of these projects to the academic growth of committee members.

Methods:

The three committee chairs designed a brief survey with 12 questions, which addressed understanding the value and benefits of work on NANOS-NOVEL projects, areas for improvement, and utility of these products in training curriculum at their institutions. Finally, the survey asked about use of the NOVEL products, and perceived value of those products for education of residents, fellows, or students. The committee chairs expect the survey results to guide their efforts to communicate value, and to identify areas where better communication might boost participation.

Results:

Of the 60 committee members, 42 (70%) completed the survey. Sixty percent of the respondents indicated that their work helped them academically or professionally. More than half of the respondents contributed submissions to NOVEL. Forty five percent listed their NOVEL publications on their curriculum vitae, and thirty percent indicate that their institution values these publications. Ninety percent use NOVEL and/or NANOS IC or NANOS NExT in their student, resident, fellow teaching. The major barrier to participation was lack of time. Several respondents desired more participation.

Conclusions:

A majority of committee members indicate that work on NANOS and NOVEL committees has helped them with academic and professional growth. NOVEL products are being used and assisting in teaching at institutions. Finding ways to communicate opportunities for participation should be helpful. The survey will help the current and future committee chairs in their efforts to provide quality improvement for those participating in these projects.

References: None.

Keywords: Miscellaneous

Financial Disclosures: licensed technology with EON Reality

Grant Support: None.

Contact Information: Sachin Kedar M.D.- Assoc. Professor in Neurology and Ophthalmology, Program Director, Neurology residency, University of Nebraska Medical Center, 988440 Nebraska Medical Center Omaha, NE 68198-8440; 402-559-8553; sachin.kedar@unmc.edu

Poster 304**EXOTROPIA IN THYROID EYE DISEASE: A CASE SERIES**

Yael Redler¹, George Saitakis², Suzanne Freitag², Jin Ma², Dean Cestari²

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Introduction:

Thyroid eye disease (TED) often causes a restrictive strabismus and most commonly affects the inferior, medial and superior recti muscles. Clinically, the most common strabismus patterns seen are hypotropias and esotropias or a combination of both. Traditionally it has been taught that the lateral recti muscles are rarely involved and that exotropias are not seen in patients with TED. We report 15 cases of isolated exotropia or in combination with a hypotropia.

Methods:

Retrospective review of patients referred to a Neuro-Ophthalmology clinic who underwent strabismus surgery between 1/1/11 and 10/31/19.

Results:

Of the 1,458 strabismus surgeries performed during the aforementioned period, 177 patients (12%) had surgery due to restrictive strabismus caused by TED, 15 out of the 177 (8.5%) patients exhibited an exotropia as a component of their misalignment and 1 patient had an isolated exotropia without the concomitant presence of a hypotropia.

Conclusions:

In our case series, we demonstrated the presence of an exotropic component in 8.5 % of our TED patients who underwent strabismus surgery. This represents a significant percentage and supports the conclusion clinicians should not exclude TED as a possible etiology in patients with an exotropia. Our data also supports the possibility that the exotropic variant of TED patients is underdiagnosed and/or underrepresented in the medical literature.

References: None.

Keywords: Adult strabismus with a focus on diplopia, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Poster 305**Assessment of Neurocognitive Consequences of Resident Call Duty Using the New MULES Rapid Picture-Naming Tool**

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Introduction:

The Mobile Universal Lexicon Evaluation System (MULES) is a tool testing the speed and accuracy of identification and naming of color images that has been investigated for sideline concussion assessment. It requires integrity of saccades, visual processing and cognition and uses a wider network of neuronal pathways than simple number-naming tools. The purpose of this study was to use MULES to evaluate neurocognitive effects of sleep deprivation in residents.

Methods:

A prospective, cohort study was conducted on surgery residents (PGY1-7) of an inner-city teaching hospital. MULES was performed before and after overnight call in the experimental group and on two consecutive days in controls. Estimates of Karolinska Sleepiness Scale (KSS) (1=extremely alert, 9=extremely sleepy), hours of sleep prior to testing and time and accuracy of MULES were recorded. Statistical analysis was performed using Chi-square and Mann-Whitney U tests and Spearman's rank correlation with SPSS-25 software. Significance was set at $p < 0.05$.

Results:

49 residents: 18 experimental on-call and 31 controls were tested. Mean (SD) age and gender were similar between the two groups: 29.56(3.99) years in the experimental group and 28.87(2.90) years in the controls ($p = 0.631$) and 33.3% female in the experimental group and 54.8% in the controls ($p = 0.146$). There were no differences in baseline MULES scores (34.87secs, experimental; 36.99secs, controls [$p = 0.29$]), in hours of sleep ($p = 0.39$) and test time changes from the first to the second day ($p = 0.233$), between the two groups. For all residents, more sleep the previous 24 hours correlated with improved testing time (Spearman's $\rho = 0.323$, $p = 0.024$). KSS ($p = 0.253$), PGY ($p = 0.246$) and age ($p = 0.470$) were not associated with MULES performance times.

Conclusions:

Residents reporting more hours of sleep demonstrated improved MULES performance compared to their baseline scores. Further research is required to confirm these results and to determine the level of sleep deprivation that negatively impacts MULES performance.

References: Davies EC, Henderson S, Balcer LJ, Galetta SL. Residency training: The King-Devick test and sleep deprivation. *Neurology* 2012;78:e103-e106. Ding ME, Mbekeani JN, Ahmed Y, Conigliaro R, Delphin E, Durstenfeld A, Jagannath A, Masters-Israilov A, Milstein M, Rabin M, Ramachandran S, Vlismas P, Yang D, Heo M, Rosenberg JB. Measurement of resident fatigue using rapid number naming. *J Neurol Sci.* 2019;397:117-122. Akhand O, Galetta MS, Cobbs L, Hasanaj L, Webb N, Drattell J, Amorapanth P, Rizzo JR, Nolan R, Serrano L, Rucker JC, Cardone D, Jordan BD, Silverio A, Galetta SL, Balcer LJ. The new Mobile Universal Lexicon Evaluation System (MULES): A test of rapid picture naming for concussion sized for the sidelines. *J Neurol Sci.* 2018;387:199-204. Cobbs L, Hasanaj L, Amorapanth P, Rizzo JR, Nolan R, Serrano L, Raynowska J, Rucker JC, Jordan BD, Galetta SL, Balcer LJ. Mobile Universal Lexicon Evaluation System (MULES) test: A new measure of rapid picture naming for concussion. *J Neurol Sci.* 2017;372:393-398.

Keywords: Ocular motility, Higher visual functions, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Poster 306**Proportion of neuro-ophthalmologic disorders in patients referred to neuro-ophthalmology for visual disturbances after cataract surgery**

Shuai-Chun Lin¹, Angie Giang¹, Maxwell Pistilli¹, Grant Liu¹, Robert Avery¹, Kenneth Shindler¹, Ali Hamedani¹, Ahmara Ross¹, Madhura Tamhankar¹

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Introduction:

Underlying ocular, systemic or neuro-ophthalmologic conditions may result in postoperative visual disturbances in patients after uneventful cataract surgery. We sought to identify the proportion of patients who had a confirmed underlying neuro-ophthalmic disorder that were referred for neuro-ophthalmic evaluation of visual disturbances after cataract surgery.

Methods:

Patients with visual disturbance after cataract surgery (onset \leq 6 months post-operative) and who were referred to neuro-ophthalmology from 2010-2019 were identified by using PennSeek-search and REDCap electronic-data-capture-tools. Data were collected on demographics, symptom onset, systemic and ocular comorbidities, neuro-ophthalmologic exam, diagnosis and management.

Results:

101 patients referred for visual disturbance, including blurry vision, reading difficulty, diplopia, eye pain, photophobia and scotoma after cataract surgery were enrolled.

33.7% of patients (34/101) were newly diagnosed with neuro-ophthalmologic diseases, including 23 patients with afferent visual pathway pathology (15 with optic neuropathies, 5 with brain tumor related optic atrophy and 3 patients with posterior cortical atrophy), while 11 patients had efferent pathway disorders (fourth nerve palsy, skew deviation, convergence/divergence insufficiency, myasthenia gravis, thyroid eye disease, ptosis and Parkinson's disease). 9/23 patients with afferent pathologies were referred due to the presence of afferent pupillary defect, disc pallor or disc edema.

There were 27.7% (28/101) patients with decompensated strabismus presenting with new onset diplopia post-operatively. 36.6% (37/101) patients had visual disturbance secondary to intraocular conditions (refractive errors, dry eye, IOL related dysphotopsia, glaucoma or retinal disease), while systemic conditions (orthostatic hypotension and inner ear disease) were identified in 2 patients (2%) as the cause of visual disturbances.

Conclusions:

Our study demonstrated that two thirds (61.4%) of the patients referred to a neuro-ophthalmology practice for post cataract surgery visual disturbances indeed had underlying neuro-ophthalmic disorders. The high percentage of true underlying neuro-ophthalmic disorders in this study suggests that some cataract surgeons generally refer patients appropriately indicating a high yield for such neuro-ophthalmology consults.

References: 1. Lundstrom M, Brege KG, Floren I, Stenevi U, Thorburn W. Impaired visual function after cataract surgery assessed using the Catquest questionnaire. *J Cataract Refract Surg.* 2000;26(1):101-108. 2. Samadi B, Lundstrom M, Kugelberg M. Improving patient-assessed outcomes after cataract surgery. *Eur J Ophthalmol.* 2017;27(4):454-459. 3. Lundstrom M, Stenevi U. Analyzing patient-reported outcomes to improve cataract care. *Optom Vis Sci.* 2013;90(8):754-759. 4. Lee MS, Rizzo JF, 3rd, Lessell S. Neuro-ophthalmologic complications of cataract surgery. *Semin Ophthalmol.* 2002;17(3-4):149-152. 5. Nayak H, Kersey JP, Oystreck DT, Cline RA, Lyons CJ. Diplopia following cataract surgery: a review of 150 patients. *Eye (Lond).* 2008;22(8):1057-1064. 6. Yanguela J, Gomez-Arnau JI, Martin-Rodrigo JC, et al. Diplopia after cataract surgery: comparative results after topical or regional injection anesthesia. *Ophthalmology.* 2004;111(4):686-692.

Keywords: Optic neuropathy, Ocular motility, Adult strabismus with a focus on diplopia

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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North American Neuro-Ophthalmology Society

46th Annual Meeting

March 7– March 12, 2020

Omni Amelia Island Plantation • Amelia Island, FL

Wednesday, March 11

6:00 am – 6:45 am	Yoga	Oceanview Room (Sunrise Tower, B level next to workout room)
6:30 am – 7:30 am	Breakfast with Exhibitors	Magnolia Ballroom
6:30 am – 7:30 am	Breakfast with the Novices	Magnolia Ballroom

Join us in the reserved YONO area at breakfast for table discussions led by senior members and /or YONOs to discuss topics relevant to aspiring or current YONOs.

6:30 am – 7:30 am	Relations to Industry - Diversifying Your Career <i>Barrett Katz, MD</i>	
6:30 am – 7:30 am	Private Practice Neuro-Ophthalmology <i>Howard R. Krauss, MD, BEEE, SM and Kevin Lai, MD</i>	
6:30 am – 7:30 am	CME Committee Meeting	Ossabaw A
6:30 am – 5:30 pm	Registration/Help Desk	Amelia Foyer
6:30 am – 7:30 am	Consortium of Pediatric Neuro-Ophthalmologists Meeting (CPNO) - All are welcome to attend <i>Facilitator: Paul H. Phillips, MD</i>	Talbot
7:30 am – 9:30 am	Skullbase Disorders and Surgical Approaches [2.0 CME] <i>Moderators: M. Tariq Bhatti, MD and Vivek Patel, MD</i>	Amelia Ballroom

This series of case presentations will provide the audience with an anatomical perspective and minimally invasive surgical approach to manage common neuro-ophthalmic neurosurgical problems.

Upon completion of this session, participants should be able to: (1) demonstrate the important neurosurgical aspects of a superior orbital fissure mass, (2) describe the potential surgical pitfalls of a superior orbital fissure mass, (3) describe the surgical planning and approach to a chiasmal lesion, (4) explain the limitations of particular surgical approaches to the optic chiasm, (5) illustrate the neurosurgical insights into the planning and execution of treating a large acute brainstem hematoma, (6) discuss the functional anatomic perspective of the vertical rami of the superior longitudinal fasciculus, and (7) describe the visual function of the vertical rami of the superior longitudinal fasciculus.

7:30 am – 7:35 am	Welcome and Symposium Overview <i>M. Tariq Bhatti, MD</i>
7:35 am – 8:15 am	“The Invisible Anatomy;” Exo- and Endophytic Neural Network <i>Amin Kassam, MD</i>
8:15 am – 8:35am	Case 1

8:35 am – 8:55 am	Superior Orbital Fissure Mass <i>Vivek Patel, MD</i> Surgical Approach <i>Amin Kassam, MD</i> Q&A/Discussion <i>M. Tariq Bhatti, MD and Vivek Patel, MD</i> Case 2 Chiasmal Compression <i>M. Tariq Bhatti, MD</i> Surgical Approach <i>Amin Kassam, MD</i> Q&A/Discussion <i>M. Tariq Bhatti, MD and Vivek Patel, MD</i>	
8:55 am – 9:15 am	Case 3 Large Acute Brainstem Hematoma <i>Vivek Patel, MD</i> Surgical Approach <i>Amin Kassam, MD</i> Q&A/Discussion <i>M. Tariq Bhatti, MD and Vivek Patel, MD</i>	
9:15 am – 9:25 am	New Frontiers: Vertical Rami of the Superior Longitudinal Fasciculus and the White Matter Chassis: A Functional Anatomic Perspective of the Subcortical Neural Network <i>Amin Kassam, MD</i>	
9:25 am – 9:30 am	Closing Remarks, Review <i>M. Tariq Bhatti, MD and Vivek Patel, MD</i>	
9:30 am – 10:00 am	Coffee with Exhibitors	Magnolia Ballroom
10:00 am – 11:25 am	2020: What's New in Low Vision [1.5 CME]	Amelia Ballroom
	<i>Moderators: Marie D. Acierno, MD and Joseph F. Rizzo III, MD</i>	

This session focuses on advancements in neuroscience in visual impairments and will look at neuroplasticity associated with visual impairments and blindness (both ocular and cerebral causes), how blind persons adapt to visual loss, compensatory behaviors related to changes occurring at the level of the brain, virtual environments as a means for blind individuals to interact with non-visual information in a meaningful manner, and explore how technology has offered new therapeutic options for patients with acquired blindness.

Upon completion of this session, participants should be able to: (1) describe how blind persons adapt to visual loss, (2) describe how compensatory behaviors are related to changes occurring at the level of the brain, (3) describe how virtual environments may be used as a means for blind individuals to interact with non-visual information in a meaningful manner, and (4) discuss how technology has offered new therapeutic options for patients with acquired blindness.

10:00 am – 10:25 am	Visual Neuro-Rehabilitative Approaches: Rehabilitative Strategies and the Role in How One Develops, Adapts, and Responds to Injury in the Visual System <i>Lotfi Merabet, OD, PhD, MPH</i>
10:25 am – 10:50 am	Virtual Reality: How to Assess Functional Vision Performance in Patients With Neurological Injury <i>Lotfi Merabet, OD, PhD, MPH</i>
10:50 am – 11:05 am	Visual Prosthetics: Enabling Technology to Give Sight to the Visually Impaired <i>Joseph F. Rizzo III, MD</i>
11:05 am – 11:15 am	Visual Rehabilitation: How Do We Empower Our Visually Impaired Patients? <i>Marie D. Acierno, MD</i>
11:15 am – 11:25 am	Discussion/Q&A

11:25 am – 12:00 pm	Jacobson Lecture- Optic Neuritis: Past, Present and Future [0.5 CME] <i>Speaker: Steven Galetta, MD</i>	Amelia Ballroom
12:00 pm – 12:15 pm	Announcements/NOVEL Update	Amelia Ballroom
12:00 pm – 12:05 pm 12:05 pm – 12:15 pm	Announcements, Valerie Biousse, MD NOVEL Update, Kathleen Digre, MD	
12:15 pm – 1:15 pm	Lunch break Lunch will be available for purchase in the meeting space. Credit card or room charge only.	Magnolia Garden
12:15 pm – 1:45 pm	Research Committee Luncheon	Talbot
12:20 pm – 1:10 pm	A Paradigm Shift for the Management of Thyroid Eye Disease (TED)* (advanced registration required) *This symposium is organized by Horizon Therapeutics.	Cumberland Ballroom

Come learn about the importance of early identification and a new treatment approach for Thyroid Eye Disease (TED) management. This presentation is intended for US healthcare professionals.

12:20 – 1:10 pm	A Paradigm Shift for the Management of Thyroid Eye Disease (TED) <i>Kimberly P. Cockerham, MD, FACS</i>	
1:15 pm – 3:15 pm	3D Anatomy [2.0 CME] <i>Moderators: M. Tariq Bhatti, MD and Vivek Patel, MD</i>	Amelia Ballroom

In this session, specially formatted 3-D atlas images will provide participants with an immersive experience outlining the detailed projections of the human visual system using innovative multi-media technology. The optic nerves, orbital, skull base, and parasellar anatomy will be navigated and described. It will also provide detailed views and relational information regarding the brain parenchyma with specific attention to the central visual pathways. Clinical and surgical correlations will be made throughout.

Upon completion of this session, participants should be able to: (1) describe the anatomical relationship between important neuroanatomical structures relevant to vision and visual processing, (2) recognize the complex organization of neuroanatomical structures sub-serving visual functions, and (3) apply this understanding of anatomy of the visual pathways to clinical practice.

1:15 pm – 3:15 pm	3D Anatomy, Amin Kassam, MD	
3:30 pm – 5: 15 pm	Skullbase Surgical Approaches - “Live” Dissection [1.75 CME] <i>Amin Kassam, MD</i>	Cumberland Ballroom

In this live cadaveric head dissection, Dr. Kassam and his colleagues will locate and define the ocular motor cranial nerves, demonstrate the dorsal-cranial approach to the superior orbital fissure, cavernous sinus and interpeduncular cistern, and detail the post-chiasmatic components of the white matter visual neural networks.

Upon completion of this session, participants should be able to: (1) apply the anatomical knowledge gained from the cadaveric head dissection to clinical practice, (2) describe the complexities and challenges in approaching the superior orbital fissure, cavernous sinus and interpeduncular cistern, and (3) recognize the post-chiasmatic components of the white matter visual neural networks.

6:30 pm – 12:00 am

Banquet

**Amelia and Magnolia
Ballrooms**

Join colleagues for a fun, casual evening of socializing, dining and dancing at the NANOS Annual Banquet! Dinner will take place in the Amelia Ballroom followed by dancing in the Magnolia Ballroom. This event is complimentary for registered attendees; guests must purchase a ticket for \$150 at the Registration Desk.

3D SKULL BASE ANATOMY

*Amin Kassam, MD
Aurora St. Luke's Medical Center
Milwaukee, WI*

LEARNING OBJECTIVES

1. Understand the fundamentals of skull base anatomy and the orbital (osseous, vascular and neural) framework
2. Describe the fundamentals of intrinsic subcortical and optic neural pathways, from the optic chiasm to the cortex, and the related neural pathways critical for visual processing.
3. Identify the differences between various anatomic windows to access the optic nerve (CN II) and ocular motor cranial nerve (CN III, CN IV, and CN VI)
4. Introduce the concept of the “13th cranial nerve”

CME QUESTIONS

1. In undertaking surgical access of the orbital and visual pathways, what are the essential principles or tenets that one should generally adhere to?
2. What are the components comprising the neural network, and how is this relevant to optic and visual pathways?
3. What is the “13th cranial nerve” and how is it relevant to current concept of subcortical white matter anatomy, in particular, the emergence of “visual cognition”?

KEYWORDS

1. Skull base
2. Orbit
3. White matter tracts
4. Cranial nerves
5. Visual Cognition

HIGHLIGHTS

In this session, participants will be first introduced to the fundamental principles of skull base and orbital anatomy. Explicitly, the concepts of radial corridors (outer osseous framework and the inner neurovascular) will be emphasized. Once the extrinsic architecture is established, the subcortical white matter tract (WMT) anatomy and neural pathways (including cranial nerves) will be highlighted and correlated with clinical case examples.

SUMMARY

Skull base and orbital surgery has witnessed a progressive anatomically-driven evolution based on three eras: osseous, vascular, and more recently neural. With the incremental understanding of microsurgical

neuroanatomy and visualization of previously unseen structures due to the rapid development of optical technology, there has been an explosive development in identifying skull base corridors. As a result, surgeons now have the ability to visualize and access previously “inaccessible” regions surrounded by often unforgiving neurovascular anatomical structures. In general, these corridors can be divided into three distinct anatomic pathways: dorsal transcranial, ventral transfacial, and in the past decade endonasal. The development of both the dorsal and ventral orbital corridors is founded on a sound understanding of microsurgical anatomy, surgical principles in accessing these corridors, and the optical technology to permit effective surgical visualization. We are now able to systematically organize both dorsal and ventral corridors and have developed an algorithmic approach considering the key components that drive safe and effective skull base and orbital surgery. The addition of exophytic (cranial nerve) and more recently, endophytic (white matter tract or the 13th cranial nerve) pathways to overall anatomical picture, plays a vital role in mitigating complications, particularly, important in an era where quality of life and cognition are valued.

CME ANSWERS

1. Orbital bone can be drilled, vessels can be moved and rerouted but the central retinal artery must be preserved. At the minimum, 2 of the 3 primary feeding constituents; however the plane of cranial nerves and white matter, ideally, should not be crossed.
2. The neural network is comprised of the exophytic (cranial nerves) and endophytic (white matter tracts) structures. Cranial nerves represent the exophytic extension of the central nervous system to the effector organs (retina and muscles, in the case of the visual systems). The subcortical white matter tracts play a role in connection of the central neural axis to higher order processing (cognitive, verbal, sensory, motor, etc) functions.
3. The 13th cranial nerve represents the white matter tracts. They have discrete boundaries and transmit afferent/efferent input and circuitry, no different than cranial nerves. However, the only anatomic difference between the 13th cranial nerve and other cranial nerves is that the 13th cranial nerve remains within the central nervous system (endophytic) as opposed to having exophytic extensions outside the central nervous system.

REFERENCES

1. Labib MA, Prevedello DM, Carrau R, Kerr EE, Naudy C, Abou Al-Shaar H, Corsten M, Kassam A. A road map to the internal carotid artery in expanded endoscopic endonasal approaches to the ventral cranial base. *Neurosurgery*. 2014;10 Suppl 3:448-471; discussion 471. doi:10.1227/NEU.0000000000000362.
2. de Lara D, Ditzel Filho LFS, Prevedello DM, Carrau RL, Kasemsiri P, Otto BA, Kassam AB. Endonasal endoscopic approaches to the paramedian skull base. *World Neurosurg*. 2014;82(6 Suppl):S121-129. doi:10.1016/j.wneu.2014.07.036.
3. Di Maio S, Ramanathan D, Garcia-Lopez R, Rocha MH, Guerrero FP, Ferreira Jr. M, Sekhar LN. Evolution and Future of Skull Base Surgery: The Paradigm of Skull Base Meningiomas. *World Neurosurgery*. 2012;78(3-4):260-275. doi:10.1016/j.wneu.2011.09.004.
4. Prevedello DM, Doglietto F, Jane JA, Jagannathan J, Han J, Laws ER. History of endoscopic skull base surgery: its evolution and current reality. *J Neurosurg*. 2007;107(1):206-213. doi:10.3171/JNS-07/07/0206.

5. Jennings JE, Kassam AB, Fukui MB, Monroy-Sosa A, Chakravarthi S, Kojis N, Rovin RA. The Surgical White Matter Chassis: A Practical 3-Dimensional Atlas for Planning Subcortical Surgical Trajectories. *Oper Neurosurg (Hagerstown)*. 2018;14(5):469-482. doi:10.1093/ons/oxp177.
6. Monroy-Sosa A, Jennings J, Chakravarthi S, Fukui MB, Celix J, Kojis N, Lindsay M, Walia S, Rovin R, Kassam A. Microsurgical Anatomy of the Vertical Rami of the Superior Longitudinal Fasciculus: An Intraparietal Sulcus Dissection Study. *Oper Neurosurg (Hagerstown)*. June 2018. doi:10.1093/ons/opy077.
7. Chakravarthi SS, Kassam AB, Fukui MB, Monroy-Sosa A, Rothong N, Cunningham J, Jennings JE, Guenther N, Connelly J, Kaemmerer T, Nash KC, Lindsay M, Rissell J, Celix JM, Rovin RA. Awake Surgical Management of Third Ventricular Tumors: A Preliminary Safety, Feasibility, and Clinical Applications Study. *Oper Neurosurg (Hagerstown)*. February 2019. doi:10.1093/ons/opy405.
8. Chakravarthi S, Fukui M, Monroy-Sosa A, Roman-Mena LPDS, Gonen L, Epping A, Celix J, Jennings J, Khalili S, Corsten M, Rovin R, Kassam AB. Revisiting the Anatomy with Physics: A Preliminary, Single-Center Experience with Its Current Surgical Platform for the Treatment of Skull Base Meningiomas. In: *Journal of Neurological Surgery Part B: Skull Base*. Vol 80. Georg Thieme Verlag KG; 2019:A136. doi:10.1055/s-0039-1679552.
9. Abbassy M, Woodard TD, Sindwani R, Recinos PF. An Overview of Anterior Skull Base Meningiomas and the Endoscopic Endonasal Approach. *Otolaryngol Clin North Am*. 2016;49(1):141-152. doi:10.1016/j.otc.2015.08.002.

VISUAL NEURO-REHABILITATIVE APPROACHES: REHABILITATIVE STRATEGIES AND THE ROLE IN HOW ONE DEVELOPS, ADAPTS, AND RESPONDS TO INJURY IN THE VISUAL SYSTEM

*Lotfi B. Merabet, OD, PhD, MPH
Massachusetts Eye and Ear, Harvard Medical School
Boston, MA*

LEARNING OBJECTIVES

1. Discuss the notions of neuroplasticity, critical period, and injury focality, and their potential impact on the recovery and rehabilitation of patients with injury to the visual system.
2. Compare different rehabilitative approaches with respect to visual field loss.
3. Discuss the different types of visual processing disorders associated with damage to higher order visual areas and their potential strategies for rehabilitation.

CME QUESTIONS

1. What is the definition of neuroplasticity and discuss its relevance with respect to recovery from brain injury?
2. What are three categories of treatment options (and give examples of each) associated with visual field loss?
3. How does damage to higher order visual areas (e.g. implicating parietal, temporal, or frontal cortices) differ in terms of their possible manifestations of visual deficits?

KEYWORDS

1. Neuroplasticity
2. Neurological injury
3. Visual field deficit
4. Higher order visual deficit
5. Rehabilitation

HIGHLIGHTS

- Neurological injury is often associated with a variety of visual impairments. In general, the profile of these impairments often bears a close association with the location, timing, and nature of the neurological injury.
- In the case of visual field loss, treatment options can be characterized as compensatory, optical, or restorative.
- Damage to higher order visual areas such as parietal and temporal cortices are characterized by deficits in spatial and object related processing respectively. In contrast, damage implicating frontal areas are often associated with difficulties with focusing and sustaining attention. Clinical examples of these cases will be presented.
- Familiarization with the concept of neuroplasticity, its potential (and constraints), can help create an operating framework to develop novel rehabilitative strategies in the setting of injury to the visual system.

SUMMARY

Patients with neurological injury can present with visual deficits that often bear close association with the location, timing, and nature of the insult. In this session, we will discuss the effect of these factors in the context of neuroplasticity as it relates to visual rehabilitation in the setting of neurological injury. We will discuss various treatment approaches for visual field loss as well the challenges associated with rehabilitation and recovery of function following damage to the higher order areas of the visual system.

CME ANSWERS

1. Neuroplasticity can be defined as the ability of the brain to change its structural and functional organization in response to development, experience, the environment, or damage. In broad terms, understanding the potential and constraints of neuroplasticity can help frame the relevance of various factors (such as the timing and focality of injury) with respect to recovery of function.
2. Treatment options for visual field loss can be characterized as compensatory, optical, or restorative. Respective examples for each include visual scanning, optical prisms, and visual rehabilitative training.
3. Neurological damage to parietal areas is often associated with spatial processing deficits (e.g. visual neglect) while damage to temporal cortical areas is often associated with difficulties in object identification (e.g. visual agnosias). Damage with frontal areas is often associated with difficulties with visual search and tracking of objects, especially in complex environments.

REFERENCES

1. Plow EB, Maguire S, Obretenova S, Pascual-Leone A, Merabet LB. Approaches to rehabilitation for visual field defects following brain lesions. *Expert Rev Med Devices*. 2009 May;6(3):291-305.
2. Mansouri B, Roznik M, Rizzo JF 3rd, Prasad S. Rehabilitation of Visual Loss: Where We Are and Where We Need to Be. *J Neuroophthalmol*. 2018 Jun;38(2):223-229.

VIRTUAL REALITY: HOW TO ASSESS FUNCTIONAL VISION PERFORMANCE IN PATIENTS WITH NEUROLOGICAL INJURY

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LEARNING OBJECTIVES

1. Identify challenges/limitations with standard ophthalmic assessments in patients with neurological injury.
2. Distinguish between assessments of visual function and functional vision.
3. Discuss the advantages of virtual reality in assessing functional visual performance.

CME QUESTIONS

1. What is the difference between an assessment of visual function and functional vision?
2. What are some of the challenges associated assessing functional vision in patients with neurological injury?
3. What are some of the advantages offered by virtual reality in assessing visual performance?

KEYWORDS

1. Functional vision
2. Neurological injury
3. Visual impairment
4. Virtual reality
5. Ecological validity

HIGHLIGHTS

- Assessing visual performance in patients with visual impairments associated with neurological injury can be challenging. Often, assessments such as visual acuity and perimetry fail to capture the nature and extent of higher order visual deficits (e.g. deficits in attention, visual search, object recognition, and spatial processing).
- Psychophysical testing using various stimulus designs and tasks can be more useful in characterizing higher order visual deficits, but often lack ecological validity. This is can be particularly problematic when testing children.
- Assessing performance using virtual reality based approaches affords the possibility to better characterize higher order visual deficits using environments that are ecologically valid and that approach real world conditions.

SUMMARY

Patients with visual impairments associated with neurological injury often present with a wide range of visual deficits. This session will discuss some of the challenges and limitations associated with assessing visual function and functional vision in these patients. We will discuss novel approaches based on virtual

reality for assessing visual performance as well as higher order cognitive functions. The value of testing using virtual reality based approaches is based on its ecological validity; that is, its ability to assess performance in settings that approach real world settings and scenarios.

CME ANSWERS

1. Visual function describes how well the eyes and basic visual system can detect a target stimulus. By varying a single parameter at a time (for example, the size of the target), testing is typically carried out in a repeated fashion under controlled testing conditions until a threshold of performance is obtained (e.g. visual acuity and perimetry). In contrast, functional vision refers to how well an individual performs while interacting with the visual environment. That is, how their vision is used in everyday activities. Characterizing functional vision involves the assessment of multiple and varying parameters captured under complex, real-life conditions as well as how well an individual is able to sustain performance over time.
2. Often patients with neurological injury will report deficits beyond changes in visual acuity. In fact, many patients may have visual acuity, contrast, color perception, and visual field function all within normal limits, or at the very least, incongruent with the extent of reported visual perceptual difficulties. These reported deficits may be more in line with difficulties in higher order visual processing (e.g. deficits in attention, visual search, object recognition, and spatial processing) and cannot be characterized with standard measure of visual function alone.
3. Virtual reality environments afford many desirable testing advantages such as testing in realistic scenarios (ecological validity), isolation of human and perceptual factors, safe, controlled, and reliable data capture, individualized testing parameters, immersive, and motivation, can transfer assessment outcomes to inform rehabilitative strategies.

REFERENCES

1. Bennett CR, Bex PJ, Bauer CM, Merabet LB. The Assessment of Visual Function and Functional Vision. *Semin Pediatr Neurol*. 2019 Oct;31:30-40.
2. Colenbrander A. Aspects of vision loss – visual functions and functional vision, *Visual Impairment Research* 5:115-136; 2003.
3. Tarr MJ, Warren WH. Virtual reality in behavioral neuroscience and beyond, *Nature Neuroscience* 5:1089-1092; 2002.

VISUAL PROSTHETICS: ENABLING TECHNOLOGY TO GIVE SIGHT TO THE VISUALLY IMPAIRED

*Joseph F. Rizzo III
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LEARNING OBJECTIVES

1. Development understanding of the conceptual foundation of visual prosthetic devices
2. Develop understanding of the psychophysical outcomes derived from retinal prosthetic devices
3. Develop perspective on how to advise patients in consideration of receiving a visual prosthetic implant
4. Develop understanding of the complexity of bringing devices to the market.

CME QUESTIONS

1. Which visual prosthetic devices have undergone human clinical trials?
 - A. Supra-choroidal
 - B. Sub-retinal
 - C. Epi-retinal
 - D. Cortex
 - E. All of the above
2. What are criteria for consideration of receiving a retinal prosthetic device?
 - A. Any form of retinal blindness
 - B. Acquired outer retinal degeneration
 - C. Vision of Light perception vision in worse affected eye
 - D. Vision of Light perception in both eyes
 - E. B and D
3. What level of vision has been reported in recipients of retinal prosthetic devices?
 - A. 20/550
 - B. Ability to read
 - C. Ability to identify specific objects on a table
 - D. Ability to navigate in unfamiliar environment
 - E. All of the above

KEYWORDS

1. Visual prostheses
2. Retinal Prostheses
3. Vision Rehabilitation

SUMMARY

The notion that a visual prosthesis could potentially restore vision to the blind was co-opted from the early to mid 20th century work of Foerster and then the renowned neurosurgeon Wilder Penfield, who

leveraged his studies of electrical stimulation in the search for epileptogenic foci to create anatomical: functional maps of the cortical surface using feedback and motor responses from awake patients. These revolutionary studies made clear that there were predictable relationships between the location and function of cortical regions, and these results were formulated to yield comprehensive maps of human visual cortex that defined (for a given individual) the correspondence between cortical coordinates and location in visual space. This knowledge suggested that electrical stimulation of the cortex with an electrode array might be able to provide meaningful visual percepts for the blind.

The field of *retinal* prosthetics, which began in the late 1980s, was enabled by the growth of the microtechnology industry, which made it possible to conceive of placing sophisticated microelectronics into the eye. Potential candidates for any type of visual prosthetic must have had normal sight early in life so that the visual cortex would have properly developed. The conceptual foundation of the retinal prosthetic field is based upon relatively selective degeneration of the outer retina, with relative preservation of the inner retina, including the retinal ganglion cells that project to the brain via the optic nerve. For any type of visual prosthetic, the goal is to restore vision by delivering electrical stimulation *distal* to the level of neural damage. For instance, to treat outer retinal degeneration, stimulation could be delivered at the inner retina or any other more distal location along the retinal calcarine pathway. But, to treat an optic neuropathy like glaucoma, stimulation would have to be delivered at or distal to the lateral geniculate body.

WHAT ARE THE COMPONENTS OF A VISUAL PROSTHESIS?

A visual prosthesis requires the means to: **1)** capture information about the visual environment; and **2)** receive operating power and deliver electrical stimulation through an array of electrodes. (Magnetic or chemical stimulation of neurons could be used, but no such device is close to human testing). In preferred embodiments, a system also would be capable of wireless modifications of the electrical stimulation paradigm to improve the quality of percepts based upon user feedback.

The ability to capture visual information from the environment can be achieved either by using an external camera (placed on a head-mounted device, like a pair of glasses) or by implanting photodiode arrays, the pixels of which will become active in accordance with the patterns of light that fall upon the device. Operating power for camera-based systems can be provided via radiofrequency (RF) transmission *or* by infra-red or laser light directed to an implanted photodiode array that would serve as a power source. Devices with these basic features have been implanted in the supra-choroidal space; sub- or epi-retinal space; and visual cortex.

The implanted components of an any implantable microelectronic device must provide hermeticity to protect the transistors and other electronic components from destruction that will occur with essentially any leakage of sodium ions into the area of the electronic elements. A prosthesis also would be required to provide at least a 10 year estimated survival time (which is assessed in specified and accepted ways).

DEVICES UNDERGOING CLINICAL TRIALS. In the 33 years since the inception of the field of retinal prosthetic devices, two companies received regulatory approval for commercial sales. In 2011, Second Sight (with its epiretinal device, the Argus) was the first company to received regulatory approval (a “CE” mark in Europe), which two years later was followed by FDA approval in the United States. Retina Implant-AG (Tubingen, Germany) then received a CE mark in 2013 for its subretinal device (Alpha-IMS, then Alpha-AMS). Currently, two companies are actively conducting clinical trials of retinal (Pixium) or cortical (Second Sight) devices for patients with either retinitis pigmentosa or age-related macular degeneration, but no retinal device is commercially available at this time. Bionic Vision Technologies (Victoria, Australia)

has developed a supra-choroidal device as a low acuity means of assisting with navigation. A photodiode array based sub-retinal device from Taiwan (Iridium, Inc) is being evaluated by the FDA.

WHAT HAVE BEEN THE PSYCHOPHYSICAL OUTCOMES? With the exception of the Optobionics, Inc. (which in 2000 was the first to perform chronic implants in humans and also the first company to declare bankruptcy in the field), the collective results of all other psychophysical tests in humans have revealed that patients who had been legally and severely blind for decades could see basic percepts, which in the best cases achieved (roughly) 20/500 vision. Patients also have shown the ability to detect motion or orientation of lines or objects on a table, or to navigate in unfamiliar environments, although there has been significant variability in outcomes among patients. And, patients often report the value of having some visual experiences even if the metrics are not compelling. These outcomes are substantial and arguably rival or surpass outcomes from any other form of vision rehabilitation, including genetic therapy. However, interpreting prosthetic-induced percepts can be arduous, and the outcomes have not provided an unambiguous improvement in quality-of-life. Drawing comparisons among different prostheses have been challenging because of varying designs of devices and testing methods; recently, an international consortium has promulgated guidelines to help standardize psychophysical testing methods.(Rizzo and Ayton, 2019)

THE FIELD OF VISUAL PROSTHETICS: EXISTENTIAL CRISIS OR UNREALIZED POTENTIAL? The initiatives to develop visual prosthetic devices for visual rehabilitation began just over 30 years ago. After seminal work by the two groups that co-founded the field (known now as Second Sight and the Boston Retinal Implant Project/Bionic Eye Technologies), the the pace of research and the diversity of technical strategies to restore vision to the blind accelerated quickly.

In the earliest days of the field of retinal prosthetics, neither NIH nor the largest private foundations for retinal research would fund the start-up ventures. There was a sentiment within our community that we had a responsibility to demonstrate the potential for this new field before expecting to receive outside funding, and as such each program had to identify seed funds to begin its work. Private foundations stepped in to support some of the earliest efforts, which yielded sufficiently enticing results that motivated some governments to support R&D programs in their countries. From that point forward, essentially all research and development conducted by the more mature research programs was supported by governmental grants across multiple countries and continents. This infusion of funds and the growing publication of research attracted increasingly large numbers of researchers into the field. Some financially invigorated programs produced promising results (summarized above) and there was significant bench-to-bedside momentum that bolstered the hope that a prosthetic would be an effective tool for visual rehabilitation. Venture capitalists had sat on the sideline since an initial investment in Optobionics, Inc. failed when that company declared bankruptcy in 2011. But, Second Sight Medical Products, Inc. received a significant strategic investment coincident with a significant federal grant that propelled its work into clinical trials, which led to regulatory approval to commercialize their device. When Medicare approved payment for its retinal prosthesis, Second Sight was a beacon of hope in the field. A growing number of companies were active in developing a range of technical options, any one of which could potentially prove to be preferential, at least for specific types of blindness. But, additional investments, especially from venture capitalists or strategic investors, would be needed to robustly continue the growth of the field.

The Beginning of an Existential Threat. The early, somewhat promising psychophysical outcomes and regulatory approvals did attract the attention of venture capitalists, but generally their (understandable) focus on a reasonable return on investment (ROI) damped enthusiasm. As the leading companies (Second

Sight and Retina Implant-AG) began to sell their devices, it quickly became obvious that the number of implants being sold was less than what would be needed to sustain the financial health of the companies. In short order, both companies ended their initiatives in retinal prosthetic device space in 2019. The earlier damping of interest became a deluge of hesitation from the VC community while it paused to recalibrate the prospects of the field.

The converging headwinds of long R&D cycles, failure to deliver unambiguously beneficial visual results, and cautious investment attitudes are creating an existential crisis for the field. However, the inability to deliver the hoped-for outcomes does not mean that future results will fail to impress. There are at least three reasons why early psychophysical results might not have met widely-held expectations. First, the companies that performed the earliest human implants did so with technologies that had not matured as much as some currently emerging approaches. Those vanguard companies could, and would likely, advance their technologies if early successes with patients generated adequate revenues that could have been used for additional R&D. Second, the regulatory environment (understandably) required that only the most severely blind patients be considered as candidates for a retinal prosthetics. Third, the field of retinal prosthetics has been learning more about the degraded neural substrate and preferred means to stimulate the neurons. The problem of how best to communicate with the neural substrate, perhaps by emulating the natural neural code, is a challenge of the highest order. Cochlear prosthetics, which are the closest device for comparison, were not successful until discovery that electrical stimulation had to be distributed temporally (i.e. phase-shifted) across electrodes. That one change in the stimulus paradigm opened the door to marked improvement in efficacy and ultimately to handsome corporate profits. The field of visual prosthetics may well benefit from an inflection point in the understanding of how better to communicate with the brain. Although success has been elusive, it could be reasonably argued that the opportunity to effectively treat blindness with a prosthesis is still within our reach. I believe that the field of visual prosthetics will succeed, despite the deflated early expectations that were driven more by the need for corporate survival than by the science, which demands more time to decipher the most promising strategies. The potential to help a large number of blind patients is the prime motivation for our research community. A more integrated and more patient alliance among scientists, physicians and the business community will be required to realize our lofty goal.

CME ANSWERS

1. E
2. E
3. E

REFERENCES

1. Rizzo J, Ayton L, et al. Harmonization of Outcomes and Vision Endpoints in Vision Restoration Trials: Recommendations from the International HOVER Taskforce. *Trans Vis Sci Tech*, 2019, in press.
2. Geruschat DR, Richards RP, et al. an analysis of observer-rated functional vision in patients implanted with the Argus II Retinal Prosthesis System at three years. *Clin Exp Optom*, 99(3):227-32, 2016.
3. Ghezzi D. Retinal Prostheses: progress toward the next generation implants. *Front Neurosci* 20, 2015.

VISUAL REHABILITATION: HOW DO WE EMPOWER OUR PATIENTS?

*Marie DiNome Acierno, MD
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Scottsdale, AZ*

LEARNING OBJECTIVES

1. To incorporate Low Vision into daily patient encounters.
2. To educate the visual impaired patient's health care team.
3. To access Low Vision Resources.

CME QUESTIONS

1. True or False: Visual Rehabilitation improves reading and visual ability.
2. True or False: Low Vision may occur due to contrast sensitivity loss.
3. True or False: Low Vision is only for visual loss due to specific causes.

KEYWORDS

1. Visual rehabilitation
2. Vision impairment
3. Low Vision

HIGHLIGHTS

If you address the concerns that are kept in the dark then, so many issues can be brought to the light of day.

Here is a key question for any patient with irreversible vision loss: "Is your vision loss making it difficult for you to participate in your daily activities?"

SUMMARY

Vision loss is vision that cannot be corrected and interferes with one's activities of daily living. Vision loss is less than 20/40, presence of a scotoma, visual field loss, or contrast sensitivity loss. We need to be able to identify patients with low vision so that we can provide education and encouragement.

It is best to refer patients for low vision support services early in one's journey of visual loss. We need to change our focus and adapt practices to recognize the importance of a referral for low vision needs and visual rehabilitation for any patient with visual impairment(s).

As healthcare providers, we have been taught well to diligently treat ocular conditions. Sometimes, we cannot cure all ocular conditions, and we need to be mindful that it is just as important to improve the patient's quality of life. Visual rehabilitation must be the standard of care for our patients losing their

vision. Low vision support should not be viewed as a last resort for only advanced visually impaired patients. Low vision services are a means to help our patients maintain and maximize their sight loss. If patients learn to compensate for their visual loss early on then, as eyesight continues to fail they will tend to do better later.

Resources:

1. AAO website and typing “**vision rehabilitation**” into the search bar or using the direct link <https://www.aao.org/low-vision-and-vision-rehab>

Here you will find:

- AAO Vision Rehabilitation Preferred Practice Pattern (PPP) Guideline
- sample letter to make PCP’s aware of a patient’s vision loss and the possibility of Charles Bonnet Syndrome
- complete listing of resources with links to: Audio Books, Magazines, News and Textbooks; Technologies to include computers, cell phones and video magnifiers; National Organizations for support.
- “**There is Something Else You Can Do.**”; six-minute video; introduction by David W. Parke II, MD, Academy CEO; production led by Joseph Fontenot, MD, Chair of the Academy’s Vision Rehabilitation committee emphasizing the impact of vision loss on the individual and the responsibility of the ophthalmologist to refer or provide vision

2. AAO website includes other educational resources under **Smart Sight** for practitioners and **Eye Smart** for patients

AAO SmartSight

- PDF Overview SmartSight** handout for health care provider to give to patients offering essential tips
- PDF SmartSight Making the most of remaining vision**
- Eye Smart** <https://www.aao.org/eye-health> patient resource for ophthalmologist-reviewed information about eye diseases and treatments, eye health news and tips for a lifetime of good eye health.

3. Vision Aware <https://www.visionaware.org>

4. Apps for Visually Impaired:

- Seeing AI** Free app; Talking camera app for those with visual impairment
- Be My Eyes** free app; “people helping people in real time”; app that connects blind and low-vision people with sighted volunteers and company representatives for visual assistance through a live video call.
- LookTel**: \$9.99; The money identifier mobile app
- KNFB Reader**: \$99.99 Reads Virtually Any Text Aloud
- TapTapSee**: free app; Identify objects through photos; is designed to help the blind and visually impaired identify objects they encounter in their daily lives.
- Color ID Free**: Discovers the Names of the Colors Around You

CME ANSWERS

1. True
2. True
3. False

REFERENCES

1. Mansouri B, Roznik M, Rizzo JF, Prasad S. Rehabilitation of Visual Loss:Where We Are and Where We Need to Be. J Neuro-Ophthalmol 38: 223-229, 2018
2. Phillips LB. Low Vision Drivers: The Ophthalmologist's Role and Responsibility. EyeNet Magazine. October 33-35, 2017

OPTIC NEURITIS: PAST, PRESENT AND FUTURE

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LEARNING OBJECTIVES

1. Discuss the role of OCT in symptomatic and asymptomatic optic neuritis
2. Discuss the role of inter-eye OCT differences in determining optic neuritis
3. Discuss the use of OCT in the diagnosis and differential of optic neuritis

CME QUESTIONS

1. Which of the following tests best distinguish a patient with MS from a control population?
 - A. High contrast letter acuity
 - B. Low contrast letter acuity
 - C. Contrast sensitivity(Pelli Robson)
 - D. Color Vision
2. The optimal inter-eye difference in retinal nerve fiber layer difference to confirm an optic nerve lesion in microns is?
 - A. 2
 - B. 5
 - C. 10
 - D. 15
3. Which of the following is true about patients with “benign MS” ?
 - A. they have less frequent episodes of optic neuritis
 - B. they have less RNFL loss compared to typical MS patients.
 - C. they have twice the frequency of optic neuritis episodes
 - D. they have no quality of life impairment.

KEYWORDS

1. Multiple sclerosis
2. Optic Neuritis
3. Optical coherence tomography
4. Low contrast letter acuity
5. Magnetic resonance imaging

HIGHLIGHTS

OCT has provided a basis for correlating structural aspects of anterior visual pathway axonal and neuronal loss with visual function in ON as well as in MS. It is now known that patients with MS have thinning of the retinal nerve fiber layer (RNFL, axons) and ganglion cell/inner plexiform layer (GCL+IPL, neurons) even in the absence of a history of acute ON. Such patients have clinically meaningful

worsening of vision and quality of life (QOL). We now also recognize that is an inter-eye RNFL and GCL difference that may predict an underlying optic nerve lesion. Newer techniques such as retinal nerve fiber layer textual analysis may provide additional sensitivity in defining more subtle forms of optic nerve injury. Our ability to separate out the anterior and posterior visual pathway contributions to RNFL loss by hemi-segmentation techniques will be important to understand the location of the disease burden in MS. When coupled with new MRI sequences such double inversion recovery images, symptomatic and asymptomatic optic nerve lesions will become easier to verify. Going forward, OCT is a powerful tool that may be used to assess neuro-repair and neuroprotective mechanisms in both acute and chronic optic nerve injury.

SUMMARY

Introduction

The Optic Neuritis Treatment Trial (ONTT) [1-6] was a classic study of the profile of optic neuritis. Importantly, the presence of magnetic resonance imaging (MRI)-detected brain lesions and oligoclonal bands [7, 8] were found to be associated with an increased risk of developing clinically definite MS (CDMS), defined by a second clinical demyelinating event. MRI was determined to be the most powerful predictor of MS risk. Patients with one or more MRI lesions at baseline had a 56% risk of CDMS at 10 years and a 72% risk at 15 years [7,9]. While visual recovery from ON as a first demyelinating event and in the setting of established MS is said to be good [5,10], studies of vision in MS have shown that patients will have continued deficits that are not well captured by high-contrast visual acuity (VA) alone [13]. Visual symptoms in MS may result from a variety of pathological processes, including inflammation, demyelination, and axonal degeneration in the afferent visual pathways [11,12]. Subclinical optic neuropathy and involvement of the optic chiasm or post-chiasmal regions of the visual pathway are common [14-15]. New antibodies have been discovered that further define subsets of patients with optic neuritis including NMO and MOG. These antibodies not only have diagnostic value but offer information about prognosis and treatment.

Significant progress has been made in understanding the additional ways to assess qualitative and quantitative visual function in patients with MS. Tests of low-contrast vision, particularly low-contrast letter acuity (LCLA), have emerged as methods that demonstrate the greatest capacity to capture visual impairment in patients with MS [16-19]. Vision-specific quality of life (QOL), measured by 25-Item National Eye Institute Visual Functioning Questionnaire (NEI-VFQ-25) and the 10-Item Neuro-Ophthalmic Supplement has been shown to be reduced among patients with worse visual function by low-contrast letter acuity and with structural changes of RNFL and GCL+IPL thinning by OCT [20-23]. Nonetheless, the optic nerve is not one of the lesion MRI lesion sites in the 2017 McDonald criteria despite its frequent involvement in MS and its ability to be a defining feature of the disorder. [24]. In this talk, we will discuss the advances in our understanding of optic neuritis and emphasize the studies that demonstrated the value of examining visual function in the setting of multiple sclerosis. Special attention will be brought to new OCT imaging criteria to confirm the presence of an optic neuropathy.[25]

Low Contrast Letter Acuity

Testing of LCLA using Sloan charts was first implemented as an exploratory outcome measure in the International MS Progressive Avonex Clinical Trial (IMPACT) study of interferon beta-1a for secondary progressive MS. Both in this study and in a heterogeneous convenience sample cohort of MS patients, it was demonstrated that LCLA was superior to HCVA, L'Anthony D-15 DS color test, and Esterman binocular visual field test in MS patients.[19] Although both Sloan and Pelli-Robson methods

distinguished MS subjects from healthy controls significantly better than HCVA, Sloan charts performed better than Pelli- Robson charts with odds ratios for worse visual function scores in MS patients of 2.41 (95% confidence interval (CI): 1.77–3.29; $p < 0.001$) for Sloan LCLA versus 1.77 (95% CI: 1.38–2.26; $p < 0.001$) for Pelli- Robson contrast sensitivity. Furthermore, only Sloan LCLA was able to distinguish MS subjects from healthy controls in the two lowest age quartiles (18–32 and 33–43 years).[19] MS patients have significantly lower LCLA scores than disease-free controls, a difference that is most pronounced at the lowest contrast Levels.[19,20] Importantly, MS and disease-free controls have similar median Snellen VA scores,13 supporting previous clinical observations that LCLA and other contrast measures capture aspects of visual function missed by HCVA. Information from these pivotal studies set the stage for use of LCLA as an outcome measure in MS research, clinical trials, and practice

Optical Coherence Tomography (OCT) in MS

Optical coherence tomography (OCT) is a non-invasive technique that is close to a tissue level *in vivo* optical biopsy of the retina. During the past decade, OCT has become increasingly recognized as a highly sensitive method for imaging the retina and optic disc. Imaging of the RNFL, both in the peripapillary region (pRNFL) and in the macula (mRNFL), represents a unique opportunity in the central nervous system to image axons without myelin sheaths (retinal ganglion cell axons are not myelinated until they traverse behind the lamina cribosa). Measures of ganglion cell layer/inner plexiform layer (GCL+IPL) thickness and total macular volume (TMV) also reflect neuronal loss in the anterior visual pathway.

OCT in Patients with MS and ON

As OCT imaging has advanced to provide retinal detail that is nearly histologic in its level of detail, autopsy studies have likewise shown that up to 94%–99% of MS patients have detectable optic nerve lesions [26, 27]. The earliest application of OCT technology to the study of ON in patients with MS was reported by Parisi et al. in 1999 [28], utilizing a first-generation OCT technology. In those patients with MS-associated ON (MSON), pRNFL thickness was reduced by an average of 46 % in eyes with an ON history, compared to disease-free control eyes. Even fellow eyes had RNFL thickness reductions of 28%. In 2005, Trip et al. [29] reported further findings using time-domain (TD-) OCT. This study revealed a 33% reduction in pRNFL thickness in eyes with a history of ON and incomplete recovery. Unaffected eyes in this study had a 27% reduction in pRNFL thickness compared to controls. Eyes with a history of ON had macular volume reductions of 11%. These first reports of OCT were thus able to show both axonal loss and retinal ganglion cell loss.

In 2010, Petzold et al. [30] performed a meta-analysis of available published reports on OCT in patients with MS and found pRNFL thinning by an average of 20.38 μm (95% CI 17.91–22.86, $n=2063$, $p<0.0001$) in MS eyes with a history of acute ON, and by an average of 7.08 μm (5.52–8.65, $n=3154$, $p<0.0001$) in MS eyes without an ON history compared to disease-free controls. Peripapillary RNFL thickness also was found to correlate with visual and neurological functioning.

In 2006, Costello et al. [31] reported that the majority of patients (approximately 75%) with acute ON, 94% of whom had a clinically isolated syndrome, will sustain 10–40 μm thinning of the pRNFL within a period of 3 to 6 months following the acute event. Importantly, pRNFL thinning to the level of 75-80 μm in that study was found to be a “threshold level” below which there were more severe decrements in visual function, as measured by automated perimetry mean deviation. To provide perspective on these measurements, normal pRNFL thickness by TD OCT is approximately 105 μm , with an estimated physiological loss due to aging of only about 0.017% per year from age 18 years onward (approximately 10–20 μm loss over 60 years) [32].

Pro et al. [33] demonstrated mild, relative thickening of the pRNFL in 8 patients with clinical retrobulbar optic neuritis (no visible optic disc swelling on ophthalmoscopy). Even though these OCT findings were subtle, and were within the range of the normal (100.7 μm in affected eye versus 92.9 μm in unaffected eye), the authors pointed out that these represented true change, as the unaffected eye remained stable over follow up. There was subsequent RNFL thinning in these affected eyes below the expected value for disease-free control eyes (approximately 105 μm) despite visual improvement [33]. The RNFL thinning was seen as early as 2-4 months following the acute ON. OCT was thus able to identify very mild, and in some cases clinically undetectable, optic disc edema in eyes with acute ON. These findings represent one way in which OCT has helped to refine the clinical profile of acute ON and of visual pathway structure in MS even in the absence of ON (see case study 1).

OCT Changes in the Subacute Phase and Recovery from ON

The time course of RNFL axonal loss following acute ON may be important for determining the “window of opportunity” for potential intervention with therapies that could protect and repair the nervous system. Reductions in pRNFL thickness in affected eyes, usually by 10–40 μm , are maximal after acute ON within 3–6 months. This pattern of rapid RNFL thinning suggests that significant axonal degeneration follows immediately after the primary demyelinating event [31, 34]. There is stabilization of RNFL thickness within 7–12 months from the beginning of the disease [34]. However, we now recognize that thinning of the GCL-IPL layer begins within weeks of the onset of acute ON and may precede the thinning of the RNFL narrowing the window of therapeutic window of neuro-repair [95]

Henderson et al. [34] performed comprehensive qualitative and quantitative visual assessments in a study of 23 patients with acute clinically isolated unilateral ON. The mean time to 90% of maximum loss from baseline in pRNFL thickness for affected eyes was 2.38 months. Ninety-nine percent of the degree of pRNFL loss occurred by an average of 4.75 months. The time of first detectable pRNFL thinning compared to the baseline fellow eye value was 1.64 months (95% CI, 0.96–2.32; $p<0.05$). Eyes with poor recovery had a significantly greater decline of RNFL from baseline to 3 months ($p=0.002$). Macular volumes also declined significantly at the time of last follow-up.

OCT in MS Subtypes

Costello et al. [35] demonstrated that patterns of OCT RNFL thinning may be able to distinguish MS disease subtypes. For ON eyes among the different MS subtypes, differences among groups were noted in the overall and temporal RNFL regions. Patients with CIS had the highest overall RNFL thickness values (mean 87.8 μm), while patients with secondary progressive MS (SPMS) had the greatest degree of thinning compared to control reference values (mean RNFL thickness 70.8 μm). For MS non-ON eyes, RNFL thickness was reduced in patients with primary progressive MS (PPMS, average 94.3 μm $p=0.04$), relapsing remitting MS (RRMS, average 99.6 μm , $p=0.02$), and SPMS (average 84.7 μm , $p<0.0001$) relative to eyes of patients with CIS (average RNFL thickness 105.7 μm). RNFL thickness may thus represent an important structural marker of disease progression.

In a study by Pulicken et al. [36], progressive MS patients showed more marked decreases in RNFL and macular volume than relapsing-remitting MS. However, even patients with “benign MS” may have pRNFL axonal loss that is as marked as that of typical RRMS and have reduced vision and QOL. While overall neurologic impairment may be mild in such cases, visual dysfunction may account for a substantial degree of disability in benign MS [37].

RNFL Thickness in Asymptomatic Fellow Eyes in ON

Thinning of RNFL has been observed not only in the eyes with a history of ON, but also in the asymptomatic fellow eyes of MS patients, as well as in MS patients without a clinical history of ON. The

average pRNFL thickness was found to be between 91.08 and 109.3 μm in the fellow eye in patients with MSON [29, 33, 36, 38-50].

In MS patients with no history suggestive of ON, the average RNFL thickness was between 93.9 and 110.9 μm [36, 50-53]. These findings emphasize the common occurrence of subclinical anterior visual pathway axonal loss in patients with MS even in eyes without history of ON. With advances in OCT techniques and MRI sequences, it will surprise few investigators that asymptomatic optic nerve lesions have been vastly underestimated in multiple sclerosis patients.

RNFL Thinning and Visual Loss

One of the most important findings that has resulted from the use of OCT MS studies is the association of RNFL thinning to visual loss, as measured by low-contrast letter acuity [23]. In 2006, Fisher et al. [41] conducted a cross-sectional study that compared RNFL thickness among MS eyes with a history of ON (MS ON eyes), MS eyes without a history of ON (MS non-ON eyes), and disease-free control eyes. These investigators found that RNFL thickness was reduced significantly among MS eyes as a group overall (92 μm) vs. controls (105 μm , $p < 0.001$, generalized estimating equation models, accounting for age and within-patient, inter-eye correlations) and particularly reduced in MS ON eyes (85 mm, $p < 0.001$). Furthermore, lower visual function scores were associated with reduced average overall RNFL thickness in MS eyes; for every 1-line decrease in low-contrast letter acuity or contrast sensitivity score, the mean RNFL thickness decreased by 4 μm . These findings supported the validity of low-contrast visual assessment and suggested a potential role for OCT in trials that may examine neuroprotective and other disease-modifying therapies. Several other investigations have demonstrated correlations between RNFL thinning and visual loss [54-56] (see case study 2). Costello et al. [57] found that RNFL thickness after an episode of isolated ON cannot be used to predict the risk of MS.

Relation of RNFL Thickness to Visual Evoked Potential (VEP) and MRI Findings

Several recent studies have highlighted the structure function-correlations provided by neuroimaging (MRI) and electrophysiological testing (visual evoked potentials) [58-61]. In a retrospective study, visual evoked potential (VEP) latency was found to be sensitive for detecting demyelination [62], while RNFL thickness reflects more structural aspects of optic nerve damage following acute ON. As might be expected, OCT RNFL thickness correlated well with VEP amplitude, but not with the latency [44]. In another study, retinal ganglion cell (RGC) axonal loss was associated with retinal dysfunction in eyes of MS patients without a history of ON and evidence of post-chiasmal involvement of the visual pathway [63]. In a study that compared 112 partners of patients with MS to a control group of 93 volunteers, abnormal VEP latency in 5 of the partners and one clinically definite case of MS was found. Studies of OCT among partners of people with MS may provide further context for this finding. [64].

In terms of brain MRI studies, RNFL thickness has been shown to reflect the volumes of brain white and gray matter as well as the normalized volumes of whole brain and white matter [54,65]. The correlations between RNFL thickness and MRI measurements of brain atrophy were more significant in the subset of patients with no clinical history of ON than in those who had an ON history in either eye. Studies also suggest that RNFL thickness measurements could be considered a marker for brain atrophy in MS [41]. The relation of RNFL thicknesses and brain parenchymal fraction (BPF), measured using high-resolution MRI was also recently shown to reflect the likely global nature of axonal and neuronal loss in MS [50]. A correlation between RNFL thickness, volume of T1 and T2 lesions, gray matter atrophy, MTR and diffusion tensor imaging measures (DTI) measurements in MS patients with or without a history of ON was also reported [40]. These MRI parameters also correlated with low-contrast letter acuity measurements, consistent with prior studies suggesting that both posterior and anterior visual pathway

disease contribute to visual function in MS [66]. Interestingly, in MS patients with optic radiation lesions, a correlation was found between the volume of the lesion and RNFL thickness ($p < 0.001$) [67].

Role for OCT in Monitoring MS Therapy Adverse Events and Efficacy

Fingolimod, an oral sphingosine-1-phosphate receptor modulator approved for treatment of MS, has been shown in clinical trials to cause macular edema in 0.3-1.2% of patients, with uveitis and other ocular pathology elevating risk [68]. Patients present with blurred vision, decreased visual acuity or eye pain. Macular edema resolves in most cases when fingolimod treatment is discontinued [68,69]. OCT studies of patients on fingolimod have shown elevations in macular volume consistent with diffuse macular edema; some of these patients were symptomatic, presenting with metamorphopsia and blurred vision [70]. Ophthalmologic evaluations, including OCT scans of the macula, are recommended before initiating treatment. Follow-up at 3-4-month intervals is also recommended.

Though not common, cases of retinopathy associated with interferon-beta 1a treatment in MS have been reported [71-74]. This retinopathy was characterized by clinical/OCT findings of retinal hemorrhages or cotton wool spots at the posterior fundus and improved with discontinuation of medication.

In a prospective study of 94 MS patients and 50 healthy subjects followed over 3 years, the authors evaluated whether treatment with interferon 1a, interferon 1b or glatiramer acetate was associated with reduced degrees of RNFL thinning. Progressive RNFL thinning was detected in both the treated and untreated groups, but untreated patients had lower mean RNFL thicknesses. Otherwise, no differences in the treatment groups were noted [75].

Another study showed that the peripapillary RNFL, ganglion cell layer thicknesses, and macular volumes measured by OCT were all reduced among patients with or without disease modifying therapy when compared with controls. The abnormal findings were more prominent for MS eyes with an ON history [76].

Microcystic Inner Nuclear Layer Abnormalities

Microcystic changes in the inner nuclear layer (MMO, microcystic macular oedema) are characterized by retinal microcysts in the inner nuclear layer and are easily identified peripherally on macular spectral-domain OCT. These findings are typically not identifiable by direct ophthalmoscopy, and may be associated with reductions in VA. In many cases, a perifoveal hyporeflective crescent shape can be seen on confocal infrared laser fundus imaging directly correlating with the area of microcysts observed on OCT (see case study 4). It has been hypothesized that inner nuclear layer microcysts associated with various forms of optic neuropathy could be either a sign of inflammation [77,78], autoantibodies against AQP4 and KIR4.1, microglial activation, blood–retina barrier breakdown or retrograde or anterograde trans-synaptic degeneration changes secondary to neurodegeneration [79,80]. Microcystic changes in the inner nuclear layers in eyes of patients with MS were first described by Gelfand et al [77]. These findings were seen in association with increased disease severity (4.7% of patients), with higher prevalence in patients with a history of ON [77]. Further evaluation of MMO found that patients with neuromyelitis optica (NMO), who are known to have a high incidence of ON, had a higher prevalence of MMO (20-26%) [81,82]. Microcystic inner nuclear layer abnormalities are not specific to MS and ON and have been found associated with other optic neuropathies, including hereditary optic neuropathy [83-93].

Segmentation and Newer trends

Thinning of the ganglion cell layer has been demonstrated to be greatest among patients with decrements in vision-specific QOL and among those with the highest degrees of visual loss [94]. In a study by Gabilondo et al., retinal changes by OCT in ON were evaluated using the latest segmentation techniques.[95] Changes in ganglion cell layer thickness within the first month were predictive of visual impairment by 6 months [93]. These studies, and others, have confirmed an important role for neuronal loss as measured by ganglion cell layer thickness in determining visual disability in MS.

OCT angiography is a newer technique that demonstrates the optic nerve blood flow, which may be reflective of the metabolic demand. This is hypothesized to be a sensitive measure of axonal loss. Wang and colleagues showed that eyes of patients with MS and ON had lower flow indices as compared to controls and MS eyes without an ON history. In addition, the flow index was abnormal in a greater proportion of eyes with a history of ON than was the peripapillary RNFL [96]. One caution in interpreting these findings might be the very high threshold (thickness below 5th percentile) for categorizing an RNFL thickness measurement as abnormal.

Optimal Inter-eye Difference in predicting an optic nerve lesion-

The current diagnostic criteria for multiple sclerosis do not include the optic nerve as lesion site. Part of the problem is that MRI imaging of the orbit has not been well studied in MS cohorts and MRI images have been limited by motion artifact. Thus, we sought to find the optimal inter-eye difference thresholds for RNFL and GCL values that were predictive of an optic nerve lesion. We found that among 1530 patients, we found an inter-eye difference of 5 microns in RNFL and 4 microns of GCL to be highly predictive of an optic nerve lesion in this cohort that had 477 patients with a history of unilateral optic neuritis.[25] These differences in structure also correlated with differences in low contrast letter acuity and quality of life. Furthermore, among the 854 patients who gave no history of optic neuritis, we found 28% of them to have a meaningful 5 micron difference in RNFL suggesting that a number of patients have asymptomatic episodes of optic neuritis.[25] Thus, using OCT we can identify both patients with symptomatic and asymptomatic optic neuritis. These values can also be tested in algorithms of patients with clinically isolated syndromes to examine their sensitivity and specificity in predicting the subsequent development of multiple sclerosis and how the optic nerve fares as a future lesion site.

Future Directions

OCT has provided a basis for correlating structural aspects of anterior visual pathway axonal and neuronal loss with visual function in ON as well as in MS. It is now known that patients with MS have thinning of the retinal nerve fiber layer (RNFL, axons) and ganglion cell/inner plexiform layer (GCL+IPL, neurons) even in the absence of a history of acute ON. Such patients have clinically meaningful worsening of vision and quality of life (QOL). We now also recognize that is an inter-eye RNFL and GCL difference that may predict an underlying optic nerve lesion. Newer techniques such as retinal nerve fiber layer textual analysis may provide additional sensitivity in defining more subtle forms of optic nerve injury. Our ability to separate out the anterior and posterior visual pathway contributions to RNFL loss by hemi-segmentation techniques will be important to understand the location of the disease burden in MS. When coupled with new MRI sequences such double inversion recovery images, symptomatic and asymptomatic optic nerve lesions will become easier to verify. Going forward, OCT is a powerful tool that may be used to assess neuro-repair and neuroprotective mechanisms in both acute and chronic optic nerve injury.

* Text above modified and updated from Rachel C. Nolan, BA; Kannan Narayana, MD; Laura J. Balcer, MD, MSCE; Steven L. Galetta, MD. Optic Coherence Tomography (OCT) and Multiple Sclerosis. In

Gryzbowski and Barboni P eds. OCT in Central Nervous System Diseases. The Eye as a window to the Brain. Springer, 201 Brain. Springer, 2015.

CME ANSWERS

1. B
2. B
3. C

REFERENCES

1. Beck RW. The Optic Neuritis Treatment Trial. Archives of Ophthalmology 106(8):1051-3, 1988
2. The clinical profile of optic neuritis. Experience of the Optic Neuritis Treatment Trial. Optic Neuritis Study Group. Archives of Ophthalmology 109(12):1673-8, 1991
3. Beck RW, Cleary PA, Anderson MM, Jr., Keltner JL, Shults WT, Kaufman DI, et al. A randomized, controlled trial of corticosteroids in the treatment of acute optic neuritis. The Optic Neuritis Study Group. New England Journal of Medicine 326(9):581-8, 1992
4. Beck RW, Kupersmith MJ, Cleary PA, Katz B. Fellow eye abnormalities in acute unilateral optic neuritis. Experience of the optic neuritis treatment trial. Ophthalmology.100(5):691-7; discussion 7-8, 1993
5. Cleary PA, Beck RW, Bourque LB, Backlund JC, Miskala PH. Visual symptoms after optic neuritis. Results from the Optic Neuritis Treatment Trial. Journal of Neuro-Ophthalmology;17(1):18-23; quiz 4-8, 1997
6. Sorensen TL, Frederiksen JL, Bronnum-Hansen H, Petersen HC. Optic neuritis as onset manifestation of multiple sclerosis: a nationwide, long-term survey. Neurology.;53(3):473-8, 1999
7. Optic Neuritis Study Group. Multiple sclerosis risk after optic neuritis: final optic neuritis treatment trial follow-up. Archives of Neurology;65(6):727-32, 2008
8. Soderstrom M, Ya-Ping J, Hillert J, Link H. Optic neuritis: prognosis for multiple sclerosis from MRI, CSF, and HLA findings. Neurology;50(3):708-14, 1998
9. Beck RW, Trobe JD, Moke PS, Gal RL, Xing D, Bhatti MT, et al. High- and low-risk profiles for the development of multiple sclerosis within 10 years after optic neuritis: experience of the optic neuritis treatment trial. Archives of Ophthalmology;121(7):944-9, 2003
10. Beck RW, Gal RL, Bhatti MT, Brodsky MC, Buckley EG, Chrousos GA, et al. Visual function more than 10 years after optic neuritis: experience of the optic neuritis treatment trial. American Journal of Ophthalmology;137(1):77-83, 2004
11. Evangelou N, Konz D, Esiri MM, Smith S, Palace J, Matthews PM. Size-selective neuronal changes in the anterior optic pathways suggest a differential susceptibility to injury in multiple sclerosis. Brain : a Journal of Neurology;124(Pt 9):1813-20, 2001
12. DeLuca GC, Williams K, Evangelou N, Ebers GC, Esiri MM. The contribution of demyelination to axonal loss in multiple sclerosis. Brain 129(Pt 6):1507-16, 2006
13. Sabadia S, Nolan R, Galetta KM et al. 20/40 or Better Visual Acuity After Optic Neuritis: Not as Good as We Once Thought? J Neuroophthalmol. Dec;36(4):369, 2016
14. Sisto D, Trojano M, Vetrugno M, Trabucco T, Iliceto G, Sborgia C. Subclinical visual involvement in multiple sclerosis: a study by MRI, VEPs, frequency-doubling perimetry, standard perimetry, and contrast sensitivity. Investigative Ophthalmology & Visual Science.;46(4):1264-8, 2005
15. Lycke J, Tolleson PO, Frisen L. Asymptomatic visual loss in multiple sclerosis. Journal of Neurology;248(12):1079-86, 2001
16. Trobe JD, Beck RW, Moke PS, Cleary PA. Contrast sensitivity and other vision tests in the optic neuritis treatment trial. American Journal of Ophthalmology;121(5):547-53, 1996

17. Balcer LJ, Baier ML, Cohen JA, Kooijmans MF, Sandrock AW, Nano-Schiavi ML, et al. Contrast letter acuity as a visual component for the Multiple Sclerosis Functional Composite. *Neurology*;61(10):1367-73, 2003
18. Baier ML, Cutter GR, Rudick RA, Miller D, Cohen JA, Weinstock-Guttman B, et al. Low-contrast letter acuity testing captures visual dysfunction in patients with multiple sclerosis. *Neurology*;64(6):992-5, 2005
19. Balcer LJ, Baier ML, Pelak VS, Fox RJ, Shuwairi S, Galetta SL, et al. New low-contrast vision charts: reliability and test characteristics in patients with multiple sclerosis. *Multiple Sclerosis*. 6(3):163-71, 2000
20. Ma SL, Shea JA, Galetta SL, Jacobs DA, Markowitz CE, Maguire MG, et al. Self-reported visual dysfunction in multiple sclerosis: new data from the VFQ-25 and development of an MS-specific vision questionnaire. *American Journal of Ophthalmology*;133(5):686-92, 2002
21. Raphael BA, Galetta KM, Jacobs DA, Markowitz CE, Liu GT, Nano-Schiavi ML, et al. Validation and test characteristics of a 10-item neuro-ophthalmic supplement to the NEI-VFQ-25. *American Journal of Ophthalmology*;142(6):1026-35, 2006
22. Mowry EM, Loguidice MJ, Daniels AB, Jacobs DA, Markowitz CE, Galetta SL, et al. Vision related quality of life in multiple sclerosis: correlation with new measures of low and high contrast letter acuity. *Journal of Neurology, Neurosurgery, and Psychiatry*;80(7):767-72, 2009
23. Sakai RE, Feller DJ, Galetta KM, Galetta SL, Balcer LJ. Vision in multiple sclerosis: the story, structure-function correlations, and models for neuroprotection. *Journal of Neuro-Ophthalmology*;31(4):362-73, 2011
24. Thompson AJ, Banwell BL, Barkhof et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol*;17:162-173, 2018
25. Nolan-Kenney RC, Liu M, Akhand O et al. Optimal Inter-eye Difference Thresholds by Optical Coherence Tomography in Multiple Sclerosis. *Ann Neurol*;85:618-629. 2019
26. Ikuta F, Zimmerman HM. Distribution of plaques in seventy autopsy cases of multiple sclerosis in the United States. *Neurology*;26(6 PT 2):26-8, 1976
27. Toussaint D, Perier O, Verstappen A, Bervoets S. Clinicopathological study of the visual pathways, eyes, and cerebral hemispheres in 32 cases of disseminated sclerosis. *Journal of Clinical Neuro-Ophthalmology*;3(3):211-20, 1983
28. Parisi V, Manni G, Spadaro M, Colacino G, Restuccia R, Marchi S, et al. Correlation between morphological and functional retinal impairment in multiple sclerosis patients. *Investigative Ophthalmology & Visual Science*;40(11):2520-7, 1999
29. Trip SA, Schlottmann PG, Jones SJ, Altmann DR, Garway-Heath DF, Thompson AJ, et al. Retinal nerve fiber layer axonal loss and visual dysfunction in optic neuritis. *Annals of Neurology*;58(3):383-91, 2005
30. Petzold A, de Boer JF, Schippling S, Vermersch P, Kardon R, Green A, et al. Optical coherence tomography in multiple sclerosis: a systematic review and meta-analysis. *The Lancet Neurology*;9(9):921-32, 2010
31. Costello F, Coupland S, Hodge W, Lorello GR, Koroluk J, Pan YI, et al. Quantifying axonal loss after optic neuritis with optical coherence tomography. *Annals of Neurology*;59(6):963-9, 2006
32. Kanamori A, Escano MF, Eno A, Nakamura M, Maeda H, Seya R, et al. Evaluation of the effect of aging on retinal nerve fiber layer thickness measured by optical coherence tomography. *Ophthalmology*;217(4):273-8, 2003
33. Pro MJ, Pons ME, Liebmann JM, Ritch R, Zafar S, Lefton D, et al. Imaging of the optic disc and retinal nerve fiber layer in acute optic neuritis. *Journal of the Neurological Sciences*;250(1-2):114-9, 2006
34. Henderson AP, Altmann DR, Trip AS, Kallis C, Jones SJ, Schlottmann PG, et al. A serial study of retinal changes following optic neuritis with sample size estimates for acute neuroprotection trials. *Brain*;133(9):2592-602, 2010

35. Costello F, Hodge W, Pan YI, Eggenberger E, Freedman MS. Using retinal architecture to help characterize multiple sclerosis patients. *Canadian Journal of Ophthalmology*;45(5):520-6, 2010
36. Pulicken M, Gordon-Lipkin E, Balcer LJ, Frohman E, Cutter G, Calabresi PA. Optical coherence tomography and disease subtype in multiple sclerosis. *Neurology*;69(22):2085-92, 2007
37. Galetta KM, Graves J, Talman LS, Lile DJ, Frohman EM, Calabresi PA, et al. Visual pathway axonal loss in benign multiple sclerosis: a longitudinal study. *Journal of Neuro-Ophthalmology*;32(2):116-23, 2012
38. Cheng H, Laron M, Schiffman JS, Tang RA, Frishman LJ. The relationship between visual field and retinal nerve fiber layer measurements in patients with multiple sclerosis. *Investigative Ophthalmology & Visual Science*;48(12):5798-805, 2007
39. Costello F, Hodge W, Pan YI, Freedman M, DeMeulemeester C. Differences in retinal nerve fiber layer atrophy between multiple sclerosis subtypes. *Journal of Neurological Sciences*;281:74–9, 2009
40. Frohman EM, Dwyer MG, Frohman T, Cox JL, Salter A, Greenberg BM, et al. Relationship of optic nerve and brain conventional and non-conventional MRI measures and retinal nerve fiber layer thickness, as assessed by OCT and GDx: a pilot study. *Journal of the Neurological Sciences*;282(1-2):96-105, 2009
41. Fisher JB, Jacobs DA, Markowitz CE, Galetta SL, Volpe NJ, Nano-Schiavi ML, et al. Relation of visual function to retinal nerve fiber layer thickness in multiple sclerosis. *Ophthalmology*;113(2):324-32, 2006
42. Grazioli E, Zivadinov R, Weinstock-Guttman B, Lincoff N, Baier M, Wong JR, et al. Retinal nerve fiber layer thickness is associated with brain MRI outcomes in multiple sclerosis. *Journal of Neurological Sciences*;268:12–7, 2008
43. Henderson AP, Trip SA, Schlottmann PG, Altmann DR, Garway-Heath DF, Plant GT, et al. An investigation of the retinal nerve fibre layer in progressive multiple sclerosis using optical coherence tomography. *Brain*;131(Pt 1):277-87, 2008
44. Klistorner A, Arvind H, Nguyen T, Garrick R, Paine M, Graham S, et al. Axonal loss and myelin in early ON loss in postacute optic neuritis. *Annals Neurology*; 64(3): 325–31, 2008
45. Merle H, Olindo S, Donnio A, Beral L, Richer R, Smadja D, et al. Retinal nerve fiber layer thickness and spatial and temporal contrast sensitivity in multiple sclerosis. *European Journal of Ophthalmology*;20(1):158-66, 2010
46. Pueyo V, Martin J, Fernandez J, Almarcegui C, Ara J, Egea C, et al. Axonal loss in the retinal nerve fiber layer in patients with multiple sclerosis. *Multiple Sclerosis*;14(5):609-14, 2008
47. Ratchford JN, Quigg ME, Conger A, Frohman T, Frohman E, Balcer LJ, et al. Optical coherence tomography helps differentiate neuromyelitis optica and MS optic neuropathies. *Neurology*.;73(4):302-8, 2009
48. Spain RI, Maltenfort M, Sergott RC, Leist TP. Thickness of retinal nerve fiber layer correlates with disease duration in parallel with corticospinal tract dysfunction in untreated multiple sclerosis. *Journal of Rehabilitation Research and Development*;46(5):633-42, 2009
49. Zaveri MS, Conger A, Salter A, Frohman TC, Galetta SL, Markowitz CE, et al. Retinal imaging by laser polarimetry and optical coherence tomography evidence of axonal degeneration in multiple sclerosis. *Archives of Neurology*;65(7):924-8, 2008
50. Toledo J, Sepulcre J, Salinas-Alaman A, Garcia-Layana A, Murie-Fernandez M, Bejarano B, et al. Retinal nerve fiber layer atrophy is associated with physical and cognitive disability in multiple sclerosis. *Multiple Sclerosis*;14(7):906-12, 2008
51. Gundogan FC, Demirkaya S, Sobaci G. Is optical coherence tomography really a new biomarker candidate in multiple sclerosis?--A structural and functional evaluation. *Investigative Ophthalmology & Visual Science*;48(12):5773-81, 2007
52. Jeanjean L, Castelnovo G, Carlander B, Villain M, Mura F, Dupeyron G, et al. [Retinal atrophy using optical coherence tomography (OCT) in 15 patients with multiple sclerosis and comparison with healthy subjects]. *Revue Neurologique*;164(11):927-34, 2008

53. Pueyo V, Ara JR, Almarcegui C, Martin J, Guerri N, Garcia E, et al. Sub-clinical atrophy of the retinal nerve fibre layer in multiple sclerosis. *Acta Ophthalmologica*;88(7):748-52, 2010
54. Sepulcre J, Murie-Fernandez M, Salinas-Alaman A, Garcia-Layana A, Bejarano B, Villoslada P. Diagnostic accuracy of retinal abnormalities in predicting disease activity in MS. *Neurology*;68(18):1488-94, 2007
55. Galetta KM, Calabresi PA, Frohman EM, Balcer LJ. Optical coherence tomography (OCT): imaging the visual pathway as a model for neurodegeneration. *Neurotherapeutics*;8(1):117-32, 2011
56. Bock M, Brandt AU, Kuchenbecker J, Dorr J, Pfueller CF, Weinges-Evers N, et al. Impairment of contrast visual acuity as a functional correlate of retinal nerve fibre layer thinning and total macular volume reduction in multiple sclerosis. *The British Journal of Ophthalmology*;96(1):62-7, 2012
57. Costello F, Hodge W, Pan YI, Metz L, Kardon RH. Retinal nerve fiber layer and future risk of multiple sclerosis. *The Canadian journal of neurological sciences*;35(4):482-7, 2008
58. Horwitz H1, Degn M, Modvig S, Larsson HB, Wanscher B, Frederiksen JL. CSF abnormalities can be predicted by VEP and MRI pathology in the examination of optic neuritis. *J Neurol.* Dec;259(12):2616-20, 2012
59. Kantorová E, Ziak P, Kurča E, Koyšová M, Hladká M, Zeleňák K, Michalik J. Visual Evoked Potential and Magnetic Resonance Imaging are More Effective Markers of Multiple Sclerosis Progression than Laser Polarimetry with Variable Corneal Compensation. *Front Hum Neurosci* Jan 22;8:10, 2014
60. Ellidag HY, Eren E, Erdogan N, Ture S, Yilmaz N. Comparison of neurophysiological and MRI findings of patients with multiple sclerosis using oligoclonal band technique. *Ann Neurosci.* Oct;20(4):149-54, 2013
61. Chirapapaian. Diagnostic value of visual evoked potentials for clinical diagnosis of multiple sclerosis.. *Doc Ophthalmol* Feb;130(1):25-30, 2015
62. Naismith RT, Tutlam NT, Xu J, Shepherd JB, Klawiter EC, Song SK, et al. Optical coherence tomography is less sensitive than visual evoked potentials in optic neuritis. *Neurology*;73(1):46-52, 2009
63. Sriram P, Wang C, Yiannikas C, Garrick R, Barnett M, Parratt J, et al. Relationship between optical coherence tomography and electrophysiology of the visual pathway in non-optic neuritis eyes of multiple sclerosis patients. *PLoS One* Aug 28;9(8):e102546, 2014
64. Hawkes CH, Chawda S, Derakshani S, Muhammed N, Visentin E, Boniface D. MRI and visual-evoked potentials in partners of multiple sclerosis patients. *Acta Neurol Scand.* Jun;125(6):424-30, 2012
65. Siger M, Dziegielewski K, Jasek L, Bieniek M, Nicpan A, Nawrocki J, et al. Optical coherence tomography in multiple sclerosis: thickness of the retinal nerve fiber layer as a potential measure of axonal loss and brain atrophy. *Journal of Neurology*;255(10):1555-60, 2008
66. Wu GF, Schwartz ED, Lei T, Souza A, Mishra S, Jacobs DA, et al. Relation of vision to global and regional brain MRI in multiple sclerosis. *Neurology.* 2007;69(23):2128-35.
67. Sinnecker T1, Oberwahrenbrock T, Metz I, Zimmermann H, Pfueller CF, Harms L, et al. Optic radiation damage in multiple sclerosis is associated with visual dysfunction and retinal thinning--an ultrahigh-field MR pilot study. *Eur Radiol* Jan;25(1):122-31, 2015
68. Zarbin MA, Jampol LM, Jager RD, Reder AT, Francis G, Collins W, et al. Ophthalmic evaluations in clinical studies of fingolimod (FTY720) in multiple sclerosis. *Ophthalmology*;120(7):1432-9, 2013
69. Turaka K, Bryan JS. Does fingolimod in multiple sclerosis patients cause macular edema? *Journal of Neurology*;259(2):386-8, 2012
70. Nolan R, Gelfand JM, Green AJ. Fingolimod treatment in multiple sclerosis leads to increased macular volume. *Neurology* 80(2):139-44, 2013;
71. Ohira M, Ito D, Shimizu T, Shibata M, Ohde H, Suzuki N. Retinopathy: an overlooked adverse effect of interferon-beta treatment of multiple sclerosis. *The Keio Journal of Medicine.*;58(1):54-6, 2009

72. Bakri SJ, Swanson JW. Asymptomatic peripheral retinal hemorrhages as a manifestation of interferon Beta 1a retinopathy. *Seminars in Ophthalmology*;30(1):56-7, 2015
73. Sallansonnet-Froment M, Roux X, de Greslan T, Bounolleau P, Taillia H, Ricard D, et al. Interferon-beta retinopathy. *Revue Neurologique*;165(11):971-4, 2009
74. Martinez de Aragon JS, Pulido JS, Hauptert CL, Blodi CF, Nielsen JS, Jampol LM. Interferon-beta-associated retinopathy. *Retinal Cases & Brief Reports*;3(1):24-6, 2009
75. Herrero R, Garcia-Martin E, Almarcegui C, Ara JR, Rodriguez-Mena D, Martin J., et al. Progressive degeneration of the retinal nerve fiber layer in patients with multiple sclerosis. *Invest Ophthalmol Vis Sci* Dec 17;53(13):8344-9, 2012
76. Tugcu B, Soysal A, Kilic M, Yuksel B, Kale N, Yigit U, et al. Assessment of structural and functional visual outcomes in relapsing remitting multiple sclerosis with visual evoked potentials and optical coherence tomography. *J Neurol Sci* Dec 15;335(1-2):182-5, 2013
77. Gelfand JM, Nolan R, Schwartz DM, Graves J, Green AJ. Microcystic macular oedema in multiple sclerosis is associated with disease severity. *Brain* 2012;135(Pt 6):1786-93.
78. Petzold A. Microcystic macular oedema in MS: T2 lesion or black hole? *The Lancet Neurology*;11(11):933-4, 2012
79. Abegg M, Dysli M, Wolf S, Kowal J, Dufour P, Zinkernagel M. Microcystic macular edema: retrograde maculopathy caused by optic neuropathy. *Ophthalmology*;121(1):142-9, 2014
80. Sotirchos ES, Saidha S, Byraiah G, Mealy MA, Ibrahim MA, Sepah YJ, et al. In vivo identification of morphologic retinal abnormalities in neuromyelitis optica. *Neurology*;80(15):1406-14, 2013
81. Gelfand JM, Cree BA, Nolan R, Arnow S, Green AJ. Microcystic inner nuclear layer abnormalities and neuromyelitis optica. *JAMA Neurology*;70(5):629-33, 2013
82. Saidha S, Sotirchos ES, Ibrahim MA, Crainiceanu CM, Gelfand JM, Sepah YJ, et al. Microcystic macular oedema, thickness of the inner nuclear layer of the retina, and disease characteristics in multiple sclerosis: a retrospective study. *The Lancet Neurology*;11(11):963-72, 2012
83. Balk LJ, Killestein J, Polman CH, Uitdehaag BM, Petzold A. Microcystic macular oedema confirmed, but not specific for multiple sclerosis. *Brain*;135(Pt 12):e226; author reply e7, 2012
84. Kisimbi J, Shalchi Z, Mahroo OA, Mhina C, Sanyiwa AJ, Mabey D, et al. Macular spectral domain optical coherence tomography findings in Tanzanian endemic optic neuropathy. *Brain*;136(Pt 11):3418-26, 2013
85. Shalchi Z, Mahroo OA, Shunmugam M, Mohamed M, Sullivan PM, Williamson TH. Spectral Domain Optical Coherence Tomography Findings in Long-Term Silicone Oil-Related Visual Loss. *Retina* Mar;35(3):555-63, 2015
86. Wolff B, Azar G, Vasseur V, Sahel JA, Vignal C, Mauget-Fayssie M. Microcystic changes in the retinal internal nuclear layer associated with optic atrophy: a prospective study. *Journal of Ophthalmology*;2014:395189, 2014
87. Tawse KL, Hedges TR, 3rd, Gobuty M, Mendoza-Santiesteban C. Optical coherence tomography shows retinal abnormalities associated with optic nerve disease. *The British Journal of Ophthalmology*;98 Suppl 2:ii30-3, 2014
88. Burggraaff MC, Trieu J, de Vries-Knoppert WA, Balk L, Petzold A. The clinical spectrum of microcystic macular edema. *Investigative Ophthalmology & Visual Science*;55(2):952-61, 2014
89. Kaufhold F, Zimmermann H, Schneider E, Ruprecht K, Paul F, Oberwahrenbrock T, et al. Optic neuritis is associated with inner nuclear layer thickening and microcystic macular edema independently of multiple sclerosis. *PloS One*;8(8):e71145, 2013
90. Bhargava P, Calabresi PA. The expanding spectrum of aetiologies causing retinal microcystic macular change. *Brain*;136(Pt 11):3212-4; author reply, 2013

91. James Pitzer Gills, Jr. and Joseph A. C. Wadsworth. Retrograde transsynaptic degeneration of the inner nuclear layer of the retina. Investigative Ophthalmology Visual Science. August vol. 6 no. 4 437-448, 1967
92. Wen JC, Freedman SF, El-Dairi MA, Asrani S. Microcystic Macular Changes in Primary Open-Angle Glaucoma. Journal of Glaucoma. Sept. 2014
93. Barboni P, Carelli V, Savini G, Carbonelli M, La Morgia C, Sadun AA. Microcystic macular degeneration from optic neuropathy: not inflammatory, not trans-synaptic degeneration. Brain. Jul;136(Pt 7):e239; author reply, 2013
94. Walter SD, Ishikawa H, Galetta KM, Sakai RE, Feller DJ, Henderson SB, et al. Ganglion cell loss in relation to visual disability in multiple sclerosis. Ophthalmology 2012 Jun;119(6):1250-7, 2013
95. Gabilondo, I., Martínez-Lapiscina, E. H., Fraga-Pumar, E., Ortiz-Perez, S., Torres-Torres, R., et al. Dynamics of retinal injury after acute optic neuritis. Ann Neurol Mar;77(3):517-28, 2015
96. Wang X, Jia Y, Spain R, Potsaid B, Liu JJ, Baumann B, et al. Optical coherence tomography angiography of optic nerve head and parafovea in multiple sclerosis. Br J Ophthalmol Oct;98(10):1368-73, 2014

Table 1. Mean reference values from recent investigations of vision, QOL, and OCT in MS

	Disease-Free Controls	All MS	MS, No History of ON	MS, History of ON
High-contrast visual acuity (VA), ETDRS, number of letters correct	59 ± 6 (n=52 eyes)	53 ± 10 (n=559 eyes)	55 ± 7 (n=301 eyes)	52 ± 12 (n=252 eyes)
<i>Binocular testing</i>	62 ± 4 (n=26 pts)	58 ± 7 (n=273 pts)	59 ± 6 (n=147 pts)	57 ± 8 (n=123 pts)
Low-contrast letter acuity (2.5%), number of letters correct	35 ± 6 (n=52 eyes)	25 ± 12 (n=550 eyes)	27 ± 11 (n=296 eyes)	23 ± 13 (n=248 eyes)
<i>Binocular testing</i>	44 ± 4 (n=26 pts)	34 ± 11 (n=273 pts)	36 ± 9 (n=147 pts)	32 ± 11 (n=123 pts)
Low-contrast letter acuity (1.25%), number of letters correct	21 ± 9 (n=52 eyes)	13 ± 11 (n=550 eyes)	15 ± 11 (n=296 eyes)	11 ± 11 (n=248 eyes)
<i>Binocular testing</i>	32 ± 5 (n=26 pts)	23 ± 11 (n=271 pts)	25 ± 11 (n=146 pts)	21 ± 12 (n=122 pts)
NEI-VFQ-25 composite score, best score=100	98 ± 2 (n=27 pts)	85 ± 15 (n=264 pts)	88 ± 14 (n=142 pts)	82 ± 15 (n=119 pts)
10-Item Neuro-Ophthalmic Supplement to the NEI-VFQ-25, best score=100	97 ± 5 (n=28 pts)	78 ± 18 (n=256 pts)	83 ± 16 (n=137 pts)	73 ± 18 (n=117 pts)
<i>Time-domain (TD) OCT</i>				
Peripapillary RNFL thickness, µm	104.5 ± 10.7 (n=219 eyes)	92.5 ± 16.7 (n=1,058 eyes)	95.6 ± 14.5 (n=730 eyes)	85.7 ± 19.0 (n=328 eyes)

Total macular volume, mm³	6.84 ± 0.36 (n=219 eyes)	6.54 ± 0.51 (n=1,058 eyes)	6.63 ± 0.48 (n=730 eyes)	6.36 ± 0.53 (n=328 eyes)
<i>Spectral-domain (SD) OCT</i>				
Peripapillary RNFL thickness, μm	93.0 ± 9.0 (n=48 eyes)	83.1 ± 12.9 (n=529 eyes)	86.4 ± 10.9 (n=287 eyes)	79.1 ± 14.1 (n=236 eyes)
Ganglion cell + inner plexiform layer (GCL+IPL), μm	88.9 ± 6.9 (n=61 eyes)	84.1 ± 8.4 (n=239 eyes)	87.0 ± 6.6 (n=150 eyes)	79.7 ± 9.2 (n=87 eyes)
Macular Thickness, μm	10.1 ± 0.4 (n=50 eyes)	9.8 ± 0.6 (n=509 eyes)	9.9 ± 0.5 (n=282 eyes)	9.7 ± 0.6 (n=221 eyes)

Abbreviations: MS = multiple sclerosis; ETDRS = Early Treatment Diabetic Retinopathy Study; QOL = quality of life ; NEI-VFQ-25 = 25-Item National Eye Institute Visual Functioning Questionnaire; TD = time-domain (OCT-3 platform); SD = spectral-domain (Cirrus platform); OCT = optical coherence tomography; RNFL = retinal nerve fiber layer.

SURGICAL APPROACHES TO THE ORBIT LIVE DISSECTION

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LEARNING OBJECTIVES

1. To describe the various surgical approaches to the orbit via the ventral endoscopic endonasal approaches (EEAs) and the dorsal transcranial approaches
2. To understand potential pathologies and treatment options that can be addressed via the respective approaches to the orbit
3. To explore current technologies which can aid in treating pathologies of the orbit via the endonasal approach

CME QUESTIONS

1. What are the inner and outer primary vascular supply network of the orbit?
2. What is the course of the central retinal artery?
3. What regions of the orbit can be approached from the endonasal perspective?

KEYWORDS

1. Expanded endonasal approach
2. Orbit
3. Skull base
4. Central retinal artery
5. Optic nerve

HIGHLIGHTS

At the end of this session, participants will be exposed to microsurgical anatomy of the anterior skull base and orbit, understand the key surgical principles in accessing the orbit, particularly from the endonasal perspective, and employ tips and tricks in addressing orbital anatomy and lesions while respecting skull base anatomic principles. Live dissections will be interactive with concomitant projection of 3D skull base anatomy.

SUMMARY

Surgery of the anterior skull base and orbit can be complex given the surrounding osseous, vascular and neural frameworks that lie within. Incremental knowledge gained in microsurgical anatomy and progressive evolution in surgical optical technology, has paved the way for the development of surgical corridors in order to facilitate and maximize safe and effective access. This live dissection will focus on anatomic and surgical principles and indications of several key ventral EEAs and dorsal transcranial

approaches to the orbit— including the superior orbital fissure, optic nerve, retinal artery, and orbital musculature— and anterior skull base.

CME ANSWERS

1. The inner circulation is formed by the ophthalmic artery and the outer circulation is composed by anastomosis with the branches of the external carotid artery that include the infraorbital, orbital branch of the middle meningeal, lacrimal, and facial arteries.
2. The central retinal artery can course inferolateral (6%), inferior (70%), or inferomedial (21%) to the optic nerve; with the site of penetration into the optic sheath near the junction of the middle and anterior one-thirds of the intraorbital optic nerve
3. Medial and inferior walls of the orbit and segments medial and inferior to the optic nerve, to a lesser extent superior, and lateral lesions are not ideal.

REFERENCES

1. McLaughlin N, Ditzel Filho LFS, Shahlaie K, Solari D, Kassam AB, Kelly DF. The supraorbital approach for recurrent or residual suprasellar tumors. *Minim Invasive Neurosurg*. 2011;54(4):155-161. doi:10.1055/s-0031-1284401.
2. Rhoton AL. The orbit. *Neurosurgery*. 2002;51(4 Suppl):S303-334.
3. Arai H, Sato K, Katsuta T, Rhoton AL. Lateral approach to intraorbital lesions: anatomic and surgical considerations. *Neurosurgery*. 1996;39(6):1157-1162; discussion 1162-1163. doi:10.1097/00006123-199612000-00018.
4. Martins C, Costa E Silva IE, Campero A, Yasuda A, Aguiar LR, Tatagiba M, Rhoton A. Microsurgical anatomy of the orbit: the rule of seven. *Anat Res Int*. 2011;2011:468727. doi:10.1155/2011/468727.
5. Matsuo S, Komune N, Iihara K, Rhoton AL. Translateral Orbital Wall Approach to the Orbit and Cavernous Sinus: Anatomic Study. *Oper Neurosurg (Hagerstown)*. 2016;12(4):360-373. doi:10.1227/NEU.0000000000001145.
6. Natori Y, Rhoton AL. Transcranial approach to the orbit: microsurgical anatomy. *J Neurosurg*. 1994;81(1):78-86. doi:10.3171/jns.1994.81.1.0078.
7. Natori Y, Rhoton AL. Microsurgical anatomy of the superior orbital fissure. *Neurosurgery*. 1995;36(4):762-775. doi:10.1227/00006123-199504000-00018.
8. Paluzzi A, Gardner PA, Fernandez-Miranda JC, Tormenti MJ, Stefko ST, Snyderman CH, Maroon JC. "Round-the-Clock" Surgical Access to the Orbit. *J Neurol Surg B Skull Base*. 2015;76(1):12-24. doi:10.1055/s-0033-1360580.
9. de Lara D, Ditzel Filho LFS, Prevedello DM, Carrau RL, Kasemsiri P, Otto BA, Kassam AB. Endonasal endoscopic approaches to the paramedian skull base. *World Neurosurg*. 2014;82(6 Suppl):S121-129. doi:10.1016/j.wneu.2014.07.036.
10. Joo W, Rhoton AL. Microsurgical anatomy of the trochlear nerve. *Clin Anat*. 2015;28(7):857-864. doi:10.1002/ca.22602.
11. Joo W, Yoshioka F, Funaki T, Rhoton AL. Microsurgical anatomy of the abducens nerve. *Clin Anat*. 2012;25(8):1030-1042. doi:10.1002/ca.22047.



North American Neuro-Ophthalmology Society

46th Annual Meeting

March 7– March 12, 2020

Omni Amelia Island Plantation • Amelia Island, FL

Thursday, March 12

6:30 am – 7:30 am

Breakfast

Magnolia Ballroom

6:30 am – 7:30 am

Breakfast with the Novices

Magnolia Ballroom

Join us in the reserved YONO area at breakfast for table discussions led by senior members and/or YONOs to discuss topics relevant to aspiring or current YONOs.

6:30 am – 7:30 am

Building Leadership Skills and the Importance of Mentorship

Lynn Gordon, MD, PhD and Peter Quiros, MD

6:30 am – 7:30 am

Surgical Neuro-Ophthalmology *Ore-ofe Adesina, MD, Lauren*

Ditta, MD and Courtney Francis, MD

6:30 am – 12:00 pm

Registration/Help Desk

Amelia Ballroom

7:30 am – 9:30 am

**New Treatments in Neuro-Ophthalmology-
2020 Trends [2.0 CME]**

Amelia Ballroom

Moderators: Bradley Katz, MD, PhD and Ahmara Ross, MD, PhD

This session will introduce and review new treatments for common diagnoses in neuro-ophthalmology. Therapeutic entities such as new FDA-approved immunotherapy, neuro-protective drugs and therapies including electrical stimulation, stem cells transplantation, and gene therapy will be discussed. This session will also review existing treatments as well as highlight new therapies on the horizon.

Upon completion of this session, participants should be able to: (1) evaluate the most recent developments in the treatment of thyroid eye disease, and (2) discuss with patients the latest research regarding treatments of optic nerve diseases, including genetic treatments, nerve regrowth treatments, and stem cell treatments.

7:30 am – 7:50 am

New Paradigm for the Treatment of Thyroid Eye Disease *Prem Subramanian, MD, PhD*

7:50 am – 8:15 am

Neuro-Ophthalmic Consequences of Immune Therapy *Lynn Gordon, MD, PhD*

8:15 am – 8:40 am

Optic Nerve Regeneration: the Future (Principles; Explanation of How It Works and Areas of Research Including Electrical Stimulation) *Kim Gokoffski, MD, PhD*

8:40 am – 9:05 am

Is It Time for Stem Cell Treatment? *Y. Joyce Liao, MD, PhD*

9:05 am – 9:30 am

Gene Therapy- Evolution and Therapeutic Applications *Patrick Yu-Wai-Man, MD, PhD*

9:30 am – 10:00 am
10:00 am – 12:00 pm

Coffee break
Strabismus: Image? Operate? [2.0 CME]
Moderators: Shannon Beres, MD and Paul H. Phillips, MD

Amelia Foyer
Amelia Ballroom

Many patients with ocular motility disorders can be diagnosed and treated after a clinical examination with no additional diagnostic testing. Other patients may require additional testing, including neuro-imaging, in order to determine the etiology and appropriate treatment of their strabismus. This case-based symposium will emphasize the important clinical findings that enable the clinician to determine if a patient with strabismus requires neuro-imaging. In addition, surgical options for the treatment of ocular motility disorders that present to neuro-ophthalmologists will be evaluated.

Upon completion of this session, participants should be able to: (1) identify clinical symptoms and signs that enable the clinician to determine whether a patient with strabismus requires neuroimaging, (2) identify the risks and benefits of various strabismus surgical procedures, and (3) identify the risks and benefits of various non-surgical procedures that treat patients with strabismus.

10:00 am – 10:14 am	Child With Crossed Eyes Since Infancy: Do I Image? Do I Operate? <i>Lauren Ditta, MD</i>
10:14 am – 10:28 am	Child With Acquired ET: Do I Image? Do I Operate? <i>Jane Edmond, MD</i>
10:28 am – 10:42 am	Adult With Acquired Diplopia at Distance: Do I Image? Do I Operate? <i>Mitchell Strominger, MD</i>
10:42 am – 10:56 am	Adult With Acquired Vertical Diplopia: Do I Image? Do I Operate? <i>Nicholas Volpe, MD</i>
10:56 am – 11:10 am	Adult With Acquired Oblique Diplopia: Do I Image? Do I Operate? <i>Hilda Capo, MD</i>
11:10 am – 11:24 am	Teenager With Acquired Strabismus: Do I Image? Do I Operate? <i>R. Michael Siatkowski, MD</i>
11:24 am – 11:38 am	Baby With Tonic Downgaze: Do I Image? Do I Operate? <i>Ellen Mitchell, MD</i>
11:38 am – 12:00 pm	Q&A

NEW PARADIGMS FOR THE TREATMENT OF THYROID EYE DISEASE

Prem S. Subramanian, MD, PhD

*Sue Anschutz-Rodgers UHealth Eye Center/University of Colorado School of Medicine
Aurora, CO*

LEARNING OBJECTIVES

1. The attendee will be able to describe the different immunological pathways by which thyroid eye disease develops.
2. The attendee will be able to recognize indications for pharmacotherapy in thyroid eye disease as they relate to severity and rapidity of disease onset and progression.
3. The attendee will be able to implement a treatment regimen and explain the anticipated benefit for the array of patient symptoms and findings that occur with thyroid eye disease.

CME QUESTIONS

1. Which thyroid disease-associated serum autoantibody is most predictive of a patient's risk for developing thyroid ophthalmopathy?
 - A. Sodium/iodide symporter
 - B. Thyroglobulin
 - C. Thyroid peroxidase
 - D. Thyroid stimulating
2. What features of thyroid eye disease that are more common in older individuals may lead to insidious and unrecognized vision loss?
 - A. Apical crowding without proptosis
 - B. Fat hypertrophy in the intraconal space
 - C. Optic nerve infiltration by fibrocytes
 - D. Transformation to lymphomatous process
3. Evidence supports the use of medical therapies for thyroid eye disease during what stage of disease development?
 - A. Prior to manifestation of orbital signs
 - B. During the active phase
 - C. When clinical findings are stable
 - D. After surgical intervention

KEYWORDS

1. Graves disease
2. Intravenous corticosteroid
3. Teprotumumab
4. Clinical activity scale score

HIGHLIGHTS

Thyroid-related ophthalmopathy (TRO) or thyroid eye disease (TED) occurs in up to 50% of patients with systemic Graves hyperthyroidism as well as a smaller percentage of patients with other autoimmune thyroid disorders such as Hashimoto thyroiditis. Some of the underlying immunological mechanisms have been studied and elucidated, including stimulatory pathways that lead to orbital fibroblast proliferation, fat hypertrophy, and extraocular muscle changes.

For a number of decades, the treatment options for patients with TED have been medical management with corticosteroids, adjuvant orbital radiation therapy, and surgical interventions to correct the sequelae of the disease including optic nerve compression, proptosis, restrictive strabismus, and periocular and eyelid tissue changes including eyelid retraction. However, recent advances have led to the development of new therapeutic strategies that employ targeted biologic agents that may alter the course of the disease rather than simply halting the inflammatory cascade; such agents offer the possibility of treating the disease without a need for subsequent surgeries by reversing orbital changes rather than merely stabilizing them.

SUMMARY

Introduction

Thyroid eye disease (TED), thyroid-related ophthalmology (TRO), and Graves eye disease are terms that have been used interchangeably to describe the characteristic complex of signs and symptoms that may accompany, follow, or precede systemic hyperthyroidism from Graves disease. A subset of patients may manifest these changes without any serologic or symptomatic evidence for thyroid dysfunction; these individuals are termed to have “euthyroid Graves ophthalmopathy.” Proliferation of normally quiescent orbital fibroblasts, fibrocytes, and adipocytes drives the changes of TED that are recognized clinically as proptosis, strabismus, and eyelid retraction. In the acute phase, orbital signs of inflammation such as chemosis, conjunctival injection, periocular swelling, orbital pain (especially with eye movement), and changes in appearance and function with time are the cardinal findings that indicate a potential response to medical and/or radiation therapy. Most TED therapies attempt to downregulate the inflammatory sequelae of this proliferation and the cytokine cascade that it generates; in doing so, the disease process may be slowed down or halted but is rarely improved with respect to remission of the signs and symptoms.

Pathogenesis

The main target of the autoimmune process that stimulates TED appears to be the TSH receptor. Antibodies against the TSH receptor bind to it and cause overstimulation of the thyroid gland and excessive release of thyroid hormone, thus causing the characteristic systemic symptoms of palpitations, heat intolerance, weight loss, hair loss, and fatigue. However, it is not the thyroid hormone itself that causes the TED-related changes; rather, it appears to be direct binding of the TSH receptor antibodies to TSH receptors on the surface of orbital fibroblasts and/or fibrocytes that invokes a stimulatory cascade that leads to both cell proliferation and recruitment of inflammatory cells that infiltrate the orbit and help to perpetuate the process. There are two primary classes of TSH receptor antibodies; those termed thyroid-stimulatory immunoglobulins (TSI) are most closely correlated with disease onset and activity. In patients with systemic Graves hyperthyroidism and no signs of TED, the levels of TSI may be predictive of the future development of ocular and orbital changes, with patients falling into the top quartile of TSI levels having a several fold increase in TED risk compared to those in the bottom quartile. The insulin-like growth factor-1 (IGF-1) receptor also is expressed on the surface of orbital fibroblasts, and its identification a number of years ago led to the observation of a potentially synergistic effect with

the TSH receptor in terms of disease activation and cellular proliferation. This effect was found to occur in a T-cell mediated fashion, and this finding also supported the notion that TED is primarily a T-cell driven disease.

More recently, stimulation of the TSH receptor on cultured TED fibroblasts has been shown to activate the phosphoinositide-3 kinase pathway and to stimulate expression of microRNAs that perpetuate the inflammatory cascade, perhaps independent of ongoing stimulation of the TSH receptor.

Smoking has been demonstrated to worsen the severity of TED and also to make its medical and surgical treatments more challenging. Indeed, the efficacy of “mainstream” TED treatments such as pulsed intravenous corticosteroids has been shown to be minimal in patients who smoke cigarettes, and the threshold exposure level for this effect appears to be quite low (about 5-10 cigarettes/day). *In vitro* studies in which orbital fibroblasts were exposed to a cigarette smoke extract showed that fibroblasts from both patients with TED and control subjects demonstrated a proliferative and adipogenic response; this occurred in a dose-dependent manner and recapitulated changes that occur when cell cultures were exposed to TNF-alpha, IL-1, and IFN-gamma. It is not known how long-lasting the systemic influence of cigarette smoking is after smoking cessation, but the observation that there may be multiple compounds in cigarette smoke that lead to its detrimental effect suggests that nicotine-only substitutes may be a viable alternative for TED patients who are attempting to quit smoking.

Therapeutic strategies

As noted, traditional therapeutic approaches have relied upon a nonspecific approach to orbital inflammation, in which corticosteroids have been the mainstay of treatment. Although there is a wealth of high-quality evidence to support the efficacy of pulsed, weekly intravenous corticosteroid infusions in the treatment of patients with active TED, the combination of potential side effects as well as the limited effect on critical symptoms and signs such as proptosis and eyelid retraction have led to the quest for more effective therapies.

Several biologic agents have been studied for the treatment of TED. Case reports and then a small case series demonstrated potential efficacy of rituximab in patients whose TED was progressing and threatening visual function despite maximal conventional medical and even surgical treatments. Improvement in visual acuity and marked reduction of disease activity appeared to be induced rapidly, within a few weeks, after 2 infusions of rituximab given 2 weeks apart. Based on these results, randomized clinical trials were designed and implemented in the US and Europe with differing study designs. These two trials, which had similar entry criteria, came to opposite conclusions regarding the effect of rituximab; one trial (European) showed superior CAS score/disease activity improvement with rituximab vs steroid therapy, while the other (American) found no difference in outcomes between subjects treated with rituximab when compared to placebo. Although the drug is not used for chronic immunosuppression and thus may not carry the same risks of serious side effects, such as progressive multifocal leukoencephalopathy (PML) as in other patients, the use of rituximab for TED remains controversial. Furthermore, because TED is thought to be mediated primarily by a T-cell driven process, there has been some concern regarding the potential mechanism by which this drug might be working; is general B lymphocyte depletion just down-regulating immune activity overall, or is there some specific mechanism by which it is having an effect? However, evidence does show that rituximab may downregulate the activity of IGF-1R+ T-cells as well.

Another biologic that has shown promise in the treatment of TED is tocilizumab, which may be familiar to many neuro-ophthalmologists because of its use in the management of patients with giant cell arteritis. This agent, which inhibits activity of the interleukin-6 (IL-6) receptor, is currently being evaluated in a larger, masked clinical trial with case series demonstrating some efficacy in both reducing disease activity and potentially in lessening proptosis, one of the most troublesome and visible signs of

TED. If this effect holds true with a greater number of patients, then treatment with tocilizumab may alter the disease course and not simply stabilize it.

Finally, the biological agent that has garnered significant interest most recently is teprotumumab, which inhibits the activity of the IGF-1 receptor. As noted above, the IGF-1 receptor shows synergistic activity with the TSH receptor in the stimulation of fibroblast and fibrocyte proliferation. Teprotumumab was originally developed as a potential anticancer drug and has been repurposed for TED because of its potential to affect the disease course itself and not just the inflammatory cascade it triggers. Initial animal studies and then phase I/II data demonstrated both safety as well as efficacy, and thus a phase III clinical trial of teprotumumab vs placebo was conducted on patients with TED of <9 months duration and minimal prior exposure to steroid therapy. Subjects received intravenous infusions every 3 weeks for 24 weeks (8 doses), and outcomes were assessed including improvement in CAS score and other soft tissue signs as well as quality of life. However, the primary outcome measure was proptosis reduction in the study eye, an outcome that had not been used in prior TED studies. When the data were analysed, it was found that a significant (approx. 3 mm) reduction in proptosis had been achieved, which is a result that is comparable to surgical decompression in many cases. Detailed orbital imaging was not performed, but it can be presumed that the effect of the drug was based on a lack of fibroblast and adipocyte proliferation and not simply by edema reduction (as other drugs that reduce edema do not have such an effect on eye position). Questions that remain to be answered include the long-term durability of the result, since we do not expect that it reduces autoantibody levels (i.e. TSI) as would an agent like rituximab. Nonetheless, because the natural history of TED is that it burns out after 12-18 months from onset, the action of teprotumumab may be sufficient to preclude the disfiguring sequelae of the disease until the autoimmune stimulation is reduced to baseline.

None of the agents described in this treatment paradigm are US FDA-approved for the indication of TED, although it is anticipated that teprotumumab may receive this approval by spring of 2020, as the drug has been designated for fast-track consideration and review.

Conclusions

Medical therapy of TED has entered a new era with the introduction of several biologic agents that could be effective in preventing long-term disease complications. A limiting factor in all analyses is that there are no long-term data (2 or more years) to demonstrate that any of these agents induce a durable and sustained effect that lasts long after the treatment(s) have been completed.

CME ANSWERS

1. D
2. A
3. B

REFERENCES

1. Tsui S, Naik V, Hoa N, et al. Evidence for an association between TSH and IGF-1 receptors. A tale of two antigens implicated in Graves' disease. *J Immunol*.181:4397-4405, 2008.
2. Cawood TJ, Moriarty P, O'Farrelly C et al. Smoking and thyroid-associated ophthalmopathy.: a novel explanation of the biological link. *J Clin Endocrinol Metab* 92:59-64, 2007.
3. Douglas R. Teprotumumab, an insulin-like growth factor-1 receptor antagonist antibody, in the treatment of active thyroid eye disease: focus on proptosis. *Eye* 33, 183-190, 2019.
4. Wong LL, Lee NG, Amarmani D, et al. Orbital angiogenesis and lymphangiogenesis in thyroid eye disease. *Ophthalmology* 123;2028-20136, 2016.

5. Perez-Moreiras JV, Alvarez-Lopez A, Gomez EC. Treatment of active corticosteroid-resistant Graves' orbitopathy. *Ophthal Plast Reconstr Surg* 30, 162-167, 2014.
6. McCoy AN, Kim DS, Gillespie EF. Rituximab (Rituxan) therapy for severe thyroid-associated ophthalmopathy diminished IGF-1R+ T-cells. *J Clin Endocrinol Metab* 99, E1294-1299, 2014.

NEURO-OPHTHALMIC CONSEQUENCES OF IMMUNE CHECKPOINT INHIBITOR THERAPY

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LEARNING OBJECTIVES

1. Attendees will be able to explain the mechanism of action of the major immune checkpoint inhibitors currently used in cancer immunotherapy.
2. Attendees will be able to describe the primary neuro-ophthalmic complications of immune checkpoint inhibition.
3. Attendees will know the therapeutic options for control of neuro-ophthalmic consequences of immune checkpoint inhibition.

KEY WORDS

1. Cancer
2. Immunotherapy
3. Optic neuropathy
4. Programmed death 1 (PD-1)
5. CTLA-4

CME QUESTIONS

1. Immune checkpoint inhibition is used in cancer immunotherapy to
 - A. Decrease the immune response to the cancer
 - B. Cause direct cell killing of the cancer cells
 - C. Enhance immune responses through release of inhibition
 - D. Enhance immune responses through direct cell killing
2. Neuro-ophthalmic complications of immune checkpoint inhibition in cancer immunotherapy
 - A. Arise from direct and immediate effect of drug infusion
 - B. Occur weeks to months after initiation of therapy
 - C. Occur as a delayed, up to 1-2 weeks, but direct effect of the drug infusion
 - D. Arise from immune cell death induced through the checkpoint inhibition
3. Therapy for severe ophthalmic complications of immune checkpoint inhibition may require the following:
 - A. Permanently discontinue immune checkpoint inhibition
 - B. Prompt institution of systemic corticosteroids
 - C. Evaluation for other potential etiologies for the ocular complication
 - D. All of the above

HIGHLIGHTS

Although immune therapy is used in many types of diseases, from control of systemic inflammatory diseases, to treatment of multiple sclerosis and other demyelinating diseases, to advances in cancer

therapy, this presentation concentrates on immune checkpoint inhibition, which is increasingly used in cancer immunotherapy.

Over the past decade, cancer immunotherapy, for which the 2018 Nobel Prize in Medicine was awarded, created a revolutionary change in the therapeutic approach for multiple types of cancers.¹ In this approach the immune system is manipulated to combat cancer through the release of normal inhibitory immune mechanisms, checkpoint pathways, in order to free up T cells to assault the cancer cells. Clinically, inhibitors of the immune checkpoint blockade pathway work through effectively upregulating natural anti-tumor immunosurveillance and have been shown to markedly improve survival of patients with specific advanced cancers.

Multiple immune checkpoint inhibitors (ICIs), monoclonal antibodies that act to block inhibitory receptors involved in T-cell downregulation, are now in clinical use and include the cytotoxic T-lymphocyte 4 (CTLA-4), programmed death (PD) through the receptor (PD-1) or ligand (PD-L1/2), or both pathways. Ipilimumab, an anti-CTLA-4 antibody was the first in this category and was approved in 2011 for the treatment of metastatic or unresectable melanoma.^{1,2} Subsequently successful targeting of the PD1 pathway was achieved and antibodies approved that target PD-1, nivolumab and pembrolizumab, and PD-L1, durvalumab, atezolizumab, and avelumab.^{3,4} The checkpoint inhibitors ipilimumab and nivolumab, in combination, were FDA-approved for dual blockade of CTLA-4 and PD-1 pathways as they provided synergistic response rates of up to 50-61% in the management of advanced melanoma.⁵

Along with the great success in treating previously unresponsive cancers came the inevitable consequences of releasing the immunologic brakes with high rates of immune related adverse events (irAEs) in patients who received the checkpoint inhibitors, higher with CTLA-4 blockade (up to 90%) than with PD-1 blockade (up to 70%).⁶⁻⁸ Although the majority of irAEs are self-limited and transient, some can lead to major morbidity or death. The most common systemic irAEs include dermatitis (rash, pruritus, vitiligo), enterocolitis (diarrhea, nausea), and endocrinopathies (thyroiditis, pancreatitis). Less common irAEs affect the lungs, liver, and kidneys.

Ophthalmic and neuro-ophthalmic consequences of immune checkpoint inhibition

Ocular irAEs are reported to occur in about 1% of treated patients, the most frequent of which is uveitis, although involvement of the optic nerve, retina, pupils, and muscles are also reported.⁹⁻¹⁸ A comprehensive review of patients treated with either anti-CTLA4 or anti-PD-1 antibodies was published in 2016 that identified 251 patients.¹⁹ In this study 93.2% of identified patients had received anti-CTLA4 therapy, however ophthalmic complications were identified in 10%, of which uveitis was present in 4.3%, conjunctivitis in 2.1%, orbital inflammation in 2.1%, and less than 1% developed optic neuropathy, retinopathy, or systemic myasthenia gravis. A prospective study of patients at a single center, along with a literature review of individuals who received anti-PD-1 or PD-L1 treatment, identified ocular complications in 0.4% and prevalence of intraocular inflammation (anterior uveitis, posterior uveitis, panuveitis) as 0.2%.¹³ This study did not specifically identify neuro-ophthalmic consequences of anti-PD-1 pathway treatments. Neuro-ophthalmic consequences of immune checkpoint inhibition can result in significant morbidity and causes other than the cancer therapy, such as metastatic disease, must be ruled out. A series of 31 patients with neuro-ophthalmic irAEs following immune checkpoint blockade therapy was recently amassed and the full documentation of these cases was submitted as an abstract for this NANOS meeting. The most common irAEs in this case series included optic nerve involvement in 11 patients with 8 patients who had bilateral optic neuritis. The other most common irAEs in this series included myasthenia gravis and extraocular muscle involvement.

In terms of uveitis, several groups identified the characteristics of patients with uveitis and the successful strategies for therapy of these ophthalmic irAEs (OirAEs). A detailed report of 14 patients with uveitis following immune checkpoint blockade was published along with a literature review of previously reported cases.¹⁴ Notably, several of these patients also had optic disc involvement, either with edema or papillitis. Optic nerve involvement in patients on immune checkpoint inhibition have been sporadically identified also in the absence of uveitis or other ocular inflammatory conditions. The majority of individuals with uveitis developed the OirAE within months of initiation of therapy, median of 63 days (range 4-161). In this study the most common cancer was melanoma, present in 31 of a total of 36 patients, which may reflect a susceptibility to ocular inflammation in these patients or may be due to the fact that melanoma was the first approved cancer indication for these medications. However a recent publication evaluated the relation between irEA as reported in the US Food and Drug Administration Adverse Event Reporting System (FAERS) and specific tumors according to the median number of coding somatic mutations and also found that the highest probability for an irEA in patients treated with anti-PD-1 therapy was in melanoma and small cell lung cancer.²⁰ Therefore it is likely that melanoma does predispose the individual to a higher probability of developing an irAE following immune checkpoint inhibition therapy. Using the FAERS database data from 2013-2018, another study identified 113 OirEAs.¹⁶ The anti-CTLA-4 ipilimumab was associated with uveitis and the PD-L1 antibody, atezolizumab, was associated with ocular inflammation. The PD-1 antibody nivolumab was associated with 60% of the cases, and both nivolumab and pembrolizumab were most highly associated with ocular myasthenia.

Neuromuscular complications following immune checkpoint inhibition have been described in multiple publications and were recently described following a systematic review of the literature which identified 30 cases of myasthenia gravis, 29 cases of neuropathy, and 22 cases of myopathy.²¹ Almost all patients developed neuromuscular symptoms within 3 months of initiation of therapy and 40% of cases has elevated serum creatinine kinase. About 25% of the patients with myasthenia were known to have had this disease prior to the onset of checkpoint inhibition. Involvement of the extraocular muscles may also resemble thyroid-associated eye disease (TED).²²

Treatment for OirEAs is not yet well-defined, however there is some evidence from the literature. In the case of uveitis, the majority of patients, but not all, respond to conventional treatment with topical, sub-tenons, or systemic corticosteroid therapy.¹⁴ In the few reported cases of optic neuritis, there was a good response to systemic steroid therapy. In the setting of neuromuscular involvement the majority of patients also responded to traditional immunomodulatory therapy, however there was also high mortality of 26% often from recurrent cancer or other complications.²¹ Depending on the severity of the irEA the different recommendations may include use of corticosteroids with or without discontinuation of the immune checkpoint inhibitor, or additional immunomodulatory agents in order to control the adverse effect. These treatment decisions must be tailored specifically for the individual patient.

SUMMARY

Development of immune checkpoint inhibitor therapy revolutionized treatment of specific cancers and resulted in increased survival for patients who would have otherwise succumbed to their disease. The therapeutic agents either target the CTLA-4 or PD-1 pathways and there is evidence for increased irAEs when the CTA-4 antibodies are used. Ocular irAEs occur in a minority of patients but result in significant morbidity. Therefore neuro-ophthalmologists must be knowledgeable about the range of observed

diseases as well as therapeutic options for resolution of these AEs. Future studies will be required to provide evidence-based guidelines for these patients.

CME ANSWERS

1. C
2. B
3. D

REFERENCES

1. Granier C, De Guillebon E, Blanc C, et al. Mechanisms of action and rationale for the use of checkpoint inhibitors in cancer. *ESMO Open* 2017;**2**(2):e000213 doi: 10.1136/esmoopen-2017-000213.
2. Hodi FS, O'Day SJ, McDermott DF, et al. Improved survival with ipilimumab in patients with metastatic melanoma. *N Engl J Med* 2010;**363**(8):711-23
3. Topalian SL, Hodi FS, Brahmer JR, et al. Safety, activity, and immune correlates of anti-PD-1 antibody in cancer. *N Engl J Med* 2012;**366**(26):2443-54
4. Brahmer JR, Tykodi SS, Chow LQ, et al. Safety and activity of anti-PD-L1 antibody in patients with advanced cancer. *N Engl J Med* 2012;**366**(26):2455-65
5. Wolchok JD, Kluger H, Callahan MK, et al. Nivolumab plus ipilimumab in advanced melanoma. *N Engl J Med* 2013;**369**(2):122-33
6. Michot JM, Bigenwald C, Champiat S, et al. Immune-related adverse events with immune checkpoint blockade: a comprehensive review. *Eur J Cancer* 2016;**54**:139-48
7. Davar D, Kirkwood JM. PD-1 Immune Checkpoint Inhibitors and Immune-Related Adverse Events: Understanding the Upside of the Downside of Checkpoint Blockade. *JAMA Oncol* 2019;**5**(7):942-43
8. Fessas P, Possamai LA, Clark J, et al. Immunotoxicity from checkpoint inhibitor therapy: clinical features and underlying mechanisms. *Immunology*. 2019 Oct 23.[Epub ahead of print] PubMed PMID: 31646612.
9. Antoun J, Titah C, Cochereau I. Ocular and orbital side-effects of checkpoint inhibitors: a review article. *Curr Opin Oncol*. 2016;**28**(4):288-94
10. Wilson MA, Guld K, Galetta S, et al. Acute visual loss after ipilimumab treatment for metastatic melanoma. *J Immunother Cancer*. 2016 Oct 18;**4**:66. eCollection 2016.
11. Abdel-Rahman O, Oweira H, Petrausch U, et al. Immune-related ocular toxicities in solid tumor patients treated with immune checkpoint inhibitors: a systematic review. *Expert Rev Anticancer Ther*. 2017;**17**(4):387-394
12. Dalvin LA, Shields CL, Orloff M, Sato T, Shields JA. Checkpoint Inhibitor Immune Therapy: Systemic Indications and Ophthalmic Side Effects. *Retina* 2018;**38**(6):1063-78
13. Bitton K, Michot JM, Barreau E, et al. Prevalence and Clinical Patterns of Ocular Complications Associated With Anti-PD-1/PD-L1 Anticancer Immunotherapy. *Am J Ophthalmol* 2019;**202**:109-17
14. Sun MM, Levinson RD, Filipowicz A, et al. Uveitis in Patients Treated with CTLA-4 and PD-1 Checkpoint Blockade Inhibition. *Ocul Immunol Inflamm* 2019:1-11
15. Douglas VP, Douglas KAA, Cestari DM. Immune checkpoint inhibitors: what neuro-ophthalmologists need to know. *Curr Opin Ophthalmol*. 2019; **30**(6):426-433.
16. Fang T, Maberley DA, Etminan M. Ocular adverse events with immune checkpoint inhibitors. *J Curr Ophthalmol*. 2019; **31**(3):319-322

17. Noble CW, Gangaputra SS, Thompson IA, et al. Ocular Adverse Events following Use of Immune Checkpoint Inhibitors for Metastatic Malignancies. *Ocul Immunol Inflamm*. 2019 Apr 23:1-6. [Epub ahead of print] PubMed PMID: 31013173.
18. Conrady CD, Laroche M, Pecan P, et al. Checkpoint inhibitor-induced uveitis: a case series. *Graefes Arch Clin Exp Ophthalmol*. 2018; **256**(1):187-191
19. Abdel-Wahab N, Shah M, Suarez-Almazor ME. Adverse Events Associated with Immune Checkpoint Blockade in Patients with Cancer: A Systematic Review of Case Reports. Nishikawa H, ed. *PLoS ONE*. 2016;11(7):e0160221. doi:10.1371/journal.pone.0160221
20. Bomze, D, Ali H, Bate A, Flatz, L. Association Between Immune-Related Adverse Events During Anti-PD-1 Therapy and Tumor Mutational Burden. *JAMA Oncol*. 2019; Aug 22. doi: 10.1001/jamaoncol.2019.3221. [Epub ahead of print]
21. Puwanant, a, Isfort M, Lacomis, D, Zivkovic SA. Clinical spectrum of neuromuscular complications after immune checkpoint inhibition. *Neuromuscul Disord*. 2019; 29(2):127-133
22. Sgiv O, Kandl TJ, Thakar SD, et al. Extraocular Muscle Enlargement and Thyroid Eye Disease-Like Orbital Inflammation Associated with Immune Checkpoint Inhibitor Therapy in Cancer Patients. *Ophthalmic Plast Reconstr Sur*. 2019;**35**:50-52.

OPTIC NERVE REGENERATION—HOW MUCH LONGER?

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LEARNING OBJECTIVES

1. Recognize the intrinsic barriers to optic nerve regeneration.
2. Differentiate between different stem cell-based approaches for generating retinal ganglion cells (RGCs).
3. Compare and contrast different approaches for overcoming limitations to RGC regeneration.
4. Appraise the potential effectiveness of current clinical trials for optic nerve regeneration.

CME QUESTIONS

1. Stem cell-derived RGCs have been shown to display all of the following characteristics EXCEPT:
 - A. Glutamate responsiveness
 - B. Intercellular transfer of cytoplasmic material
 - C. Expression of RGC specific markers including Brn3 and CD171
 - D. Dendritic arborization
2. To date, all of the following show promise as potential solutions for guiding regenerating axons to their appropriate distal targets in the diencephalon EXCEPT:
 - A. Electrical fields
 - B. Scaffolds
 - C. Peripheral nerve grafts
 - D. Myelin associated proteins
3. Failure of mTOR and JAK/STAT pathway up-regulation to restore the optokinetic reflex after optic nerve crush injury in mice was a result of:
 - A. Lack of myelination along regenerated axons
 - B. Failure to form new synapses with the superior colliculus
 - C. Failure to regenerate axons
 - D. Aberrant regeneration

KEYWORDS

1. Optic nerve regeneration
2. Retinal ganglion cell
3. Inducible pluripotent stem cells

HIGHLIGHTS

Introduction

In mammals, axon regeneration after injury is the rule for the peripheral nervous system (PNS) but the exception when it comes to the central nervous system (CNS). The limited regenerative capacity of the CNS was thought to be cell intrinsic until experiments demonstrated that CNS axons readily grow into

peripheral nerve grafts.¹ These landmark studies demonstrated that extrinsic environmental factors can override intrinsic limitations to regeneration in the CNS. These early studies fueled investigations to identify growth-permissive molecules within the PNS and growth-inhibitory molecules within the CNS, with the hope that manipulating their relative levels would unlock the regenerative capacity of the CNS.

Cell-intrinsic and Cell-extrinsic Barriers to Optic Nerve Regeneration

Cell-intrinsic limitations to regeneration are established during development when the CNS transitions from a state of proliferation to one of differentiation. Some organs, such as the skin and liver, retain a reserve of pluripotent cells through their differentiation phase which serve to regenerate and replace damaged cells in the adult organ. Other organs, such as the CNS, do not retain pluripotent cells. Intracellular signaling pathways that have been shown to induce transcriptional cascades and epigenetic changes that underlie neuronal maturation in the CNS include cyclic adenosine monophosphate (cAMP), mammalian target of rapamycin (mTOR), and Kruppel Like Factor 4.² Accordingly, down regulation of these molecules in axotomized neurons has been associated with variable rates of RGC axon regeneration.³⁻⁵

Cell extrinsic barriers to axon regeneration can be divided into two major groups: myelin and glial scar. Myelin is a group of fatty proteins produced by glial cells whose function is to insulate and speed electrical conduction along axons. Myelin byproducts are shed from axons when injured and are cleared by Schwann cells and blood-borne macrophages in the PNS.⁶ The absence of Schwann cells in the CNS is thought to account, in part, for the relatively poor axon regeneration seen in the CNS. Additionally, reactive astrocytes elaborate a glial scar comprised of chondroitin sulphate proteoglycans in response to injury.⁷ This scar is thought to create an inhospitable environment for axonal regeneration, serving as a mechanical barrier to growth. Neutralization of these barriers to axon regeneration will be necessary for development of effective neuro-regenerative and cell-replacement based strategies for optic nerve regeneration.

Neuro-regenerative Approaches

Current strategies for neuro-regeneration or approaches to rescue degenerating axons have focused on providing neurotrophic support such as with nerve growth factor (NGF) and brain-derived neurotrophic factor.⁸ The rationale for these approaches stem from the finding that neurons depend on retrograde transport of endosomes containing neurotrophic factors for survival.⁹ The hope was that by providing neurotrophic support, RGCs could be kept alive longer, increasing the opportunity for axon regeneration. The problem however is that increased neuronal survival did not equate to new axon formation^{10,11}. Others have tried preventing apoptosis¹² and preventing axon retraction as strategies to slow optic nerve degeneration.¹³

More targeted approaches aimed at resetting cell intrinsic programs to pro-axonogenic states have been met with greater success. Activation of growth-promoting molecules such as mTOR and Janus kinase/signal transducers and activators of transcription (JAK/STAT) have been associated with long distance RGC axon regeneration after optic nerve crush injury.³⁻⁵ There are a number of caveats, however, associated with these approaches. First, these therapies appear to benefit only a subset of RGCs: activation of mTOR or overexpression of oncomodulin and insulin-like growth factor 1 selectively promoted regeneration of alpha-RGCs which comprise only 6% of the total RGC population.¹⁴ Second, the efficacy of mTOR and JAK/STAT in directing optic nerve regeneration have only been demonstrated when their levels were upregulated before or concurrently with axon injury^{3,15}, which has limited clinical application. Third, although some of these regenerated axons formed functional synapses with neurons in the superior colliculus, animals did not show improvement on visual aptitude testing.⁴ This lack of

improvement likely occurred because the newly formed axons were left unmyelinated. Partial restoration of visual function could be achieved with 4-aminopyridine (4-AP), a voltage-gated potassium channel blocker.

Cell-Replacement Approaches

The first step in developing cell replacement-based strategies for optic nerve regeneration requires a reliable, high volume source of healthy RGCs. The discovery that human embryonic stem cells (hESCs) and more recently inducible pluripotent stem cells (iPSCs) could be trans-differentiated into RGCs has turned optic nerve regeneration from science fiction to possibility. iPSCs are somatic cells such as skin fibroblasts that have been reverted to an immature state through enhanced expression of four transcription factors (Oct3/4, Sox2, c-Myc, and Klf4).^{16,17} Currently, there are two different methods for generating RGCs from stem cells (hESCs and iPSCs): 1) organoid differentiation and 2) planar differentiation. Organoids are self-organizing, three-dimensional miniature organs developed in vitro from pluripotent stem cells while planar culture consists of two-dimensional cultures. Generally, trans-differentiation involves exposing these cells to different cocktails of growth factors. RGCs can be observed in culture as early as day 15 of differentiation and have been observed to form dendritic arborization. Significant work is being performed to understand which of these methods is the most robust for producing RGCs that resemble the native RGC. On one hand, organoids have been shown to express the same sequence of transcription factors that characterize endogenous retinal development (e.g. Brn3 and CD171) and to self-organize into layers similar to the developing optic cup.^{18,19} Whole-cell voltage clamp recordings demonstrate that planar-derived RGCs are glutamate responsive.²⁰ It appears that RGCs can be readily purified from either culture technique suggesting that one day, patients may serve as their own source for RGC transplantation. A limitation to using autologous iPSCs, however, is that any underlying genetic predispositions to neuro-degeneration would still be present in the cells used to generate new RGCs.

A barrier to current cell-replacement therapies is the poor rate of RGC integration into the ganglion cell layer of the retina after intravitreal injection, between 1-7%²¹. Cited causes of poor integration include: 1) structural obstacles to the ganglion cell layer (GCL), such as the retinal inner limiting membrane (ILM) and extracellular matrix (ECM) and 2) post-injection inflammatory responses, including immune-mediated clearance of the transplanted cells. Remarkably, ILM peeling was associated with increased integration rates in ex vivo cultures.²² Of the RGCs that migrated into the GCL, many displayed normal RGC-like arboritic structures that formed functional synapses with the host retina.

Of the few RGCs that integrate into the host retina, many sprouted axons that grew towards the optic nerve head but few (~10%) grew past the lamina cribrosa and into the optic nerve.²¹ Some had hoped that recapitulating the pathways that guided optic nerve development could be used to direct the growth of regenerating axons. This hope, however, was met with limited success: ephrin-A2 expression in the superior colliculus was found to have an inhibitory effect on RGC axon regeneration.²³ A similar effect was reported with semaphorin-3A. Recently, our group has found success with the application of electric fields (EFs). We found RGC axons exhibited cathode-directed growth when exposed to an EF in vitro.²⁴ The efficacy of such currents on directing RGC axon regeneration in vivo after optic nerve crush injury are currently under active investigation in our lab and preliminary experiments show promising results. Alternative strategies for directing optic nerve regeneration include fabricated scaffolds^{20,25} and autologous grafts from the PNS.

The question of whether regenerated axons will establish new, functional synapses with the diencephalon remains a significant question in the field of optic nerve regeneration. Attempts to

recapitulate the ‘retinal waves’ that primed the developing visual system have been met with promising success. In one of these experiments, Lim crushed one optic nerve and sutured the non-lesioned eye shut, forcing all light input to the visual cortex to come from the lesioned optic nerve. High contrast visual stimulation in conjunction with mTOR activation enhanced RGC regeneration after crush injury and lead to partial recovery of visual function including the optokinetic reflex, the visual cliff test, and the looming avoidance response.¹⁵

SUMMARY

Depending on the rate and severity of RGC degeneration, different optic neuropathies stand to benefit from neuro-protective, neuro-regenerative, or cell replacement-based strategies. Although promising, significant barriers still exist before stem cell based therapies can be translated to the clinical arena. Currently, only one clinical trial (NCT01920867/ NCT03011541) is listed on Clinicaltrials.gov that proposes to use stem cells to restore vision in patients blinded by various eye diseases. This trial however does not aim to replace lost cells but rather hopes to provide neurotrophic support to dying cells.²⁶ Given the recent disastrous outcomes of patients with age-related macular degeneration who lost significant vision after intravitreal injection with adipose-derived stem cells²⁷, we urge caution before endorsing premature trials.

CME ANSWERS

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REFERENCES

1. Richardson, P. M., McGuinness, U. M. & Aguayo, A. J. Axons from CNS neurons regenerate into PNS grafts. *Nature* **284**, 264-265, doi:10.1038/284264a0 (1980).
2. Yang, P. & Yang, Z. Enhancing intrinsic growth capacity promotes adult CNS regeneration. *Journal of the neurological sciences* **312**, 1-6, doi:10.1016/j.jns.2011.08.037 (2012).
3. Sun, F. *et al.* Sustained axon regeneration induced by co-deletion of PTEN and SOCS3. *Nature* **480**, 372-375, doi:10.1038/nature10594 (2011).
4. Bei, F. *et al.* Restoration of Visual Function by Enhancing Conduction in Regenerated Axons. *Cell* **164**, 219-232, doi:10.1016/j.cell.2015.11.036 (2016).
5. Park, K. K. *et al.* Promoting axon regeneration in the adult CNS by modulation of the PTEN/mTOR pathway. *Science* **322**, 963-966, doi:10.1126/science.1161566 (2008).
6. Schwab, M. E. Repairing the injured spinal cord. *Science* **295**, 1029-1031, doi:10.1126/science.1067840 (2002).
7. Pearson, C. S., Mencio, C. P., Barber, A. C., Martin, K. R. & Geller, H. M. Identification of a critical sulfation in chondroitin that inhibits axonal regeneration. *Elife* **7**, doi:10.7554/eLife.37139 (2018).
8. Gokoffski KK, P. M., Alas B, Lam P. Neuro-protection and Neuro-regeneration of the Optic Nerve: Recent Advances and Future Directions. *Current opinion in neurology* **In Press** (2019).
9. Harrington, A. W. & Ginty, D. D. Long-distance retrograde neurotrophic factor signalling in neurons. *Nat Rev Neurosci* **14**, 177-187, doi:10.1038/nrn3253 (2013).
10. Goldberg, J. L. *et al.* Retinal ganglion cells do not extend axons by default: promotion by neurotrophic signaling and electrical activity. *Neuron* **33**, 689-702 (2002).

11. Mesentier-Louro, L. A. *et al.* Nerve Growth Factor Role on Retinal Ganglion Cell Survival and Axon Regrowth: Effects of Ocular Administration in Experimental Model of Optic Nerve Injury. *Mol Neurobiol* **56**, 1056-1069, doi:10.1007/s12035-018-1154-1 (2019).
12. Ahmed, Z. *et al.* Ocular neuroprotection by siRNA targeting caspase-2. *Cell death & disease* **2**, e173, doi:10.1038/cddis.2011.54 (2011).
13. Tanna, A. P. & Johnson, M. Rho Kinase Inhibitors as a Novel Treatment for Glaucoma and Ocular Hypertension. *Ophthalmology* **125**, 1741-1756, doi:10.1016/j.optha.2018.04.040 (2018).
14. Duan, X. *et al.* Subtype-specific regeneration of retinal ganglion cells following axotomy: effects of osteopontin and mTOR signaling. *Neuron* **85**, 1244-1256, doi:10.1016/j.neuron.2015.02.017 (2015).
15. Lim, J. H. *et al.* Neural activity promotes long-distance, target-specific regeneration of adult retinal axons. *Nat Neurosci* **19**, 1073-1084, doi:10.1038/nn.4340 (2016).
16. Takahashi, K. & Yamanaka, S. Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. *Cell* **126**, 663-676, doi:10.1016/j.cell.2006.07.024 (2006).
17. Yu, J. *et al.* Induced pluripotent stem cell lines derived from human somatic cells. *Science* **318**, 1917-1920, doi:10.1126/science.1151526 (2007).
18. Aparicio, J. G. *et al.* Temporal expression of CD184(CXCR4) and CD171(L1CAM) identifies distinct early developmental stages of human retinal ganglion cells in embryonic stem cell derived retina. *Experimental eye research* **154**, 177-189, doi:10.1016/j.exer.2016.11.013 (2017).
19. Meyer, J. S. *et al.* Optic vesicle-like structures derived from human pluripotent stem cells facilitate a customized approach to retinal disease treatment. *Stem Cells* **29**, 1206-1218, doi:10.1002/stem.674 (2011).
20. Sluch, V. M. *et al.* Differentiation of human ESCs to retinal ganglion cells using a CRISPR engineered reporter cell line. *Sci Rep* **5**, 16595, doi:10.1038/srep16595 (2015).
21. Venugopalan, P. *et al.* Transplanted neurons integrate into adult retinas and respond to light. *Nature communications* **7**, 10472, doi:10.1038/ncomms10472 (2016).
22. Johnson, T. V., Bull, N. D. & Martin, K. R. Transplantation prospects for the inner retina. *Eye* **23**, 1980-1984, doi:10.1038/eye.2008.376 (2009).
23. Symonds, A. C. *et al.* EphA5 and ephrin-A2 expression during optic nerve regeneration: a 'two-edged sword'. *Eur J Neurosci* **25**, 744-752, doi:10.1111/j.1460-9568.2007.05321.x (2007).
24. Gokoffski, K. K., Jia, X., Shvarts, D., Xia, G. & Zhao, M. Physiologic Electrical Fields Direct Retinal Ganglion Cell Axon Growth In Vitro. *Investigative ophthalmology & visual science* **60**, 3659-3668, doi:10.1167/iovs.18-25118 (2019).
25. Johansson, F., Carlberg, P., Danielsen, N., Montelius, L. & Kanje, M. Axonal outgrowth on nano-imprinted patterns. *Biomaterials* **27**, 1251-1258, doi:10.1016/j.biomaterials.2005.07.047 (2006).
26. Weiss, J. N., Levy, S. & Benes, S. C. Stem Cell Ophthalmology Treatment Study: bone marrow derived stem cells in the treatment of non-arteritic ischemic optic neuropathy (NAION). *Stem Cell Investig* **4**, 94, doi:10.21037/sci.2017.11.05 (2017).
27. Kuriyan, A. E. *et al.* Vision Loss after Intravitreal Injection of Autologous "Stem Cells" for AMD. *The New England journal of medicine* **376**, 1047-1053, doi:10.1056/NEJMoa1609583 (2017).

IS IT TIME FOR STEM CELL TREATMENT?

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LEARNING OBJECTIVES

1. Identify the key issues in stem cell therapy relevant to neuro-ophthalmic diseases.
2. Compare and contrast the different targets and approaches for stem cell transplantation and vision restoration.
3. Formulate a plan for discussing stem cell treatment with patients who ask for your advice.

CME QUESTIONS

1. Which one of the following regenerative treatments appear to promote functional recovery in neuro-ophthalmic diseases?
 - A. Transplantation of oligodendrocyte precursor cells
 - B. Transplantation of retinal ganglion cells
 - C. Visual stimulation
 - D. Fingolimod
 - E. All of the above
2. Which of the following barriers to successful transplantation of retinal cells may be overcome by treatment with metformin?
 - A. Differentiation of oligodendrocytes
 - B. Breakdown of extracellular matrix barriers
 - C. Formation of functional synapses
 - D. Post-injection inflammation
3. Which of the following statements about fingolimod is TRUE?
 - A. It has been shown to support Müller cell function
 - B. It promotes retinal ganglion cell (RGC) differentiation
 - C. It enhances the survival of transplanted neural stem cells in vitro
 - D. It reduces the interval required for human embryonic stem cell (hESC) differentiation

KEYWORDS

1. Stem cell transplantation
2. Neuroprotection
3. Remyelination
4. Human embryonic stem cells (hESC)
5. Induced pluripotent stem cells (iPSC)

HIGHLIGHTS

Introduction

Stem cell transplantation is being explored as a treatment for vision loss associated with both ocular and neurologic diseases. This need arises because of the limited capacity for endogenous repair after injury in the mammalian central nervous system. Vision loss in optic neuropathies is associated with the loss of retinal ganglion cell activity, which leads to reduced regenerative capacity and further loss of retinal ganglion cells and oligodendrocytes. Stem cell transplantation can potentially enhance survival of neurons or glia (cell protection) or replace the neurons and glia that are lost (cell replacement). There are considerable donor and host issues to overcome that impact the differentiation, integration, and long-term survival of the transplanted cells. A variety of transplantable stem cells, delivered as cell suspensions or as preformed 3D patches or organoid structures, are in development.¹

Complexity of the visual pathway

Major hurdles for successful cell transplantation include integration into the host and reconstruction of the neural circuitry. Regenerative therapy to restore vision is complex because of the (1) multiple cell types that are dysfunctional or lost in the neuron-glia-vascular niche as a result of disease, (2) the injured, adult environment, and (3) the necessity to reconstruct precise retinotopic representation of the visual space over the long distance of the visual pathway. In blinding diseases, both neurons and glial cells are typically lost or disrupted. For example, macular degeneration involves the loss of not only the photoreceptors, but also the retinal pigment epithelium and Müller cells that maintain and support the photoreceptors. In optic neuropathies, not only are the retinal ganglion cells (RGCs) lost, but also the optic nerve head astrocytes, and the oligodendrocytes and astrocytes in the optic nerve that support normal RGC function. There is now evidence that new myelinating oligodendrocytes can be generated throughout life and are influenced by the levels of neuronal activity.²⁻⁴ Thus, injury to the RGC axons also leads to loss of the oligodendrocytes. This loss of oligodendrocytes means loss of cells that support the RGC axons and the loss of cells that support efficient signal transduction via saltatory conduction.

Lessons from retinal degeneration

Stem cell therapy has been extensively studied for age-related macular degeneration (AMD) and other retinal degenerations.^{5,6} Treatment of these diseases, associated with extensive photoreceptor degeneration, has focused on transplantation of stem cells as dissociated cells, a retinal patch, or a sheet. Part of the reason that treatment of these diseases with stem cell transplantation is attractive is because transplanted cells only need to make one synaptic connection to a bipolar cell. The relatively intact inner retina in AMD allows the realistic possibility that cell replacement in the outer retina may restore vision. Also, studies with retinal prosthetic devices have shown that patients appear to retain a retinotopic map even after extensive outer retinal degeneration if the retina can be stimulated appropriately.⁷

In contrast to AMD, stem cell transplantation to treat optic neuropathies is more challenging because of the lower likelihood of reconstituting a circuit when the pre- and post-synaptic neurons are far apart.⁸ New cells need to establish connections within the retina and also extend axons to precise targets in the lateral geniculate nucleus (LGN).⁹ In addition, in order to maintain efficient signal transduction along the axon, the axon must be myelinated, another hurdle to vision restoration.⁸

Donor factors

The efficacy of stem cell transplantation depends on factors from the donor cells as well as the recipient retina. The differentiation of human embryonic stem cells (hESCs) and induced pluripotent stem cells

(iPSCs) toward retinal lineages has progressed rapidly in the last decade, but there are still extended time lines for the generation of retinal neurons and high variability in the differentiation process. Drawing again from the example of photoreceptor transplantation, young, post-mitotic photoreceptors from young donor photoreceptors were found to integrate more readily than retinal cells isolated at earlier or later ontogenetic stages.¹⁰ Enrichment of the transplanted cells with the desired neurons can increase integration. Transplantation of dissociated cells may be impacted by enzymatic and mechanical dissociation, leading to fewer cells integrating into the host retina. Cells that are part of a sheet or patch appear to have better survival and host integration.

Host factors

Host factors that may impact successful transplantation include the age of the host, chronicity and severity of the disease, remodeling of the host retina, inflammation within the host retina, and degeneration of the post-synaptic cell bodies. The method by which the donor cells are delivered may also impact graft integration, due to the host response. For instance, although subretinal or intravitreal injections may be good ways to deliver donor cells to treat retinal degenerations, these techniques may induce undesirable responses in the host, such as gliosis and inflammation. This induced gliosis and inflammation may be layered over gliosis and inflammation already caused by the disease process, adversely impacting transplantation efficiency and limiting maximal regeneration.⁸ Transplantation of retinal neurons may also be limited by the extracellular matrix in the inner retina, which forms a physical barrier to transplanted cells. The extracellular matrix may be breached using matrix metalloproteases or bacterial enzymes, facilitating migration and synaptogenesis of transplanted cells. However, these compounds may injure the host retina.⁶

Transplantation of autologous cells

First-in-human safety studies of stem cell transplantation have been done using autologous (from self) or allogeneic (donated) cells. Examples of autologous stem cells include bone marrow-derived mesenchymal stem cells or iPSCs derived from the skin fibroblasts of the host. Autologous cells may help prevent further neuronal degeneration via cell-cell protective mechanisms. In a study of ten patients with AMD, autologous bone marrow-derived CD34⁺ hematopoietic stem and progenitor cells were isolated from the patients and injected intravitreally.¹¹ This therapy was found to be safe, and there was significant improvement in best-corrected visual acuity at every follow-up visit and in mean sensitivity threshold at 6, 9 and 12 months post treatment.¹¹ In a study of ten patients with non-arteritic anterior ischemic optic neuropathy (NAION), autologous bone marrow-derived stem cells were injected and also found to be safe.¹²

Transplantation of allogeneic cells

Allogenic cells are cells that are generated and banked from selected donors. For example, hESCs may be grown in vitro, differentiated, and transplanted. The cells can also be grown as a 3D retinal organoid¹³ or on a synthetic matrix and then transplanted into the subretinal space as a patch.^{14,15} Transplantation of pre-formed retinal patches or sheets appears to be superior to transplantation of dissociated cells grown as a confluent sheet. Two phase I/II studies involving 18 patients with AMD or Stargardt disease with 4-year follow up have shown that it is possible to safely implant hESC-derived retinal pigment epithelial cells.¹⁶ More than half of treated patients in these studies experienced successful cellular engraftment as well as sustained improvements in visual acuity. Although there was a case of postoperative infectious endophthalmitis, there was no evidence of malignant transformation of the transplanted cells or rejection-related inflammation.¹⁶ Unexpectedly, in addition to integration of transplanted cells, researchers have observed examples of donor-host cell fusion.^{17,18} Specifically, some host cells acquired proteins otherwise expressed only by donor cells. This observation indicates that the

beneficial effects of stem cell transplantation may not be solely related to integration of the donor cells into the host retina.

The role of visual stimulation in functional recovery

Neuronal activity is important for the survival of retinal ganglion cells,¹⁹ axotomized optic nerves,²⁰ and oligodendrocytes.²⁻⁴ The mammalian central nervous system has limited regenerative capacity after injury. However, enhancement of neural activity, combined with elevation of the cell-growth-promoting pathway involving mammalian target of rapamycin (mTOR), has been shown to promote RGC axon regeneration and to rescue a subset of visual behaviors.²¹ This observation indicates that visual stimulation using high-contrast stimuli may be an important adjunct therapy for functional recovery after optic nerve injury.

Targeting oligodendrocytes in functional recovery

Although neurons have historically been the focus of stem cell transplantation, glial cells such as oligodendrocytes are also affected by optic nerve injury, and functional recovery also requires restoration of these cells. Abnormal oligodendrocytes have been observed in animal models of NAION²² and in glaucoma.²³ Loss of oligodendrocytes also plays an important role in the vision loss associated with central nervous system diseases such as multiple sclerosis (MS), stroke, and traumatic brain injury. Current therapeutic strategies remain deficient in promoting remyelination because mature, differentiated oligodendrocytes do not seem to remyelinate.^{24,25} Although most patients with MS do not generate new oligodendrocytes, a subset of individuals with very aggressive MS do generate new oligodendrocytes in normal-appearing white matter.²⁶ This observation indicates there may be some residual capacity for the genesis of oligodendrocytes in the adult brain, and that oligodendrocyte-directed therapy using cell transplantation may be a promising means to enhance functional recovery. This approach has the potential to enhance the remaining neural circuits, which may be simpler or more effective than reconstituting neurons or the neural circuitry.

Embryonic stem cells can be differentiated into oligodendrocyte precursor cells or mature oligodendrocytes in vitro,^{25,27,28} and transplantation of oligodendrocyte precursor cells has been shown to be neuroprotective in animal models of optic neuropathies.^{9,29} Transplantation of oligodendrocyte precursor cells into animal models of glaucoma leads to increased RGC survival, but only when concomitantly activated by inflammation.²⁹ Transplantation of autologous mesenchymal stem cells have also been shown to induce oligodendrocyte differentiation and generation of myelin-like sheaths.³⁰ Despite the exciting possibility of enhancing functional recovery using oligodendrocyte-directed cell therapy, there are also important limitations. Like neuron-directed cell transplantation, oligodendrocyte-directed therapy may also be affected by donor and host factors. At this time, differentiation protocols for human oligodendrocyte precursor cells are heterogeneous and lengthy (55-150 days in vitro). Although adult oligodendrocyte precursor cells have limited regenerative capacity, one group has recently demonstrated that treatment with metformin may restore the responsiveness of oligodendrocytes to pro-differentiation signals.³⁰

Pharmacologic manipulation of oligodendrocyte precursor cells or oligodendrocytes may be an exciting way to enhance functional recovery without cell transplantation. Screening a large number of drugs that are already FDA-approved, one group demonstrated that miconazole and clobetasol have the potential to enhance oligodendrocyte differentiation and remyelination in vitro and in an animal model of multiple sclerosis.³¹ It is not yet clear if the use of these drugs leads to functional recovery. The oral drug fingolimod, a sphingosine 1-phosphate (S1P) receptor analog, approved as an immunomodulator for the treatment of relapsing-remitting MS, has been shown to enhance remyelination.³² Fingolimod has been

shown to increase survival of neural stem cells and enhance their development into mature oligodendrocytes in vitro.³³ In vivo, there is also evidence that fingolimod increases the efficacy of transplanted human iPSC-derived neural progenitors in an animal model of demyelination.³⁴

What to tell patients

It is too early to recommend stem cell transplantation for the treatment of optic neuropathies. At the cellular level, vision restoration requires reconstitution of the neuron-glia-endothelial niche at the retina and the optic nerve. At the systemic level, vision restoration depends on reconstitution of the degenerating or degenerated retino-geniculo-cortical pathways. Successful stem cell transplantation into the retina or the optic nerve will involve manipulation of the donor cells and modification of the recipient environment.

In addition to the challenges of stem cell therapy described above, it is critical that we develop and validate objective methods to evaluate the efficacy of these treatments. Such measurements must evaluate both the form and function of the transplanted cells. These measurements will likely include high-resolution imaging, such as optical coherence tomography and adaptive optics, as well as electrophysiology and/or functional magnetic resonance imaging.

Although we do not want our patients to be without hope, our role as physicians is to realistically inform our patients about the current state of stem cell therapy and caution them against the consequences of undergoing unproven treatments. As treatments become available in the future, they should be carefully vetted, and physicians should only consider recommending therapies that are registered with clinicaltrials.gov. Patients affected by blinding diseases may be both vulnerable and desperate, and therefore must be cautioned against the possibilities of physical harm, psychological harm, and financial costs. Desperate patients seeking vision restoration may perceive that the lack of any benefit is the worst possible outcome of unproven therapies and may not be mindful of the potential for further harm.

In summary, stem cell transplantation provides an opportunity to replace cells and to repair or restore visual function in blinding diseases. These therapies will almost certainly involve both neurons and glia. There are still substantial challenges to overcome before regenerative therapies can effectively and safely restore functional vision in patients with neuro-ophthalmic diseases. Although there are currently limited options for the treatment of retinal degenerations and optic neuropathies, the results of current studies will help form the foundation for future trials for the treatment of these conditions.

CME ANSWERS

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REFERENCES

1. Stern JH, Tian Y, Funderburgh J, et al. Regenerating Eye Tissues to Preserve and Restore Vision. *Cell Stem Cell* 2018;22:834-849.
2. Foster AY, Bujalka H, Emery B. Axoglial interactions in myelin plasticity: Evaluating the relationship between neuronal activity and oligodendrocyte dynamics. *Glia* 2019;67:2038-2049.

3. Nagy B, Hovhannisyan A, Barzan R, Chen TJ, Kukley M. Different patterns of neuronal activity trigger distinct responses of oligodendrocyte precursor cells in the corpus callosum. *PLoS Biol* 2017;15:e2001993.
4. Gautier HO, Evans KA, Volbracht K, et al. Neuronal activity regulates remyelination via glutamate signalling to oligodendrocyte progenitors. *Nat Commun* 2015;6:8518.
5. Chichagova V, Hallam D, Collin J, et al. Cellular regeneration strategies for macular degeneration: past, present and future. *Eye (Lond)* 2018;32:946-971.
6. Gasparini SJ, Llonch S, Borsch O, Ader M. Transplantation of photoreceptors into the degenerative retina: Current state and future perspectives. *Prog Retin Eye Res* 2019;69:1-37.
7. Caspi A, Roy A, Dorn JD, Greenberg RJ. Retinotopic to Spatiotopic Mapping in Blind Patients Implanted With the Argus II Retinal Prosthesis. *Invest Ophthalmol Vis Sci* 2017;58:119-127.
8. Calkins DJ, Pekny M, Cooper ML, Benowitz L, Lasker IloA, Glaucomatous Neurodegeneration P. The challenge of regenerative therapies for the optic nerve in glaucoma. *Exp Eye Res* 2017;157:28-33.
9. Johnson TV, Bull ND, Martin KR. Transplantation prospects for the inner retina. *Eye (Lond)* 2009;23:1980-1984.
10. Santos-Ferreira TF, Borsch O, Ader M. Rebuilding the Missing Part-A Review on Photoreceptor Transplantation. *Front Syst Neurosci* 2016;10:105.
11. Cotrim CC, Toscano L, Messias A, Jorge R, Siqueira RC. Intravitreal use of bone marrow mononuclear fraction containing CD34(+) stem cells in patients with atrophic age-related macular degeneration. *Clin Ophthalmol* 2017;11:931-938.
12. Weiss JN, Levy S, Benes SC. Stem Cell Ophthalmology Treatment Study: bone marrow derived stem cells in the treatment of non-arteritic ischemic optic neuropathy (NAION). *Stem Cell Investig* 2017;4:94.
13. Mellough CB, Collin J, Queen R, et al. Systematic Comparison of Retinal Organoid Differentiation from Human Pluripotent Stem Cells Reveals Stage Specific, Cell Line, and Methodological Differences. *Stem Cells Transl Med* 2019;8:694-706.
14. Vitillo L, Tovell VE, Coffey P. Treatment of Age-Related Macular Degeneration with Pluripotent Stem Cell-Derived Retinal Pigment Epithelium. *Curr Eye Res* 2019;1-11.
15. da Cruz L, Fynes K, Georgiadis O, et al. Phase 1 clinical study of an embryonic stem cell-derived retinal pigment epithelium patch in age-related macular degeneration. *Nat Biotechnol* 2018;36:328-337.
16. Schwartz SD, Tan G, Hosseini H, Nagiel A. Subretinal Transplantation of Embryonic Stem Cell-Derived Retinal Pigment Epithelium for the Treatment of Macular Degeneration: An Assessment at 4 Years. *Invest Ophthalmol Vis Sci* 2016;57:ORSFc1-9.
17. Waldron PV, Di Marco F, Kruczek K, et al. Transplanted Donor- or Stem Cell-Derived Cone Photoreceptors Can Both Integrate and Undergo Material Transfer in an Environment-Dependent Manner. *Stem Cell Reports* 2018;10:406-421.
18. Nickerson PEB, Ortin-Martinez A, Wallace VA. Material Exchange in Photoreceptor Transplantation: Updating Our Understanding of Donor/Host Communication and the Future of Cell Engraftment Science. *Front Neural Circuits* 2018;12:17.
19. Goldberg JL, Espinosa JS, Xu Y, Davidson N, Kovacs GT, Barres BA. Retinal ganglion cells do not extend axons by default: promotion by neurotrophic signaling and electrical activity. *Neuron* 2002;33:689-702.
20. Watanabe M, Fukuda Y. Survival and axonal regeneration of retinal ganglion cells in adult cats. *Prog Retin Eye Res* 2002;21:529-553.
21. Lim JH, Stafford BK, Nguyen PL, et al. Neural activity promotes long-distance, target-specific regeneration of adult retinal axons. *Nat Neurosci* 2016;19:1073-1084.

22. Goldenberg-Cohen N, Guo Y, Margolis F, Cohen Y, Miller NR, Bernstein SL. Oligodendrocyte dysfunction after induction of experimental anterior optic nerve ischemia. *Invest Ophthalmol Vis Sci* 2005;46:2716-2725.
23. Son JL, Soto I, Oglesby E, et al. Glaucomatous optic nerve injury involves early astrocyte reactivity and late oligodendrocyte loss. *Glia* 2010;58:780-789.
24. Crawford AH, Tripathi RB, Foerster S, et al. Pre-Existing Mature Oligodendrocytes Do Not Contribute to Remyelination following Toxin-Induced Spinal Cord Demyelination. *Am J Pathol* 2016;186:511-516.
25. Czepiel M, Boddeke E, Copray S. Human oligodendrocytes in remyelination research. *Glia* 2015;63:513-530.
26. Yeung MSY, Djelloul M, Steiner E, et al. Dynamics of oligodendrocyte generation in multiple sclerosis. *Nature* 2019;566:538-542.
27. Alsanie WF, Niclis JC, Petratos S. Human embryonic stem cell-derived oligodendrocytes: protocols and perspectives. *Stem Cells Dev* 2013;22:2459-2476.
28. Neman J, de Vellis J. A method for deriving homogenous population of oligodendrocytes from mouse embryonic stem cells. *Dev Neurobiol* 2012;72:777-788.
29. Bull ND, Irvine KA, Franklin RJ, Martin KR. Transplanted oligodendrocyte precursor cells reduce neurodegeneration in a model of glaucoma. *Invest Ophthalmol Vis Sci* 2009;50:4244-4253.
30. Rivera FJ, de la Fuente AG, Zhao C, et al. Aging restricts the ability of mesenchymal stem cells to promote the generation of oligodendrocytes during remyelination. *Glia* 2019;67:1510-1525.
31. Najm FJ, Madhavan M, Zaremba A, et al. Drug-based modulation of endogenous stem cells promotes functional remyelination in vivo. *Nature* 2015;522:216-220.
32. Yazdi A, Ghasemi-Kasman M, Javan M. Possible regenerative effects of fingolimod (FTY720) in multiple sclerosis disease: An overview on remyelination process. *J Neurosci Res* 2019.
33. Zhang Y, Li X, Ciric B, et al. Effect of Fingolimod on Neural Stem Cells: A Novel Mechanism and Broadened Application for Neural Repair. *Mol Ther* 2017;25:401-415.
34. Yazdi A, Mokhtarzadeh Khangahi A, Baharvand H, Javan M. Fingolimod Enhances Oligodendrocyte Differentiation of Transplanted Human Induced Pluripotent Stem Cell-Derived Neural Progenitors. *Iran J Pharm Res* 2018;17:1444-1457.

GENE THERAPY - EVOLUTION AND THERAPEUTIC APPLICATIONS

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LEARNING OBJECTIVES

1. Describe the methods available for gene delivery
2. Compare the different methods being developed for targeted genome editing
3. Critically review the clinical applications of gene therapy

CME QUESTIONS

1. What is the most commonly used gene delivery system for ocular gene therapy?
 - A. Liposomes
 - B. Adenoviral vectors
 - C. Adeno-associated viral vectors
 - D. Lentiviral vectors
 - E. Retroviral vectors
2. Which of the following neurotrophic factors are being considered for mutation-independent gene therapy?
 - A. Brain-derived neurotrophic factor (BDNF)
 - B. Ciliary neurotrophic factor (CNTF)
 - C. Basic fibroblast growth factor (FGF)
 - D. Glial cell-derived neurotrophic factor (GDNF)
 - E. All of the above
3. Which of the following methods can be used for targeted genome editing?
 - A. Zinc-finger nucleases (ZFN)
 - B. Transcription activator-like effector nucleases (TALEN)
 - C. RNA-guided nucleases (CRISPR/Cas9)
 - D. All of the above
 - E. None of the above

KEYWORDS

1. Gene therapy
2. Genome editing
3. Mitochondrial diseases
4. Neurodegenerative diseases
5. Viral vectors

HIGHLIGHTS

A. Introduction

Gene therapy is an attractive treatment strategy for both inherited and acquired late-onset neurodegenerative diseases (1). Over the past three decades, significant advances have been made in gene delivery methods and achieving more targeted and sustained expression of the gene of interest. The promising results obtained from preclinical studies have led to an increasing number of human clinical trials to investigate the safety and efficacy of gene therapy approaches for a broad range of disorders, in particular those involving the eye and the central nervous system.

B. Delivery Methods

Both viral and non-viral strategies have been developed for the transfer of DNA material and these are being further refined to circumvent the host immune response (2). An effective and safe surgical technique for gene delivery is also an important consideration and depending on the tissues that are being targeted, there may be specific technical barriers that need to be overcome. The aim is to ensure reproducible transgene expression over a sufficient period of time and optimally, at physiological levels to minimise potential adverse effects (3). The eye is an ideal target organ for gene therapy due to its relative immune privilege and the easier anatomical access, with intravitreal injections being favoured to target retinal ganglion cells (RGCs) and subretinal injections for outer retinal disorders.

C. Gene Therapy Paradigms

Gene therapy can be classified into broad categories based on the disease group and the mode of action of the transgene, namely, (i) gene replacement; (ii) gene addition or augmentation; and (iii) optogenetics (1). Gene replacement is the obvious strategy for monogenic diseases caused by known mutations that result in haploinsufficiency, i.e. there is not sufficient amount of the wild-type protein to sustain normal cellular function. The pioneering work in the field of inherited retinal diseases has recently led to the approval by the Food and Drug Administration (FDA) of the first gene therapy product for Leber congenital amaurosis, caused by recessive *RPE65* mutations (4). There is currently an ongoing gene therapy programme using allotopic expression for Leber hereditary optic neuropathy (LHON) caused by the m.11778G>A mitochondrial DNA mutation. Gene addition or augmentation with neurotrophic factors is being investigated for more complex diseases such as glaucoma and Parkinson disease. A key attraction of this neuroprotective strategy is its broader applicability to neurodegenerative diseases with the opportunity to supplement a combination of neurotrophic factors targeting different pathways. Optogenetics takes a different approach to cell rescue by imparting light sensitivity onto neurons (4). This property is achieved with the transfection of bacterial opsin genes encoding for light-gated ion channels that have the ability to create an action potential. The modulation of neuronal activity with optogenetics is being considered for inherited retinal diseases characterised by selective photoreceptor degeneration and for central nervous system disorders caused by an imbalance between inhibitory and excitatory pathways, such as Parkinson disease.

D. *In Vivo* v/s *Ex Vivo* Gene Therapy

Regenerative medicine with embryonic stem cells (ESCs) or induced pluripotent stem cells (iPSCs) is now moving into an accelerated clinical phase of development. The differentiation of human-derived stem cell populations into the cell types that are lost in a particular disorder is only the first step as these *ex vivo* cells then need to be transferred not only in the correct anatomical location, but also positioned appropriately to make the right connections (5). In the case of RGCs, the long pathway from the inner retina to the lateral geniculate nucleus and the strict retinotopic arrangement pose considerable challenges. Genetic engineering of ESCs and iPSCs is a synergistic approach that can be employed to enhance the function of the transplanted cells or to correct the underlying genetic defect if these stem cells have been established from an individual carrying a specific mutation. In contrast, for *in vivo* gene therapy, novel methods for molecular editing are used to target and correct the genetic defect in

differentiated cells (6). The gene editing technologies that are being considered for translational applications include zinc-finger nucleases (ZFN), transcription activator like effector nucleases (TALEN), and RNA-guided nucleases (CRISPR/Cas9).

SUMMARY

Gene therapy has moved firmly from the bench to the bedside with the potential to transform the management of both rare monogenic diseases and late-onset neurodegenerative diseases that are posing considerable societal burden in an aging population. Although considerable progress has been made over the past three decades, there are still a number of technical challenges related to optimal gene delivery and transgene expression that need to be resolved. Importantly, the long-term safety and efficacy of the various technologies that are being employed require tight oversight and the cost implications of bringing these novel treatments to market, and ultimately to patients cannot be underestimated.

CME ANSWERS

1. (C) Adeno-associated viral vectors
2. (E) All of the above
3. (D) All of the above

REFERENCES

1. Yu-Wai-Man P. Genetic manipulation for inherited neurodegenerative diseases: myth or reality? *Br J Ophthalmol*. 2016;100(10):1322-31.
2. Slivac I, Guay D, Mangion M, Champeil J, Gaillet B. Non-viral nucleic acid delivery methods. *Expert Opin Biol Ther*. 2017;17(1):105-118.
3. Kay MA. State-of-the-art gene-based therapies: the road ahead. *Nat Rev Genet*. 2011;12(5):316-28.
4. Dalkara D, Duebel J, Sahel JA. Gene therapy for the eye focus on mutation-independent approaches. *Curr Opin Neurol*. 2015;28(1):51-60.
5. Kaufmann KB, Büning H, Galy A, Schambach A, Grez M. Gene therapy on the move. *EMBO Mol Med*. 2013;5(11):1642-61.
6. Naldini L. Gene therapy returns to centre stage. *Nature*. 2015; 526(7573): 351-60.

CHILD WITH CROSSED EYES SINCE INFANCY: DO I IMAGE? DO I OPERATE?

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LEARNING OBJECTIVES

1. The attendee will be able to recognize the key clinical features of Duane retraction syndrome.
2. The attendee will be able to clinically differentiate Duane retraction syndrome from other causes of esotropia in early childhood.
3. The attendee will be able to describe management strategies, including indications for surgery and surgical techniques for patients with Duane retraction syndrome.

CME QUESTIONS

1. True or False: Surgery is always the first line of treatment for patients with Duane retraction syndrome.
2. What clinical examination finding should help in differentiating Duane retraction syndrome from a sixth nerve palsy in a child with esotropia?
 - A. incomitant strabismus
 - B. limited adduction of the affected eye
 - C. anomalous head position
 - D. limited abduction of the affected eye
3. True or False: The diagnosis of Duane retraction syndrome is made radiographically.

KEY WORDS

1. Duane retraction syndrome
2. Esotropia
3. Co-contraction
4. Abduction deficit
5. Incomitant strabismus

SUMMARY

Duane retraction syndrome, or Duane syndrome (DS), is a common congenital ocular movement disorder characterized by absent lateral rectus innervation by the abducens nerve, along with aberrant innervation to the lateral rectus from oculomotor nerve branches.^{1,2} This anomalous innervation results in unique clinical findings that differentiate it from other forms of strabismus and ocular misalignment. Most cases are sporadic, unilateral, and more frequently occur in females (60%) and left eyes (58-72%).^{3,4,5} Although DS generally presents as an isolated disorder, associated ocular and systemic findings can be seen in approximately 33% of cases.⁶

DS with associated esotropia is by far the most common presentation. The signature clinical features are abnormal horizontal eye movements, with a deficiency of abduction, which can mimic a sixth nerve palsy. There is palpebral fissure widening on abduction, modest reduction of adduction, and globe retraction on adduction, best identified by a narrowing of palpebral fissure due to co-contraction of the medial and lateral recti.

Differentiating DS from other causes of esotropia, such as sixth nerve palsy or infantile esotropia, can be challenging, particularly in young, uncooperative infants and children. Patients with infantile esotropia present by six months of age with a structurally normal eye, normal ductions, and a comitant strabismus pattern, whereas incomitant strabismus is characteristic of DS and sixth nerve palsies. In both infantile esotropia and sixth nerve palsy, there is usually a large angle of deviation in primary position. In DS, there is marked limitation to abduction, however patients may be orthotropic or have only a small strabismic deviation (usually an esotropia $< 15^\Delta$) in primary position, due to tonic innervation to the lateral rectus. Globe retraction and eyelid findings will be absent in cranial nerve six palsies and infantile esotropia. Also, limitation of abduction may improve with elevation or depression in DS, which is not true of cranial nerve six palsy. A further point of differentiation is that in esotropic DS, limited adduction of the affected eye frequently results in a small-angle exotropia on gaze opposite to the side of the affected eye, a finding not present in an isolated sixth nerve palsy.⁴

A diagnosis of DS can be made from clinical features alone and does not warrant routine neuroimaging. Concerning management, many patients do not need surgery, and observation is preferred, especially in young children. Children with DS rarely complain of diplopia, often maintain good binocular sensory fusion with a slight head position, and usually do not have amblyopia.⁷ A cycloplegic refraction should be performed on all children with esotropia to identify an accommodative component, which may correct residual esotropia.

Indications for surgery include a large compensatory head posture or manifest deviation in primary position that reduces binocular fusion or causes amblyopia. Additional considerations are large upshoots or downshoots or unacceptable globe retraction. A number of surgical procedures have been described and continue to evolve in an effort to improve abduction deficits and increase the field of single binocular vision.^{8,9} The degree of medial rectus tightness and lateral rectus co-contraction must be considered and can be assessed with forced duction testing. Medial rectus recessions may be sufficient to restore binocular alignment in the primary position. A transposition procedure with or without augmentation (Foster Augmentation) with a posterior fixation suture may prove effective to improve abduction, head turn, and expand the range of binocular single vision.¹⁰ Resections are generally avoided as they can exacerbate globe retraction or limit adduction. However, resections have proven effective in select cases.¹¹

Case

An eight-month-old healthy, Caucasian male baby presents with inward crossing of the eyes since birth. Visual behavior is normal for age, he objects equally to occlusion with either eye, has a small angle alternating esotropia with inability to abduct past midline bilaterally. Cycloplegic refraction reveals no significant refractive error.

Differential diagnosis

- Infantile esotropia
- Bilateral cranial nerve VI palsy
- Duane retraction syndrome

Case diagnosis

This is a case of Duane retraction syndrome, a unique spectrum of ocular motility disorders that can be associated with esotropia, with other clinical findings that differentiate it from other causes of esotropia in children.

CME ANSWERS

1. False
2. B
3. False

REFERENCES

1. De Respinis P, Caputo A, Wagner R, et al. Duane's retraction syndrome. *Surv Ophthalmol.* 38:257-8, 1993.
2. Doyle, Jefferson J, Hunter David G. Transposition procedures in Duane retraction syndrome. *J AAPOS*; 23:5-14, 2019.
3. Kahn AO, Oystreck D. Clinical characteristics of bilateral Duane syndrome. *J AAPOS*;10:198-201, 2006.
4. Raab EL. Clinical features of Duane's syndrome. *J Pediatr Ophthalmol* 23(2):64-68, 1986.
5. Shainberg MJ. Duane syndrome. *Am Orthop J* 50:30-35, 2000.
6. Cross HE, Pfaffenbach DD. Duane's retraction syndrome and associated congenital malformations. *Am J Ophthalmol.*70:442-9, 1972.
7. Tomac S, et al. Duane's retraction syndrome: its sensory features. *Ophthalmic Physiol Opt.* 27:579-83, 2007.
8. Laby DM, Rosenbaum AL: Adjustable vertical rectus muscle transposition surgery. *J Pediatr Ophthalmol Strabismus*, 31:75, 1994.
9. Miller JM, Demer JL, Rosenbaum AL: Effect of transposition surgery on rectus muscle paths by magnetic resonance imaging. *Ophthalmol*;100:475, 1993.
10. Molarte AB, Rosenbaum AL. Vertical rectus muscle transposition surgery for Duane syndrome. *J Pediatr Ophthalmol Strabismus* 27:171-177, 1990.
11. Kraft SP. Lateral rectus resection strabismus surgery in unilateral Duane Syndrome with esotropia and limited abduction. *Binocular vision & strabismus quarterly.* 25(3) : 149-157, 2010.

CHILD WITH ACUTE ACQUIRED COMITANT ESOTROPIA: DO I IMAGE? DO I OPERATE?

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LEARNING OBJECTIVES

1. Distinguish between accommodative esotropia and pediatric acute acquired comitant esotropia (AACE)
2. Recognize the warning signs for presence of intracranial pathology
3. Develop a management strategy for AACE and concurrent Chiari I malformation (CM-I)

CME QUESTIONS

1. Which condition/finding is associated with acute acquired comitant esotropia?
 - A. Hydrocephalus
 - B. Lateral rectus under-action
 - C. Uncorrected hyperopia
 - D. Monocular occlusion
2. What is the leading symptom/sign in patients symptomatic of Chiari I malformation?
 - A. Papilledema
 - B. Headache with a Valsalva
 - C. Nystagmus
 - D. Bowel incontinence
3. Which statement is true of abducens palsy in children?
 - A. The esotropia may quickly become comitant
 - B. Esotropia is typically equal at distance and near
 - C. Often associated with inferior oblique over-action
 - D. Does not lead to complaints of diplopia because children suppress the second image

KEYWORDS

1. Acute acquired comitant esotropia (AACE)
2. Accommodative esotropia
3. Chiari I malformation
4. Divergence insufficiency esotropia

SUMMARY

Acute acquired comitant esotropia (AACE) is an unusual presentation of esotropia in children. AACE is considered rare, but no statistical data is available regarding its actual incidence or prevalence. AACE is characterized by a relatively large angle of esotropia, complaints of diplopia, and minimal refractive error, distinguishing it from accommodative esotropia which is associated with moderate to high hyperopia, history of intermittency, and no diplopia.

The historical classification of AACE is based on weak or absent evidence but continues to be cited in the literature. AACE is categorized into 3 types: Type 1 (Swan type): AACE following monocular occlusion/disruption of fusion; Type II (Franceschetti type): idiopathic (“due to physical or psychologic stress”); type III (Bielschowsky type): AACE associated with myopia. Other conditions reported to be associated with AACE include decompensated monofixation syndrome, anisometropia with tenuous fusion, and most recently, neurologic conditions such as posterior fossa tumors and Chiari I malformation.

Intracranial pathology is rare in children who present with isolated AACE

According to recent literature, intracranial pathology is rare in children who present with isolated AACE without other signs or symptoms of neurologic disease.^{1,2} Buch and Vinding reported a series of 48 children with AACE. One patient with no other neurologic signs was found to have a thalamic tumor (AACE possibly unrelated). The remaining 2 children with intracranial pathology (pontine glioma and pseudotumor cerebri) had additional obvious signs or symptoms (papilledema, headache, nystagmus).² Interestingly, ET greater at distance than near was a highly specific risk factor for intracranial disease.

Chiari I malformation is usually asymptomatic in children and rarely presents as isolated AACE

CM-I is a common finding in both children and adults with a prevalence between 0.24% and 3.6%. It is a widely held notion that the vast majority of CM-I are “benign” – asymptomatic or minimally symptomatic. The most common symptoms/signs of clinically significant CM-I are: Valsalva-induced occipital headache and syringomyelia. Other less frequent symptoms include neck pain, vertigo, upper extremity weakness/numbness, ataxia, dysarthria, dysphagia, and gaze evoked nystagmus. One case series of 427 children with asymptomatic CM-I concluded that “the likelihood of developing a neurologic deficit after presentation with “benign CM-I is less than 1%”.³ In this series, AACE was not a symptom/sign of CM-I.

AACE has been associated with CM-I

Several case reports and small series exist of children and adults with AACE presumed to be secondary to Chiari I malformation.^{4,5,6,7,8,9, 10, 11, 12} Ophthalmic examination findings that were associated with resolution or improvement of AACE after CM-1 surgery were: divergence insufficiency esotropia (D>N ET) and end-gaze nystagmus. In addition, rapid recurrence of esotropia after initially successful strabismus surgery would also raise the suspicion for a neurologic cause and warrants CM-1 surgical evaluation.

Occipital decompression or bilateral medial rectus recession?

The critical question is whether the CM-I is causing the AACE, making occipital decompression the treatment of choice, or whether the CM-I is “benign” and the AACE is unrelated, making strabismus surgery the treatment of choice. It is difficult to draw conclusions from the published literature for the following reasons: some studies combined adults with children (etiologies of AACE likely different), some authors deemed “improvement” of the esotropia after occipital decompression as an indication that CM-I was causative, some authors concluded that AACE was secondary to intracranial pathology that was diagnosed many years later (possibly unrelated), and some reports of children undergoing occipital decompression for CM-I did not detail whether the children were experiencing the symptoms of CM-I (primarily from the ophthalmic literature).

Diffuse infiltrating pontine glioma (DIPG) rarely presents with isolated AACE (Put lower down and check reference order)

DIPG has been reported to cause AACE in children.¹ Over 50% of patients present with the classical triad of cranial nerve deficits (abducens and facial nerve paresis), cerebellar signs (ataxia, dysmetria, and dysarthria) and long tract signs (hyperreflexia, upward Babinski and decreased strength). Symptoms are typically present for a short period of time prior to diagnosis. Isolated AACE, without other more typical neurologic signs and symptoms, is a rare presentation in patients harboring a DIPG.

Conclusion

- AACE, in an otherwise asymptomatic child, is rarely the initial sole presenting sign of a posterior fossa tumor or CM-I. AACE is idiopathic in many/most children.
- Neuro-imaging is indicated in a child with a history of tussive/Valsalva headache, neck pain, ataxia, cranial nerve palsies, papilledema, nystagmus, upper extremity numbness or paresthesias, or other indicators of neurologic disease.
- In a child with AACE and CM-I, possible ophthalmic indicators that neurosurgical treatment is indicated are: divergence insufficiency esotropia (distance esotropia > near), end-gaze nystagmus, rapid recurrence of esotropia after initially successful strabismus surgery.
- Whether children with isolated AACE require neuroimaging is controversial
- A child with AACE, with or without CM-I, who is otherwise asymptomatic, with ET that is equal at distance and near (D=N ET) or is greater at near than distance (N>D ET), strabismus surgery should be considered as primary treatment.

Case

6 YO child presents with acute onset of comitant esotropia and complaints of binocular diplopia and is otherwise asymptomatic. Exam: 20/20 vision each eye, uncorrected, 25 PD esotropia (ET) at distance and near viewing, 25 ET in all positions of gaze, full ductions and versions, no nystagmus, normal fundus exam and cycloplegic refraction revealing +1.00 OU. MRI brain with and without contrast reveals Chiari I malformation.

Six months later the deviation is unchanged and the child remains otherwise asymptomatic. A bilateral medial rectus recession is performed resulting in orthotropia and restoration of stereopsis.

Differential diagnosis

Acute acquired comitant esotropia due to benign causes (idiopathic, decompensation of esophoria, etc)

Acute acquired comitant esotropia due to neurologic condition (Chiari I malformation, posterior fossa tumor)

Accommodative esotropia

Abducens palsy

Final case diagnosis

Acute acquired esotropia, idiopathic, unrelated asymptomatic Chiari I malformation

CME ANSWERS

1. D
2. B
3. A

REFERENCES

1. Warren, K, Diffuse Intrinsic Pontine Glioma: Poised for Progress, *Frontiers in Oncology*, Pediatric Neuro-Oncology Section, Pediatric Oncology Branch, National Cancer Institute, National Institutes of Health, Volume 2, Article 205, December 2012
2. Buch, H, Vindings, T, Acute Acquired Comitant Esotropia of Childhood: a Classification based on 48 Children, *Acta Ophthalmologica Scandinavica Foundation, Acta Ophthalmol.*, 2015;93:568-574
3. Leon, T, Kuhn, E, Arynchyna, A, Smith, B, Tubbs, R, Johnston, J, Blount, J, Rozzelle, C, Oakes, W, Rocque, B, Patients with “benign” Chiari I malformation require surgical decompression at a low rate, *J Neurosurg Pediatric.*, 2019, 23:498-506
4. Aitken, L, Lindan, C, Sidney, S, Gupta, N, Barkovich, A, Sorel, M, Wu, Y, Chiari Type I Malformation in a Pediatric Population, *Pediatr Neurol* 2009, 40:449-454
5. Passo, M, Schults, WT, Talbot T, Palmer EA, Acquired Esotropia. A Manifestation of Chiari I Malformation, *J. Clin Neuro-Ophthalmol.*, 1984;4:151-154
6. Bixenman, WW, Laguna, JF, Acquired Esotropia as Initial Manifestation of Arnold-Chiari Malformation, *J Pediatric Ophthalmol Strabismus*, 1987;24:83-86
7. Akman, A, Dayanir, V, Sanac, AS, Kansu, T, Acquired Esotropia as Presenting Sign of Cranio-Cervical Junction Anomalies, *Neuro-Ophthalmol.*, 1995;15:311-314
8. Lewis, AR, Kline, LB, Sharp, JA, Acquired Esotropia due to Arnold Chiari I Malformation, *J Neuro-Ophthalmol.*, 1996;16:49-54
9. Biousse, V, Newman, NJ, Petermann, SH, Lambert, SR, Isolated Comitant Esotropia and Chiari I Malformation, *Am J Ophthalmol.*, 2000 Aug; 130(2):216-220
10. Imes, RK, Quinn, TA, Acute Comitant Esotropia in Chiari I Malformation, *Ophthalmology* 2001;108:834
11. Deefort-Dhellemmes, S, Denion, E, Bouvet-Drumare, I, Hache, JC, Dhellemmes, P, Resolution of Acute Acquired Comitant Esotropia after Suboccipital Decompression for Chiari I Malformation, *Am J Ophthalmol.*, 2003;133:723-25
12. Pokharel, D, Siatkowski, RM, Progressive Cerebellar Tonsillar Herniation with Recurrent Divergence Insufficiency Esotropia, *J AAPOS*, 2004 Jun;8(3):286-7

ACQUIRED DIVERGENCE INSUFFICIENCY IN AN ADULT: DO I IMAGE? DO I OPERATE?

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LEARNING OBJECTIVES

1. The attendee will be able to recognize the key clinical features of adult onset Divergence Insufficiency Esotropia (DIET).
2. The attendee will be able to understand the anatomical orbital changes that lead to adult onset Divergence Insufficiency Esotropia.
3. The attendee will be able to describe management strategies, including indications for prisms and surgery, in patients with adult onset Divergence Insufficiency Esotropia.

CME QUESTIONS

1. An 83- year-old with parkinsonism presents with double vision when driving. On examination they are orthotropic at near and have a 12 prism diopter esotropia at distance. Ductions are full. These findings are consistent with what diagnosis?
 - A. Adult onset divergence insufficiency (DIET)
 - B. Convergence insufficiency
 - C. Intranuclear ophthalmoplegia
 - D. Bilateral 6th nerve palsy
2. An elderly patient complains of horizontal diplopia when driving. On external examination you note a deep superior sulcus, mild ptosis, and high lid creases in both eyes. These finding are consistent with what diagnosis?
 - A. Adult onset divergence insufficiency esotropia (DIET)
 - B. Bilateral 6th nerve palsy
 - C. Breakdown of a congenital strabismus
 - D. Thyroid orbitopathy
3. What is the most appropriate initial treatment for a small angle esotropia (i.e. 4 prism diopters) in a patient with adult onset divergence insufficiency esotropia?
 - A. Base out prisms glasses
 - B. Base in prism glasses
 - C. Bilateral medial rectus recessions
 - D. Loop myopexy of the superior rectus and lateral rectus

KEY WORDS

1. Divergence Insufficiency
2. Esotropia
3. Strabismus
4. Diplopia

SUMMARY

Adult onset divergence insufficiency (DIET) is a well-recognized condition that appears to be more prevalent now that the population is aging and staying more active. DIET is a more recent descriptive term of the clinical findings, but has also been referred to as “Divergence weakness in adults”, “Age related distance esotropia,” “Distance esotropia in the elderly,” and a variation of “Sagging eye syndrome.” Initially DIET was thought to be a mild 6 nerve palsy and neuro-ophthalmologists tended to evaluate these patients with neuroimaging, systemic work up, (including myasthenia and thyroid associated orbitopathy), and possibly lumbar puncture testing. In most cases, these tests are non-diagnostic. However, anatomical and high resolution orbital imaging studies performed by Joe Demer et. al. show that the pathophysiology is most likely involutional changes in the connective tissue band between the lateral rectus and superior rectus muscles (LR/SR band).¹ This causes the lateral rectus muscle and its orbital pulley to sag inferiorly and thus diminish its ability to abduct at distance. Thus if neuroimaging is to be obtained, coronal fine cuts of the orbit are necessary to demonstrate the inferior displacement of the lateral rectus and often the stretching of the LR/SR band with nasal displacement of the superior rectus. In some elderly patients with underlying neurodegenerative diagnoses such as Parkinsonism, DIET may occur from a neurological etiology.

Treatment of DIET is dependent on the amount of esotropia causing the double vision and patient expectations. For small angles less than 12 prism diopters, ground in prisms can be used to neutralize the double vision at distance. However this can induce an exotropia at near. Most patients can fuse a small exodeviation. However, patient with neurodegenerative disease may manifest both DIET and a concomitant convergence insufficiency. In these cases separate reading spectacles may be required either without the base out prism, or with base in prism.

An additional option for patients with large angle esotropia is strabismus surgical repair or press on prisms. In patients who are not surgical candidates, long-term press on prisms can be advantageous. The dilemma, however, arises in those patients with small angles but who no longer need spectacles for distance and wish to function without glasses. In these cases medial rectus (MR) recessions have been described and can be successful. The only caveat is that the standard dose response curve is lower and more MR recession is required per angle of deviation. For larger angles of deviation, bilateral MR recession, or MR recession with lateral rectus (LR) resection is an option. Standard dose response curves as well are lower and must be adjusted. Although unpublished, this author performs an in office prism adaptation test to determine the largest extent of the deviation and also considers surgery for a larger angle that induces a slight exophoria, but for which the patient can fuse both at distance and near. This anticipates that because involutional changes are progressive over time, the DIET may increase and slight overcorrection may be desirable to delay additional surgery.

In most instances adult onset divergence insufficiency esotropia is a clinical diagnosis based on the patient's symptoms and findings. However one must be cognizant that this could be the presentation of early onset 6th nerve palsy, myasthenia gravis, or thyroid orbitopathy. Thus in some instances serologic testing and neuroimaging is necessary to rule out these other potentially more serious disorders. However, once recognized, treatments including prisms or strabismus surgical repair can alleviate the diplopia and restore quality of life.

Case

An 83 year old woman with mild Parkinsonism presents with the relatively acute onset of double vision when driving following cataract extraction. She has a history of being mildly myopic and states that she

never had double vision before. Her acuity was 20/50 in both eyes prior to the cataract extraction. The double vision is described as horizontal with one image slightly next to the other. It is not present at near. She now no longer needs glasses to see for far away and uses an over the counter +3.00 reader. On examination her acuity is 20/25 in both eyes with good near stereo. Color vision is full with no afferent pupillary defect. External examination reveals slightly sunken orbits with a deep superior sulcus, high lid crease and mild ptosis. Motility examination is remarkable for a 6 diopter esotropia on cover/uncover testing that builds to 8 diopters on alternate cover testing. On right and left end horizontal gaze there is an 8 diopter esotropia. Ductions reveal a minimal -1 limitation on abduction of both eyes. At near she is orthotropic. The remainder of her examination is remarkable only for her well centered posterior chamber lenses and normal macula.

Differential diagnosis

- Myasthenia Gravis
- Bilateral cranial nerve VI palsy
- Thyroid associated orbitopathy
- Adult onset divergence insufficiency esotropia

Case diagnosis

This patient presents with the classic findings of adult onset Divergence Insufficiency Esotropia. This includes an elderly individual, horizontal diplopia at distance, lack of or less diplopia at near, and external findings of a deep superior sulcus, mild ptosis, and a high lid crease. Motility examination reveals an incomitant esotropia worse at distance than near. Ductions are essentially full with only a slight limitation to abduction. There may be a small vertical incomitant component and there is lack of fatigability.

CME ANSWERS

1. A
2. A
3. A

REFERENCES

1. Chaudhuri Z and Demer JL.: Sagging eye syndrome: connective tissue involution as a cause of horizontal and vertical strabismus in older patients, JAMA Ophthalmol 131:619,2013.
2. Mittleman D. : Age related distance esotropia, J AAPOS 10:212, 2006.
3. Repka MA and Dowing E.: Characteristics and surgical results in patients with age-related divergence insufficiency esotropia,. J AAPOS 18:370, 2014.
4. Ridley-Lane M, Lane E, Yeager LB, et al.: Adult-onset chronic divergence insufficiency esotropia: clinical features and response to surgery, J AAPOS 20:117, 2016.

ADULT WITH ACQUIRED VERTICAL DEVIATION: DO I IMAGE? DO I OPERATE?

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LEARNING OBJECTIVES

1. The attendee will be familiar with the differential diagnosis of vertical diplopia
2. The attendee will be able to recognize the unique clinical settings and exam findings in adults with different causes of acquired vertical misalignment
3. The attendee will know when work-up is indicated and methods available for treating diplopia in this setting

CME QUESTIONS

1. Which of the following findings is more common in acquired versus congenital fourth nerve palsy?
 - A. Diplopia worse in upgaze
 - B. Eye pain
 - C. Ipsilateral exaggerated superior sulcus
 - D. Facial asymmetry
 - E. Symptomatic diplopia with 4 prism diopters hypertropia
2. Motility findings typical of a right fourth nerve palsy can present with similar findings as:
 - A. Thyroid eye disease resulting in “tight” right superior rectus
 - B. Myasthenia affecting primarily the left inferior rectus
 - C. Entrapment of the right inferior rectus
 - D. Thyroid disease involving the left inferior rectus
 - E. Alternating skew deviation
3. Which of the following conditions are matched with their presentation most accurately?
 - A. Myasthenia gravis with acute symptoms and normal eyelid exam
 - B. Acquired fourth nerve palsy with acute symptoms and hypertropia worse in ipsilateral upgaze
 - C. Thyroid eye disease with chronic chin down position and eyelid retraction
 - D. Congenital fourth nerve palsy with chronic symptoms and inferior oblique overaction
 - E. Skew deviation with absence of other neurologic symptoms and good fusional amplitudes

KEYWORDS

1. Hypertropia
2. Fourth nerve palsy
3. Schwannoma
4. Vertical double vision
5. Inferior oblique overaction

SUMMARY

Fourth nerve or superior oblique palsies are exceedingly common in outpatient neurologic and ophthalmic practice. Along with thyroid eye disease they are amongst the most common conditions encountered, particularly in an outpatient setting. When evaluating a patient with acute symptoms consistent with vertical, binocular double vision, both the history and motility exam will generally point to a specific “localization” before any work up is performed. A critical question on historical evaluation is the setting in which the symptoms develop. Obviously, a previous history of head trauma would be a common setting for acquired fourth nerve palsy as well as orbital trauma as a common setting for injured or entrapped extraocular muscles leading to double vision. The tempo of symptom onset is another critical feature. Although many patients don’t recognize the chronic features of longstanding misalignment, most will offer a description of some binocular duress or intermittent double vision for longstanding problems such as congenital fourth nerve palsies. If the patient went from no symptoms at all to having acute vertical double vision, the presentation would be more concerning for an acute skew deviation/brain stem event or vasculopathic fourth nerve palsy. The other important feature is to identify any historical aspects that would suggest thyroid disease or myasthenia gravis, most importantly variability and eyelid changes. Patients should also be questioned as to whether their symptoms are more noticeable or prevalent in certain positions of gaze. The most important features in this setting are the worsening of fourth nerve palsies in contralateral gaze and more specifically acquired fourth nerve palsies in contralateral down gaze and congenital fourth nerve palsies generally in contralateral up gaze. A patient with chronic symptoms that are intermittent, usually have this on the basis of good fusional amplitudes and gaze dependent double vision. Also consider asking the patient to review old photographs to look for chronic head tilts to suggest a congenital fourth nerve palsy.

On the examination, assessing the facial appearance for asymmetry is important in that patients with congenital fourth nerve palsies often have relative hypoplasia on the effected side.^{1,2} Similarly looking at the orbit and testing for the hypoesthesia in the first division of the fifth cranial nerve is important in the setting of previous orbital trauma. Finally, looking carefully for signs of myasthenia gravis, particularly eyelid twitch or fatigue in up gaze, in the setting of ptosis, are critical features of the external exam. Most important is the assessment of ductions and versions and quantification of the deviation. The examiner should have a reliable way, either with alternate cover testing or red glass/Maddox rod testing, to quantify the deviation, and based on that quantification attempt to localize the dysfunctional muscle or nerve. Most acquired fourth nerve palsies follow the three-step test with worsening of the hypertropia in contralateral gaze and ipsilateral head tilt. Worse symptoms in contralateral downgaze is more common with acquired palsies.³ Change in the deviation with head tilt may be less obvious in congenital fourth nerve palsies. The examiner should estimate the amount of torsional misalignment both based on the patient’s description and with testing with double Maddox rod. This is particularly important in the setting of closed head trauma where bilateral fourth nerve palsies can be difficult to detect particularly if they are asymmetric. Other features of acquired bilateral fourth nerve palsy would be a V-pattern horizontal strabismus along with a relatively small primary position deviation and alternating hypertropia. One of the most important clues to congenital and longstanding deviations is the presence of good fusional amplitudes. This can be accessed simply by placing increasing amounts of vertical prism in front of one eye and seeing if the patient can maintain single vision. Anything more than 3 prism diopters in the vertical plane would suggest increased vertical fusional aptitude.

After careful history and examination almost all patients with a history of trauma can be assigned a specific localization for their double vision (orbital injury or traumatic fourth nerve palsy). Similarly,

patients with thyroid eye disease can be identified based on abnormal eyelid position, chin up position, a vertical deviation worse in up gaze and other typical stigmata of thyroid disease. This can occasionally be occult and assessment of the eye muscles either with ultrasound or neuroimaging should facilitate diagnosis. Patients with minimal restriction of the contralateral inferior rectus can behave very similarly to patients with ipsilateral fourth nerve palsies (e.g. right IVth looks similar to tight left IR) . Generally, patients with skew deviations have other neurologic symptoms and have been recognized to present in a setting in which they developed other posterior fossa dysfunction. There are occasional patients who after recovering from a brain injury or a stroke for example will have deviations that are best interpreted as a skew deviation although these patients generally will have been worked up and there is not a specific indication for further testing. Finally, in patients with exams consistent with fourth nerve palsy, it is relatively easy to distinguish congenital palsies from acquired. Patients with congenital palsies generally do not require work up and are recognized by the inferior oblique over action and good fusional aptitudes along with the absence of torsional symptoms. In patients with acquired fourth nerve palsies, the majority are going to have recognized trauma, a vasculopathic history, and rarely, as in the case presented, some type of occult neoplasm. The patients with trauma do not need additional work up. Although there is good evidence to suggest that patients with acute onset of cranial nerve palsies would benefit from imaging to diagnose occult significant neurologic disease, including tumors and ischemia,⁴ in the group of patients with fourth nerve palsy that is isolated, the yield is lower and it may be reasonable to follow the patient anticipating spontaneous recovery. While in the case presented it was important to do an MRI to identify the schwannoma so that appropriate prognostic discussions could be had with the patient, particularly as it relates to surgical intervention, it would not change the management in the absence of other neurologic symptoms. Generally, patients with chronic, non-congenital, fourth nerve palsies should be imaged to identify these types of benign skull base lesions.^{5,6}

Patients with hypertropia can generally be managed either with prism spectacles or strabismus surgery. Many patients particularly with congenital fourth nerve palsies can benefit from prism spectacles that correct some of the deviation and can improve some of their symptoms.⁷ There is presumably little harm in having patients use prism and they certainly can be offered as a temporary or a permanent option as the patient is having a work up or being followed. Some patients with acquired fourth nerve palsies can benefit from using a prism for instance when reading although this is less likely to be successful because of torsional misalignment and limited fusional amplitude. Patients with thyroid disease can sometimes do well with prisms because they have already found that they can maintain a head position that is associated with comfortable fusion and the prism glasses help neutralize that head position.

Most patients with acquired symptomatic vertical strabismus can be effectively treated with strabismus surgery. In the case of thyroid eye disease this is generally done through recessing vertical eye muscles that have restriction sometimes using non-absorbable sutures, and depending on surgeon preference, the use of an adjustable suture can be quite effective. In patients with congenital fourth nerve palsies, there is almost always benefit from inferior oblique recession or myectomy and depending on the pattern of the deviation, sometimes additional surgery can include inferior rectus weakening on the contralateral side or superior rectus weakening on the ipsilateral side. There is a subset of patients with superior oblique tendon laxity which may benefit from superior oblique tuck procedure.^{2,8} In patients with acquired fourth nerve palsies, generally with small deviations in down gaze, some combination of contralateral inferior rectus weakening and ipsilateral inferior oblique weakening will improve ocular alignment.

Case

A 54 yo man, with no history of trauma, presents with a 3 year history of increasing vertical binocular double vision. His symptoms are worse in down gaze and are present all of the time. Exam findings include typical findings of left hypertropia worse in right and down gaze with limited fusional amplitudes and excyclotropia of 6 degrees. Work up (MRI) reveals schwannoma of the left fourth nerve and he is managed with contralateral inferior rectus recession.

Differential diagnosis

- Differential Diagnosis of Acquired Vertical Deviation
 - Fourth nerve palsy
 - Thyroid eye disease
 - Skew
 - Myasthenia
 - Orbital trauma
 - Decompensated hyperphoria

Final case diagnosis

This patient has an acquired fourth nerve palsy resulting from a schwannoma who presented with chronic symptoms although with symptoms worse in downgaze and without increased fusional amplitudes.

CME ANSWERS

1. E
2. D
3. D

REFERENCES

1. Greenberg MF, Pollard ZF. Ocular plagiocephaly: ocular torticollis with skull and facial asymmetry. *Ophthalmology*, 107:173, 2000
2. Helveston EM, Mora JS, Lipsky SN, Plager DA, Ellis FD, Sprunger DT, Sondhi N. Surgical treatment of superior oblique palsy. *Trans Am Ophthalmol Soc.*, 94, 315 1996
3. Ivanir Y, Trobe JD. Comparing Hypertropia in Upgaze and Downgaze Distinguishes Congenital From Acquired Fourth Nerve Palsies. *J Neuroophthalmol*. 37, 365, 2017
4. Tamhankar MA, Bioussé V, Ying GS, Prasad S, Subramanian PS, Lee MS, et al. Isolated third, fourth, and sixth cranial
5. nerve palsies from presumed microvascular versus other causes: a prospective study. *Ophthalmology*.11, 2264, 2013
6. Elmalek VI, Younge BR, Bioussé V, Leavitt JA, Moster ML, et al. Clinical course and prognosis of trochlear nerve schwannomas. *Ophthalmology*, 6, 2011, 2009
7. Feinberg AS, Newman NJ. Schwannoma in patients with isolated unilateral trochlear nerve palsy. *Am J Ophthalmol*, 127,183, 1999.
8. Tamhankar MA, Ying GS, Volpe NJ., Success of prisms in the management of diplopia due to fourth nerve palsy.
9. *J Neuroophthalmol*, 31:206, 2011
10. Komori M, Suzuki H, Hikoya A, Sawada M, Hotta Y, Sato M. Evaluation of Surgical Strategy Based on the Intraoperative Superior Oblique Tendon Traction Test. *PLoS One*.11(12), 2016

ADULT WITH ACQUIRED OBLIQUE DIPLOPIA: DO I IMAGE? DO I OPERATE?

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LEARNING OBJECTIVES

1. Learn how to evaluate a patient with acquired oblique diplopia.
2. Recognize how to distinguish thyroid eye disease from other causes of oblique diplopia, such as superior oblique palsy.
3. Understand the management principles of a patient with thyroid eye disease, including the surgical treatment of strabismus.

CME QUESTIONS

1. A 56-year-old woman complains of recent onset of binocular oblique diplopia. Motility examination reveals a right hypertropia that increases in upgaze and a small esotropia that worsens in left gaze. External examination demonstrates bilateral superior scleral show. Which of the following is the most likely diagnosis?
 - A. Right superior oblique palsy
 - B. Thyroid eye disease
 - C. Dorsal midbrain syndrome
 - D. Myasthenia gravis
2. Which of the following clinical tests is most useful in differentiating a superior oblique palsy from thyroid eye disease?
 - A. Force generation
 - B. Tensilon
 - C. Versions
 - D. Forced ductions
3. A patient with thyroid eye disease demonstrates bilateral upper eyelid lid retraction that improves in downgaze, a right hypertropia that measures 6 prism diopters in primary position and 12 degrees of excyclotropion. Which of the following is the most appropriate surgical treatment?
 - A. Recess the right superior rectus muscle
 - B. Recess the left inferior rectus muscle
 - C. Recess both inferior rectus muscles
 - D. Recess right inferior oblique muscle

KEY WORDS

1. Oblique diplopia
2. Thyroid eye disease
3. Hypertropia
4. Restrictive strabismus
5. Superior oblique palsy

SUMMARY

Thyroid eye disease (TED) is an autoimmune condition typically characterized by an initial acute inflammatory phase, followed by a fibrotic phase that may affect orbital tissues and extraocular muscles.^{1,2} It is usually associated with hyperthyroidism (85%), but may occur in euthyroid (5%) or hypothyroid (10%) individuals.³ The annual adjusted incidence rate is 16 women and 3 men per 100,000 population.³ Cigarette smoking increases the risk of TED by 7-8 times.³

TED and superior oblique (SO) palsy are the most common causes of hypertropia in adult patients, and differentiating them can be challenging.⁴ In both, sensorimotor exam frequently reveals excyclotorsion and a hypertropia that increases in adduction. External findings, the 3-step test, a compensatory head posture and forced duction testing may help distinguish TED from SO palsy. Classic external findings of TED include eyelid retraction (fixation duress may contribute to upper eyelid retraction), lid lag, proptosis, periorbital edema, conjunctival injection over horizontal rectus muscles and conjunctival chemosis. The 3-step test will frequently be positive in SO palsy. In addition, SO palsy is typically accompanied by a contralateral head tilt, while TED is more frequently associated with a chin-up (if predominantly inferior rectus involvement), or face turn (if incomitant esotropia). Forced ductions are positive in TED and usually negative in SO palsy.

To confirm a TED diagnosis and determine activity of disease, evaluation may include a thyroid panel (TSH, T3 free T4) and assessment of thyroid antibodies (thyroid stimulating immunoglobulin [TSI], thyroid binding inhibitory immunoglobulin [TBII], thyrotropin receptor antibody [TRAb], thyroid peroxidase antibody [TPO]).

Routine imaging is not necessary if the classic external findings of TED are present, forced ductions are positive, thyroid antibody titers are elevated and there is no evidence of optic nerve compromise. However, if diagnosis is uncertain, echography or orbital CT or MRI scans can be helpful. Extraocular muscle involvement is frequently bilateral, with muscles demonstrating enlargement of the muscle belly with sparing of the tendon, and high reflectivity on A-scan.

Medical management of TED inflammatory phase includes smoking cessation, ocular lubricants, selenium, steroids, radiation, and biologics. Surgical treatment, if necessary, should be carried out using a stepwise approach, starting with thyroidectomy (controversial), orbital decompression (if significant proptosis or optic nerve compression), strabismus surgery and lastly eyelid surgery.

Indications for strabismus surgery include binocular diplopia, a deviation in primary position or a compensatory head posture. The main goal is to achieve single binocular vision in primary position and downgaze. Surgery should be deferred until alignment and antibody titers are stable or improving. Assessment of torsion and degree of tightness of the extraocular muscles by forced duction testing pre-operatively and intra-operatively help determine which extraocular muscles to include in the surgical plan.⁵ Recession procedures of the tight muscles are preferred. Adjustable sutures may be useful, as normal dose-response curves do not always apply to these patients.^{5,6} A mild undercorrection may be desirable, as post-operative drifts towards overcorrection are not uncommon.⁷

Case

Healthy adult with onset of binocular oblique diplopia after sinus infection. Symptoms do not fluctuate throughout the day. Diplopia is worse in upgaze. Exam reveals a moderate angle hypertropia, worse in adduction, with a small angle esotropia and 8 degrees of excyclotorsion.

Differential diagnosis

1. Thyroid eye disease
2. Superior oblique palsy
3. Myasthenia gravis
4. Orbital myositis
5. Orbital floor fracture

Final diagnosis

Thyroid eye disease is frequently responsible for binocular oblique diplopia, as it can cause restrictive strabismus most commonly involving the inferior and medial rectus muscles.

CME ANSWERS

1. B
2. D
3. C

REFERENCES

1. Harrad R. Management of strabismus in thyroid eye disease. *Eye (Lond)* 2015;29(2):234-237.
2. Seiff SR, Wagner LH. Management of graves myopathy: Thyroid-associated orbitopathy: when should we operate? *J AAPOS*. 2018;22(4):251-252.
3. McAlinden C. An overview of thyroid eye disease. *Eye Vis (London)* 2014;1:9
4. Tamhankar MA, Kim JH, Ying G-S, et al. Adult hypertropia: a guide to diagnostic evaluation based on review of 300 patients. *Eye (Lond)* 2011; 25(1): 91–96
5. Dagi LR. Management of Graves myopathy: Understanding and managing vertical strabismus from thyroid eye disease. *J AAPOS*. 2018;22(4):252-255.
6. Volpe NJ, Mirza-George N, Binenbaum G. Surgical management of vertical ocular misalignment in thyroid eye disease using an adjustable suture technique. *J AAPOS*. 2012;16(6):518-522.
7. Peragallo JH, Velez FG, Demer JL, Pineles SL. Postoperative drift in patients with thyroid ophthalmopathy undergoing unilateral inferior rectus muscle recession. *Strabismus*. 2013;21(1):23-28.

ATYPICAL STRABISMUS IN CHILDHOOD: DO I IMAGE? DO I OPERATE?

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LEARNING OBJECTIVES

1. To recognize differences between adults and children with strabismus due to myasthenia gravis.
2. To utilize neuro-imaging cost-effectively in children with atypical strabismus patterns.
3. To employ proper indications for extraocular muscle surgery in children with myasthenic strabismus.

CME QUESTIONS

1. The coexistence of ptosis and ophthalmoplegia at diagnosis of MG is:
 - A. More common in children than adults
 - B. More common in adults than children
 - C. Equally common in adults and children
2. Which of the following is more common in myasthenic strabismus in adults as compared to children?
 - A. Esotropia
 - B. Hypertropia
 - C. Strabismus fixus
 - D. Suppression
3. Which of the following is associated with greater success following eye muscle surgery for strabismus due to MG?
 - A. Positive AchR antibodies
 - B. Poor response to corticosteroids
 - C. Stability of deviation for one year
 - D. Age > 50 years

KEY WORDS

1. Strabismus
2. Myasthenia gravis
3. Incomitant
4. Strabismus fixus

SUMMARY

Myasthenia gravis (MG) is an autoimmune disorder involving the neuromuscular junction of skeletal muscles. Adult and pediatric prevalence estimates are approximately 2-30 and 1-5 per million person years, respectively; 10-15% of all cases occur in children.^{1,2} Ocular findings include incomitant strabismus and ptosis, and the pupils are clinically spared.

There are various subtypes of pediatric MG, including transient neonatal forms from infants born to myasthenia mothers, and congenital types due to structural or biomechanical deficits in the acetylcholine receptors as opposed to autoimmune receptor blocking or modifying molecules.^{3,4} The most common form, however, is the juvenile form (JMG), which has many clinical similarities to the adult form. However, children with this condition are less likely to have either AchR or MUSK antibodies. When the latter are present, patients are more prone to respiratory crisis and have a less predictable response to therapy.⁵ Children with JMG have positive antibodies in about 40% of those with purely ocular symptoms, and 75% of those with generalized disease. Approximately 40% of the 40% antibody-negative children seroconvert over 2 years.⁶

Diagnostic and treatment strategies for JMG are similar to those for adult disease. They include antibody assay, pharmacologic testing, single-fiber EMG, and the rest and ice tests, as well as pyridostigmine, corticosteroids, azathioprine, rituximab, tacrolimus, plasmapheresis, IVIG, mycophenylate mofetil, and thymectomy respectively.

There are a number of differences in the clinical presentation and course of MG in children vs adults. Obviously, development of amblyopia is a concern in children, occurring in 25-50% of patients. Fortunately, treatment is successful in over 90% of cases.⁷ Children also have a higher rate of associated autoimmune diseases such as thyroid dysfunction, idiopathic arthritis, myositis, and asthma, occurring in almost 10% of children.⁸ While ptosis is common in all patients with MG, children appear to have a greater incidence of exotropia as opposed to esotropia, as well as vertical strabismus; in addition over half (up to 70%) of children have both ptosis and ophthalmoplegia on initial diagnosis.⁹ Myasthenia may be a great mimicker in both children and adults, but the converse is true as well, i.e., what appears to be MG may actually be intracranial disease, and children may have MG plus other conditions.¹⁰ Neuroimaging should be considered in all atypical cases, when additional findings are present, serology is negative, or pharmacologic testing is equivocal. Response of ptosis to pyridostigmine appears equal to or better than in adults, and generalization rates are lower in children.^{11,12} However, response of ophthalmoplegia is less robust, even when corticosteroids or other systemic agents are used, though all patients eventually stabilize.¹²

Strabismus surgery may be considered after disease has been maximally controlled and the ductions and alignment have been stable for at least 6-12 months. One relatively rare type of stabilization which occurs mainly in children is that of "strabismus fixus," whereby there is total or near-complete ophthalmoplegia bilaterally and a moderate to large angle deviation, generally exotropia (due to orbital geometry). Results may be unpredictable as innervation and tonus may be globally but asymmetrically impaired throughout agonist-antagonist pairs. Nevertheless, acceptable outcomes are achieved in a majority of patients, though multiple procedures may be required.¹³ Many surgeons prefer recessions as a first approach when possible due to ease of reversibility.

Case 1

An eight-year old boy presents with acquired diplopia and unilateral ptosis. Exam reveals ipsilateral ptosis and adduction deficit, with contralateral elevation deficit. The family are undocumented residents and have no funds for neuroimaging.

Differential diagnosis

- Unilateral nuclear third nerve palsy
- Partial bilateral third nerve palsy
- Myasthenia gravis

Case diagnosis

This case represents myasthenia gravis mimicking brainstem disease. Careful analysis of the strabismus would require multiple intracranial lesions to cause the clinical picture, making myasthenia a more likely etiology.

Case 2

A 10 year old child with antibody-positive and edrophonium-positive generalized myasthenia gravis has been treated for 4 years, with resolution of ptosis and bulbar and systemic symptoms. For 3 years he has had diffuse ophthalmoplegia bilaterally, with only trace ductional movements in any direction. Alignment in primary gaze is XT 30 at distance, 40 at near. There is no diplopia with or without prism correction. The family desires an opinion on strabismus surgery.

Differential diagnosis

- strabismus fixus due to myasthenia gravis
- chronic progressive external ophthalmoplegia
- bilateral cavernous sinus syndrome

Case diagnosis management

The phenomenon of strabismus fixus, though rare, is well known among strabismologists. This child meets indications for strabismus surgery, which was performed without complication.

CME ANSWERS

1. A
2. A
3. C

REFERENCES

1. Carr AS, Cardwell, CR, McCarron PO, et al. A systematic review of population based epidemiological studies in myasthenia gravis. *BMC Neurology* 10:46, 2010..
2. Phillips LH 2nd, Torner JC, Anderson MS, et al. The epidemiology of myasthenia gravis in central and western Virginia. *Neurology*. 42:1888-93, 1992.
3. Tellez-Zenteno JF, Hernandez-Ronquillio L, Salinas V, et al. Myasthenia gravis and pregnancy: clinical implications and neonatal outcome. *BMR Muschoekeletal Disord* 5:42, 2004.
4. Kinali M, Beeson D, Pitt MC, et al. Congenital myasthenia syndromes in childhood: diagnostic and management challenges. *J Neuroimmunol* 201-202:6-12, 2008.
5. Skjei KL, Lenon VA, Kuntz NL. Muscle specific kinase autoimmune myasthenia gravis in children: a case series. *Neuromuscul Disord* 23:874-82, 2013.
6. Anlar B, Senbil N, Kose G, et al. Serological follow-up in juvenile myasthenia: clinical and acetylcholine receptor antibody status of patients followed for at least 2 years. *Neuromuscul Disord* 15:355-57, 2005.
7. Ortiz S, Borchert M. Long-0term outcomes of pediatric ocular myasthenia gravis. 115:1245-48, 2008.
8. Chiang LM, Darras BT, Kang PB. Juvenile myasthenia gravis. *Muscle and Nerve*. 39:423-31, 2009.
9. Kim J-H, Hwang J-M, Hwang Y, et al. Childhood ocular myasthenia gravis. *Ophthalmol* 110:1458-62, 2003.

10. Moorthy G, Behrens, MM, Drachman DB et al. Ocular pseudomyasthenia or ocular myasthenia "plus": a warning to clinicians. *Neurology* 39:1150-54, 1989.
11. Pineles SL, Avery RA, Moss HE, et al. Visual and systemic outcomes in pediatric ocular myasthenia gravis. *Am J Ophthalmol* 150:453-59, 2010.
12. Ortiz S, Borchert M. Long-term outcomes of pediatric ocular myasthenia gravis. *Ophthalmol* 115:1245-48, 2008.
13. Peragallo JH, Velez FG, Demer, JL, et al. Long-term follow-Up of strabismus surgery for patients with ocular myasthenia gravis. *J Neuroophthalmol* 33:40-44, 2013.

CHILD WITH LIMITED UPGAZE: DO I IMAGE? DO I OPERATE?

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LEARNING OBJECTIVES

1. The attendee will be familiar with the differential diagnosis of dorsal midbrain syndrome (DMS).
2. The attendee will be able to recognize the unique clinical settings and examination findings in children with dorsal midbrain syndrome.
3. The attendee will know the diagnostic workup of a child with limited upgaze.

CME QUESTIONS

1. Which of these is not a feature of dorsal midbrain syndrome?
 - A. Divergence insufficiency
 - B. Convergence retraction nystagmus
 - C. Impaired up gaze
 - D. Lid retraction
2. An 8-month-old is evaluated for ptosis, limitation of extraocular movements, and a normal pupil exam. These findings are suggestive of:
 - A. Periventricular leukomalacia (PVL)
 - B. Encephalitis
 - C. Congenital fibrosis of the extraocular muscles (CFEOM)
 - D. Interventricular haemorrhage (IVH)

KEY WORDS

1. Dorsal midbrain syndrome
2. Tonic downgaze
3. Convergence retraction nystagmus
4. Light near dissociation

SUMMARY

Dorsal midbrain syndrome (DMS) is a supranuclear vertical gaze palsy secondary to lesions damaging the vertical gaze center in the posterior commissure of the dorsal midbrain. The syndrome is characterized by the following: (1) light-near dissociation, (2) paralysis of conjugate up gaze, and (3) convergence-retraction nystagmus during attempted upward saccades. Lid retraction also called Collier's sign in primary position may also be present.

It is important to differentiate this from other conditions which can present with impaired upgaze in a young patient. With benign tonic downgaze of infancy, infants are neurologically normal and symptoms usually resolve within weeks to months.¹ With congenital fibrosis of the extraocular muscles (CFEOM), there is bilateral blepharoptosis with variable restriction of horizontal gaze in addition to vertical gaze.² Leigh syndrome is a mitochondrial disorder characterized by milestone regression within the first year of

life, poor tone, ataxia, and abnormal neuroimaging. Some of the ophthalmic findings include ptosis, refractive error, strabismus, reduced extraocular motility, and optic atrophy³.

The question is whether to image or not in tonic downgaze. Neuroimaging is indicated when there is any history of milestone regression, seizures, abnormal visual behavior, or signs or symptoms of raised intracranial pressure. Additionally, if the symptoms do not improve or resolve on follow-up over a few months, imaging is recommended.^{4,5} Any signs or symptoms of DMS warrants neuroimaging.

DMS causes significant residual motility disturbances unless there is early correction of the underlying cause.⁶ After the eye movement restriction has been present for > 6 months - 1 year with no further expected changes, strabismus surgery can be considered. Abnormal head posture due to the inability to elevate the eyes is an indication for surgery, however, the associated retraction nystagmus and convergence spasm can make surgical correction challenging.⁶ There are limited reports with regards to surgical approaches in correcting eye movement abnormalities in DMS. Suggested procedures include bilateral full tendon upward transpositions of the medial and lateral recti, bilateral inferior rectus recessions, and bilateral superior rectus resections combined with bilateral inferior rectus recession⁶. Posterior fixation suture of the medial rectus muscles may reduce the effects of convergence spasm⁷.

Case

4-month-old boy presented to the pediatric ophthalmology clinic for “funny eye movements” noted by the pediatrician at the 2-month visit. Examination findings included macrocephaly, convergence-retraction nystagmus, sun setting sign, and bilateral lid retraction. Dilated examination revealed bilateral optic atrophy.

Differential diagnosis

- Impaired upgaze – differential
 - Normal infants – 2%
 - Not present during sleep
 - Upgaze normal with head rotations
 - Lids and pupils normal
 - Resolves by 6 months
 - No need for neuroimaging
 - Congenital fibrosis of the extraocular muscles (CFEOM)
 - Ptosis
 - Restriction of eye movements
 - Pupils normal
 - Family history of similar features
 - No need for neuroimaging
 - Neurologic disease – ie. Leigh disease, periventricular leukomalacia (PVL), intraventricular hemorrhage (IVH)
 - Neonate with respiratory or feeding difficulties
 - Progressive neurologic deficits
 - History of prematurity
 - History of regression of milestones
 - Seizures
 - Delay in motor and speech milestones
 - Needs neuroimaging

- Dorsal midbrain syndrome- clinical characteristics
 - Lid retraction
 - Impaired upgaze
 - Pupils with light near dissociation
 - Convergence retraction nystagmus
 - Needs neuroimaging
- Dorsal midbrain syndrome
 - Differential
 - Hydrocephalus,
 - Tumor
 - Midbrain hemorrhage
 - Encephalitis
 - Trauma
 - Image – Yes
 - Treatment
 - Underlying cause
 - Strabismus surgery

Case diagnosis

This is a case of dorsal midbrain syndrome aka Parinaud’s syndrome, a condition that should be in the differential in the evaluation of children with limitation of up gaze.

CME ANSWERS

1. A
2. C

REFERENCES

1. Allen NM, Tibussek D, Borusiak P, King MD. Images in neonatal medicine. Benign **tonic downgaze** of infancy. Arch Dis Child Fetal Neonatal Ed. 2010 Sep;95(5):F372
2. Heidary G, Mackinnon S, Elliott A, Barry BJ, Engle EC, Hunter DG. Outcomes of strabismus surgery in genetically confirmed congenital fibrosis of the extraocular muscles. J AAPOS. 2019 Sep 18.
3. Åkebrand R, Andersson S, Seyedi Honarvar AK, Sofou K, Darin N, Tulinius M, Grönlund MA. Ophthalmological characteristics in children with Leigh syndrome - A long-term follow-up. Acta Ophthalmol. 2016 Sep;94(6):609-17
4. V.S. Miller, A.M. Packard. Paroxysmal downgaze in term newborn infants J Child Neurol, 13 (1998), pp. 294-295
5. Fernández-Alvarez E. Transient benign paroxysmal movement disorders in infancy. Eur J Paediatr Neurol. 2018 Mar;22(2):230-237.
6. Buckley EG, Holgado S. Surgical treatment of upgaze palsy in Parinaud's syndrome. J AAPOS. 2004 Jun;8(3):249-53.
7. A Spielmann, J Ritcher. La chirurgie oculomotrice dans le syndrome de Parinaud Ophtalmologie, 3 (1989), pp. 157-159
8. S.A Buckley, J.S Elston. Surgical treatment of supranuclear and internuclear ocular motility disorders Eye, 11 (1997), pp. 377-380

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