Red Rock Casino
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Las Vegas, NV

March 16-21, 2019

North American Neuro-Ophthalmology Society

1975-2019

North American Neuro-Ophthalmology Society

45th Annual Meeting

March 16 – March 21, 2019
Red Rock Casino, Resort & Spa • Las Vegas, Nevada

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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 COMMERICAL 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.

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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 29.25 AMA PR Category 1 Credits. Physicians should claim only the credit commensurate with the extent of their participation.

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

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Key: P = Planner; F = Faculty

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Saturday, March 16

8:00 am – 12:00 pm	**NANOS Board Meeting**	**Veranda DE**
2:00 pm – 7:30 pm	**Registration/Help Desk**	**5th floor Registration Desk**
3:00 pm – 4:30 pm	**Orbital and Sellar Lesions-Neuro-Radiology Pearls and Pitfalls** *Moderator: Madhura Tamhankar, MD*	**Red Rock Ballroom**

This session is designed to provide participants working in multi-disciplinary programs with important points of information regarding selection of appropriate imaging modalities and sequences within those modalities, as well as strategies for image analysis to precisely evaluate pathology involving the optic nerves and other cranial nerves that affect vision. This session will: 1) review MR and CT imaging protocols for intra-orbital pathology, pathology of the visual pathway, and other cranial nerves 2) discuss the evaluation of intra-orbital neoplasia including primary orbital tumors and tumors/pathology that secondarily involve the orbit through direct growth from surrounding areas (paranasal sinuses, bone), perineural spread, and metastatic disease and 3) discuss sellar and parasellar pathology that may involve/compress the visual pathway and/or extend to the cavernous sinuses.

Upon completion of this session, participants should be able to: 1) determine if cross-sectional imaging is necessary 2) select the best test when imaging is necessary 3) describe their role in communicating with their neuroradiologists to optimize protocol selection 4) identify when specialized high resolution MR imaging is necessary 5) identify MR protocols and sequences for evaluating sellar and parasellar disease and 6) discuss imaging findings that distinguish neoplastic from inflammatory disease.

3:00 pm – 4:30 pm	**Orbital and Sellar Lesions- Neuro-Radiology Pearls and Pitfalls,** *Laurie Loevner, MD*

6:00 pm – 7:30 pm	**Opening Reception (All are welcome!)**	**Pavilion Ballroom**

Sunday, March 17

6:00 am – 6:45 am	**Yoga**	**Pavilion Ballroom**
6:30 am – 7:30 am	**Breakfast**	**Charleston Ballroom**
6:30 am – 5:30 pm	**Registration/Help Desk**	**5th floor Registration Desk**
7:30 am – 9:30 am	**Frank B. Walsh (I)** *Co-Chairs: Madhura Tamhankar, MD and Grant Liu, MD* *Walsh Host Committee: Kenneth Shindler, MD, PhD, Robert Avery, DO, MSCE,*	**Red Rock Ballroom**

Ahmara Ross, MD, PhD, and Ali Hamedani, MD, MHS
Neuro-radiologist: Laurie Loevner, MD
Neuro-pathologist: Zissimos Mourelatos, 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 course, 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.

Moderators: Kenneth Shindler, MD, PhD and Ahmara Ross, MD, PhD

7:30 am – 7:45 am	**Welcome and Intro to Mobile App**
7:45 am – 8:05 am	**A Zebra Among Zebras**, *Peter W. Mortensen, MD*
8:05 am – 8:25 am	**The Great Masquerade**, *Bart K. Chwalisz, MD*
8:25 am – 8:45 am	**Chalky Pallid Edema**, *Daniel L. Kornberg, MD*
8:45 am – 9:05 am	**A-deno What's Going On!** *Christine Greer, MD*
9:05 am – 9:25 am	**Go with your Gut Feeling**, *Paul R. Freund, MD, MSc, FRCSC*
9:25 am – 9:30 am	**Wrap-up**

9:30 am – 10:00 am	**Coffee break**	**Charleston Ballroom**
10:00 am – 12:00 pm	**Frank B. Walsh (II)**	**Red Rock Ballroom**

Moderators: Grant Liu, MD and Robert Avery, DO, MSCE

10:00 am – 10:20 am	**Fire and Ice**, *Mary D. Maher, MD*
10:20 am – 10:40 am	**Unexplained Becomes Explained**, *Jinu Han, MD*
10:40 am – 11:00 am	**A Trip Through the Wormhole**, *Anne Kao, MD*
11:00 am – 11:20 am	**Three's a Crowd**, *Kanwal S. Matharu, MD*
11:20 am – 11:40 am	**Don't Drink the Water**, *Devon A. Cohen, MD*
11:40 am – 11:45 am	**Morning Wrap-up**

12:00 pm – 12:30 pm	**Lunch**	**Charleston Ballroom**
12:00 pm – 12:30 pm	**International Relations Committee Meeting**	**Veranda E**
12:00 pm – 1:00 pm	**Fellowship Directors Committee Meeting**	**Veranda AB**
12:30 pm – 2:30 pm	**Poster Session I: Clinical Highlights**	**Red Rock Ballroom A-C**

12:30 pm – 1:30 pm	**Odd Numbered Posters**
1:30 pm – 2:30 pm	**Even Numbered Posters**

2:30 pm – 3:00 pm	**Business Meeting**	**Red Rock Ballroom**
3:00 pm – 5:15 pm	**Frank B. Walsh (III)**	**Red Rock Ballroom**

Moderators: Madhura Tamhankar, MD and Ali Hamedani, MD, MHS

3:00 pm – 3:20 pm	**Every Rose Has Its Thorn**, *William J. Anderson, BS*
3:20 pm – 3:40 pm	**Not the Rolling Stones**, *Ari A. Shemesh, MD*
3:40 pm – 4:00 pm	**Fooled Thrice**, *Jonathan A. Micieli, MD, CM*
4:00 pm – 4:20 pm	**At the Crossroads**, *Konstantinos Douglas, MD, DVM, MBA*
4:20 pm – 4:40 pm	**Just the Two of Us**, *Dan Milea, MD, PhD*
4:40 pm – 5:00 pm	**Turbulence Fluid Waves and the Black Hole**, *Stella Y. Chung, MD, MS*
5:00 pm – 5:15 pm	**Closing Remarks**

5:30 pm – 6:00 pm	**Walsh Committee Meeting**	**Veranda D**
5:45 pm – 6:45 pm	**Members-in-Training Reception**	**Veranda F**

(All students, residents and fellows-in-training are encouraged to attend.)

Frank B. Walsh: Session I
Moderators: Kenneth Shindler, MD, PhD and Ahmara Ross, MD, PhD

Frank B. Walsh: Session II
Moderators: Grant Liu, MD and Robert Avery, DO, MSCE

Frank B. Walsh: Session III
Moderators: Madhura Tamhankar, MD and Ali Hamedani, MD, MHS

"A Zebra Among Zebras"

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History & Exam

61-year-old man with Type 2 diabetes and hypertension presented to outside hospital ED with fever, headache, and neck pain. Onset of neck pain was one week prior, with worsening of symptoms following chiropractic manipulation. Patient was evaluated at outpatient clinic one day prior and given Medrol Dosepak for degenerative disc disease. In the ED, he had fever 102.5F, headache, neck pain, and right-sided blurry vision followed by rapid development of chemosis, proptosis, ophthalmoplegia, and nonreactive right pupil. Labs revealed leukocytosis and elevated lactate. Chest X-Ray revealed pulmonary nodules and C-spine CT revealed retropharyngeal abscess. CT head was unremarkable. Patient was started on broad spectrum antibiotics and was transported. After transfer to the medical ICU, ophthalmology was stat paged for loss of vision in his right eye during transport. Ophthalmology arrived minutes later and was the first team at bedside. Our examination was notable for visual acuity hand motions 1' (right) and 20/200 (left), fixed and dilated right pupil with afferent pupillary defect, intraocular pressure 60 (right) and 26 (left), and omnidirectional ophthalmoplegia bilaterally. Anterior segment was notable for right-sided chemosis and proptosis with fixed, dilated pupil. Fundus examination was unremarkable. Right lateral canthotomy and cantholysis performed, with pressure decreasing to 30. ENT performed bedside laryngoscopy, with no concern for fungal etiology. Bedside ultrasound demonstrated thrombus in the right internal jugular vein. We immediately discussed the case with neurosurgery, oculoplastics, medical ICU team, and ENT, with urgent angiogram strongly recommended. Shortly thereafter, patient reported loss of vision in the left eye, with bilateral fixed and dilated pupils. Due to acute worsening of his condition, angiogram was not obtained. CT orbit demonstrated bilateral cavernous sinus thrombosis, bilateral internal jugular thrombi, and retropharyngeal abscess. Patient was continued on broad spectrum antibiotics and intubated. He became unresponsive and succumbed to infection the following day.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

"A Zebra Among Zebras"

Answer

Final Diagnosis

Given the patient's retropharyngeal abscess, bilateral pulmonary nodules, and bilateral internal jugular vein thrombi, the patient was diagnosed with Lemierre's syndrome. He developed bilateral cavernous sinus thrombosis, which rarely occurs from Lemierre's. Karkos et al., 2009, noted that cavernous sinus thrombosis only occurred in roughly 5% of cases. Interestingly, his blood cultures returned positive for Staph aureus rather than Fusobacterium, which causes roughly 90% of Lemierre's cases. Most patients with Lemierre's syndrome present in their second or third decade of life (median age 22), though there have been cases documented in patients ranging from 2 months old to 78 years old. Lemierre's syndrome has a 5% mortality rate, and the patient's rapid decline may be attributed to his atypical presentation, especially given the development of bilateral cavernous sinus thrombosis. The administration of steroids one day prior to his hospitalization may have contributed to his decline.

Summary of Case

In summary, we have a 61 year-old man with type 2 diabetes who was walking, talking, and in his usual state of health one day prior to presentation. He presented with bilateral cavernous sinus thrombosis, retropharyngeal abscess, bilateral pulmonary nodules, and bilateral internal jugular vein thrombi after being started on steroids one day prior to presentation. ENT evaluation ruled out fungal etiology. Because all these pathologies presented simultaneously, it was presumed that all were due to an infectious etiology which disseminated. Furthermore, the patient was given steroids the day prior to presentation, which may have exacerbated the spread of his infection. Despite being started on vancomycin and piperacillin-tazobactam, the patient's status declined rapidly over several hours, with progressively worsening mental status. Patient was evaluated by neurosurgery, and no endovascular surgical options were recommended. Patient was continued on antibiotics but died the following day. Blood cultures and retropharyngeal abscess cultures returned positive for Staphylococcus aureus following his death.

Struggle/Dilemma of the Clinical Presentation Description

Patient was in his usual state of health and diagnosed with degenerative disc disease the prior day. He was started on steroids and acutely decompensated. Initially, he only had unilateral ophthalmologic manifestations, and we were concerned about cavernous carotid fistula. Given his diabetes and rapid progression, we also considered Mucor. We strongly recommended angiogram, which we could not obtain given his worsening condition. CTA head/neck demonstrated bilateral internal jugular thrombi and bilateral cavernous sinus thrombosis.

Keywords: Cavernous sinus syndrome, Thrombosis, Jugular veins, Proptosis, Optic Neuropathy

References

1. Karkos PD, Asrani S, Karkos CD, Leong SC, Theocari EG, et al: Lemierre's syndrome: a systematic review. Laryngoscope 2009; 119: 1552-9.

"The Great Masquerade"

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History & Exam

A 56-year-old man with unremarkable prior history complained of visual and somatosensory disturbances. Five months prior, he had an episode of being unable to see oncoming traffic. He developed transient visual disturbances lasting minutes in the left hemifield, e.g., the right sides of people's faces looked as if they were melting. His family noticed a tendency to veer toward the left when walking. Optometry evaluation was unrevealing. Four months later he had an episode of sudden difficulty using his left hand, prompting a hospital admission. An MRI brain was performed, and showed multiple areas of restricted diffusion. A workup for stroke etiologies was negative apart from mildly elevated inflammatory markers. Upon discharge, aspirin and atorvastatin were added to his medications. He continued to have episodes of left hand and face numbness about twice weekly and occasional episodes of left-sided visual disturbances. He developed intermittent intense left temple pain occurring 1-2x/week. He presented emergently again with a transient episode of left facial droop, left arm numbness and brief confusion. Neuro-ophthalmic exam revealed: visual acuities of 20/20 OD, 20/25 OS, previously known color blindness, and otherwise excellent afferent and efferent function. Perimetry showed an inferior arcuate defect OS. The fundi appeared normal. OCT showed normal disc and foveal contours but suggested thickened choroid. Fluorescein angiography was notable for delayed A-V and choroidal filling. Repeat brain MRI showed enlargement of the previously noted diffusion-positive areas. An extensive laboratory evaluation was notable for mildly elevated inflammatory markers and LDH, otherwise negative infectious, autoimmune, paraneoplastic and hypercoagulable studies. LP showed mildly elevated protein and elevated IgG. CT torso showed three distinct lobulated retroperitoneal masses, biopsy of which revealed large B-cell lymphoma. Brain biopsy was performed. This showed minimally hypercellular brain parenchyma with abnormal atypical cells within vessels, establishing a diagnosis of intravascular lymphoma.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

"The Great Masquerade"

Answer

Final Diagnosis
Intravascular lymphoma causing slowly enlarging multifocal cerebral infarcts and chorioretinal slow perfusion, associated with systemic lymphoma.

Summary of Case
This patient presented with recurrent transient multifocal neurological disturbances, including visual distortions in a hemifield. Unusually, consecutive brain MRIs showed multifocal "slow strokes", with enlargement of the same diffusion-restricted areas over time. In addition to the cerebral findings, neuro-ophthalmic evaluation found thickened choroid and slow perfusion of the retinal and choroidal circulations. Systemic lymphoma was found, but the connection with the ocular and cerebral findings was made when brain biopsy revealed intravascular lymphoma. Intravascular lymphoma is rare but a notorious mimic of numerous neurologic conditions, including embolic disease and vasculitis. It is a particularly important differential in cryptogenic multifocal stroke. There are few documented ophthalmic cases, but any part of the eye can be affected, and involvement of uveal, retinal and choroidal blood vessels has been pathologically demonstrated. Symptoms arise when tumor foci obstruct organs' blood supply. The diagnosis is established by a finding of large lymphoma cells in small/medium blood vessels in skin, muscle, brain or other organs. It usually occurs de novo, but intravascular lymphoma in the setting of systemic lymphoma has been reported, which may represent embolization of neoplastic lymphocytes, or clonal evolution with loss of expression of chemokine receptors for extravasation.

Struggle/Dilemma of the Clinical Presentation Description
- The seriousness of the presentation, and the unusual aspects of the case, including progression of infarcts in the same area, failed to be recognized initially - Confirmation of intravascular lymphoma is important even if systemic lymphoma is present as treatment differs - The retinal and choroidal perfusion abnormalities were likely caused by sludging of tumor cells in the respective vasculature, as demonstrated pathologically by Papalas et al. (see references)

Keywords: Complications of cancers, retinopathy, Vascular disease of the brain and the eye, Vascular Arterial (Ischemic stroke)

References
• Beristain X, Azzarelli B – The neurologic masquerade of intravascular lymphomatosis. Arch Neurol.2002;59:439-443. • Chapin JE, Davis LE, Kornfeld M, Mandler RN - Neurologic manifestations of intravascular lymphomatosis. Acta Neurol Scand.1995;91:494-9. • Fonkem E, Dayawansa S, Stroberg E, et al. - Neurological presentations of intravascular lymphoma (IVL): meta-analysis of 654 patients. BMC Neurology.2016;16:9 • Freedman AS, AsterJC, Boer-Auer A. - Intravascular large cell lymphoma. UpToDate. Accessed 10/25/2018 • Papalas JA, Proia AD, Cummings TJ – Hematolymphoid malignancies with intraocular intravascular involvement: report of 2 cases. Annals Diagn Pathol.2011;15(4):286-90. • Tahsili-Fahadan P, Rashidi A, Cimino J, et al. - Neurologic manifestations of intravascular large B-cell lymphoma.Neurol Clin Pract.2016;6:55-60.

“Chalky Pallid Edema”

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History & Exam

A 52 year-old woman with hypertension, insulin dependent type II diabetes, mild non-proliferative diabetic retinopathy in both eyes, obstructive sleep apnea, paroxysmal atrial fibrillation, obesity and multifactorial end-stage renal disease (ESRD) complained of four days of a dark scotoma in the inferior portion of the right eye that began right after hemodialysis. The scotoma migrated inferiorly and enlarged over four days. One month prior to presentation she developed intermittent jaw pain on chewing, worse on the right side. On ophthalmic examination, visual acuity was count fingers at three feet for the right eye and 20/60 with pinhole improvement to 20/25 in the left eye. There was a 2+ relative afferent pupillary defect (RAPD) in the right eye. The anterior segment examination was notable only for bilateral mild nuclear sclerosis. Fundus examination of the right eye showed 360° optic disc edema with chalky temporal pallor and a flame hemorrhage superior to the disc. The left optic disc was without edema or pallor with a 0.2 cup to disc ratio. In light of the presence of jaw claudication and pallid edema, an arteritic anterior ischemic optic neuropathy (AION) due to giant cell arteritis (GCA) was suspected. Fluorescence angiogram demonstrated leakage of the right optic disc with normal retinal and choroidal filling. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were elevated to 90 mm/hr and 4.3 mg/dL, respectively, but platelet count was normal at 229 per uL. Brain MRI revealed several punctate acute infarcts across several vascular territories including the bilateral high frontal and left occipital white matter, as well as a punctate focus of restricted diffuse at the insertion of the right optic nerve head. Neck MRA showed no significant stenosis. Head MRA showed no signs of inflammation in the temporal artery walls.

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Grant Support: None.

"Chalky Pallid Edema"

Answer

Final Diagnosis
AION of the right eye accompanied by jaw claudication, followed later by PION in the left eye, all secondary to calciphylaxis of branches of the common carotid artery. Concomitant bilateral punctate subcortical infarcts presumably a result of calciphylaxis as well.

Summary of Case
The patient was hospitalized and received 1 g/day of intravenous methylprednisolone for three days followed by oral prednisone at 80 mg/day. A right temporal artery biopsy (TAB) showed intimal calcific deposits but was without granulomatous inflammation or vasculitis. Three weeks after initial presentation, the patient noted new headaches despite steroid usage. Visual acuity dropped to hand motions in the right eye and visual fields showed severe diffuse vision loss. Visual acuity and fields were full in the left eye. Despite the patient's relatively young age and negative TAB, GCA was still considered a possibility given the prominent jaw claudication. Prednisone was tapered to 40 mg/day over months. Seven months after presentation, prednisone had been increased back up to 40 mg a day due to recurrent headaches and jaw claudication. Despite this, the patient developed dyschromatopsia and superior disturbance in her left eye. Visual acuity in the left eye remained 20/20, but visual fields showed a new superior altitudinal visual field defect. Fundus examination showed no disc edema or pallor of the left eye, and a left posterior ischemic optic neuropathy (PION) was diagnosed. The patient was hospitalized for further intravenous methylprednisolone. The patient also noted a new dark lesion over the left inguinal region. A biopsy of the skin lesion was consistent with calciphylaxis. In conjunction with nephrology, the patient was treated with sodium thiosulphate and the steroids were quickly tapered down. With the clinical context of calciphylaxis seen in the skin lesions, the TAB was reviewed with pathology who reinterpreted the calcific deposits of the temporal artery as consistent with calciphylaxis. A diagnosis of AION, PION and jaw claudication, all due to calciphylaxis of branches of the common carotid artery was made.

Struggle/Dilemma of the Clinical Presentation Description
Our patient presented with acute vision loss and a history of jaw claudication along with high inflammatory markers (ESR and CRP) concerning for GCA. She also had multiple systemic risk factors for non-arteritic ischemic optic neuropathy (NA-AION) and a disc-at-risk in the fellow eye. It was not until after her vision loss in the second eye that the she presented with skin lesions which were found to be due to calciphylaxis, suggesting the true diagnosis.

Keywords: Giant cell arteritis, Temporal artery biopsy, Ischemic optic neuropathy

References
Nordborg E, Nordborg C. Giant cell arteritis: Epidemiological clues to its pathogenesis and an update on its treatment, Rheumatology 42(3), 413–21, 2003. Al-Absi AI, Wall BM, Cooke CR. Medial arterial calcification mimicking temporal arteritis. Am J Kidney Dis 44(4), 73–8, 2004. Sivertsen MS, Strøm EH, Endre KMA, Jørstad ØK. Anterior Ischemic Optic Neuropathy Due to Calciphylaxis. J Neuroophthalmol 38(1), 54–6, 2018. Roverano S, Ortiz A, Henares E, Eletti M, Paira S. Calciphylaxis of the temporal artery masquerading as temporal arteritis: a case presentation and review of the literature. Clin Rheumatol 34(11), 1985–8, 2015. Awwad ST, Ghosn S, Hogan RN. Calciphylaxis of the temporal artery masquerading as temporal arteritis. Clin Experiment Ophthalmol 38(5), 511–3, 2010.

“A-Deno What's Going On!”

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History & Exam

A 68 year-old Hispanic female with hypertension, type II diabetes mellitus, panhypopituitarism after pituitary adenoma resection 30 years prior and subsequent radiation therapy presented with decreased vision in the left eye and severe headache. The patient’s vision in the left eye declined in the preceding four months until she could no longer see light. She described a constant pressure within her left eye and 10/10 headache for nine months. The headaches were similar to the headaches she experie---nced prior to her initial tumor resection. She had presented to an outside emergency department several times given these symptoms and was suspected to have a recurrent pituitary adenoma. Recently, she had become somnolent without focal deficits. Her medications included levothyroxine, hydrocortisone and oral hypoglycemics and there had been no recent change. Her labs were notable for profound hyponatremia. Ophthalmic exam was notable for 20/60 and NLP vision, amaurotic pupil, and RAPD OS. Intraocular pressures and cranial nerves III-VII were normal. There was no proptosis or ocular adnexal abnormality or findings on slit lamp exam. The cup-to-disc ratio was 0.4 bilaterally with mild-moderate pallor of the left optic nerve. Visual field of the right eye showed diffuse depression. MRI brain with and without contrast demonstrated a 16x19x24 mm heterogenous sellar, suprasellar lesion contiguous with the left optic nerve. Within the mass, there was a non-enhancing T1 and T2 hypointense components thought to be consistent with cystic changes and calcification. The peripheral margins exhibited heterogenous nodular enhancement, which extended through the sellar floor to the sphenoid sinus, involving the left optic chiasm and optic nerve. CT head showed sella and clival erosion, no evidence of sinus disease. These findings were believed to be consistent with an invasive pituitary adenoma. The patient was referred for surgical resection at which point a diagnostic procedure was performed.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“A-Deno What's Going On!”

Answer

Final Diagnosis

Pituitary aspergillosis is rare and presenting symptoms are often indistinguishable from pituitary adenoma1. In both circumstances, the most common symptoms are headache, vision disturbances and endocrinological abnormalities1,2 . Severe to excruciating headache has been reported in up to 87% of patients with pituitary adenoma 3. As such, the preoperative diagnosis of pituitary aspergillosis is difficult, especially in an immune-competent patient without extensive sinus disease. The clinician must have a high degree of suspicion in recurrent cases of pituitary adenoma which were previously treated with radiation, for atypical possibilities. These include infectious processes such as fungal infiltration, in particular in diabetic patients.

Summary of Case

This case highlights the clinical presentation of what appears to be a routine recurrent pituitary adenoma: endocrine abnormalities, headache, and vision loss in a relatively healthy patient with a previous adenoma history. Given her history of radiation to the sella, radiation optic neuropathy was also entertained. However, pathologic specimens collected during subtotal tumor resection demonstrated lymphocytes as well as fungal hyphae, and prominent in areas of necrosis on H & E stained sections. GMS stain highlighted fungal hyphae. Synaptophysin staining showed small nests of anterior pituitary cells and there was no loss of reticulin framework. Such findings do not support a diagnosis of recurrent adenoma or radiation necrosis. Given the predominately septated hyphal fragments and bulbous expansions, a mold organism was at the top of the differential. The patient was started on amphotericin and micafungin to cover aspergillosis and mucor, while fixed tissue samples were processed for PCR. Ultimately, PCR analysis of tissue demonstrated aspergillosis positivity. The patient was transitioned to voriconzale and amphotericin with a targeted duration of treatment of about one year. Interval MRI imaging at month two and three demonstrated stability of disease. At month five, ophthalmology follow-up demonstrated interval improvement of the right visual field.

Struggle/Dilemma of the Clinical Presentation Description

Factors leading to an incorrect preoperative diagnosis were multifactorial, largely driven by the patient’s relatively typical presentation as well as anchoring bias. Given that the patient’s adenoma had previously required resection followed by radiation and the fact that MRI findings showed an enlarged sellar mass compressing the left optic nerve, diagnoses entertained included recurrent adenoma versus radiation optic neuropathy. However, subtle radiologic findings could have pointed to the diagnosis.

Keywords: headaches

References

1. Liu J, You C, Tang J, Chen L. Fungal pituitary abscess: Case report and review of the literature. Neurology India. 2013;61(2):210. https://www.ncbi.nlm.nih.gov/pubmed/23644345. doi: 10.4103/0028-3886.111168. 2. Lee JH, Park YS, Kim KM, et al. Pituitary aspergillosis mimicking pituitary tumor. AJR. American journal of roentgenology. 2000;175(6):1570-1572. https://www.ncbi.nlm.nih.gov/pubmed/11090377. doi: 10.2214/ajr.175.6.1751570. 3. Levy MJ, Matharu MS, Meeran K, Powell M, Goadsby PJ. The clinical characteristics of headache in patients with pituitary tumours. Brain : a journal of neurology. 2005;128(Pt 8):1921-1930. https://www.ncbi.nlm.nih.gov/pubmed/15888539. doi: 10.1093/brain/awh525.

“Go with Your Gut Feeling”

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History & Exam

71 year-old man noticed a ”smudge” in his central vision when reading that was gradually progressing over a year. Medical history was significant for one episode of hemorrhagic colitis requiring colectomy 28 years ago diagnosed as Crohn's disease, atrial fibrillation, and congenital dyschromatopsia. He worked as psychiatrist, did not drink alcohol, and quit smoking many years ago. Vision was 20/80 in the right eye and 20/60 in the left. Formal visual fields were full with bilateral decrease in foveal sensitivity. Foveal granularity was noted and retinal referral was made, however, no evidence of maculopathy was seen by retinologist. One year later, vision changed to 20/50 and 20/300. There was now questionable bilateral optic nerve pallor. CBC, ESR, CRP, ACE, ANA, VDRL, Vitamin B12 and folate were all normal except for mild leukopenia and thrombocytopenia. MRI brain/orbits without contrast was performed and was normal. Testing for LHON was negative. Multifocal ERG showed decreased cone responses. Patient was re-evalauted by the retinal service, but no diagnosis was made. Vision continued to deteriorate to 20/200 and CF a year later. Investigations for neuromyelitis optica (NMO antibody testing with ELISA technique and contrast-enhanced MRI brain/spine) were negative. OCT of the RNFL was normal with no thinning of the papillomacular bundle. Patient was lost to follow-up for 4 years before returning to clinic 7 years after initial presentation, now with 20/400 and CF visual acuities. Visual fields demonstrated larger central scotomas in each eye. RNFL OCT remained unchanged, however, OCT of the macular ganglion cell complex demonstrated severe bilateral thinning. The following tests were performed: CBC, ESR, CRP, ANA, VDRL, ACE, Vitamin B12, Folate, NMO antibodies (cell-based assay technique), anti-MOG antibodies, and MRI brain/orbits/spine with contrast. All testing was negative again except for mild leukopenia and thrombocytopenia. A diagnostic procedure was performed.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

"Go with Your Gut Feeling"

Answer

Final Diagnosis
Bilateral symmetric optic neuropathy secondary to chronic arsenic toxicity.

Summary of Case
Serum heavy metal screening was performed. Unexpectedly, the level of arsenic was 5x upper limit of normal. This was confirmed on repeated testing 1 month later. Patient's partner was tested with normal results. Detailed questioning for possible sources of environmental, occupational, or recreational exposures that would put patient at risk of arsenic exposure were all unrevealing. Since serum arsenic is cleared within 24-48 hours of exposure, there was continuing exposure to arsenic. When asked whether he has any hobbies, patient thought and responded that he goes to his remote cottage weekly. When partner's normal testing was brought up, the patient said that he always goes to his cabin alone. When asked about the water source at the cottage, patient immediately recalled the water was well-sourced and not municipal. Reviewing his medical history, remote history of hemorrhagic colitis requiring colectomy was consistent with acute arsenic poisoning. When deed of purchase for the cottage was located, it was identified that hemorrhagic colitis occurred 3 months after the cottage was was bought 28 years ago. Pathology slides from the colectomy were retrieved and re-examined by several gastrointestinal pathologists who agreed that the samples were not consistent with previous diagnosis of Crohn's colitis. A research laboratory with the capability to perform Total Reflection X-ray Fluorescence (TXRF) was contacted and a sample of the colonic tissue excised 28 years ago was analyzed. Arsenic content of the colon was measured and was found to be 5.9 ppb, 3 to 10 times the mean arsenic concentrations found in visceral organs of normal subjects. Well water from the cottage is currently being tested. In retrospect, persistent mild leukopenia and thrombocytopenia were also consistent with arsenic toxicity. Thus, in this case, chronic exposure to arsenic for 28 years caused slowly progressive toxic optic neuropathy.

Struggle/Dilemma of the Clinical Presentation Description
Optic neuropathy secondary to heavy metal toxicity is not well known and its incidence in the Western world is rare. As a result, screening for heavy metal toxicity is not routinely performed for patients with symmetric optic neuropathies. The paucity of objective abnormalities, and the very long time that elapsed from initial presentation until objective evidence of optic neuropathy was seen, resulted in misdirected investigations into causes of a potential maculopathy.

Keywords: Optic Neuropathy, Afferent visual pathways, Nutritional, Toxic

References
Dang, Jaiswal, Somasundaram. Distribution of Arsenic in Human Tissues and Milk. The Science of the Total Environment, 29, pp 171-175, 1983. Graeme, Pollock. Heavy Metal Toxicity, Part I: Arsenic and Mercury. The Journal of Emergency Medicine, 16(1), pp 45–56, 1998. Vahidnia, van der Voet, de Wolff. Arsenic neurotoxicity - A review. Human & Experimental Toxicology, 26, pp 823–832, 2007.

"Fire and Ice"

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History & Exam

A 14 year-old boy, with ADHD on amphetamine and dextroamphetamine, presented with headache and bilateral decreased vision. Seven days prior, he began experiencing bilateral non-positional frontal headache unresponsive to NSAIDS that did not wake him from sleep. Five days prior, he felt fatigued and noticed blurry vision and decreased color perception. He denied pain on eye movement and ocular tenderness. He was brought to medical attention when he no longer could see the food on his plate. He was camping in the Catskills one week before his headache began; he denied tick bites, fever, URI, nausea, vomiting, diarrhea and stiff neck but had a red, itchy rash on his dorsal foot. There was no history of hypertension, diabetes, heart disease, anemia or recent blood loss. He had no prior history nor a family history of headache. His acuity was HM OD and 20/500 OS, and no control AO/HRR color plates were seen. There were large dense cecocentral scotomas OU. A right RAPD was present. EOMS and saccades were intact. Slit lamp examination was unremarkable OU with normal tensions. There was disc edema and peri-papillary hemorrhages OU with a large peri-papillary cotton-wool spot OD. Retinal veins were engorged OU. MRI of the orbits showed enlarged, enhancing, tortuous orbital and pre-chiasmatic optic nerves, sparing the chiasm, with globe flattening. The brain was normal. Lumbar puncture opening pressure was 180 mm/H2O. There were 3 RBC in the CSF and 12 WBC with 95% lymphocytes, 3% monocytes, 1% neutrophils and 1% eosinophils. CSF glucose was 63, and protein was 31. The CBC revealed a WBC of 10.9 with a differential of 65% neutrophils, 26% lymphocytes, 5% monocytes, 3% eosinophils and 1% basophils. Hemoglobin was 14.3. Hematocrit was 40.1. BUN was 14. Creatinine was 0.47. AST was 33. ALT was 13.

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Grant Support: None.

"Fire and Ice"

Answer

Final Diagnosis
Anti-myelin oligodendrocyte glycoprotein (anti-MOG) sydrome

Summary of Case
He was treated empirically intravenously with acyclovir, ceftriaxone, and 1 gram/day of methylprednisolone. On day two, the patient's vision was correctable to 20/400 OD,and 20/125 OS. Testing returned negative for Lyme, RPR, quantiferon gold, ACE, ANA and anti-double stranded DNA. The CSF returned negative for meningitis and encephalitis panel and Epstein Bar PCR. Vision improved to 20/200 OD and 20/30 OS on day 3. After 5 days of IV methylprednisolone, the patient was discharged on 40 mg oral prednisone. Serum studies sent to the Mayo Clinic returned negative for anti-aquaporin 4 antibodies and positive for anti-myelin oligodendrocyte glycoprotein (anti-MOG) antibodies with titer of 10.8. One week later, his vision was 20/40 OD and 20/20-1 OS. Since return to baseline had not been achieved, prednisone was increased to 60 mg per day for 2 weeks. Two weeks after discharge, his vision was 20/30-2 OD and 20/25+2 OS. Prednisone was reduced to 50 mg per day for 2 weeks followed by a 10 mg taper each week. Acuity at one month from discharge was 20/20+3 OU and 6/6 AO/HRR color plates OU. One month after discharge, repeat MRI of the orbits revealed resolution of optic nerve enhancement and decrease nerve size. Continued immunomodulation was planned.

Struggle/Dilemma of the Clinical Presentation Description
The markedly swollen optic nerves, hemorrhages and CWS OD suggested an aggressive infiltration or aggressive childhood glioma. The longitudinally involvement of the orbital and intracranial nerves sparing the chiasm, however, suggested anti-MOG antibody optic neuritis (ON). Recently 4/47 of anti-MOG optic neuritis patients had disc hemorrhages. Two anti-MOG ON eyes have had neuro-retinitis with disc hemorrhage one having CWS.

Keywords: Autoimmune diseases, Magnetic resonance imaging, optic nerve, Retina, Demyelinating disease

References
Biotti, et al. "Optic Neuritis in Patients with Anti-MOG Antibodies Spectrum Disorder: MRI and Clinical Features from a Large Multicentric Cohort in France." Journal of Neurology, vol. 264, no. 10, pp. 2173–2175, 2017. Chen, et al. "Myelin Oligodendrocyte Glycoprotein Antibody–Positive Optic Neuritis: Clinical Characteristics, Radiologic Clues, and Outcome."American Journal of Ophthalmology, vol 195, pp 8-15, 2018. Lee and Mays. "Anti–Myelin Oligodendrocyte Glycoprotein Optic Neuritis or Neuroretinitis?" JAMA Ophthalmology, vol. 136, no. 10, 2018. Moura, Frederico Castelo, et al. "Anti-MOG (Myelin Oligodendrocyte Glycoprotein)–Positive Severe Optic Neuritis with Optic Disc Ischaemia and Macular Star." Neuro-Ophthalmology, vol. 39, no. 6, pp. 285–288, 2015. Ramanathan, Sudarshini, et al. "Radiological Differentiation of Optic Neuritis with Myelin Oligodendrocyte Glycoprotein Antibodies, Aquaporin-4 Antibodies, and Multiple Sclerosis." Multiple Sclerosis Journal, vol. 22, no. 4, pp. 470–482, 2015.

“Unexplained Become Explained”

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History & Exam

7 years old male presented to the ophthalmology clinic for the evaluation of low vision. He was born with caesarean section after an uneventful pregnancy at 38 weeks, 4.05kg. The mother denied any perinatal hypoxia, ischemia or head injury during delivery. He first visited pediatric neurology clinic for hypotonia at the age of 6 months. He started to walk when he was 18 months. He showed delayed development and have mild intellectual disability with intelligence quotient (IQ) of about 77-80. He is taking methylphenidate for attention deficit hyperactivity disorders. He can communicate well with others and, he can walk and run without any support. Cycloplegic refraction showed –cyl0.50 axis 180 in the right eye and +sph0.50 –cyl0.50 axis180 in the left eye. His best corrected visual acuity was 20/100 in the both eyes. Extraocular motility examination showed full duction and version. Alternate cover test showed orthophoria at distance and near. When covering one eye, jerk nystagmus beating toward uncovered eye was noted, which is consistent with latent nystagmus. Slit lamp examination showed normal, and dilated fundus examination revealed diffuse optic atrophy in both eyes. Spectral-domain optical coherence tomography showed thinning of retinal nerve fiber layer in both eyes. Electroretinography with skin electrode was performed and the results was inconclusive. Brain magnetic resonance imaging was not remarkable. Biochemistry test showed normal lactate to pyruvic acid ratio. Neurological examination showed normal cerebellar function and gait. Other cranial nerve examination was normal. Further diagnostic testing was then performed.

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"Unexplained Become Explained"

Answer

Final Diagnosis

Bosch-Boonstra-Schaaf optic atrophy syndrome (BBSOAS)

Summary of Case

Targeted next-generation sequencing was performed on genomic DNA obtained from patient's blood. We foundnovel heterozygous NR2F1c.513C>G:p.Tyr171Ter nonsense mutation (MIM 132890, RefSeq accession number NM_005654.4). This variant has not been found in any genomic database (1000Genome, Exome Variant Serer, ExAC Browser or gnomAD Browser, accessed in September 2018). The c.513C>G mutation is located in functional DNA-binding domain, and it was ascribed to be pathogenic according to American College of Medical Genetics Guidelines and in silicopredictions (CADD:37, FATHMM:0.9857). In light of molecular genetic testing, Bosch-Boonstra-Schaaf optic atrophy syndrome (BBSOAS) was diagnosed. BBSOAS is an autosomal dominant disorder characterized by delayed development, moderate intellectual disability, and optic atrophy. Bosch et al. reported 6 unrelated patients with optic nerve atrophy associated with developmental delay and intellectual impairment. NR2F1encodes a conserved orphan nuclear receptor protein, and it is mainly expressed at high levels in the optic nerve, thalamus, and pallidum. NR2F1 has a nuclear receptor structure with two main domains, a functional DNA-binding domain and a ligand-binding domain with two highly conserved sequence regions. This protein is important for neurodevelopment, including oligodendrocyte differentiation, cortical patterning, guidance of thalamocortical exon, and optic nerve development. Ophthalmologic abnormalities in BBSOAS showed variable optic disc abnormalities, including optic nerve hypoplasia, pale discs, and disc excavation. In addition to visual and cognitive dysfunctions, patients with BBSOAS manifested hypotonia (75%), seizures (40%), autism spectrum disorder (35%), oromotor dysfunction (60%), thinning of corpus callosum (53%), and hearing deficits (20%). The recognition of this rare clinical syndrome had implications for avoiding unnecessary numerous investigation and genetic counselling, as it was reported as developmental anomaly, not a progressive in nature.

Struggle/Dilemma of the Clinical Presentation Description

Optic nerve atrophy in children can be caused by trans-synaptic degeneration as a part of cortical visual impairment or genetic causes. Several syndromic forms of optic neuropathy are known, so accurate diagnosis is difficult. In addition, existence of neurological features in some mitochondrial optic neuropathies such as LHON-plus or DOA-plus create an initial diagnostic dilemma. Comprehensive genetic testing using targeted panel can lead to the correct diagnosis.

Keywords: Optic atrophy, Optic Neuropathy, Hereditary, Cerebral blindness, Developmental and congenital anomalies

References

1. Bosch DG, Boonstra FN, Gonzaga-Jauregui C, Xu M, de Ligt J, et al. NR2F1 mutations cause optic atrophy with intellectual disability. Am J Hum Genet 2014, 94(2):303-309. 2. Yamaguchi H, Zhou C, Lin SC, Durand B, Tsai SY, et al. The nuclear orphan receptor COUP-TFI is important for differentiation of oligodendrocytes. Developmental biology 2004, 266(2):238-251. 3. Chen CA, Bosch DG, Cho MT, Rosenfeld JA, Shinawi M, el al. The expanding clinical phenotype of Bosch-Boonstra-Schaaf optic atrophy syndrome: 20 new cases and possible genotype-phenotype correlations. Genet Med 2016, 18(11):1143-1150. 4. Kaiwar C, Zimmermann MT, Ferber MJ, Niu Z, Urrutia RA, et al. Novel NR2F1 variants likely disrupt DNA binding: molecular modeling in two cases, review of published cases, genotype-phenotype correlation, and phenotypic expansion of the Bosch-Boonstra-Schaaf optic atrophy syndrome. Cold Spring Harb Mol Case Stud 2017, 3(6). 5. Al-Kateb H, Shimony JS, Vineyard M, Manwaring L, Kulkarni S, et al. NR2F1 haploinsufficiency is associated with optic atrophy, dysmorphism and global developmental delay. Am J Med Genet A 2013,161a(2):377-381.

“A Trip Through the Wormhole”

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History & Exam

The patient initially presented to me at age 19 years with a "throbbing, aching pressure" behind her right eye and swelling of the right upper eyelid. Her pain was worse in lateral gaze, although she denied diplopia. She had been prescribed 60mg of prednisone by the referring provider, which reduced the swelling but not the degree of soreness. A review of the chart indicated that she had been having similar symptoms intermittently for eight years. Her visual acuity was 20/15 in the right eye, 20/20 in the left eye. Her pupils were briskly reactive; there was no relative afferent pupillary defect. Color vision was intact in both eyes. She had -1 adduction and abduction deficits in her right eye; her ductions were otherwise full. Exophthalmometry measured the right eye as 2mm more proptotic than the left eye. There was no lid lag in downgaze and no resistance to retropulsion on either eye. The right upper eyelid was 1mm more ptotic than the left. On slit lamp examination she had episcleral and scleral injection laterally on the right eye without chemosis. The remainder of the slit lamp and fundus examinations were unremarkable.

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Grant Support: None.

"A Trip Through the Wormhole"

Answer

Final Diagnosis
Orbital cysticercosis

Summary of Case
A 21 year-old Filipino woman had recurrent orbital inflammation for 10 years. She first presented to her pediatrician at age 11 years with intermittent swelling of her right cheek and lower eyelid. CT scan showed soft tissue swelling and sinusitis; MRI showed similar findings. She underwent a biopsy that confirmed chronic sinusitis. For the next two years, her symptoms persisted. An MRI was repeated and showed enlargement of the right medial and inferior rectus muscles with a "tiny rim-enhancing fluid collection along the belly of the medial rectus adjacent to the optic nerve." Given her orbital findings and history of sinusitis, she was referred to rheumatology to assess for granulomatous polyangiits (GPA). It was determined that GPA was unlikely and orbital biopsy was recommended. Three years after initial presentation she underwent a right orbital biopsy that showed only non-granulomatous inflammation. For the next five years she continued to have intermittent flares of subcutaneous nodules on her forehead, scalp, ear, and eyelids that were treated with pulse doses of steroids. She declined repeat biopsy and was transitioned to methotrexate, but she would continue to have flares of orbital inflammation. Ten years after initial presentation, she agreed to repeat orbital biopsy. Pathology showed only "focal patchy inflammation consisting of neutrophils, eosinophils, and lymphocytes." She declined further surgery and continued on methotrexate until April 2018, when she underwent a third orbital biopsy. A larval form consistent on pathologic examination with cysticercosis was extracted from the superonasal orbit, not contiguous with an extraocular muscle. The patient underwent treatment with albendazole and prednisone and had resolution of symptoms.

Struggle/Dilemma of the Clinical Presentation Description
Recurrent orbital inflammation incompletely responsive to treatment with prednisone and methotrexate.

Keywords: Orbital inflammation, infection

References
None.

“Three's a Crowd”

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History & Exam

A 2 year-old male boy was referred for painless, progressive proptosis in the right eye over a one year. The patient had no history of trauma, personal or family history of malignancy, or orbital inflammation, and had an unremarkable past medical history. On exam, the patient had fix and follow vision OU with no APD, and normal IOP of 16 and in both eyes. Motility exam demonstrated moderate deficits in all fields of gaze in the right eye, and were normal in the left eye. External exam noted subtle axial proptosis in the right eye. Slit lamp and dilated fundus exam were normal for both eyes. A fat-suppressed orbital MRI scan showed enlargement of all extraocular muscles in the right eye and significant orbital congestions with straightening of the optic nerve and axial proptosis without significant globe deformation. Laboratory workup was unrevealing with normal CBC, thyroid panel, IgG panel, lysozyme, and angiotensin-converting enzyme. An anterior orbitotomy with right lateral rectus muscle incisional biopsy was performed. Intraoperatively, the muscle was thick and difficult to cut. The tissue demonstrated low-grade spindle cell fibrosis based on trichrome Masson stain without significant nuclear pleomorphism or mitotic activity, confirmed with a Ki-67 index of less than 1%. Immunohistochemical stain were diffusely positive for vimentin and CD34, and negative for beta catenin, S-100 protein, ERG and BCL-2. The patient was monitored for several months with stable proptosis, motility limitations and vision. As the child aged, the child was noted to have a high astigmatism OD, managed with spectacles and patching. Serial MRIs were performed with stable right orbital findings. Interval dilated fundus exam revealed no optic nerve edema or atrophy. The decision was made to continue to monitor, given the stability and good vision.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

"Three's a Crowd"

Answer

Final Diagnosis
Diffuse-type Infantile Orbital Fibromatosis

Summary of Case
A 2 year-old male with painless, progressive proptosis and motility deficits in the right eye over a one year period transferred to our hospital for diagnosis and management. MRI Brain and orbits imaging demonstrated multiple right extraocular muscles enlargement. With a negative laboratory work-up, an extraocular muscle biopsy with histopathology examination indicated a diffuse-type spindle cell tumor. Instead of debulking the muscles, the patient has been observed with stable proptosis, motility deficits and vision.

Struggle/Dilemma of the Clinical Presentation Description
To our knowledge, this is the first case of diffuse-type infantile orbital fibromatosis. Given the patient's age, this case illustrates the difficulty in identifying an undescribed clinical disease that masquerades as a more common disease. The clinical presentation, neuroimaging, and negative laboratory workup supported the decision for an incisional biopsy. Histopathology examination established a definitive diagnosis of diffuse-type infantile fibromatosis. The clinical course, management, and treatment of this diagnosis is not defined in pediatric cases.

Keywords: Fibrous dysplasia, Orbit, Pediatric

References
1. Moro A, De Angelis P, Gasparini G, et al. Orbital Desmoid-Type Fibromatosis: A Case Report and Literature Review. 2013. 2. Hidayat AA, Font RL. Juvenile Fibromatosis of the Periorbital Region and Eyelid: A Clinicopathologic Study of Six Cases. Arch Ophthalmol. 1980;98(2):280-285. 3. Hayashi K, Katori N, Otsuki Y, Ohno-Matsui K. Clinicopathological study of three cases of infantile fibromatosis of the orbit. Int Ophthalmol. 2014;34(5):1097-1106. 4. Campbell RJ, Garrity JA. Juvenile fibromatosis of the orbit: A case report with review of the literature. Br J Ophthalmol. 1991;75(5):313-316. 5. Hartstein ME, Thomas SM, Ellis LS. Orbital desmoid tumor in a pediatric patient. Ophthal Plast Reconstr Surg. 2006;22(2):139-141.

"Don't Drink the Water"

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History & Exam

A 19-year-old right-handed man presented with a 3 year history of episodic headaches, right hemiparesis, and progressive vision loss OU. Beginning in the fall of 2015, he developed stepwise deterioration in vision OU in association with severe headaches. Initial evaluation at an outside hospital showed VA 20/40 OD and 20/50 OS with bilateral optic disc pallor. MRI of the orbits showed no abnormalities. VA worsened to 20/200 OU by January 2016 and fields showed central scotoma OU and a left homonymous hemianopia. LHON testing was negative. CSF analysis showed 1 WBC, protein 36 mg/d, IgG index 0.66 (<0.6), (+) oligoclonal bands, with negative AFP, cytology, and Lyme. He was started on IV followed by oral steroids in February 2016 with improvement in the visual field, but no improvement in VA. Mycophenolate was started on April 2016 with no improvement and therefore discontinued. He continued having attacks of nausea, headache, worsening vision, and then developed right hemiparesis. Repeat orbital MRI in March 2017 showed left optic nerve enhancement. In April 2017 he was started on rituximab, but became lethargic after the second infusion, and his neurological status deteriorated after the third infusion (October 2017). He began behaving unusually – saying inappropriate things and developed excessive thirst that led to drinking toilet water. In November of 2017 he developed left-sided weakness and became wheelchair bound. Repeat orbital MRI showed persistent left optic nerve enhancement and T2 hyperintensity of the right basal ganglia and cortical spinal tracts. His cognition declined thereafter to the point that he had difficulty expressing himself. In March 2018, on presentation to our institution, he was unable to follow commands, had severe cognitive impairment and spasticity throughout. VA was LP OU. Pupils were minimally reactive to light. Dilated funduscopic exam showed severe bilateral optic nerve pallor with normal retina.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

"Don't Drink the Water"

Answer

Final Diagnosis
Germinoma with bilateral optic nerve infiltration

Summary of Case
Cranial and orbital MRI showed marked evolution of thickening and enhancement of the left optic nerve, diffuse T2 signal change in the white matter including corpus callosum and internal capsule extending through the brainstem, patchy multifocal T2 signal change in the brainstem, evolution of encephalomalacia in the left cerebral peduncle, and contrast enhancement of cranial nerves 3 and 6. Repeat CSF analysis showed 7 oligoclonal bands, an elevated IgG index of 1.0, 2 WBCs, and mild elevation in total protein at 51. CSF cytology and autoimmune encephalopathy panel were negative. Serum AFP was 2.9 (nl <6) and beta HCG 1.2 (nl <1.4). CSF beta human chorionic gonadotropic was 3.5 (nl <1) and AFP was < 0.5. Free thyroxine was 0.8, Testosterone was 270. Prolactin was 17.4 (nl 4-15.2). Morning cortisol was 6.4 (nl 7-25). Desmopressin led to improvement in his polydipsia and polyuria and he was felt to have central diabetes insipidus. Full body positron emission tomography scan that revealed no evidence of fluorodeoxyglucose (FDG)-avid malignancy. There was mild FDG activity associated with the left optic nerve. The next step was to proceed with a tissue diagnosis at the most likely highest yield site with lowest risk – the left optic nerve. The pathologic findings from the left optic nerve biopsy were consistent with germinoma. The nerve was completely replaced by a population of neoplastic cells with large nuclei with prominent nucleoli and abundant pale eosinophilic to clear cytoplasm. The cells expressed the germ cell markers (i.e. PLAP, Oct4 and SALLA4) with a small number of T lymphocytes present. Only a minimal number of optic nerve fibers remained at the periphery of the nerve (as outlined on the pathology slides by NF & LFB/PAS stains).

Struggle/Dilemma of the Clinical Presentation Description
Despite presenting in 2015 with severe optic nerve pallor OU, orbital MRI at that time did not show optic nerve enhancement. The optic nerve didn't enhance on imaging until 2017 and only affected the left optic nerve, despite bilateral vision loss. An infiltrative process is expected to show enhancement at onset and be present bilaterally as both were affected clinically. Ultimately, the optic nerve findings didn't help the diagnosis until biopsy.

Keywords: optic nerve, Tumor, Optic atrophy

References
None.

“Every Rose Has Its Thorn”

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History & Exam

A 26-year-old woman presented with a one-year history of horizontal binocular diplopia on far-right gaze. During a routine eye examination for contact lenses, she was found to have a gaze paretic nystagmus on far-right gaze. The patient also offered a one-year history of right-sided instability and balance issues. MRI was done, and she was admitted to our institution for further evaluation and management. Further history revealed that she experienced diplopia in primary position after running a mile. She denied headache, nausea, vomiting, and other visual symptoms. She denied antecedent trauma or illness. She denied variability of diplopia or associated ptosis. Neuro-ophthalmologic examination showed 20/20 vision bilaterally, with normal pupils and color vision. External examination revealed mild orbicularis weakness. Corneal sensation was mildly reduced in both eyes. Motility showed a mild right esotropia on right gaze from a subtle sixth nerve paresis. There was a gaze paretic nystagmus in right gaze as well. Slit lamp examination was normal. Fundus examination was normal with pink optic nerves. General neurologic examination showed no other focal deficits. MRI was reviewed; CT head and MRI spine were additional tests performed. Spinal fluid analysis was not done because of concerns for herniation. Numerous laboratory studies were performed. A diagnostic procedure was performed.

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Grant Support: None.

"Every Rose Has Its Thorn"

Answer

Final Diagnosis

Rosette-forming glioneuronal tumor (although another low grade glioneuronal tumor could not be negated)

Summary of Case

The MRI brain showed multiple T1 hypointense T2 hyperintense cystic lesions within the posterior fossa involving the cerebellar vermis, right cerebellar hemisphere, and brainstem. Possible scolices were identified within multiple cysts on T1 images, leading to a high suspicion for parasitic infection, specifically neurocysticercosis (NCC). MRI of the spine showed similar intramedullary lesions extending from brainstem to involve the upper cervical spinal cord. CT of the head demonstrated a single area of calcification in the right cerebellum. An extensive infectious disease, auto-immune, and paraneoplastic evaluation was pursued. Consultation with neurocysticercosis experts at the CDC was obtained. The possibility of coenurosis secondary to Taenia multiceps, T. serialis, T. brauni, or T. glomerata was considered as well. Infectious workup for Echinoccocus, Toxoplasmosis, and TB was negative. Stool ova and parasites was similarly negative. Serum testing for NCC with enzyme-linked immunoelectrotransfer blot (EITB) was sent to the CDC. Auto-immune and paraneoplastic work up were negative. Treatment for a presumed parasitic infection with anti-helminthic therapy after steroid pre-treatment was entertained. However, after further discussion with the CDC, this option was reevaluated due to the high lesion burden and potential massive inflammatory response. There was also growing skepticism for a parasitic etiology of the lesion, a biopsy was obtained for definitive diagnosis. Pathology was diagnostic for a low grade glioneuronal tumor with characteristics suggestive of a rosette-forming glioneuronal tumor (RGNT). Some cells showed oligodendroglioma-like features, however this was ruled out based on the absence of 1p 19q codeletion on chromosomal microarray. RGNT is a glioneuronal tumor that may show oligodendroglioma-like areas and is found in the fourth ventricle, and rare RGNT cases have been reported with similar multi-loculated gross and radiologic morphology. However, this potential diagnosis could not be definitively established on histopathology as the tumor failed to show characteristic rosettes with synaptophysin positive cores.

Struggle/Dilemma of the Clinical Presentation Description

Both neurocysticercosis and glioneuronal tumors can have similar radiographic features with calcifications and multiple cystic lesions in the posterior fossa. The suggestion of possible scolex within multiple cysts on MRI and exposure to a household contact who traveled to a disease-endemic area strongly favored parasitic infection. After extensive laboratory workup was unrevealing and consultation with the CDC, only biopsy of the lesion confirmed the lesion as a low grade glioneuronal tumor.

Keywords: infection, Tumor, Nystagmus

References

1. Yang C, Fang J, Li G, Li S, Ha T, Wang J, et al. Histopathological, molecular, clinical and radiological characterization of rosette-forming glioneuronal tumor in the central nervous system. Oncotarget. 2017;8(65):109175-90. 2. Medhi G, Prasad C, Saini J, Pendharkar H, Bhat MD, Pandey P, et al. Imaging features of rosette-forming glioneuronal tumours (RGNTs): A Series of seven cases. Eur Radiol. 2016;26(1):262-70. 3. Zhang J, Babu R, McLendon RE, Friedman AH, Adamson C. A comprehensive analysis of 41 patients with rosette-forming glioneuronal tumors of the fourth ventricle. J Clin Neurosci. 2013;20(3):335-41. 4. Marhold F, Preusser M, Dietrich W, Prayer D, Czech T. Clinicoradiological features of rosette-forming glioneuronal tumor (RGNT) of the fourth ventricle: report of four cases and literature review. J Neurooncol. 2008;90(3):301-8. 5. Gao L, Han F, Jin Y, Xiong J, Lv Y, Yao Z, et al. Imaging features of rosette-forming glioneuronal tumours. Clin Radiol. 2018;73(3):275-82. 6. Kim SW, Kim MK, Oh SM, Park SH. Racemose cysticercosis in the cerebellar hemisphere. J Korean Neurosurg Soc. 2010;48(1):59-61.

"Not the Rolling Stones"

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History & Exam

A 68-year-old woman presented to the clinic complaining of "bouncing" vision when waking up at night for one month. Two years ago, she experienced discrete episodes of spinning for seconds provoked by head movements, which resolved spontaneously. Her ocular motor and vestibular exams were normal aside from apogeotropic nystagmus (brought on by roll more than Dix-Hallpike testing), most intense in right roll test (Figure 1). The general neurological examination was unremarkable except for mild difficulty in tandem gait. She was diagnosed with apogeotropic horizontal canal (HC) benign paroxysmal positional vertigo (BPPV) and underwent treatment with repositioning maneuvers and head-shaking in the clinic and with vestibular PT, although there was no change in symptoms or nystagmus. Given refractory positional nystagmus, contrast-enhanced MRI of the brain was ordered and was unremarkable. Over the next several weeks, balance worsened, positional symptoms persisted, and dizziness was experienced constantly without provocation. Examination was now notable for gaze-evoked with rebound nystagmus, saccadic smooth pursuit and VOR suppression, horizontal head shaking induced downbeat nystagmus and ataxic gait. Positional apogeotropic nystagmus was still present. Paraneoplastic panel was unrevealing (ANNA-1/2/3, PCA-1/2/Tr, Amphiphysin, CRMP-5, VGKC, VGCC, GAD-65, Ma/Ta and ZIC4), as was CT chest, abdomen and pelvis and other labs to investigate a progressive cerebellopathy (negative/normal CRP, ESR, Vitamins B1/B12/ E, Cu, celiac panel, anti-TPO, HIV and +ANA titer of 1:320, which was a chronic finding). Given continued deterioration, she was admitted for expeditious LP and PET scan. Repeat contrast-enhanced brain MRI was normal. Lumbar puncture demonstrated normal WBC, protein and glucose levels. Extensive CSF studies were negative including: gram stain, Cryptococcus, VDRL, HSV/CMV/VZV PCR, WNV-IgG, Mycobacteria/Whipple's PCR, Oligoclonal IgG, Autoimmune panel, Cytology and Flow cytometry. She underwent whole-body FDG-PET that was notable for symmetric cerebellar hypometabolism (Figure 2). Further diagnostic testing was performed.

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"Not the Rolling Stones"

Answer

Final Diagnosis
Sporadic Creutzfeldt-Jakob disease (sCJD)

Summary of Case
A 68 yo female initially presented with BPPV-like symptoms and nystagmus, but then developed a progressive cerebellopathy over two months. Extensive infectious, paraneoplastic and inflammatory studies of serum and CSF were unremarkable. FDG-PET was notable for symmetric cerebellar hypometabolism (Figure 2). Although there was nothing clearly indicative of an autoimmune process (i.e., negative paraneoplastic/autoimmune panel, absence of CSF pleocytosis), given the potential to decrease morbidity and mortality, she was treated empirically with methylprednisolone followed by IVIg, without improvement. New ocular motor findings at that time included bilaterally abnormal head impulse testing (with relative sparing of vertical canals), divergence insufficiency, and centripetal nystagmus. She was then discharged for rehabilitation. She continued to deteriorate neurologically, which led to readmission. Her Montreal Cognitive Assessment score declined from 25/30 (first admission) to 20/30, and myoclonic jerks were apparent. The constellation of rapidly progressive dementia (RPD), visual symptoms, ataxia and myoclonus, were highly concerning for Creutzfeldt-Jakob disease (CJD). A third brain MRI was notable for subtle patchy thalamic T2/FLAIR hyperintensities with restricted diffusion (figure 3). Continuous EEG monitoring revealed left posterior temporal sharp waves. Repeat LP demonstrated tau protein (>4000 pg/ml, reference range 0-1149), positive 14-3-3 protein and positive Real-time quaking induced conversion (RT-QuIC), confirming the diagnosis of CJD. She was transitioned to hospice and passed away 6 months after experiencing the initial positional symptoms. An autopsy was performed, and the pathology report is pending at this time (this will be Figure 4).

Struggle/Dilemma of the Clinical Presentation Description
The patient presented with positional vertigo and nystagmus that appeared benign, although red flags were soon apparent. There was no response to repeated repositioning maneuvers, and ocular motor abnormalities developed. This prompted further testing including brain MRI (normal) and FDG-PET, which showed symmetric cerebellar hypometabolism that could have been indicative of autoimmune encephalitis or CJD. The patient deteriorated despite immunotherapy. Eventually, abnormal MRI, her clinical exam/course, and a positive RT-Quic confirmed CJD.

Keywords: Vertigo, Eye movements, Cerebellum, Creutzfeld-Jacob disease

References
1. Seung-Han Lee, Sang-Jun Park, Jae-Hwan Choi, Tai-Seung Nam, Central Positional Nystagmus Associated with Cerebellar Tumors, Neurology, Volume 86, 16 Supplement, 2016. 2. Jeong-Yoon Choi, Ji Hyun Kim, Hyo Jung Kim, Stefan Glasauer, Ji-Soo Kim, Central Paroxysmal Positional Nystagmus - Characteristics and Possible Mechanisms, Neurology, Volume 84, Page 2238-46, 2015 3. Aaron Foutz, Brian S. Appleby, Clive Hamlin, Xiaoqin Liu, Sheng Yang et al, Diagnostic and Prognostic Value of Human Prion Detection in Cerebrospinal Fluid. Annals of Neurology, Volume 81, Page 79-92, 2017. 4. Brian S. Appleby, Kristin K. Appleby, Peter V. Rabins, Does The Presentation of Creutzfeldt-Jakob Disease Vary By Age of Presumed Etiology? A meta-analysis of the past 10 years, The Journal of Neuropsychiatry and Clinical Neurosciences, Volume 19, Page 428-435, 2007.

"Fooled Thrice"

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History & Exam

A 40-year-old healthy man presented with a one-month history of left ptosis and binocular horizontal diplopia. Examination revealed normal afferent visual function. He had left ptosis and there was limitation of elevation, depression, adduction and a dilated, sluggishly reactive pupil in the left eye. CT angiogram was normal and MRI of the brain with contrast revealed an enhancing mass extending along the course of the left oculomotor nerve suggestive of a schwannoma. Lumbar puncture was normal and neurosurgery advised against biopsy. He received fractionated radiation therapy (50Gy) and a short-course of dexamethasone for a presumed left oculomotor nerve schwannoma and his ptosis and diplopia started to improve two weeks after treatment. Follow-up MRI six months after treatment showed further decrease in the size of the lesion and his diplopia in primary position resolved. Eighteen months after treatment, his double vision returned and repeat MRI demonstrated stability in the size of the cisternal portion, but an increase in the size of the cavernous and intra-orbital portion of the left oculomotor nerve mass. Due to the relatively prompt response to radiation and dexamethasone, the possibility of an inflammatory lesion was considered. An extensive workup including CT of the chest/abdomen/pelvis was normal. He was also started on mycophenolate mofetil as he did not tolerate corticosteroids well. One month later, he suddenly lost vision in his left eye and examination revealed hand motions vision with a left relative afferent pupillary defect, left ptosis and complete left ophthalmoplegia. The right eye had normal visual acuity and motility. Repeat MRI demonstrated interval enlargement of the mass with compression of the left optic nerve at the orbital apex. Repeat lumbar puncture was normal and after 5 days of high-dose intravenous methylprednisolone, his vision in the left eye worsened to no light perception. A diagnostic procedure was performed.

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Grant Support: None.

"Fooled Thrice"

Answer

Final Diagnosis
Malignant oculomotor nerve sheath tumor

Summary of Case
He underwent left orbital apex decompression and biopsy of the lesion. Pathology revealed a high-grade malignant peripheral nerve sheath tumor. There was a fascicular architecture with staghorn-like vasculature, heterologous cartilage formation, and high mitotic activity. After tissue diagnosis, mycophenolate and corticosteroids were stopped. Whole-body PET-CT was performed and was negative for metastatic disease. After extensive discussion among multiple services, he underwent resection of the tumor via a left cranio-orbital zygomatic craniotomy with extradural clinoidectomy and exenteration of the frontal and ethmoidal sinuses and orbit. The tumor surrounded the carotid artery and extracapsular dissection was not possible. One month after surgery, repeat MRI revealed that the tumor had significantly increased in size particularly in the region of the left cavernous sinus. Due to the aggressive nature of the tumor, further surgery was not recommended and he underwent fractionated radiation therapy over 6 weeks and received two doses of cisplatin. Follow-up MRI one month after radiation and chemotherapy demonstrated decreased tumor size in the region of the left sella and cavernous sinus. The visual function in his right eye remained normal. This malignant tumor was likely present initially and the radiation therapy produced a response large enough to improve his symptoms, but insufficient to eradicate the tumor. This resulted in a recurrence of his symptoms 18 months after radiation therapy. Although a malignant transformation was possible, the unusual reduction in size seen after his initial treatment and the relatively short latency period argued against this. Malignant oculomotor nerve sheath tumors are extremely rare and have been reported in a 9-year-old boy with additional cranial nerve schwannomas [1] and a 72-year-old man with a complete, pupil-sparing oculomotor nerve palsy that completely resolved after surgical resection.[2]

Struggle/Dilemma of the Clinical Presentation Description
We were thrice fooled by his third nerve palsy. First, aneurysmal compression had to be promptly ruled out. Second, despite the classic MRI appearance of a benign schwannoma, our patient's recurrence of diplopia and rapid growth of the oculomotor nerve mass over one year after radiation therapy, raised doubt as to that diagnosis. Third, the quick initial response to radiation/dexamethasone raised the possibility of an inflammatory lesion, but he worsened with immunosuppressive therapies.

Keywords: 3rd Nerve palsy, Radiation

References
1. Kozic D, Nagulic M, Ostolic J, et al. Malignant peripheral nerve sheath tumor of the oculomotor nerve. Acta Radiol 2006;47(6):595-8. 2. Fard MA, Montgomery E, Miller NR. Complete, pupil-sparing third nerve palsy in a patient with a malignant peripheral nerve sheath tumor. Arch Ophthalmol 2011;129(6):813-4.

"At the Crossroads"

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History & Exam

A 54-year-old female former smoker presented with vertical diplopia, left facial pain and left forehead weakness. She previously had thyroidectomy for a noncancerous nodule and abdominal hysterectomy for fibroids. She reported a two-year history of worsening facial pain and numbness that started as a sore spot above the left eyebrow, and over months progressed to involve the left forehead and cheek. This pain was initially responsive to steroids but became persistent, severe, and unresponsive to treatment. Within a few months of the onset of the pain, the patient developed oblique binocular diplopia that also worsened over time. In addition, she lost the ability to move the forehead on that side, although the rest of the face appeared normal. Exam was notable for left-sided cranial nerve findings: partial CNIII palsy, complete CNIV and CNVI palsies, left-sided hypesthesia in the V1-2 distribution, and weakness of the temporal branch of left frontal nerve. Later, left eye chemosis, injection and inferior keratopathy were also present. Skin and ENT exams were normal. MRI with contrast revealed asymmetric enhancement of left cavernous sinus; on further review there was extension along the left frontal and vidian nerves. CT chest/abdomen/pelvis showed a benign hepatic cyst. PET scan only showed reduced uptake in the extraocular muscles, secondary to the cranial nerve palsies. An extensive laboratory work-up was unrevealing, including serologies for connective tissue diseases, ANCA, sarcoidosis, Lyme and syphilis. Four lumbar punctures yielded normal CSF and cell counts, including cytology and flow. The patient and was managed with escalating doses of steroids, which were initially given orally but then transitioned to IV. She was admitted to an outside hospital for severe refractory pain, and transferred to our institution. A diagnostic left frontal nerve biopsy was obtained, and showed moderately differentiated, keratinizing squamous cell carcinoma with intraneural and perineural involvement.

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Grant Support: None.

"At the Crossroads"

Answer

Final Diagnosis
Intracranial squamous cell carcinoma with unknown primary origin, which in addition to involvement of the cranial nerves in the cavernous sinus (III, IV, VI, V1, V2) included branches of the ipsilateral facial nerve.

Summary of Case
A middle-aged former smoker developed progressive facial pain associated with an unusual combination of involvement of the ipsilateral cranial nerves (CNs) in the cavernous sinus (III, IV, VI, V1, V2) and branches of the ipsilateral facial nerve. Her presentation was initially steroid responsive, though the diplopia and facial pain continued to progress. MRI showed contrast enhancement of the cavernous sinus, and on further review, involvement of the ipsilateral frontal and vidian nerve was appreciated. The vidian nerve likely served as a conduit for facial nerve involvement. Workup was initially unrevealing, and for two years, the diagnosis remained idiopathic cavernous sinus inflammation (Tolosa-Hunt syndrome). After the pain became uncontrollable with IV steroids and narcotics, a left frontal biopsy which yielded the diagnosis of squamous cell carcinoma (SCC) infiltrating multiple CNs. Neither dermatologic nor otolaryngologic evaluation revealed an obvious primary, thus this is presumed to be primary intracranial SCC. Intracranial SCC with unknown primary origin is a rare condition that presents insidiously with multiple cranial nerve involvement and facial pain without systemic manifestations. The rarity of this diagnosis, initially subtle clinical findings and equivocal imaging studies can delay appropriate diagnosis and treatment of such cases (Bourque et al, 2017)[1]. Histopathologic evidence of neural involvement portends a poor prognosis (Erkan et al, 2017)[2]. We believe this to be an extraordinary case of primary intracranial involvement with a unique pattern of cranial nerve abnormalities.

Struggle/Dilemma of the Clinical Presentation Description
This case of intracranial squamous cell carcinoma of unknown primary origin and an unusual pattern of multiple cranial nerve manifestations presented a formidable diagnostic challenge, with an initially extensive negative workup.

Keywords: Intracranial tumors, Cranial nerve palsies, Facial pain, Perineural invasion

References
[1] Pierre R Bourque and others, '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, 2017 <http://dx.doi.org/https://doi.org/10.1016/j.jocn.2016.09.022>. [2] Serkan Erkan and others, 'Clinical Perineural Invasion of the Trigeminal and Facial Nerves in Cutaneous Head and Neck Squamous Cell Carcinoma: Outcomes and Prognostic Implications of Multimodality and Salvage Treatment', Head and Neck, 2017 <http://dx.doi.org/10.1002/hed.24607>.

"Just the Two of Us"

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History & Exam

A 63-year-old female patient of Chinese ethnicity was referred for unexplained visual loss in her right eye, discovered incidentally 1 month before presentation. Her past medical history revealed quiescent asthma and a benign cyst in the left lung, excised 27 years earlier. The patient had no vascular risk factors and was not smoking. On examination, best-corrected vision was counting fingers in the right eye and 6/7.5 in the left eye, associated with severe color vision loss in the right eye. There was a dense right relative afferent pupillary defect, but the remainder of the neuro-ophthalmic examination was normal, including fundoscopy, ocular motility and other cranial nerves functions. There was a dense visual field defect in the right eye and a Cirrus OCT disclosed normal retinal nerve fiber layer thickness in both eyes. The presumptive diagnosis was unexplained right retrobulbar optic neuropathy. A brain MRI disclosed an enhancing mass involving the anterior right clivus and apex, infiltrating the ipsilateral cavernous sinus, highly suggestive of meningioma. Excision of the tumor was decided by the neuro-surgical team, and pathology confirmed a WHO Grade III parapapillary chordoid meningioma. Post-operatively, the patient had an ispilateral iatrogenic pupil-involving 3rd nerve palsy, an ipsilateral 4th nerve palsy and developed a right soleal vein thrombosis, treated symptomatically. However, the patient's main post-operative complaint was persistent coughing.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

"Just the Two of Us"

Answer

Final Diagnosis
Intra-meningioma tumor-to-tumor metastasis of previously undiagnosed lung adenocarcinoma.

Summary of Case
The persistent coughing prompted re-evaluation of the pre-operative chest X ray, which disclosed non-specific nodules. A chest CT-scan showed multiple pulmonary nodules and confluent mediastinal lymphadenopathies consistent with a metastatic process. A whole body PET scan confirmed hypermetabolic enlarged bilateral hilar and mediastinal lymphadenopathy and FDG-avid right supraclavicular lymph nodes. Bronchoscopy with broncho-alveolar lavage was performed, completed by trans bronchial needle aspiration, revealing a tumour with cribriform and papillary architecture, positive for TTF1 and CK7, confirming the diagnosis of lung adenocarcinoma. The initial meningioma diagnosis was challenged and reviewed, confirming presence of meningothelial cells, but also showing evidence of additional intrameningeal metastatic adenocarcinoma, suggesting a final diagnosis or tumour-to-tumour metastasis. The papillary/glandular portion of the meningeal tumor was indeed identical (positive CK7, TTF-1 and Napsin) with the sample analyzed in the lung biopsy. The patient declined chemotherapy, but underwent adjuvant brain radiotherapy (60Gy, 30 fractions). Five months post-operatively, the patient recovered 6/12 vision in the previously blind eye and visual fields improved significantly. Sequential follow-up brain MRIs over 6 months showed no recurrence of the tumor.

Struggle/Dilemma of the Clinical Presentation Description
The patient was initially diagnosed incorrectly (or rather incompletely) with meningioma, due to the radiological MRI appearance of the lesion and to the imperfect pathology evaluation. Subsequently, the patient was also diagnosed with metastatic lung carcinoma, which was not coincidental. Re-evaluation of the pathology from the two biopsy sites confirmed tumor-to-tumor metastasis into the meningioma. The adenocarcinoma metastasis was locally more invasive than the meningeal component of the tumour, requiring specific treatment.

Keywords: Tumor, Optic Neuropathy, metastatic carcinoma, optic nerve, Compressive optic neuropathy

References
1/ Sohail S, Karambizi DI, Baker A, Groh DM, Toms SA. A Comparative Report on Intracranial Tumor-to-Tumor Metastasis and Collision Tumors. World Neurosurgery 2018;116:454-463 2/ Caroli E, Salvati M, Giangaspero F, Ferrante L, Santoro A. Intrameningioma metastasis as first clinical manifestation of occult primary breast carcinoma. Neurosurg Rev 2006;29:49–54.

“Turbulence, Fluid Waves, and the Black Hole”

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History & Exam

A 61-year old male developed an acute exacerbation superimposed on a 3-month relapsing and remitting course of painless eyelid swelling beginning in the right upper lid progressing to involve both upper and lower eyelids, malar area, and temporalis. He provided photographic documentation of dramatic waxing and waning course, sometimes preventing him from opening his eyelids (Figure 1). His condition was poorly responsive to repetitive courses of antibiotics and corticosteroids, but showed mild improvement with compressive dressing. The patient denied a pulse synchronous bruit. However, when questioned about auditory symptoms, he described a “rushing fluid” sound when he digitally compressed the eyelid tissues. He denied previous trauma or surgery. He worked as a truck driver and had strong inclination to “selfies”, providing ample documentation of his waxing and waning course of eyelid edema. Examination showed severe right upper and lower eyelid demarcation extending to the malar and temporalis areas, without tenderness, erythema, or proptosis. The remainder of the slit lamp and funduscopic examinations were normal. CT orbit obtained prior to presentation reported “significant right periorbital swelling without other abnormalities" but images were unavailable. T1 orbital fat suppressed contrast enhanced axial and coronal imaging and T2 axial and FLAIR images demonstrated diffuse enhancement and enhancing collection of the fluid in the right upper eyelid, malar, and temporalis regions on T1 sequences (Figure 2A and 2B) that were bright on T2 (Figure 2C) and demonstrated signal suppression on FLAIR (Figure 2D). Radiology report summarized the findings as “large phlegmon or abscess overlying the orbit without post-septal involvement.” CBC with differential, urinalysis, HIV, and blood culture were normal. A biopsy was performed for intra-operative study to confirm the diagnosis.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

"Turbulence, Fluid Waves, and the Black Hole"

Answer

Final Diagnosis

Non-traumatic CSF blepharocele. Blepharocele results from an intermittent accumulation of CSF in eyelid tissues secondary to a cranio-orbital fistula between the subarachnoid space and the eyelid.1 Cranio-orbital fistulas are uncommon complications associated with cranio-orbital trauma and surgery. As orbital pressure is typically higher than that in the nose or ear, rhinorrhea and otorrhea are the most common manifestations of CSF leakage, while CSF accumulation in the eyelid and orbit rarely occurs. Beta 2-transferrin is a protein found exclusively in CSF and perilymph, tested extensively in skull base and spinal surgeries for detection of CSF with a sensitivity of 94 to 100% and specificity of 98 to100%.3 The diagnosis of non-traumatic CSF blepharocele was supported by critical review of neuroimaging. MRI FLAIR studies appeared to follow the characteristics of CSF, and CT studies revealed an area of bony dehiscence after Beta-2 transferrin confirmation of CSF in tissue. A craniotomy directly identified the site of CSF fistula, which was successfully repaired.

Summary of Case

A lateral orbitotomy with surgical biopsy of eyelid, temporalis, and lacrimal gland was performed. Final pathology reported "no inflammation" in all biopsy samples. Intra-operative cultures of lacrimal gland grew rare coagulase negative Staphylococcus epidermidis. Tissue culture grew both S.epidermidis and Staphylococcus hominis. Intra-operative findings included pink-tinged fluid emanating from glistening tissue without a well-defined fluid pocket. The surgeon could sweep his hand like a squeegee over the surgical wound and produce more glistening fluid. Intra-operative specimen was sent for Beta 2-transferrin, a highly specific marker for CSF, which subsequently confirmed the fluid to be CSF. Patient was diagnosed with non-traumatic CSF blepharocele. Prior CT imaging was acquired post-operatively and careful inspection identified an unreported defect in the frontal bone of the lateral right orbital roof (Figure 3A and B). A supraorbital craniotomy confirmed a lateral frontal bone defect (Figure 4A), and an overlying dural defect that was repaired using a collagen matrix and calcium hydroxyapatite cement (Figure 4B). The patient's symptoms and imaging findings subsequently resolved. CSF blepharocele is an extremely rare complication of trauma, most commonly occurring in children. Non-traumatic spontaneous blepharocele is nearly unknown. We add to a limited literature on the spontaneous development of this entity, which includes another single additional case report that was associated with a congenital lesion (Table 1). In both cases, a causative bony defect was identified in the orbital roof, and repair resolved the eyelid edema.

Struggle/Dilemma of the Clinical Presentation Description

Persistent waxing and waning eyelid and facial edema refractory to antibiotic and corticosteroid therapy that is inconsistent with blepharochalasis, infection, or trauma may occur in the absence of trauma. Here we present an atypical presentation of non-traumatic occult spinal fluid leak, confirmed with Beta 2- transferrin testing. Presence of FLAIR attenuation of the high signal T2 facial fluid supports low protein content, appears to follow the imaging characteristics of CSF, signifying CSF fistula.

Keywords: Eyelids, MRI, skull base

References

1. Chandra N, Ojha BK, Chandwani V, Srivastava C, Singh SK, Chandra A. A rare case of posttraumatic eyelid swelling: cerebrospinal fluid blepharocele. J Neurosurg Pediatr. 2013; 11(3):242-4. 2. Germano R, Silva M, Germano F, Brandao M, Germano C, de Souza B, Kawai R, Germano J. Eyelid liquoric fistula secondary to orbital meningocele. Revista Brasiliera de Oftalmologica. 2015; 74(1).

Poster Session I: Clinical Highlights in Neuro-Ophthalmology
Sunday, March 17th- 12:30 pm – 2:30 pm
Authors will be standing by their posters during the following hours:
Odd Numbered Posters: 12:30 pm – 1:30 pm
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1	Nivolumab-associated anti-MOG antibody positive Optic Neuritis	Gabrielle R. Bonhomme
2	Recurrent optic neuritis secondary to relapsing MOG antibody-associated demyelination syndrome	Gerard L. Hershewe
3	Unilateral papilledema due to subdural hematoma related with pre-existing arachnoid cyst	Ileok Jung
4	Masquerades of giant cell arteritis evident on temporal artery biopsy	Jonathan A. Micieli
5	Isolated Optic Neuropathy due to Folate Deficiency with associated Iron Overload	Charles Maitland
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7	Ethambutol Induced Optic Neuropathy: A Case Series	Serena Zaman
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9	Abnormal posterior visual pathway MRI in an elderly woman with LHON	Zakeya M. Al-Sadah
10	Transient Visual Loss induced by Pregnancy	Sophie Bonnin
11	An Atypical Case of Orbital Rhabdoid Tumor	Jennifer N. Danesh
12	Neurovascular disorders with isolated ocular signs and symptoms	Kumudini Sharma
13	Myelin Oligodendrocyte Glycoprotein Antibody (MOG-IgG)-Positive Optic Perineuritis	Gregory P. Van Stavern
14	Concurrent Embolic Anterior Ischemic Optic Neuropathy and Retinal Artery Occlusion with Acute silent ischemic Stroke	Xiaojun Zhang
15	Recurrence of chiasmitis secondary to systemic lupus erythematosus	Glauco B. Almeida
16	Bilateral Optic Neuropathies from Infiltrative B-Cell Lymphoma	Eliecer Arosemena
17	Incipient Optic Neuritis	Marc A. Bouffard
18	High altitude associated non-arteritic ischemic optic neuropathy	Yin Allison Liu
19	Pembrolizumab induced optic neuropathy in a patient with laryngopharyngeal carcinoma	Yin Allison Liu

20	Mitochondrial ND5 gene heteroplasmic mutation (m.G13042A), in a patient with Leigh-LHON overlap syndrome	Inbal Man Peles
21	Bilateral optic neuropathy following treatment with nivolumab for metastatic cutaneous melanoma	Maria E. Mayorga
22	The Eagle Head in My Right Eye! A Case of Paracentral Acute Middle Maculopathy	Tarek A. Shazly
23	Unusual Manifestation of Histopathologic Confirmed Metastatic Esophageal Carcinoma	Dilip A. Thomas
24	Paracentral Acute Middle Maculopathy in the Setting of New Onset Giant Cell Arteritis	Jane Bailey
25	Bitemporal Hemianopsia and Significant Binasal GCL–IPL Thinning In Chiasmal Hemioptic Hypoplasia	Jose I. Benavides
26	Vitreopapillary Traction Masquerading as Papilledema	Joseph Chacko
27	Concurrent CRAO with Arteritic AION in Eosinophilic Granulomatosis with Polyangiitis	Anuchit Poonyathalang
28	Heterochromia and ocular ischemia resulting from Neurofibromatosis I-related optic pathway glioma	Imran Jivraj
29	The Localizing Value of the Relative Afferent Pupillary Defect in Patients with Efferent Ocular Disease	Aroucha Vickers
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31	Anorexic disc or compressed disc	Sneh Dhannawat
32	All is Well - A diagnostic and management challenge	Manasa Gunturu
33	Severe Susac syndrome in a patient with active ulcerative colitis	Nicolae Sanda
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35	Traumatic Optic Tract Syndrome with a Decade-Old Head Trauma	Jack G. Mouhanna
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38	Meningocele, a Protective Finding in Patient with Pulsatile Tinnitus and Brain Imaging Features Suggesting PTCS	Katarzyna Slota
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40	Papilledema: initial sign of an INF2 mutation	David W. Rastall
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44	Longest Involvement of Visual Pathway in Neuromyelitis Optica Spectrum Disorder	Bunyada Chinkulkitnivat

45	Accidental ophthalmic artery Onyx embolisation for meningioma-Vision lost in an attempt to preserve	Tonse Ashwini Kini
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48	Multifocal Stroke from Ozone Gas Emboli	Paul R. Freund
49	Single-photon emission computerized tomography (SPECT) in MRI negative Cortical Blindness Post Anoxic Brain Insult	Nagham Al-Zubidil
51	External Carotid-Facial Vein Fistula Masquerading as Carotid-Cavernous Fistula	Ankur A. Mehra
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54	A Case of Neuromyelitis Optica Presenting with Orbital Inlammation	Lucy A. Bailey
55	Marginal Zone Lymphoma Causing Superior Sagittal Sinus Stenosis and Intracranial Hypertension	Mhafrin Basta
56	Ipilimumab and Nivolumab associated VKH like Immune Related Adverse Events	Johanna D. Beebe
57	A Diagnostically Challenging Case of Neurosarcoidosis in the Era of Highly Sensitive Tests	Konstantinos Douglas
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60	New biomarkers in inflammatory demyelinating diseases of the central nervous system (CNS)	Mathias Falck Schmidt
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62	Isolated inferior rectus palsy due to orbital lymphoma	Jin Hwangbo
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66	Papilledema due to Cryptococcal Meningitis in Immunocompetent Patients	Chun-Hsiu Liu
67	Papilledema and bilateral optic neuropathy: dual mechanism for visual loss in patient with leptomeningeal carcinomatosis	Henry Liu
68	Bilateral optic perineuritis secondary to giant cell arteritis	Eun Hye Oh
69	LHON-MS patient with long-term non-response to Idebenone shows improvement after 4-AP Usage	William Sultan
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71	Ocular Manifestation of Systemic Disease	Mangayarkarasi Thandampallayam Ajjeya Gowder

72	Bilateral Uveitis Presentation in a Patient with Giant Cell Arteritis	Nagham Al-Zubidi
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75	Sequential Bilateral Vision Loss due to Lymphomatous Infiltration of the Anterior Optic Pathways	Nitsan Duvdevan Strier
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78	First case of melanoma-associated retinopathy with conjunctival melanoma	Jeanne Lafortune
79	Myelin Oligodendrocyte Glycoprotein Antibody-Associated Optic Neuritis with Sjögren's Syndrome	Aman Mittal
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81	Rapidly progressing retinal dystrophy in Spinocerebellar Ataxia 7 (SCA7): A case report of three brothers	Gideon Nkrumah
82	Case of Heidenhain Variant Creutzfeldt-Jakob Disease Presenting with Homonymous Quadrantanopia and Corresponding Nuclear Imaging Findings	Shivkumar Bhadola
83	Vertical Gaze Palsy with Bilateral Third Nerve Palsy and Contralateral Hemiparesis	Karthika Bhaskaran
84	Optic Neuritis and Intracranial Hypertension caused by Chronic Lymphocytic Leukemia	Poonam Bansal
85	Optic Nerve: A window to Neurosyphilis	Mirta Arana
86	Cobalt-chromium toxicity and late-onset disease conversion in LHON – is there a causal link?	Neringa Jurkute
87	Diagnostic of micro adenoma pituitary in patients pediatric	Alexa G. Méndez Vázquez
88	Ophthalmoparesis and Optic Neuropathy in a Woman with Catastrophic Antiphospholipid Syndrome	Pai-Huei Peng
89	A Case of an Esophageal Adenocarcinoma Causing Infiltrative Optic Neuropathy and Carcinomatous Meningitis	Tatiana Bakaeva
90	A Case of Posterior Reversible Encephalopathy Syndrome Presenting as Obstructive Hydrocephalus	Alexander S. Barsam
91	Delayed Development of a Dural AV Fistula and PTEN Hamartoma Syndrome in Pseudo-Idiopathic Intracranial Hypertension	Doria M. Gold
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93	Cerebellar Stroke and Prostaglandin	Wolliez Jean-Philippe
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95	Neurosarcoidosis Masquerading as Cavernous Sinus Meningioma	Omar Solyman

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98	The Treatment of Chronic Papilledema Secondary to a Dural Arteriovenous Fistula	Amanda J. Wong
99	Disseminated Adult Atypical Teratoid Rhabdoid Tumor causing Dorsal Midbrain Syndrome	Colleen C. Yard
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106	Ophthalmic manifestations and diagnostic of Friedreich Syndrome	Alexa Guadalupe Méndez Vázquez
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108	Multi-modal Imaging of Retinal Capillary Hemangioblastoma	Johnny X. Li
109	Case Report: Idiopathic Presentation of Raeder's Paratrigeminal Neuralgia	Matthew N. Parvus
110	Destructive Rhino-Orbital IgG4-Related Disease	Amadeo R. Rodriguez
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112	Anti-Hu associated Gaze Palsy Associated with Recurrent Small Cell Lung Cancer	Samantha Goldburg
113	Paraneoplastic Downbeat Nystagmus Secondary to Metastatic Prostatic Carcinoma	Gerard L. Hershewe
114	Dissociated Pendular Nystagmus in Oculopalatal Tremor with Bilateral Inferior Olivary Hypertrophy	Seung-Han Lee
115	The Use Of Positional Head Impulse Test In Vertical Nystagmus: Evidence For Vestibular Imbalance	Joao Lemos
116	Exacerbation of Oscillopsia and Nystagmus from Reading Aloud in Superior Semicircular Canal Dehiscence	Angela Oh
117	Fourteen Syndrome and Fifteen Syndrome: Horizontal Gaze Palsy Plus Unilateral Seventh and Sixth Nerve Paresis	Berthold Pemp
118	Traumatic Ophthalmoplegia In A Pediatric Patient	Scott A. Davis
119	A Case of Pendular Nystagmus: Delayed Onset of Infantile Nystagmus	Hak Seung Lee
120	Bilateral abducens palsy in West Nile Meningoencephalitis	Anika Tandon

121	A Case of Acute Leukemia Presenting as Acute 6th Nerve Palsy	Malek A. Alrobaian
122	Tolosa-Hunt Syndrome: A Case Series of Atypical Presentations	Melody Merati
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Category: Orbital and Eyelid Disorders		
127	Superior Ophthalmic Vein Thrombosis from Orbital Cellulitis in Setting of Trauma	Jamie Choi
128	Pseudo von Graefe's Sign following Operative Vaginal Delivery	Swati Handa
129	Bilateral Eyelid Apraxia Secondary to Bilateral Paramedian Mesencephalic Stroke Treated with Botulinum A Toxin Injection	Emily Li
130	Misdiagnose of Carotid Cavernous Fistulas, who´s to blame?	Macarena Clementi
131	Spontaneous dehiscence of the lateral orbital wall	Tiffany C. Ho
132	Pembrolizumab-associated Diplopia Secondary to Orbital Pseudotumor	Shira S. Simon
133	Orbital Myositis Triggering Oxygen-responsive Cluster Headache	Vivian Paraskevi Douglas
134	Walsh to the Rescue: Case of Neurosarcoidosis with Vasogenic Edema and Pachymeningitis	Sravanthi Vegunta
135	Vertical Diplopia: An Unusual Manifestation of Silent Sinus Syndrome	Venkatkrish M. Kasetty
136	Checkpoint inhibitor associated orbital inflammation masquerading as ocular myasthenia gravis and thyroid eye disease	Marisa Tieger
Category: Pupil		
137	Relative afferent pupillary defect with contralateral demyelinating midbrain lesion in a patient with Charcot’s Triad	Bryce Buchowicz

Poster 1
Nivolumab-associated anti-MOG antibody positive Optic Neuritis

Gabrielle Bonhomme[1], Deepak Soneji[2]

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Introduction:
Nivolumab has been associated with neurotoxicity. We present a case of MOG-antibody optic neuritis associated with Nivolumab use.

Description of Case(s):
A 46-year-old man presented with four days of sub-acute vision loss in his left eye. History reveals stage III B-cell chronic lymphocytic lymphoma and squamous cell carcinoma of the tongue. Squamous cell carcinoma progressed, with metastasis to liver and bone and Hypogammaglobulinemia treated by IVIG. Medications included cephalexin, clindamycin, nivolumab, and fluocinolone. Initial Visual acuity was 20/20 on the right and Hand Motion on the left, with a left afferent pupillary defect. Color perception was 11/11 in the right and 0/11 in the left by Ishihara plates. Ocular motility was full bilaterally, with pain on eye movement. Dilated ophthalmoscopy revealed optic nerves without disk edema or pallor. Retinal and neurologic examination were unrevealing. Gadolinium-enhanced MRI Brain/orbits revealed T2 hyperintensity and post-contrast enhancement of the left intra-orbital optic nerve, without associated cerebral lesions. Nivolumab was held. Lumbar puncture and serologies for infections, paraneoplastic, and autoimmune disorders were obtained. Given clinical presentation of optic neuritis without evidence of infection, 1 gram of IV methylprednisolone was administered daily for three days. He was discharged on 1 mg/kg oral Prednisone oral taper. Anti-MOG antibodies were positive (1:1000). At follow up, visual acuity had improved to 20/30 in the left eye.

Conclusions, including unique features of the case(s):
Optic Neuritis may be considered in the differential diagnosis of unilateral vision loss in the setting of Nivolumab treatment. Should NMO IgG prove negative, anti-MOG antibody may be considered to evaluate for this phenotype of NMO seronegative demyelination, with a high rate of recurrence.

References: Myelin Oligodendrocyte Glycoprotein Antibody (MOG-IgG)-Positive Optic Neuritis: Clinical Characteristics, Radiologic Clues, and Outcome. Chen JJ, Flanagan EP, Pittock JS, et al. American Journal of Ophthalmology 2018; 185: 8 – 15. Spain L, Walls G, Julve M, O'Meara K, Schmid T, Kalaitzaki E, Turajilic S, Gore M, Rees J, and Larkin J. Neurotoxicity from immune-checkpoint inhibition in the treatment of melanoma: a single center experience and review of the literature. Annals of Oncology 2017; 28: 377-385. Boisseau W, Touat M, Berzero G, Savatovsky J, Marabelle A, Touitou V, Ricard D, Malouf G, Psimaras D. Safety of treatment with nivolumab after Ipilimimab -related meningoradiculitis and bilateral optic neuropathy. European J Cancer 2017; 83: 28-31.

Keywords: Optic neuritis, Magnetic resonance imaging, metastatic carcinoma

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Poster 2
Recurrent optic neuritis secondary to relapsing MOG antibody-associated demyelination syndrome

Gerard Hershewe[1], Joshua Gratwohl[2], Clinton Kolseth[1], Munadel Awad[1], Jerad Hershewe[2]

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Introduction:
Recurrent optic neuritis has been associated with demyelinating diseases including anti-MOG syndrome. We describe a 12 year old girl with relapsing acute optic neuritis responsive to oral steroids and IVIG.

Description of Case(s):
A 12-year-old girl was evaluated with blurred vision and low-grade orbital pain OD. BCVA: OD CF and OS 20/20. CV: 0 of 6 HRR plates OD. There was a 2.1 log unit RAPD OD. There was 3+ hyperemic disc edema OD. HVF showed a dense central scotoma OD. RNFL thickness was increased at 338 microns OD. MRI scan of the orbit showed focal enlargement and enhancement of the intraorbital right optic nerve. MRI scan of the brain, cervical, and thoracic spine with gadolinium were normal. The NMO IgG was normal. The patient clinically improved following treatment with I.V. Solu-Medrol followed by an oral steroid taper. Eight days later- BCVA: 20/20 OU! There was resolving disc edema OD. Following discontinuation of the oral prednisone, there was an interval worsening of her central vision OD- BCVA: OD 20/40. There was minimal disc edema and 1+ temporal pallor of the optic nerve. HVF showed both a dense inferior altitudinal defect and a superotemporal altitudinal defect. The anti-MOG antibody was elevated at 1:100. There was clinical improvement following treatment with a second course of I.V. Solumedrol, IVIG, and low dose prednisone therapy- BCVA: 20/20 OU! There was 1-2+ temporal pallor of the optic nerve and a normal HVF.

Conclusions, including unique features of the case(s):
Relapsing MOG antibody associated demyelination can be seen in pediatric patients. Anti-MOG patients are typically steroid responsive, but 70% of episodes treated with oral prednisone relapsed at doses of less than 10 mg or within 2 months of cessation. Immunotherapy with either IVIG or Rituxan in combination with low dose steroids may help to prevent relapses in these patients.

References: Zhou, Y; Jia, X; Yang, H; Chen, C;Sun, X; Peng, L; Kermode, AG; Qui, W. Myelin oligodendrocyte glycoprotein (MOG) antibody-associated demyelination: comparison between onset phenotypes. European Journal of Neurology. 2018 Aug 28. Peng, A et. al. Retinal nerve fiber layer thickness in optic neuritis with MOG antibodies: A systematic review and meta-analysis. Journal of Neuroimmunology. 2018 Sep 11. Zhou, Y et.al. Myelin oligodendrocyte glycoprotein (MOG) antibody-associated demyelination: comparison between onset phenotypes. (accepted for publication but not yet published) Ungureanu, A; de Seze, J; Ahle, G; Sellal, F; Myelin oligodendrocyte glycoprotein antibodies in neuromyelitis optica spectrum disorder. Revue Neurologique. 2018.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 3
Unilateral papilledema due to subdural hematoma related with pre-existing arachnoid cyst

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Introduction:
Papilledema is caused by increased intracranial pressure and is commonly bilateral. This case describes unilateral papilledema due to a structural anomaly combined with subdural hematoma.

Description of Case(s):
A 38-year-old man with diplopia and tinnitus for 3 days visited to the clinics. He had a history of newly developed headache on the left side 2 months ago. The initial magnetic resonance imaging (MRI) of the brain demonstrated the large arachnoid cyst in the left middle cranial fossa. The headache was slowly aggravated, which was followed by diplopia. He had no ptosis, isocoric pupil and no relative afferent pupillary defect. The movements of extracular muscles were intact bur the patient reported the horizontal diplopia during far and leftward gaze. The fundus photography showed unilateral papilledema in the left eye and follow-up MRI demonstrated the subdural hematoma in the left frontoparietotemporal convexity related to arachnoid cyst. In a T2-weighted image, the subarachnoic space of the left optic nerve was observed as distended due to the increased amount of cerebrospinal fluid. Marked widening of the bulbar part of the optic nerve adjacent to the posterior sclera was also identified.

Conclusions, including unique features of the case(s):
Unilateral papilledema can be encountered in a certain patient with special anatomical structures such as unilateral subdural hematoma related to pre-existing arachnoid cyst.

References: None.

Keywords: High intracranial pressure/headache, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 4
Masquerades of giant cell arteritis evident on temporal artery biopsy

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Introduction:
Temporal artery biopsy (TAB) may not only confirm the diagnosis of giant cell arteritis (GCA), but also reveal atypical histopathological signs to support other diagnoses. We present three cases where temporal artery biopsy revealed an alternative diagnosis (ANCA-associated vasculitis, multiple myeloma, and thromboangiitis obliterans) in patients with a history suggestive of GCA.

Description of Case(s):
A 75-year-old man presented to the emergency room with a 2-month history of weight loss, fever, and chills that did not respond to multiple courses of antibiotics. He later developed temporal headache, jaw claudication and bilateral vision loss from a right anterior ischemic optic neuropathy and left ischemic optic neuropathy and retinopathy. TAB revealed no inflammation in the wall of the temporal artery, but a small obliterative vasculitis in the vasa vasorum. This led to the diagnosis of ANCA-associated vasculitis. A 77-year-old woman presented with a one-day history of sudden vision loss in her left eye from a left anterior ischemic optic neuropathy. She felt fatigued and unwell and had elevated inflammatory blood markers. TAB revealed no significant inflammation, but disruption of the inner elastic lamina and accumulation of amyloid. This led to further investigations and a diagnosis of multiple myeloma. A 50-year-old man presented with right temporal headache, protrusion of a non-tender nodule in his right temporal region and blurred vision in both eyes. He reported that one of his toes turned black and he had an intense sharp and burning pain in his extremities.TAB revealed a thrombo-occlusive vasculitis and he was diagnosed with thromboangiitis obliterans (Buerger's disease).

Conclusions, including unique features of the case(s):
TAB is not only important for a diagnosis of GCA, but may reveal findings to support additional diagnoses. This has implications for the increased use of non-invasive alternatives such as ultrasound and omission of histopathological analysis in the diagnosis of patients suspected of having GCA.

References: None.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 5
Isolated Optic Neuropathy due to Folate Deficiency with associated Iron Overload

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Introduction:
Isolated Optic neuropathy due to folate deficiency is rarely reported. Poor dietary practices, malabsorption, and/or tobacco/alcohol abuse are responsible. We examined a patient with blinding optic neuropathies and isolated folic acid deficiency. After initial replacement therapy serologic investigation subsequently revealed high ferritin and iron saturation levels with negative genetic testing for hemochromatosis consistent with the diagnosis of Iron Overload Syndrome. There are no reports of blindness associated with Iron Overload Syndrome.

Description of Case(s):
Nonspecific leg aching developed simultaneously. Past Medical history was remarkable for absence of visual, neurologic, or constitutional disease. The patient was a modest drinker without history of any GI disturbance or history of poor nutrition or alcohol abuse. Physical Exam: Visual acuity exam showed 20/200 OD, 20/80 OS, color vision 0/6 (HRR color plates). Humphreys Visual Field revealed relative cecocentral scotoma and arcuate fiber defects in both eyes. Funduscopic examination demonstrated full nerve fiber bundles.

Conclusions, including unique features of the case(s):
The case is unique in that folate deficiency developed in isolation and unrelated to previously reported commonly associated pathologies. The relationship between folate deficiency and Iron Overload Syndrome is problematic. There are no reported cases of Iron Overload Syndrome causing optic neuropathy. The relationship between the two conditions will be discussed.

References: None.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 6
Anti Tuberculosis Therapy causing Neuroretinopathy

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Introduction:
Ethambutol and less commonly, Isoniazid are well documented causes of toxic optic neuropathy. This manifests as reduced visual acuity, colour vision deficits and visual field defects. We present an interesting case where the neuropathy progressed at least 12 months after drug cessation, with atypical electrophysiology findings.

Description of Case(s):
A 35 year old male of Pakistani origin, with normal renal function, presented with blurred vision in both eyes of several week duration. He had completed a 2 month course of standard doses of Ethambutol, Pyrazinamide, Rifampicin and Isoniazid, and was continuing the latter 2 drugs as per protocol. The visual acuities were 6/60 bilaterally, pupils were reactive with no afferent defect, the Ishihara test plate could not be visualised, and the fundi as well as optic nerve heads looked normal. The visual fields showed centrocaecal scotomas, and the nerve fibre layer OCT showed temporal thinning with diffuse macular ganglion cell layer loss. Isoniazid was promptly discontinued. Alternative diagnoses were investigated for and an MRI head and orbits, nutritional and heavy metal screen, ACE/ syphilis serology and vasculitic markers were normal. The absence of uveitis made TB optic neuritis unlikely. ISCEV standards electrophysiology revealed an abolished pattern VEP and reduced flash VEP. The ERG was found to be electronegative with a photopic ERG suggesting normal cone function. The rod responses were unexpectedly severely reduced and delayed. Macular ganglion cell layer and nerve fibre layer loss continued at least 12 months after cessation of anti-TB therapy, with a most recent visual acuity of 1/60 in both eyes.

Conclusions, including unique features of the case(s):
This is the first case in the literature of anti-TB therapy associated with severe rod dysfunction. The neuro-ophthalmologist must be alert to the varying sites of toxicity, and the potential for continued damage to the macular ganglion cell layer and nerve fibre layer after drug cessation.

References: 1) Lee EJ, Kim SJ, Choung HK, Kim JH, Yu YS. Incidence and clinical features of ethambutol-induced optic neuropathy in Korea. Journal of Neuroophthalmology. Dec;28(4):269-77 2008 2) Chamberlain PD, Sadaka A, Berry S, Lee AG. Ethambutol Optic Neuropathy. Current Opinion in Ophthalmology. Nov;28(6):545-55. 2017 3) Lai TY, Chan WM, Lam DS, Lim E. Multifocal electroretinogram demonstrated macular toxicity associated with ethambutol related optic neuropathy. British Journal of Ophthalmology. Jun;89(6):774-5. 2005 4) Kulkarni HS, Keskar VS, Bavdekar SB, Gabhale Y. Bilateral optic neuritis due to isoniazid. Indian Journal of Pediatrics Jun;47(6):533-5 2010 5) Kardon RH, Morrisey MC, Lee AG. Abnormal multifocal electroretinogram (mfERG) in ethambutol toxicity. Seminars in Ophthalmology. Oct-Dec;21(4):215-22 2006.

Keywords: Optic neuropathy, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease

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Grant Support: None.

Poster 7
Ethambutol Induced Optic Neuropathy: A Case Series

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Introduction:
Optic neuropathy is a rare but potentially sight-threatening adverse effect of the anti-tuberculous agent ethambutol. The consequences can be devastating, with early diagnosis and cessation of medication critical in preventing irreversible visual loss. Royal College of Ophthalmologists in the United Kingdom recently revised its guidelines in regards to baseline assessment prior to commencement of the medication, advising that baseline assessment must be performed by the prescriber.

Description of Case(s):
We describe four patients seen in the neuro-ophthalmology clinic between 2010 and 2018 in whom there was established optic neuropathy secondary to ethambutol. We outline their clinical journeys and highlight similarities in their presentations, co-pathology and recovery. All affected patients were older (mean age 63.5). The mean time from starting ethambutol to onset of visual symptoms was 3.5 months, with one patient identified at the asymptomatic stage following referral from an infectious disease specialist given duration and dose of ethambutol. A renal dialysis patient developed severe ethambutol toxicity despite appropriate adjustment of ethambutol levels. The mean final visual acuity (VA) was 0.22 OD 0.26 OS. The mean time for visual improvement to best recorded VA was 7.5 months.

Conclusions, including unique features of the case(s):
We outline these cases to highlight that vision may continue to deteriorate rapidly despite cessation of therapy, and that age and co-existing renal disease are risk factors for toxicity. In addition, an asymptomatic patient and a case of co-existent abducens palsy highlighted the requirement for baseline screening and supports screening at intervals as patients may not be aware of early, subtle defects. In our service, patients on ethambutol undergo opportunistic questioning regarding visual symptoms and at least 4 monthly visual acuity and Ishihara colour vision testing by trained nursing staff working alongside the physicians in charge of their care. With prompt cessation of ethambutol, none of our patients had a VA of less than 0.48.

References: None.

Keywords: Optic neuropathy, Miscellaneous

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Poster 8
Morning Glory Disc Anomaly with an ipsilateral Optic Nerve Glioma

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Introduction:
Morning glory disc anomaly (MGDA) is a congenital disorder characterized by the funnel shape disc excavation with radiating retinal vessels. MGDA is sometimes associated with midline developmental or vascular malformations. On evaluation for visual function, MGDA and concurrent ipsilateral optic nerve enlargement were found. This case is to report a rare CNS association with MGDA and to alert the importance of systemic evaluation in congenital Optic nerve anomalies.

Description of Case(s):
11yrs ago, a 5-year-old girl was referred to my clinic because of strabismus and amblyopia of left eye. At the first visit, VA OD 20/20 OS 20/200 with RAPD +3 OS and left exotropia 15pd were noticed. On fundus exam, left optic disc showed characteristic MGDA. Magnetic resonance imaging studies revealed enlargement of the prechiasmatic ipsilateral optic nerve which consistent with glioma. With long-term follow-up for optic nerve tumor, there is no change in tumor size and visual field. Upon amblyopia treatment, visual acuity was preserved from 20/200 at the initial visit to 20/100 at the last visit.

Conclusions, including unique features of the case(s):
In conclusion, I recommend that any patient with MGDA take CNS imaging for evaluation of varies midline defect and vascular abnormalities as well as visual functions. Early recognition and management of amblyopia are essential to enhance visual acuity. Especially this patient was followed up to 11 years for concurrent optic nerve glioma. This case is unique to report a rare CNS association with MGDA and long-term follow-up. And it is important to recognize the importance of systemic evaluation and amblyopia management in congenital Optic nerve anomalies.

References: 1. Morning glory disc anomaly with an ipsilateral enlargement of the optic nerve pathway D.Thoma, I. Nijs, P.Demarel, I. Casteels Europian J of Pediatric Neurology, 21; 787-798, 2017 2. Morning Glory Disc Anomaly in Association with Ipsilateral Optic nerve Glioma P. Bandopadhayay, L Dagi, N Robison, L Goumnerrova, N Ullrich Arch Ophthalmol vol 130: 1082-1083, 2012.

Keywords: Pediatric neuro-ophthalmology, Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 9
Abnormal posterior visual pathway MRI in an elderly woman with LHON

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Introduction:
LHON generally occurs in younger males. We present an unusual case.

Description of Case(s):
A 79-year-old woman was admitted to the University hospital for delirium. The patient had noted bilateral painless visual loss OU 3 months earlier. She has a history of severe COPD, chronic hypoxic respiratory failure, aortic aneurysm, B12 deficiency, hypertension, a protracted history of alcohol abuse and poor nutritional intake due to alcoholism. She was a heavy smoker. She had no giant cell arteritis symptoms. Her exam showed oriented woman on oxygen. She had a visual acuity of counting fingers OU with constricted visual fields OU, pupils measured 5 mm OU with 1 + equal OU with no RAPD, normal ocular motility. Trigeminal and facial nerves were intact. Normal anterior segment exam and intraocular pressures. Her optic nerves appeared normal. A full-field ERG was normal OU. A pattern VER showed a P-100 of 143.5 ms on the right and 148.5 ms on the left which was delayed OU. ON OCT and retinal OCT were normal OU. Labs showed a normal CBC, BMP, NMO, thiamine, B12, syphilis testing, paraneoplastic panel, ACE and ESR. A contrasted MRI scan of the brain and orbits showed scattered foci of chronic microangiopathic changes. LP was normal. Negative MS profile. CT chest, abdomen and pelvis showed no malignancy. A second contrasted brain and orbital fat suppressed MRI showed an abnormal signal in the optic chiasm extending partially into the cisternal optic nerves as well as posteriorly into the optic pathways on FLAIR. Blood testing for LHON revealed with a heteroplasmic G>A nucleotide substitution at mitochondrial position 11778.

Conclusions, including unique features of the case(s):
This is an unusual case of LHON presenting in a 79 year old female with an abnormal MRI FLAIR signal in optic chiasm extending to cisternal optic nerve and optic pathways posteriorly.

References: None.

Keywords: Genetic Disease, Optic neuropathy, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 10
Transient Visual Loss induced by Pregnancy

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Introduction:
During pregnancy, because of estrogen stimulation, Pituitary gland almost always enlarge and can sometimes exceeding 100 % and return to normal within six month after post partum. It usually does not expand to the extrasellar area to cause symptoms such as headache or vision impairement. In some rares cases the mass effect threaten the vision.

Description of Case(s):
In 2012, a 26-year-old woman experienced a severe isolated left eye decreased vision to 20/200 occuring at the 7th month of her first pregnancy witch resolved spontaneously after birth. Two years later, the second pregnancy had the same effect. The MRI showed increased size of the hypophysis pushing up the chiasma. Vision quickly recovered within few weeks of post partum period, the size returned to normal. In 2016 she discovered her pregnancy because of the blurring vision of her left eye. The pregnancy was interrupted for a fetal malformation and vision quickly recovered. She was referred to a neuro ophthalmologist in 2017 and asked for visual risk of a fourth pregnancy. At this time, visual acuity and visual field were normal. Posterior fundus exam showed normal optic nerves normal OCT. Cerebral MRI was also normal.

Conclusions, including unique features of the case(s):
We can reasonably assume decreased vision is due to a left compressive optic neuropathy induced by the mass effect of physiological enlargement of the pituitary gland. We can assume that even if the risk of permanent visual impairment, or other mass effect complications should not be so high, otherwise it would have been previously reported in the litterature. We can't predict that a fourth pregnancy will be totally safe, knowing that the third episode of compression occurred in the early months of pregnancy. Repetitive physiological compression from enlargement of pituitary gland has never been reported. ophtalmologistes should be aware of this potentially threatening condition.

References: Dinc H and co. Pituitary dimensions and volume measurements in pregnancy and post partum: MR assessment. Acta Radiol. 1998; 39(1): 649 Ennaifer H and Co. Developed diplopia due to a pituitary macroadenoma during pregnancy Pan African Medical Journal. 2018;29:39. Inoue T and Co. Loss of vision due to a physiologic pituitary enlargement during normal pregnancy. Graefes Arch Clin Exp Ophthalmol. 2007; 245(7): 104951

Keywords: Optic neuropathy, Neuroimaging, Perimetry

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Grant Support: None.

Poster 11
An Atypical Case of Orbital Rhabdoid Tumor

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Introduction:
Malignant rhabdoid tumor of the orbit is rare and can present with findings similar to a glioma but portends a more aggressive course and poor prognosis. We present the case of a child with a rapidly growing orbital tumor that initially presented with findings mimicking that of an optic nerve glioma.

Description of Case(s):
A previously healthy 6-month-old boy presented to the emergency room with 1 week of progressive ocular misalignment and proptosis of the left eye. CT orbits was ordered by the ER, which showed fusiform enlargement of the left optic nerve isolated to the orbit with mild enhancement post contrast, most consistent with an optic nerve glioma. At this time, fundus exam showed significant left optic nerve edema and a cherry red spot consistent with central retinal artery occlusion. Urgent MRI obtained 1 week later revealed an infiltrative enlargement of the left optic nerve as well as a large mass in the intraconal space. Biopsy specimen was consistent with rhabdoid tumor. The patient eventually underwent left orbital exenteration and radiation therapy.

Conclusions, including unique features of the case(s):
Biopsy specimen was found to have a homozygous deletion of tumor suppressor gene SMARCB1 (also known as INI1) gene on Chromosome 22. Given these findings, the team was concerned about a germline 22q11 deletion, thus whole exome sequencing was performed. Gene studies were performed and showed normal 22q11 of peripheral blood, indicating that deletions in tumor were spontaneous in nature. .22q11 deletion has been associated with a variety of syndromes, not all of which are associated with a mutation in tumor suppressor SMARCB1, but those that are have been associated with rhabdoid tumor oncogenesis (primarily in the kidney). Other atypical features of this presentation include young age, rapid growth and CRAO (likely related to rapid growth) which has never been reported in this context.

References: 1. Verma A, Morriss C. Atypical teratoid/rhabdoid tumor of the optic nerve. Pediatr Radiol. 2008;38(10):1117-21. 2. Biswas B, Bhushan B, Jayakumar N et al (1999) Teratoid malignant medulloepithelioma of the optic nerve: report of a case and review of the literature. Orbit 18:191–196 3. Judkins AR, Eberhart CG, Wesseling P. Atypical teratoid/rhabdoid tumor. World Health Organization Classification of tumors of the central nervous system. Lyon: IARC Press; 2007. p. 147–9. 4. Chakrapani AL, White CR, Korcheva V, et al. Congenital extrarenal malignant rhabdoid tumor in an infant with distal 22q11.2 deletion syndrome: the importance of SMARCB1. 5. Mahdi Y, Kharmoum J, Alouan A, et al. Primary atypical teratoid/rhabdoid tumor of the optic nerve: a rare entity in an exceptional location. Diagn Pathol. 2015;10:47.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 12
Neurovascular disorders with isolated ocular signs and symptoms

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Introduction:
Neurovascular disorders include aneurysms, vascular malformations, venous sinus obstruction and AVfistulas etc. We present two cases of neurovascular disorders with isolated ocular findings.

Description of Case(s):
Case I: 14 year boy sent from neurosurgery with a diagnosis of cavernous sinus angioma. Patients had diplopia for 2 months and a history of cellulites at left angle of mouth. Examination showed esotropiaOD with abduction restriction, rest of the examination was normal. Magnetic Resonance Imaging (MRI) showed seller mass with contrast enhancement, right paraseller extension, Internal Carotid Artery (ICA) pushed peripherally suggestive of cavernous angioma. Neuro-radiologist reviewed the MRI and reported the sac like outpouching of right cavernous ICA with indication of turbulent flow and intense post contrast enhancement suggestive of mycotic aneurysm of right cavernous ICA. Digital subtraction angiogram confirmed the ICA aneurysm. The patient underwent the parent vessel occlusion of right ICA with good cross circulation. Case II: 33 year male had sudden onset of painful visual lossOD. The doctor noted light perceptionOD, 6/9OS and diagnosed retrobulbar neuritis and gave methylpred injections. Ten days later patient came to us, examination showed vision 6/18OD, 6/6OS, RAPD inOD with impaired colour vision. Fundii revealed temporal pallorOD with normal discOS. Perimetery showed bitemporal hemianapia OU with central scotomaOD. Visual evoked response was normalOU. Initial MRI demonstrated the haemorrhage in suprasellar region on right side tracking along right optic tract. Repeat MRI after 2 weeks revealed minimal patchy enhancement in a small space occupying lesion in relation to optic chiasma on right with partly resolved bleed indicative of a cavernous angioma with bleed. The patient underwent right pterional craniotomy with excision of lesion.

Conclusions, including unique features of the case(s):
Case I: MRI findings of the turbulent flow in the lesion helped in making the diagnosis of mycotic aneurysm. Case II: Optochiasmatic cavernous angioma is rare and not encapsulated, hence recurrent haemorrhages are common.

References: Deltomme M, Schroeven M, Lawson ML, etal. MRI and MRA features of a saccular mycotic aneurysms of the cavernous carotid artery resulting from invasive aspergillus sinusitis. Journal of the Belgium Society of radiology 2015;99(2):76-79. Cloud GC, Ric PM, Markus HS. Serial MRI of a mycotic aneurysm of the cavernous carotid artery. Neuroradiology 2003;45:546-549. Alafaci C. Cavernous malformation of the optic chiasm: An uncommon location. Surg Neurol Int 2015:6:60. SonDW. Cavernous malformation of the optic chiasm: Case report. Journal of Korean neurosurgical society 2008:44(2):88-90.

Keywords: Neuroimaging, Optic neuropathy, Interventional neuroradiology

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Poster 13
Myelin Oligodendrocyte Glycoprotein Antibody (MOG-IgG)-Positive Optic Perineuritis

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Introduction:
Optic perineuritis can be a manifestation of infectious and systemic inflammatory disorders, but the majority of cases are idiopathic. MOG-IgG-positive optic neuritis has been reported to be associated with optic nerve sheath enhancement. We report the clinical features, imaging findings, serological evaluation and treatment response of optic perineuritis patients with positive MOG-IgG.

Description of Case(s):
Two patients presented with pain with eye movements with minimal or no central visual acuity loss. Optic nerve sheath enhancement was noted with MR imaging consistent with optic perineuritis (OPN). Optical coherence tomography revealed mild retinal nerve fiber layer thickening. Both patients were positive for MOG-IgG in serum and responded well to steroid administration with complete resolution of symptoms. One patient suffered multiple relapses requiring chronic immunosuppression while the other has not had recurrence after tapering of the prednisone over 12 months follow up.

Conclusions, including unique features of the case(s):
This report describes 2 patients with clinical, radiographic and therapeutic response consistent with optic perineuritis. MOG-IgG likely accounts for many cases of previously described idiopathic optic perineuritis. Mild vision loss with optic nerve sheath enhancement on MRI should prompt testing for MOG-IgG. Identification of this entity might provide guidance for treatment and prevent unnecessary further investigations.

References: 1. Bergman O, Andersson T, Zetterberg M. Optic perineuritis: a retrospective case series. Int Med Case Rep J. 2017;10:181-188. doi:10.2147/IMCRJ.S125972 2. Jitprapaikulsan J, Chen JJ, Flanagan EP, et al. Aquaporin-4 and Myelin Oligodendrocyte Glycoprotein Autoantibody Status Predict Outcome of Recurrent Optic Neuritis. Ophthalmology. 2018;125(10):1628-1637. doi:10.1016/j.ophtha.2018.03.041 3. López-Chiriboga AS, Majed M, Fryer J, et al. Association of MOG-IgG Serostatus With Relapse After Acute Disseminated Encephalomyelitis and Proposed Diagnostic Criteria for MOG-IgG–Associated Disorders. JAMA Neurol. July 2018. doi:10.1001/jamaneurol.2018.1814 4. 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;195:8-15. doi:10.1016/j.ajo.2018.07.020.

Keywords: Optic neuropathy, Demeylinating disease, Neuroimaging

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Poster 14

Concurrent Embolic Anterior Ischemic Optic Neuropathy and Retinal Artery Occlusion with Acute silent ischemic Stroke

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Introduction:

Embolic acute retina artery occlusion(RAO) is a well-known prodromal event for acute cerebral ischemic stroke[1] and embolic anterior ischemic optic neuropathy(AION) is very rarely reported[2, 3]. Silent acute cerebral infarct concurrent with ARO is usually found in the anterior circulation(1,4-6). We report a case of concurrent embolic AION and RAO with acute silent ischemic stroke involving brainstem.

Description of Case(s):

70-y-o Caucasian female with PMHx of diabetes, hypertension, CAD, mechanical aortic valve, atrial fibrillation on Warfarin, bilateral carotid endarterectomy(CEA) presented with acute painless vision loss OD. She had a left femoral artery angiography 5 days before the visual onset at which time Warfarin was held. On the 2nd day of onset she was documented with 2 small emboli in the branches of retinal artery OD. ESR was found at 63 and CRP 9.7. She was started with prednisone 80mg daily with concern of CRAO secondary to GCA, then referred to neuro-ophthalmologist who recommended her to ED for stroke evaluation. Visual acuity was finger count OD and 20/25 OS. Fundus exam by direct ophthalmoscope showed mild diffuse optic disc swelling OD with a right RAPD. No other focal neurological deficit. An infected wound and cellulites was found on the left heel with positive culture of pseudomonas and MRSA. MRI of brain demonstrated lacunar infarction of left pons and right caudate nucleus. She was started on Heparin. On day 6 of onset, VA stayed as HM and fundus examination showed flame shape hemorrhage on the temporal edge of right optic disc. Patient was discharged on Warfarin. One month follow up showed massive hemorrhage on optic disc and cherry red spot with stable vision.

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

Embolic AION is very rare especially with concurrence of ARO and acute silent cerebral infarct. It suggests embolism as possible mechanism of AION hence prompt the appropriate stroke workup and management.

References: 1. Biousse V. Acute Retinal Artery Ischemia: an Emergency Often Ignored. Am J Ophthalmol, 2016, 157(6): 1191-1121. 2. Coca M, Palau AEB, Morgan M, et al. Embolic Anterior Ischemic Optic Neuropathy Associated with a Hollenhost Plaque. JAMA, 2015, 133(2): e143264. 3. Portnoy S, Beer P, Packer AJ et al. Embolic Anterior Ischemic Optic Neuropathy. J of clinical neuro-ophthalmology,1989,9(1), 21-25. 4. Helenius J, Arsava EM, Goldstein J, et al. Concurrent Acute Brain Infarcts in Patients with Monocular Vision Loss. Ann Neurol 2012, 72, 286-293. 5. Lee J, Kim SW, Lee SC. Co-occurrence of acute retinal artery occlusion and acute ischemic stroke: Diffusion-weighted MRI Image Study. Am J Ophthalmol, 2014; 157: 1231-1238. 6. Zhang L, Zhang J, Kim R, et al. Risk of Acute Ischemic Stroke in Patient with Monocular Vision Loss of Vascular Etiology J neuro-ophthalmology, 2018, 38: 328-33.

Keywords: Optic neuropathy, Vascular disorders, Stroke Trauma, Neuroimaging

Financial Disclosures: The authors had no disclosures.

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Poster 15
Recurrence of chiasmitis secondary to systemic lupus erythematosus

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Introduction:
Ophthalmologic manifestations involving optic nerve and chiasm occur in only 1% of systemic lupus erythematousus (SLE) patients1. For diagnosis purposes it is worthy to consider that in some cases imaging exams can be found without alterations2,3.

Description of Case(s):
A 29 year old, female, was diagnosed with SLE in 2014 and used immunosuppressant treatment during this period. In March of 2017 reported an episode of sudden waking visual blurred, associated with high intensity diffuse headache. At ophthalmologic examination, she presented 20/150 visual acuity both eye (BE), biomicroscopy, tonometry, fundoscopy and ocular motility without alterations BE. The photomotor reflex examination demonstrated reduced and symmetrical reflexes BE (+3) associated with bilateral bitemporal visual field loss, compatible with chiasmal lesions. Laboratory data included an elevated erythrocyte sedimentation. The other exams: lumbar puncture (including oligoclonal banding), magnetic resonance imaging (MRI) (brain, orbit, pituitary and spinal cord) and angioresonance did not identify any abnormalities. Intravenous methylprednisolone was performed and an improvement on clinical aspects could be seen after fifteen days (visual acuity 20/25 in both eyes and visual field without alterations). After 8 months, the patient had a new headache and loss of inferior bitemporal visual field. A new MRI and neurological evaluation were performed without alterations. Intravenous methylprednisolone was indicated resulting in an improvement of the clinical aspects and visual field.

Conclusions, including unique features of the case(s):
Although immunosuppressed and without other clinical complaints, the episodes of chiasmitis were the only manifestation presented by the patient, in the face of an apparently controlled disease.

References: None.

Keywords: Neuro-ophth & systyemic disease (eg. MS, MG, thyroid), Visual fields, Vascular disorders

Financial Disclosures: The authors had no disclosures.

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Poster 16
Bilateral Optic Neuropathies from Infiltrative B-Cell Lymphoma

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Introduction:
Lymphomatous optic nerve (ON) infiltration is uncommon, often with delay in diagnosis.

Description of Case(s):
A 62yo woman with painful, progressive blurred vision OS received oral prednisone with improvement of symptoms, recurrent with steroid discontinuation. One month later, vision was 20/20OD, 20/30OS, with left RAPD and severe left ON edema. Head CT showed left ON sheath calcifications; brain/orbit MRI showed left ON enhancement and enlarged cervical and retropharyngeal lymph nodes. CSF analysis showed slightly elevated protein. Extensive testing, including aquaporin4 antibodies, was abnormal only for elevated ESR (70). She received intravenous and PO steroids for presumed optic neuritis. Two months later, vision was 20/25OD and CFOS, with left RAPD and severe left ON edema. Brain/orbit MRI showed decreased enhancement of the left ON and decreased lymph node size. Four months later (one year after presentation), neuro-ophthalmological examination showed vision 20/80OD and NLPOS, very swollen right ON, pale and swollen left ON, and multiple retinal hemorrhages suggesting old artery occlusion OS. MRI showed infiltrative diffuse left ON enhancement extending across the chiasm to the right ON. CSF analysis/fine needle aspiration of lymph nodes demonstrated CD20+ mature B-cell lymphoma. Final diagnosis was nodal marginal zone lymphoma (MZL) with CNS involvement stage IV.

Conclusions, including unique features of the case(s):
The global incidence of MZL is 10% of all non-Hodgkin lymphomas. MZL has three subtypes: extranodal, splenic and nodal MZL. Extranodal MZL, the most common type of lymphoma affecting the orbit (60% of cases), uncommonly involves the ON (3% of cases). We found no reported cases of nodal MZL affecting the orbit or the ON. Nodal MZL is a low-grade lymphoma, frequently presenting with advanced-stage disease. Delay in diagnosis >6 months is standard. MRI findings are nonspecific, including enlargement of the ON, enhancement of the ON sheath, and even tramtracking. >80% of patients have complete remission after treatment, usually chemotherapy combined with steroids.

References: - Grimm, McCannel, Omuro, etal. Primary CNS lymphoma with intraocular involvement: International PCNSL Collaborative Group Report. Neurology. 71(17),1355-1360, 2008. - GadegaardOlsen, Heegaard, Orbital lymphoma, Survey of Ophthalmology 1-22, 2018. - Kim, Mendoza, Rashid, Hayek, Grossniklaus, Optic nerve lymphoma: report of two cases and review of the literature, Surv Ophthalmol, 60(2):153-165, 2015. - Ahle, Touitou, Cassoux, Bouyon, Humbrecht, et al, Optic nerve infiltration in primary central nervous system lymphoma. JAMA Neurol, Nov1;74(11), 1368-1373, 2017. - DeSouza, Hooten, Lack, John, Martin, Bilateral central retinal artery occlusion associated with bilateral lymphoproliferative infiltrative optic neuropathy, Ocul Oncol Pathol, 3:229–234, 2017. - Kanamalla, The optic nerve tram-track sign, Radiology, 227(3):718–9, 2003. - Cuneo, Castoldi, Marginal zone B-cell lymphoma, Atlas Genet Cytogenet Oncol Haematol, 10(3):180-183, 2006. - Chen, Nodal marginal zone lymphoma (NMZL), Atlas Genet Cytogenet Oncol Haematol. In press.

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

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Poster 17
Incipient Optic Neuritis

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Introduction:
Optic neuritis typically entails discrete attacks of rapidly-evolving, transiently painful vision loss with recovery over weeks to months. Though nadir acuity and prognosis vary according to etiology (e.g., multiple sclerosis, NMO, anti-MOG), the natural history of each attack is generally similar. However, the classic natural history of optic neuritis has exceptions. Atypical resolution of optic neuritis is well described (i.e., chronic relapsing inflammatory optic neuropathy), but atypical onset of optic neuritis is poorly defined. We describe 3 patients with unusually protracted courses between symptom onset and progression to typical optic neuritis. We term this early, forme fruste disease state "incipient optic neuritis."

Description of Case(s):
We performed a retrospective chart review of 3 patients who presented with forme fruste optic neuritis who evolved into a more classic phenotype. Patient 1 (female) presented at age 48 with a history of lupus and lymphoma on hydroxychloroquine, mycophenolate, ibrutinib, bendamustine, and 1 dose of rituximab for painless blurred vision OD with 20/20 acuity, normal perimetry, and mild disc edema. MRI revealed right optic nerve enhancement which persisted for 4 years without vision loss or treatment. AQP4 was positive. 5 years after presentation, she developed painful acute vision loss with recurrent optic nerve enhancement. Patients 2 and 3 (30F, 38M) were evaluated for painless disc edema OU with no immune history, vascular risk factors, or immunosuppressant use. Visual acuity, color vision, MRI brain/orbits, lumbar puncture, and infectious work-up were normal in both. Each had visual field defects and progressed to a more classical optic neuritis phenotype after 3 and 6-10 weeks with development of painful eye movements and rAPD, respectively, with eventual resolution of disc edema and good outcome.

Conclusions, including unique features of the case(s):
Optic neuritis typically entails rapidly-evolving, painful vision loss but may be preceded by a variably-protracted period of forme fruste, incipient disease.

References: None.

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

Financial Disclosures: The authors had no disclosures.

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Poster 18
High altitude associated non-arteritic ischemic optic neuropathy

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Introduction:
Hypobaric hypoxia in extreme high altitude leads to optic disc edema, cotton wool spots, and retinal vascular changes [1-3]. High altitude associated non-arteritic anterior ischemic optic neuropathy (NAION) has been described [4-7]. In this study, we examined the clinical manifestations of 5 cases of high altitude-associated NAION.

Description of Case(s):
Three patients developed vision loss during vacation (Yellowstone National Park [8,000 ft], Sierras [14, 505 ft], and camping). One occurred while working as a mountain climber, and one noted blurred vision at sea level and then developed worsening vision while at Bryce Canyon (8000 ft) 5 days later. Average age at presentation was 56 (48-74) years. All patients were evaluated by a neuro-ophthalmologist within 3-21 days of symptom onset. Regarding risk factors, all patients (except a monocular patient) had disc-at-risk in the contralateral eye, and none had optic disc drusens or vascular risk factors. Three patients were diagnosed with obstructive sleep apnea and treated. Three patients' vision worsened, and one improved. Visual acuity was 20/20 to 20/70 at presentation and 20/70 to counting fingers at ≥6 months. Automated static perimetry revealed averaged mean deviation of -18.3 dB at presentation and -22.1 dB at ≥6 months. Average retinal nerve fiber layer thickness was 281 (80-348) microns at onset and 60 (55-80) microns at ≥6 months. Average macular ganglion cell complex was 59 (50-79) microns at onset and 50 (43-54) microns at ≥6 months. Four patients had subsequent high-altitude exposure, but none developed further events.

Conclusions, including unique features of the case(s):
NAION can occur in association with moderate high-altitude exposure. These patients are younger, had disc-at-risk, relatively mild obstructive sleep apnea, and no vascular risk factors. There was a high proportion of visual deterioration over days to weeks and relatively severe thinning on OCT. High altitude exposure may be a precipitating factor for NAION.

References: 1. Hackett, P.H., High altitude cerebral edema and acute mountain sickness. A pathophysiology update.Adv Exp Med Biol, 1999. 474: p. 23-45. 2. Willmann, G., et al., Update on high altitude cerebral edema including recent work on the eye.High Alt Med Biol, 2014. 15(2): p. 112-22. 3. Schatz, A., et al., Optic nerve oedema at high altitude occurs independent of acute mountain sickness.Br J Ophthalmol, 2018. 4. Bandyopadhyay, S., et al., Anterior ischaemic optic neuropathy at high altitude.Indian J Ophthalmol, 2002. 50(4): p. 324-5. 5. De Bats, F., et al., [Role of intolerance to hypoxia in the occurrence of anterior bilateral ischaemic optic neuropathy at high altitude].J Fr Ophtalmol, 2010. 33(10): p. 724-7. 6. Tian, X., et al., Retinal changes following rapid ascent to a high-altitude environment.Eye (Lond), 2018. 32(2): p. 370-374. 7. Distefano, A.G. and B.L. Lam, Non-Arteritic Anterior Ischemic Optic Neuropathy in Pilots.Aerosp Med Hum Perform, 2018. 89(11): p. 1005-1007.

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

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Poster 19
Pembrolizumab induced optic neuropathy in a patient with laryngopharyngeal carcinoma

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Introduction:
Pembrolizumab is a programmed death-1 receptor monoclonal antibody that is currently approved by the U.S. FDA for treating head and neck cancers. Intraocular inflammation (uveitis) following treatment withis a rare but clinically important event, described in approximately 1 percent of treated patients (1-5).

Description of Case(s):
A 48-year-old female presented with left ear hearing loss in 2015, pain with chewing in October 2017, and worsening left-sided cheek swelling, proptosis, facial pain and nasal discharge in 2/2018. Biopsy showed left maxillary sinus squamous cell carcinoma. Chemoradiation was started. She received a 1st dose of pembrolizumab on 7/5/2018. In 7/2018, after just two doses, she experienced sudden complete vision loss in the left eye. By 7/28/2018, her right eye also went blind. Repeat MRI brain w/wo showed compression of the optic apparatus. Pembrolizumab was discontinued. Palliative chemoradiation was initiated in 7/2018. Her first ophthalmology visit was in 9/2018. Visual acuity was NLP OU. Right pupil was fixed at 7 mm and the left was fixed at 4 mm. Afferent pupillary defect was absent. She had nearly complete, bilateral ophthalmoplegia. There was 50% decrease to touch in left CN V1-V3. Right optic nerve was tilted with mild pallor and peripapillary hemorrhage. There was large, left facial swelling/edema with left eye proptosis. Bullous conjunctival chemosis was overlying the left lower lid and the cornea was neurotrophic with dense punctate epithelial erosions. Left optic disc was tilted, pallid and with peripapillary hemorrhages covered by vitreous hemorrhage appearing like central retinal vein occlusion.

Conclusions, including unique features of the case(s):
With a close relationship between exposure to Pembrolizumab and bilateral vision loss to no light perception, it is suspicious that there was a causal effect. The vision loss was described as an immune-related adverse reaction caused by the drug. Our patient also had optic nerve compression due to tumor progression.

References: 1. Aaberg MT1, Aaberg TM Jr. PEMBROLIZUMAB ADMINISTRATION ASSOCIATED WITH POSTERIOR UVEITIS. Retin Cases Brief Rep. 2017 Fall;11(4):348-351. 2. Hanna KS1. A Rare Case of Pembrolizumab-Induced Uveitis in a Patient with Metastatic Melanoma. Pharmacotherapy. 2016 Nov;36(11):e183-e188. 3. Acaba-Berrocal LA1, Lucio-Alvarez JA1, Mashayekhi A1, Ho AC2, Dunn JP2, Shields CL1. Birdshot-like Chorioretinopathy Associated With Pembrolizumab Treatment.JAMA Ophthalmol. 2018 Oct 1;136(10):1205-1207. 4. Robert C, Schachter J, Long GV, et al. Pembrolizumab versus Ipilimumab in Advanced Melanoma. N Engl J Med 2015; 372:2521. 5. Ribas A, Hamid O, Daud A, et al. Association of Pembrolizumab With Tumor Response and Survival Among Patients With Advanced Melanoma. JAMA 2016; 315:1600.

Keywords: Optic neuropathy

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Grant Support: None.

Poster 20
Mitochondrial ND5 gene heteroplasmic mutation (m.G13042A), in a patient with Leigh-LHON overlap syndrome

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Introduction:
We describe the first case report of Leigh/LOHN overlap syndrome associated with mitochondrial 13042G>A mutation.

Description of Case(s):
Over 4 years, a male teenager suffered from ophthalmoplegia (WEBINO), parkinsonism, seizures, cognitive and behavioral deterioration (after alcohol consumption), and finally, sub-acute vision loss. Ocular structure was normal, VEP was pathological. CSF lactate levels were high, MRS demonstrated a lactate peak. Repeated MRI revealed bilateral periaqueductal and midbrain encephalomalacia lesions, and after vision loss, also a slight enhancement of optic chiasm. Repeated WES genetic tests showed normal mitochondrial sequence. Muscle biopsy was normal. Brain biopsy showed spongiform changes with fibrillary and cellular gliosis. When visual deterioration occurred, neuro-ophthalmologist suspected LHON acute phase and suggested starting Idebenone treatment, despite lack of genetic confirmation. Genetic tests were repeated, a mitochondrial heteroplasmic mutation in the ND5 gene (13042G>A) was found.

Conclusions, including unique features of the case(s):
For mitochondrial diseases it is not unusual that the same mutation results in different phenotypes possibly caused by additional nuclear modifying genes or epigenetic factors(1). 13042G>A mutation was reported in patients with a Leigh like syndrome (INO, ataxia, increased lactate)(2), patients with a MELAS/MERRF overlap syndrome(3), and an Italian family with LHON-like optic neuropathy, retinopathy and cataract, strokes and early deaths(1). Our patient presented features of both Leigh like syndrome and LOHN-like optic neuropathy. According to the international consensus statement on the clinical and therapeutic management of LHON(4), "Idebenone should be started as soon as possible in patients with disease less than 1 year". Since first genetic tests of our patient failed to reach a diagnosis, the dilemma was whether to treat with Idebenone, despite lack of genetic confirmation. Repeated tests confirmed diagnosis, and revealed higher mutational loads in urinary epithelium than in blood. This suggests a strong selection against the mutant mtDNA in a fast turnover tissue, similar to other severe mtDNA pathogenic mutations(1,5).

References: 1. Valentino ML, Barboni P, Rengo C, Achilli A, Torroni A, Lodi R, Tonon C, Barbiroli B, Fortuna F, Montagna P, Baruzzi A, Carelli V. The 13042G -.A/ND5 mutation in mtDNA is pathogenic and can be associated also with a prevalent ocular phenotype. J Med Genet 2006;43:e38. 2. Blok M.J., Spruijt L., de Coo I.F., Schoonderwoerd K., Hendrickx A., Smeets H.J. 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(4):e74 3. Naini AB, Lu J, Kaufmann P, Bernstein RA, Mancuso M, Bonilla E, Hirano M, DiMauro S. Novel mitochondrial DNA ND5 mutation in a patient with clinical features of MELAS and MERRF. Arch Neurol 2005;62:473–6. 4. Carelli V., Carbonelli M., de Coo I.F., Kawasaki A., Klopstock T., Lagrèze W.A., La Morgia C., Newman N.J., Orssaud C., Pott J.W.R., et al. International Consensus Statement on the Clinical and Therapeutic Management of Leber Hereditary Optic Neuropathy. J. Neuroophthalmol. 2017;37:371–381 5. Rahman S, Poulton J, Marchington D, Suomalainen A. Decrease of 3243ARG mtDNA mutation from blood in MELAS syndrome: a longitudinal study. Am J Hum Genet 2001;68:238–40.

Keywords: Genetic Disease, Optic neuropathy, Ocular Motility

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Grant Support: None.

Poster 21
Bilateral optic neuropathy following treatment with nivolumab for metastatic cutaneous melanoma

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Introduction:
Immune checkpoint inhibitors are powerful tools in the management of malignancy. Their mechanism of action is inducing an endogenous autoimmune state to fight metastatic cancers. However, they have been associated with systemic and ocular side effects. The purpose is to describe an ophthalmic side effect of nivolumab in a patient with metastatic cutaneous melanoma.

Description of Case(s):
A 71 year old male presented with dimmed vision and dyschromatopsia in both eyes for 3 months. He had a history of stage III metastatic cutaneous melanoma treated with ipilimumab+nivolumab (4 cycles), then nivolumab (24 cycles), with good tumor control. Presenting visual acuity was 20/20 OU, with normal pupil response. Fundus examination showed mild bilateral optic nerve edema, visual fields (VF) showed marked constriction. Treatment with nivolumab was discontinued. Head and orbit MRI and spinal fluid were normal. Serology for atypical optic neuropathies and paraneoplastic syndromes was negative. Follow-up VF worsened, with constriction 10° from fixation OU and decreased VA in OS. Treatment was initiated with prednisone with no response, then plasma exchange (PLEX) was performed with significant improvement in VF, VA and dyschromatopsia for 3 weeks. At which point, VF and dischromatopsia started to worsen progressively, and VA decreased to 20/40 OU, so a new round of PLEX was performed and azatioprine was started, with no further decline of vision or visual fields. OCT shows marked loss of fibers OU.

Conclusions, including unique features of the case(s):
Checkpoint inhibitors are new tools in the management of previously incurable malignancies. Although ocular immune related adverse events are rare, they should be considered after starting nivolumab and even after cessation of the medication. Every patient with a history of metastatic malignancy treated with nivolumab presenting with new ocular symptoms must be examined to rule out side effects of checkpoint inhibitors. Also a choroidal mass due to metastatic disease and paraneoplastic syndromes should be considered.

References: None.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 22
The Eagle Head in My Right Eye! A Case of Paracentral Acute Middle Maculopathy

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Introduction:
An 83-year-old male presented with a sudden painless onset of a seeing an eagle-head-shaped dark spot in the center of his right eye. His past medical history was significant for spinal stenosis. Past ocular history was significant for mild ocular dryness, bilateral cataract extraction 4 years prior to presentation, and right epiretinal membrane (ERM).

Description of Case(s):
Examination revealed visual acuity of 20/25 OU, 8/8 Ishihara plates OU, and normal pupillary reactions without afferent pupillary defect. Slitlamp and dilated fundus examination were unremarkable apart from bilateral pseudophakia and right ERM. On an Amsler grid, the patient was able to demonstrate a dark spot few degrees inferotemporal to fixation. Spectral-domain Optical Coherence Tomography (SD-OCT) showed normal macular thickness OU with a mild ERM in the right eye. Additionally, it showed a subtle hyper-reflectivity in the middle retinal layers of the juxta foveal region of the right macula. OCT Angiography revealed focal loss of the deep capillary plexus in the shape of an eagle head. Systemic stroke workup was unremarkable.

Conclusions, including unique features of the case(s):
Paracentral Acute Middle Maculopathy (PAMM) is an OCT-based diagnosis in patients with retinal capillary ischemia and persistent scotomas. This relatively new entity was first reported in 2013 by Sarraf and interpreted as a possible more superficial variant of Acute Macular Neuroretinopathy (AMN). It is characterized by hyperreflective lesions visible at the level of the inner nuclear layer (INL) in patients presenting with acute onset of a negative scotoma. Additionally, PAMM demonstrates grey lesions visible on near-infrared reflectance imaging. Workup to rule out cardiovascular risk factors is recommended. Diffuse lesions may be a sign of an occult central retinal artery occlusion mandating to rule out underlying carotid disease or giant cell arteritis. PAMM should be considered in patients presenting with paracentral negative scotomas especially in the absence of an afferent pupillary defect.

References: Rahimy E, et al. Paracentral Acute Middle Maculopathy What We Knew Then and What We Know Now. Retina, The Journal of Retinal and Vitreous Diseases 2015, Vol 35, 10 Sarraf D, Rahimy E, Fawzi AA, et al. Paracentral Acute Middle MaculopathyA New Variant of Acute Macular Neuroretinopathy Associated With Retinal Capillary Ischemia. JAMA Ophthalmol. 2013;131(10):1275–1287. Chen X, et al. Spectrum of retinal vascular diseases associated with paracentral acute middle maculopathy. Am J Ophthalmol 2015;160(1):26–34.

Keywords: Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Non-organic visual disorders, Visual fields

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Grant Support: None.

Poster 23
Unusual Manifestation of Histopathologic Confirmed Metastatic Esophageal Carcinoma

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Introduction:
Intraocular metastasis from esophageal carcinoma are rare. Cases of esophageal carcinoma with metastasis to the choroid have been infrequently reported, especially in ophthalmic literature, and to our knowledge, none have included histopathology.

Description of Case(s):
A white male in his late 60s was referred for evaluation of left orbital mass. The patient presented with transient vision loss OS, intermittent "pressure-like" headaches originating from behind the left eye, and central vision loss. Two years ago, he was diagnosed with esophageal adenocarcinoma. Uncorrected VA was 20/30 OD and HM OS with RAPD. Temporal constriction and central scotoma OS were noted on confrontation VF. EOM was full. Fundus examination OS showed circumferential peripapillary retinal elevation, most pronounced infratemporally. OCT revealed diffuse irregular and undulating contour to the choroid RPE and retina. MRI revealed an intraconal left orbital mass arising from the uvea. Transconjunctival lateral orbitotomy was performed. A violaceous mass was seen emanating from the temporal aspect of the sclera 15 mm posterior to the lateral rectus insertion. A shave biopsy revealed clusters of tumor cells in an infiltrative pattern and desmoplastic stroma. Tumor cells showed significant pleomorphism, apoptosis, and mitotic activity. Immunostaining with cytokeratin-7 supported the diagnosis of metastatic esophageal adenocarcinoma. The patient was referred to the ocular oncology service with no evidence of systemic disease otherwise. He was treated with IMRT with partial resolution and subjective improvement.

Conclusions, including unique features of the case(s):
Ocular manifestations of metastatic esophageal adenocarcinoma depend on its location; symptoms include vision loss, diplopia, and VF defects. This can be seen bilaterally or unilaterally, and may be the presenting symptom. Our case presented with a central scotoma with visual loss, which has rarely been reported and histopathologic confirmation even less common. It is important to differentiate between metastases and primary choroidal melanoma. Confirmatory biopsy can rarely be obtained but is useful for determination of definitive management.

References: None.

Keywords: Tumors, Orbit/ocular pathology, Neuro-ophth & systyemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 24
Paracentral Acute Middle Maculopathy in the Setting of New Onset Giant Cell Arteritis

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Introduction:
Paracentral acute middle maculopathy (PAMM) is a condition in which ischemia of the deep retinal capillary plexus causes distinctive hyperreflective lesions in the inner nuclear layer on high resolution SD-OCT.

Description of Case(s):
An 80-year-old woman noticed acute onset of a central gray lacy or snowflake pattern disrupting the vision of the right eye. Two months prior she had developed new temporal headaches that worsened despite occipital nerve blocks, associated with scalp tenderness and jaw claudication. Past medical history was significant for breast cancer in remission, treated with surgery and chemotherapy one year prior, as well as Grave's disease and hypertension. Several of her antihypertensive medications were recently increased due to worsening hypertension. Review of systems revealed a 10 pound weight loss and night sweats but no polymyalgia rheumatica symptoms. Visual acuity was 20/20-2 OD and 20/20 OS. Pupils, motility, and visual fields were normal. Fundus exam showed normal discs and vessels. Right macula showed blunted foveal reflex and subtle parafoveal retinal whitening that corresponded to hyperreflective areas of the inner nuclear layer on OCT. OCT angiography showed decreased flow in the deep capillary plexus OD. Left macula was normal. ESR was 21 mm/hr, and CRP was mildly elevated at 1.1 mg/dL. Temporal artery biopsy showed granulomatous inflammation in the intima, muscularis, and adventitia with neovascularization within the vessel wall. Her headache improved dramatically on oral prednisone, and her visual disturbance and macular changes gradually improved over several months.

Conclusions, including unique features of the case(s):
PAMM can be caused by hypoperfusion associated with either venous or arterial occlusions. Although PAMM has been reported in 2 patients with GCA and cilioretinal artery occlusion, our patient did not appear to have a cilioretinal artery and to our knowledge, PAMM has not been reported as a presenting sign of giant cell arteritis in the absence of cilioretinal artery occlusion.

References: Chen, Rahimy, Sergott, Nunes, Souza. Spectrum of retinal vascular diseases ssociated with paracentral acute middle maculopathy. Am J Ophthalmol,160, 26-34, 2015. Pichi, Fragiotta, Freund, Au, Lembo. Cilioretinal artery hypoperfusion and its association with paracentral acute middle maculopathy. Br J Ophthalmol doi: 10.1136/bjophthalmol-2018-312774. [Epub ahead of print] 2018. Rahimy, Sarraf. Paracentral acute middle maculopathy spectral-domain optical coherence tomography feature of deep capillary ischemia. Curr Opin Ophthalmol, 25(3):207-12, 2014.

Keywords: Neuro-ophth & systyemic disease (eg. MS, MG, thyroid), Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Vascular disorders, Pupils Retina, Miscellaneous

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Poster 25
Bitemporal Hemianopsia and Significant Binasal GCL–IPL Thinning In Chiasmal Hemioptic Hypoplasia

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Introduction:
Chiasmal hemioptic hypoplasia has been described among diverse congenital optic nerve anomalies, associated to septo-optic dysplasia. These anomalies will produce different defects of the visual field according to their presentation form. It has been demonstrated by Optical Coherence Tomography (OCT) a close correlation between damage of the chiasmatic visual pathway with an axonal and ganglion cells loss in corresponding nasal area of the retina.

Description of Case(s):
We present a 67 y.o. female illiterate patient who comes for evaluation with chief complaint of progressive visual loss with no relevant medical or family history. During the evaluation she presented an alternate esotropia of 40 prism diopters and limited abduction in both eyes, conjugate horizontal nystagmus, best corrected visual acuity of 20/100 in both eyes, chromatic vision of 4/5 plates in both eyes. Pupils were normal and the intraocular pressure as well with bilateral cataracts of NO5, NC5 by LOCS III classification, which justified the visual loss. The optic nerve was initially described with temporal pallor, with nasal hypoplasia and band atrophy. The Humphrey Visual Fields showed a bitemporal hemianopsia with respect of the vertical meridian and Cirrus OCT showed binasal GCL-IPL thinning. Cerebral MRI was performed, and it showed hypoplasia of the corpus callosum, agenesis of septum pellucidum, and chiasmal hypoplasia.

Conclusions, including unique features of the case(s):
Chiasmal hemioptic hypoplasia is a congenital defect associated to the septo-optic dysplasia that may present a bitemporal hemianopsia with respect of the vertical meridian and a GCL-IPL complex thinning of the nasal hemiretina, mimicking a chiasmal compression in asymptomatic patients.

References: 1- Hoyt WF. Rios-MontenegroEN. Berens MM. et al. Homonymous hemioptic hypoplasia: Fundoscopic features in standard and red free ilumination in three patients with congenital hemiplegia. Br J Ophthalmology 1972; 56: 537-545. 2- Monteiro ML, Leal BC, Rosa AA & Bronstein MD (2004): Optical coherence tomography analysis of axonal loss in band atrophy of the optic nerve. Br J Ophthalmol 88: 896–899. 3. T.J. Biega, Z.P. Khademian and G. Vezina. Isolated Absence of the Optic Chiasm: A Rare Cause of Congenital Nystagmus. Am Journal of Neuroradiology February 2007, 28 (2) 392-393. 4- Tieger MG, Hedges TR III, Ho J, Erlich-Malona KN, Vuong LN, Athappilly GK, Mendoza-Santiesteban CE. Ganglion cell complex loss in chiasmal compression by brain tumors. J Neuroophthalmol. 2017; 37: 7-12.

Keywords: Visual fields, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 26
Vitreopapillary Traction Masquerading as Papilledema

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Introduction:
This case study emphasizes the importance of using OCT to look for vitreopapillary traction in atypical cases of suspected papillitis, NAION, or papilledema.

Description of Case(s):
60-year-old gentleman was referred for evaluation of disc edema. He reported central flashes of light in the right eye for two months followed by a cloudy blindspot. Humphrey visual field showed an enlarged blindspot in the right eye and infero-nasal defect in the left eye. On exam, vision was 20/25 and 20/20. He had 4+ optic disc edema, 2+ vitreous cell, and a mild epiretinal membrane in the right eye and mild disc drusen in the left eye. He reported that one week prior to the onset of visual symptoms he was bitten by a tick, so he was started on doxycycline for possible papillitis secondary to tick-borne disease. Subsequently, a work-up for etiologies of papillitis was negative. At one month follow-up, the patient's disc edema and vitreous cell in the right eye remained unchanged while the left eye had developed 1-2+ disc edema in the interim. One month later, magnetic resonance imaging of the brain and orbits was ordered to rule out mass lesion as a cause of bilateral disc edema and was unremarkable. Lumbar puncture was performed with an opening pressure of 25 cm H2O and normal cerebrospinal fluid studies. Optical coherence tomography (OCT) of the discs revealed vitreopapillary traction syndrome in both eyes four months from initial visit. He was referred to the retina service for surgical evaluation and underwent pars plana vitrectomy in both eyes sequentially. Follow-up OCT showed dramatic improvement in the vitreous traction, and the patient reported subjective improvement in vision.

Conclusions, including unique features of the case(s):
OCT should be utilized in the work-up of optic disc edema in middle-aged and older adults, since impending posterior vitreous detachment is prevalent in this age group.

References: None.

Keywords: Optic neuropathy, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 27
Concurrent CRAO with Arteritic AION in Eosinophilic Granulomatosis with Polyangiitis

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Introduction:
Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare systemic necrotizing vasculitis characterized by peripheral neuropathy, pulmonary involvement, and eosinophilia. EGPA has been associated with a number of ocular conditions, including retinal vascular occlusion, ocular motor cranial neuropathy, and optic neuropathy. We describe a case report of a concurrent central retinal artery occlusion(CRAO) with arteritic anterior ischemic optic neuropathy(AION).

Description of Case(s):
A 44-year-old woman presented with acute painless severe visual loss in her right eye. Her past medical history included deep vein thrombosis in her leg, for which she was treated with warfarin. Her visual acuity was hand motion in the right eye and 20/20 in the left eye. Right relative afferent pupillary defect was present. The fundoscopic examination revealed diffuse whitening of retina with cotton wool spots. Right optic disc was chalky white and edematous, whereas left fundus appeared normal. Fundus fluorescein angiography(FFA) demonstrated delayed arterio-venous transit time along with choroidal hypoperfusion, consistent with CRAO and arteritic AION in the right eye. Laboratory evaluation revealed an ESR of 14 mm/hour, C-reactive protein level of 66.35 mg/dl and 44% peripheral eosinophilia. During last year, she recently had worsening of asthma, recurrent paranasal sinusitis along with mononeuropathy of left peroneal nerve. The diagnosis of EGPA was made based on constellation of eosinophilia, mononeuropathy, asthma and paranasal sinus abnormalities. Patient was given high-dose corticosteroid combined with pulsed intravenous cyclophosphamide. Her vision was improved to 20/60 in the right eye and the left eye remains unaffected.

Conclusions, including unique features of the case(s):
The most consistent diagnosis is EGPA-associated CRAO concurrent with arteritic AION. The patient's visual improvement may have been the result of early diagnosis and immunosuppressive therapy. Therefore, we suggest that EGPA patients should undergo complete neuro-ophthalmic evaluations. Visual improvement may be achieved by early diagnosis and prompt treatment by immunosuppressive agents.

References: 1. Churg J, Strauss L. Allergic granulomatosis, allergic angiitis, and periarteritis nodosa. Am J Pathol 1951;27:277–301. 2. Masi AT, Hunder GG, Lie JT, Michel BA, Bloch DA. The American College of Rheumatology 1990 criteria for the classification of Churg- Strauss syndrome (allergic granulomatosis and angiitis). Arthritis Rheum 1990;33:1094–100.

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

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Poster 28
Heterochromia and ocular ischemia resulting from Neurofibromatosis I-related optic pathway glioma

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Introduction:
NF1-OPG are typically benign optic nerve tumors arising in childhood which may be associated with visual loss from optic neuropathy, impaired extraocular motility, and proptosis. While optic disc edema, pallor, or choroidal folds are commonly observed, iris and retinal vascular sequelae arising from NF1-OPG are exceedingly rare (1-4).

Description of Case(s):
An 11-month-old girl presented with iris heterochromia and left proptosis. She had reduced visual acuity in the left eye, a RAPD, impaired extraocular motility, and cutaneous evidence of NF1. MRI demonstrated a large optic nerve tumor and enhancement of the iris. EUA revealed hypotony, extensive dilated iris vessels and blood in Schlemm's canal. The posterior segment examination revealed optic disc elevation and optociliary shunt vessels, a cilioretinal artery occlusion, dilated and tortuous retinal veins with retinal capillary non-perfusion, a clinical picture most consistent with ocular ischemic syndrome and venous stasis retinopathy. A stereotactic-guided optic nerve biopsy was performed and histopathology was consistent with low grade pilocytic astrocytoma. The patient was enrolled in a clinical trial of Vinblastine +/-Bevacizumab.

Conclusions, including unique features of the case(s):
Intraocular involvement from NF1-OPG is exceedingly rare (1, 2, 4) . Other potentially malignant tumors, such as optic nerve medulloepithelioma, must be considered in the differential diagnosis. In adults, there are reported cases of malignant OPG presenting with central retinal vein occlusion (5, 6). In the setting of known NF1, typical OPG do not require histopathologic confirmation; even in aggressive cases, optic nerve biopsy is associated with significant risk of visual loss with limited diagnostic utility. However, optic nerve biopsy may be considered to confirm the diagnosis of OPG when intraocular involvement is observed to exclude a malignant optic nerve tumor, particularly in the setting of severe pre-existing severe visual loss in the affected eye. Ocular ischemic syndrome with venous stasis retinopathy is a rare and devastating cause of visual loss resulting from NF1-OPG.

References: 1. Shields JA, Shields CL, De Potter P, Milner RS. Choroidal neovascular membrane as a feature of optic nerve glioma. Retina. 1997;17(4):349-50. 2. Gupta V, Sabri K, Whelan KF, Viscardi V. Rare case of optic pathway glioma with extensive intra-ocular involvement in a child with neurofibromatosis type 1. Middle East Afr J Ophthalmol. 2015;22(1):117-8. 3. Eghtedari M, Fattahi SF, Owji N, Ashraf MJ, Khalili MR, Geramizadeh B. Optic nerve glioma with complete intraocular extension. J Curr Ophthalmol. 2016;28(4):228-31. 4. de Keizer RJ, de Wolff-Rouendaal D, Bots GT, Thomeer RT, Brouwer OF, Vielvoye GJ. Optic glioma with intraocular tumor and seeding in a child with neurofibromatosis. Am J Ophthalmol. 1989;108(6):717-25. 5. Yatziv Y, Bukstein F, Segev Y, Kesler A. Adult optic nerve glioma presenting as central retinal vein occlusion. Retin Cases Brief Rep. 2007;1(1):33-5. 6. Balachandran C, Millar MJ, Murali R, Bulliard C, Malcolm CM, Maloof A. Malignant optic glioma presenting as an acute anterior optic neuropathy. Retina Cases Brief Rep. 2009;3(2):156-60.

Keywords: Pediatric neuro-ophthalmology, Tumors, Orbit/ocular pathology, Orbit, Pupils Retina

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Poster 29
The Localizing Value of the Relative Afferent Pupillary Defect in Patients with Efferent Ocular Disease

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Introduction:
Although the relative afferent pupillary defect (RAPD) is a well-known objective, rapid assessment of the afferent visual system, the localizing significance of the RAPD is particularly critical in some cases of efferent ocular disease. We present a case where the chief complaint was diplopia and the examination of the efferent pathway disclosed a strabismus. Neuroimaging studies of the brain were normal but orbital imaging confirmed a structural lesion. The importance of detection of an RAPD should be emphasized as part of the preoperative orthoptic measurements prior to strabismus surgery.

Description of Case(s):
An 86-year-old vasculopathic female presented with chronic painless binocular vertical diplopia. Initial orthoptic evaluation revealed strabismus for which she underwent surgery. Despite surgical intervention, she continued to complain of double vision over the following year and underwent a second strabismus surgery. She then noted "smoky" vision on leftward gaze. She was referred to the retina specialist who noted a left epiretinal membrane with macular edema, but no intervention was recommended. She continued to complain of decreased vision of the left eye and was subsequently referred to the neuro-ophthalmology department. At that visit, patient was noted to have a left RAPD and a left dense inferior altitudinal field defect. MRI orbit revealed an avidly enhancing extra-axial mass invading the left orbital apex.

Conclusions, including unique features of the case(s):
Patients with a chief complaint of diplopia are usually assumed to have efferent disease. The finding of chronic and stable ocular misalignment may lead to a decision for strabismus surgery. Preoperative imaging studies of the brain may be negative in patients with an orbital lesion and dedicated orbital imaging (e.g., Magnetic resonance imaging of brain and orbit with gadolinium and fat suppression) may be necessary. The presence of an efferent sign (eg. incomitant strabismus) and an RAPD should be considered to be an orbital apex lesion until proven otherwise.

References: None.

Keywords: Adult strabismus with a focus on diplopia, Ocular Motility, Orbit/ocular pathology, Tumors

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Grant Support: None.

Poster 30
Homonymous Hemianopsia after PRES and Immune Reconstitution Inflammatory Syndrome in HIV/AIDS

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Introduction:
Posterior reversible encephalopathy syndrome (PRES) is characterized by transient vasogenic cerebral edema with multiple etiologies and typically presents with seizures, headache, visual disturbance and mental status changes. Immune reconstitution inflammatory syndrome (IRIS) is defined by clinical criteria including atypical presentation of opportunistic infections, tumors or inflammation, decreased viral load (VL) and increased CD4 lymphocytes. To our knowledge, only two cases associating PRES with IRIS in HIV/AIDS have been described.

Description of Case(s):
A 26-year-old, non-compliant woman with congenital HIV/AIDS was admitted for acute respiratory failure due to multi-lobular pneumonia. Blood and sputum cultures identified Haemophilus influenza and IV antibiotics were instituted. HAART (highly active antiretroviral therapy) was initiated a week later and was subsequently augmented with two other antiretroviral preparations. This resulted in decreased viral load (105,590 to 75 copies) and development of episodic headaches, confusion, hypertension and epileptic seizures. T2-weighted MRI revealed bilateral, diffuse, cortical and subcortical hyperintensity (leucoencephalopathy), more pronounced posteriorly. EEG showed left occipital and parietal spikes with diffuse slowing. Lumbar puncture was negative for JC virus making progressive multifocal leucoencephalopathy unlikely. Diagnosis of PRES associated with IRIS was made. Anti-hypertensive and anti-epileptic therapy was added to her regimen, with good effect. She was discharged in stable condition with CD4=21; VL=174. Five months after discharge, she was readmitted due to headaches. Ophthalmology was consulted to rule out CMV retinitis. She had no visual complaints and bilaterally, had uncorrected visions of 20/20, reactive pupils without RAPD, normal color vision and normal anterior and posterior segments. Visual fields revealed right homonymous hemianopsia. MRI showed complete resolution of leucoencephalopathic changes and minor decreased volume of the left occipital lobe. MRA was normal.

Conclusions, including unique features of the case(s):
PRES may occur in the setting of IRIS in HIV/AIDS and may result in persistent neurologic sequelae. Patients with PRES should have neuro-ophthalmic assessment including perimetry.

References: 1. French MA1, Price P, Stone SF. Immune restoration disease after antiretroviral therapy. AIDS. 2004 Aug 20;18(12):1615-27. 2. Lamy C, Oppenheim C, Mas JL. Posterior reversible encephalopathy syndrome. Handb Clin Neurol. 2014;121:1687-701. 3. Fugate JE, Rabinstein AA. Posterior reversible encephalopathy syndrome: clinical and radiological manifestations, pathophysiology, and outstanding questions. Lancet Neurol. 2015 Sep;14(9):914-925. 4. Weiss ZF, Rich J, Wing EJ. Posterior reversible encephalopathy syndrome in a patient with HIV/AIDS and immune reconstitution syndrome: a case study and literature review. Oxf Med Case Reports. 2018 Aug 20;2018(8):omy046.

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

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Poster 31
Anorexic disc or compressed disc

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Introduction:
Primary intracranial germ cell tumors represent 3-5% of all central nervous system tumors and occur most commonly in the pineal and suprasellar region with a male preponderance. Germinomas interestingly are more common in males when they involve pineal gland but more common in females when involving suprasellar region.

Description of Case(s):
15 years old anorexic female was admitted for evaluation of severe weight loss. She also had trouble with her vision, endocrine abnormalities, and an episode of seizure episode with some confusion on the day of admission. She never had menses Ophthalmology evaluation was remarkable for decreased vision, constricted visual fields and pale optic discs OU. All her symptoms including her not started her menses, weight loss, vomiting, visual disturbance and pale nerves were initially attributed to anorexia and vomiting. But given her pale optic nerves, episode of seizure and confusion she got an MRI which showed a large enhancing sellar-suprasellar mass with calcification suggestive of craniopharyngioma. On biopsy after partial resection she was found to have germinoma.

Conclusions, including unique features of the case(s):
Germinomas in pediatric age group can masquerade as psychiatric disorders and it is important to rule out organic causes in all patients. Neuroimaging can sometimes provide new insight into diagnosing patients with complex presentation and unclear diagnosis.

References: None.

Keywords: Tumors, Neuroimaging, Pediatric neuro-ophthalmology, Non-organic visual disorders, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

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Poster 32
All is Well - A diagnostic and management challenge

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Introduction:
Ganglioglioma are rare, slow-growing neoplasm with high predilection for temporal lobe. Low-grade gangliogliomas typically curable by surgery and has excellent prognosis. High-grade gangliogliomas managed with total resection and sometimes followed by radiation. The cases reported in literature with edema in the optic chiasm and tract were secondary to sellar/suprasellar tumors, high grade gliomas, aneurysm and had visual dysfunction.

Description of Case(s):
A 48-year-old woman experienced 2 years of gradually worsening right hemiparesis. History of hypothyroidism on levothyroxine. Neurologic examination showed right lower face weakness and right hemiparesis with brisk reflexes and positive Babinski. Visual acuity was 20/15OU with no RAPD. Color vision, extraocular movements and fundus exam were normal. MRI-brain showed large heterogeneously enhancing solid-cystic lesion in left thalamus with extensive edema extending into optic chiasm and bilateral optic tracts. The ESR, CRP, ACE, ANA, RPR were normal. CT CAP did not reveal a systemic tumor. Stereotactic brain biopsy was non-diagnostic. Oral prednisone was initiated. HVF, OCT RNFL, OCT Ganglion cell layers OU were normal. Repeat imaging after two weeks of oral steroids, showed no change in lesion size with some improvement in edema. Brain PET scan showed small focus of increased FDG activity in the lesion. Repeat biopsy favored WHO grade1 ganglioglioma. Although pathologically it was low-grade, patient declined clinically and radiologically. She was started on bevacizumab followed by temozolamide. Significant improvement was noted on follow-up brain imaging and clinically.

Conclusions, including unique features of the case(s):
The relatively mild initial neurologic symptoms and the lack of visual dysfunction with intact RNFL and GCL despite extensive radiologic involvement of the lesion was a diagnostic dilemma in the face of a non-diagnostic brain biopsy. A second biopsy revealed grade 1 ganglioglioma and treatment was challenging as the tumor was deemed not resectable due to the location, requiring radiation followed by chemotherapy.

References: A national perspective of adult gangliogliomas Kunal Varshneya, J. Manuel Saemiento, Mirian Nuno, Carlito Lagman, Debraj Mukherjee, Karla Nuno, Harish Babu, Chirag G Patil (August 2016) Cerebral Gangliogliomas: Preoperative Grading using FDG-PET and 201Tl-SPECT Patricia K. Kincaid, Suzie M. El-Saden, Sung-Hye Park, and Barry W. Goy (may 1998) Intracranial ganglioglioma: clinicopathological and MRI findings in 16 patients D. Zhanga, T.D. Henningb, L.-G. Zoua, L.-B. Huc, L. Wena,*X.-Y. Fengd, S.-H. Daia, W.-X. Wanga, Q.-R. Suna, Z.-G. Zhange (Jan 2008) Reversible Edema-Like Changes Along the Optic Tract Following Pipeline-Assisted Coiling of a Large Anterior Communicating Artery Aneurysm. Biagia La Pira; Waleed Brinjikji; Christopher Hunt; John J Chen; Giuseppe Lanzino MR imaging study of edema-like change along the optic tract in patients with pituitary region tumors. Saeki N, Uchino Y, Murai H, Kubota M, Isobe K, Uno T, Sunami K, Yamaora A. AJNR Am J Neuroradiol. 2003 Oedema along the optic tracts due to pituitary metastasis. Saeki N, Murai H, Kubota M, Fujimoto N. Br J Neurosurg. 2001.

Keywords: Tumors, Neuroimaging, Higher visual functions, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 33
Severe Susac syndrome in a patient with active ulcerative colitis

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Introduction:
The triad - encephalopathy, visual disturbances and hearing loss - characterizes Susac syndrome, a rare vasculopathy with unclear etiology and pathogeny. Herein, we report a severe Susac syndrome in a patient with active ulcerative colitis, condition causing various types of cerebral lesions and presenting cochlear and ocular involvement.

Description of Case(s):
A 64-year-old woman with medical history of ulcerative colitis and currently treated with oral prednisone, presented with gradual change in behavior. 9 months before presentation, she experienced sudden vertigo followed by left hearing loss. Audiogram showed raised thresholds on the left and MRI revealed multiples infra and supra-tentorial T2/FLAIR hyperintensities and leptomeningeal, bilateral vestibular and right cochlear gadolinium enhancement. Symptoms partially recovered after corticotherapy. 1 week before presentation, she exhibited progressive change in behavior. Initial neurological examination noted disorientation, disinhibition, cognitive and attention impairment. MRI showed multiple small infra and supra-tentorial ischemic lesions, some involving corpus callosum and exhibiting a “snowball” aspect, others involving the left external capsule and presenting a “string of pearls” disposition; T1 post-gadolinium showed leptomenigeal enhancement, mainly infratentorial. Ophthalmological exam revealed yellow, non-refractile retinal arterial plaques, occlusion of distal branches of central retinal artery and fluorescein leakage . CSF showed only elevated total proteins and moderately elevated Il-6 . Complex immunological, onconeuronal, infectious and prothrombotic state workup showed only increased d-dimers and increased activity of factor VII and factor von Willebrand. Colonoscopy revealed severe active ulcerative colitis. Due to the severe presentation she benefited from an aggressive treatment including corticotherapy, IV immunoglobulins, cyclophosphamide and methotrexate followed by favorable clinical and radiological evolution at 3 months follow-up.

Conclusions, including unique features of the case(s):
To our knowledge this case represent a second report of severe Susac syndrome associated with active ulcerative colitis. We suggest that inflammatory bowel disease might interfere directly with the vasculopathic processes of Susac syndrome or indirectly through an increased procoagulant state.

References: 1. Susac JO, Hardman JM, Selhorst JB. Microangiopathy of the brain and retina. Neurology. 1979;29:313 LP-313. 2. Fine S, Nee J, Thakuria P, Duff B, Farraye FA, Shah SA. Ocular, Auricular, and Oral Manifestations of Inflammatory Bowel Disease. Dig Dis Sci. Springer US; 2017;62:3269–3279. 3. Rodríguez-Martínez, J. A., and A. Echarri-Piudo. "Síndrome de Susac en un paciente con colitis ulcerosa". Gaceta medica de Mexico 153.7 (2017): 924-927.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 34
Hipoxic - ischemic Encephalopathy

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Introduction:
Hipoxia and hypoperfusion are the responsible mechanisms for the development of hipoxic- ischemic encephalopathy of CNS. Visual cortex is an unusual target. Common causes of hipoxic- ischemic encephalopathy in adults are cardiac arrest, severe hypotension, trauma and drowning. In children, the leading causes are neonatal anoxia, abusive trauma and dehydration. Clinical manifestations of hipoxic- ischemic encephalopathy include bilateral vision loss in all cases and, less frequently, Balint- Holmes syndrome . (1) Although enduring damage to occipital cortex can be caused by hipoxic- ischemic encephalopathy (2), neuroimaging may be normal or misinterpreted as normal due to subtle signs that might be overlooked.(1) Differential diagnosis with psychogenic causes is mandatory. (1)

Description of Case(s):
A 47 year- old woman presented with a 30 years long bilateral loss of vision. She first noticed it after a cardiorespiratory arrest caused by an asthma crisis, which required hospitalization and mechanic respiratory assistance with induced pharmacological coma. Her neurologist's diagnosis was hipoxic- ischemic encephalopathy. MRI and VEP were normal. Examination revealed bilateral visual acuity of 20/20. Central scotomas in lower right quadrants were present in both eyes. OCT showed thinning of macular halves in each eye anatomically correlated to visual field findings.

Conclusions, including unique features of the case(s):
Neuroimaging can be normal or incorrectly interpreted as normal due to subtle signs in hipoxic- ischemic encephalopathy. (1) This case is unique because it shows OCT findings strongly correlated to visual field defects that reflect retrograde degeneration in a case of hipoxic- ischemic encephalopathy with normal neuroimaging. OCT may provide evidence of disease and emerge as a new tool in such cases, consequently ruling out differential diagnosis as psychogenic causes.

References: 1. Parmar HA, Trobe JD. Hipoxic-Ischemic Encephalopathy with Clinical and Imaging Abnormalities Limited to Occipital Lobe. J Neuro-Ophthalmol. 2016;36(3):264-269. 2. Margolin E, Sachin K, Trobe JD. Isolated Cortical Visual Loss with Subtle Brain MRI Abnormalities in a Case of Hipoxic-Ischemic Encephalopathy. J Neuro-Ophthalmol. 2007;27(4):292-296.

Keywords: Higher Visual Cortical functions, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Higher visual functions, Visual fields, Neuroimaging

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Poster 35
Traumatic Optic Tract Syndrome with a Decade-Old Head Trauma

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Introduction:
Lesions of the optic tract lead to subtle clinical features that may be under-recognized. Optic tract syndrome is characterized by a triad of a contralateral relative afferent pupillary defect (RAPD), contralateral homonymous hemianopia and contralateral bow-tie optic atrophy. This report outlines the rare and scarcely reported traumatic optic tract syndrome with corroborating MRI, retinal nerve fiber layer (RNFL) and, for the first time in the literature, ganglion cell-inner plexiform layer (GCIPL) findings.

Description of Case(s):
A 22-year-old female presents with a one-year history of decreased vision in the left eye and a remote history of head trauma from a mountain biking accident at age 13. She was comatose on a ventilator for three weeks following the accident. She noticed decreased vision in the right eye four months post-injury and recently in the left eye, which was likely a sudden realization given her stable Humphrey visual field (HVF). On afferent exam, she had excellent visual acuity and color vision with both eyes, but a subtle 1+ right RAPD and a right-sided visual field defect to confrontation were noted. Efferent exam was normal, as were the anterior segment, maculae and vessels. Detailed inspection of the posterior segment, however, revealed mild nasal and temporal right optic nerve pallor. HVF showed somewhat incongruous right homonymous hemianopia. Optical coherence tomography for RNFL and GCIPL showed thinning in both eyes, more prominently in the nasal and temporal aspects of the right optic nerve and the nasal aspect of the right macula, respectively. Finally, MRI demonstrated left optic tract atrophy.

Conclusions, including unique features of the case(s):
Although rare, traumatic optic tract syndrome should be on the differential in cases with an appropriate history and head trauma. Once suspected, patients should be carefully assessed for the specific triad and subtle signs that accompany optic tract lesions on exam and imaging and may otherwise be easily missed.

References: None.

Keywords: Optic nerve trauma and treatment, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Neuroimaging, Stroke Trauma, Visual fields

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Grant Support: None.

Poster 36
Idiopathic Intracranial Hypertension: Cerebrospinal Fluid Leak Complicated By Meningitis

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Introduction:
Idiopathic intracranial hypertension (IIH) is defined by signs and symptoms of increased intracranial pressure (ICP), elevated ICP with normal cerebrospinal fluid (CSF) composition, and without another cause of elevated ICP. IIH is increasingly recognized as a cause of spontaneous CSF leak from pressure-induced skull base erosion. Patients may have minimal leak-related symptoms (e.g., rhinorrhea, low-pressure headache, or bacterial meningitis). Diagnosis of IIH typically occurs following surgical leak repair with subsequent elevated ICP and associated symptoms.

Description of Case(s):
A 55-year-old obese woman with a history of migraine and tension-type headaches presented with headache for five days with acute worsening for one day. The headache was throbbing, holocephalic and maximal at the left temple, worse with any position change, and initially mild until becoming acutely severe with associated nausea and photophobia. On examination, the patient was afebrile, without nuchal rigidity, and with a normal neurological exam. Laboratory studies showed mild neutrophilic leukocytosis and elevated inflammatory markers. Noncontrast head CT demonstrated partially effaced sulci, empty sella, and tonsillar ectopia concerning for intracranial hypertension. MRI Brain demonstrated an empty sella and trace fluid in the left sphenoid sinus, read as likely related to sphenoidal mucosal disease given absence of CSF rhinorrhea. MRV Brain showed narrowing of the lateral transverse sinuses. The patient subsequently developed clear fluid leaking from her left nare. A reservoir test was positive for clear fluid rhinorrhea. Cisternogram confirmed a CSF leak with focal dehiscence in the left sphenoid sinus posterior wall. Notable CSF studies comprised elevated opening pressure of 38 cmH2O and lymphocytic pleocytosis. Broad-spectrum antibiotics and acetazolamide were initiated and the patient underwent surgical repair of the leak and ventricular shunt placement.

Conclusions, including unique features of the case(s):
The unifying diagnosis was that of likely chronically increased ICP from undiagnosed IIH resulting in bone erosion and CSF leak complicated by meningitis. The patient improved markedly with treatment.

References: None.

Keywords: Pseudotumor Cerebri, Skull Base, High intracranial pressure/headache, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 37
Non-Idiopathic Intracranial Hypertension

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Introduction:
Patient is a 29 year old female with history of Stargardt disease diagnosed in 2010 referred for papilledema.

Description of Case(s):
Patient is of normal weight with a BMI of 24.88 without history of tetracycline or estrogen use. She was placed in a clinical trial for Stargardt disease in 2016. There were three study groups included in the trial: 1 placebo arm, and 2 treatment arms with different doses of a vitamin A derivative study drug. Early in 2017, she was found to have new papilledema with normal imaging and a lumbar puncture with bland CSF studies and an opening pressure of 38.5 cm H2O. As the trial was ongoing, we were unable to find out which medication she was taking, but it was assumed she was in one of the vitamin A treatment arms causing her new papilledema. She was started on acetazolamide and the study drug was discontinued with resolution of papilledema. She was later re-challenged with the study drug at a lower dose a few months later, after which unfortunately the papilledema returned. She was restarted on acetazolamide with resolution of papilledema again. The two year Stargardt study ended and the patient discontinued both the study drug and acetazolamide without return of papilledema after six months of follow-up.

Conclusions, including unique features of the case(s):
Vitamin A intoxication is a known possible precipitant to increased intracranial pressure and papilledema. Despite having no official report of the study medication that our patient received, it was assumed this patient had received on of the two doses of the vitamin A derivative that subsequently lead to the papilledema. She was treated with acetazolamide with resolution and after the study drug was discontinued she has been stable with eventual taper off of acetazolamide without return of papilledema.

References: None.

Keywords: High intracranial pressure/headache, Pseudotumor Cerebri, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 38
Meningocele, a Protective Finding in Patient with Pulsatile Tinnitus and Brain Imaging Features Suggesting PTCS

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Introduction:
Pulsatile tinnitus is a diagnostically challenging and commonly subjective symptom. It is a sensation of whooshing, whistling, humming that is unilateral or bilateral and is synchronized with heart beat. Origin may be arterial, arteriovenous or venous. It frequently resolves with distal pressure over the ipsilateral jugular vein. In pseudotumor cerebri syndrome (PTCS) origin of pulsatile tinnitus is likely venous due to turbulent flow through narrowed transverse venous sinus. Patients with PTCS typically present with headaches (90%) and transient visual obscurations (70%). Many patients have transverse sinus stenosis as result of chronic elevation of intracranial pressure which in turn leads to fibrosis resulting in narrowed appearance of dural sinus on venous imaging. Patients with PTCS can have abnormal findings on MRI including empty sella, transverse sinus stenosis, widened optic nerve sheath, and posterior globe flattening of orbits. In addition high intracranial pressure (ICP) can lead to spontaneous meningoceles, which could become a source of CSF leak.

Description of Case(s):
Our patient presented with pulsatile tinnitus, without headaches or transient visual obscurations and without papilledema on exam. Opening pressure was 26cm H2O. A diagnosis of PTCS was suggested but not made. as she fulfilled the MRI criteria (transverse sinus stenosis, widened perioptic nerve sheaths, partially empty sella). She was found to have meningoceles on brain imaging. After larger pressure gradient was found on catheter angiography, she underwent venous sinus stenting with complete resolution of tinnitus.

Conclusions, including unique features of the case(s):
The finding of meningoceles may have been clinically protective and precluded development of headaches by deflecting symptoms of elevated ICP in this patient.

References: None.

Keywords: High intracranial pressure/headache, Neuroimaging, Pseudotumor Cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 39
You DON'T need VITAMINES

Haydee Martinez[1], Mariana de Viirgiliis[2], Antonio Cairine[3], Lidia Sarotto[4], Mirta Arana[4], Macarena Clementi[4], Lucrecia Bazzino[3], Violeta Millet[4]

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Introduction:
IIH in Pediatric population is associated with very different etiologies. Hypervitaminosis A due to excessive ingest has been cited as one of them. We present a girl 5 years old who daily and "for a long time" took 2 multivitamin complex that included low dosis of Vitamine A – because her mother thought it was good for her with no medical prescription – and every day a moisturizing cream with 600.000 IU Vit A. She developped a typical IHH with cephalea, diplopía and typical findings in MRI.

Description of Case(s):
Description: The girl was brought by her parents referring 72 hs of cephalea associated with horizontal diplopia. No obesity, no personal relevant history. Examination showed decreased visual acuity OD 10/20 OS 14/20 – Bilateral Papilledema and RPAD OD. MRI with prominent subarachnoid space around the optic nerves, flattening of the posterior sclera, intraocular protrusion of the optic nerve head, vertical tortuosity of the optic nerves. LP 50 mmHg, normal CSF. VF: generalized depression. OCT: generalized increase of RNFL. Blood Retinol test supported the suspected hipervitaminosis 0.68mg/ml (NV: 0.25-0.43). With acetazolamide and supression of Vit A, complete recovery was obtained.

Conclusions, including unique features of the case(s):
Conclusion: The etiology of this case of IIH is very inusual. It seems that both factors, oral ingest of Vitamine A and dermic absorption due to the emolient cream, contribute in developping IH. Other important aspect to consider is the parents, and also popular judgement, about the benefits of vitamines without evaluating the danger of hipervitaminosis.

References: -"Sight-threatening pseudotumor cerebri asssociated with excess vitamin A supplementation" James D Benzimra, Sumu Simon, Alexandra J Sinclair, Susan P Mollan. Practical Neurology April, 2018 -"Clinical spectrum of the pseudotumor cerebri in children: Etiological, clinical features, treatment and prognosis "Hüseyin PerCorrespondence information about the author Hüseyin Per, Mehmet Canpolat, Hakan Gümüş, Hatice Gamze Poyrazoğlu, Ali Yıkılmaz, Sarper Karaküçük, Hakkı Doğan, Sefer Kumandaş, Erciyes University, Faculty of Medicine, Department of Pediatrics, Division of Pediatric Neurology, Kayseri, Turkey. -"A Review of Pediatric. Idiopathic Intracranial Hypertension." David L. Rogers, MD. Pediatric Clinics 2018 -Treatment Response in Pediatric Patients With Pseudotumor Cerebri Syndrome. Tovia E, Reif S, Oren A, Mitelpunkt A, Fattal-Valevski A. Neuroophthalmol. 2017.

Keywords: Pseudotumor Cerebri, Pediatric neuro-ophthalmology, Ocular Motility, Neuroimaging, High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 40
Papilledema: initial sign of an INF2 mutation

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Introduction:
Idiopathic Intracranial Hypertension (IIH) is the most common cause of papilledema in young women, however ~93% of patients have a BMI>25 (3) – IIH patients with low BMI should warrant a more robust clinical work-up.

Description of Case(s):
A thin 25-year-old female presented with transient visual obscurations, headaches, and pulsatile tinnitus. A diagnosis of IIH was made after bilateral disc edema, an opening pressure of 320mm Hg on lumbar puncture, and no lesions or vascular anomalies on brain imaging were observed. Visual symptoms and headaches initially resolved with acetazolamide, however several months later, she developed worsening headaches refractory to acetazolamide, paresthesia in her hands and feet, hallucinations, and horizontal binocular diplopia. She was hospitalized and found to have focal segmental glomerular sclerosis (FSGS) and developed extremity weakness, requiring a wheelchair to ambulate. Lumbar puncture showed 420 WBCs and electromyogram (EMG) showed mixed sensory/motor demyelination and axonal loss. Treatment with intravenous immunoglobulin and plasma exchange failed to produce clinical improvement, prompting genetic testing which revealing a missense mutation in the N-terminal inhibitory domain of the INF2 gene, a rare condition associated with Charcot-Marie-Tooth (CMT) dominant intermediate E and FSGS type 5.

Conclusions, including unique features of the case(s):
Mutations in the N-terminal inhibitory domain of the INF2 gene are known to cause disorganization of the cytoskeleton in neurons and myelinating cells via early termination of actin filaments,(2) causing CMT,(4,5) FSGS,(1,4) and CNS changes including ventricular dilation, however this is the first detailed report of the ocular manifestations of the disease due to its rarity, severity, and phenotypic heterogeneity. Atypical presentations of common diseases should be closely followed for further clinical developments, as additional atypical findings make rare diseases increasingly likely. In this case, the patient's demographics (i.e. BMI=16.3) was atypical for IIH and close follow-up of other atypical features resulted in the correct diagnosis.

References: Brown, Elizabeth J et al. "Mutations in the formin gene INF2 cause focal segmental glomerulosclerosis" Nature genetics vol. 42,1 (2009): 72-6. Korobova, Farida et al. "An actin-dependent step in mitochondrial fission mediated by the ER-associated formin INF2" Science (New York, N.Y.) vol. 339,6118 (2013): 464-7. Bruce, B. B., et al. "Atypical idiopathic intracranial hypertension Normal BMI and older patients." Neurology 74.22 (2010): 1827-1832. Boyer, Olivia, et al. "INF2 mutations in Charcot–Marie–Tooth disease with glomerulopathy." New England Journal of Medicine 365.25 (2011): 2377-2388. Werheid, Friederike et al. "Underestimated associated features in CMT neuropathies: clinical indicators for the causative gene?" Brain and behavior vol. 6,4 e00451. 4 Mar. 2016, doi:10.1002/brb3.451.

Keywords: Pseudotumor Cerebri, Genetic Disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 41
Isolated Acquired Primary Crocodile Tears

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Introduction:
The crocodile sheds tears as a physiologic response to mastication. Humans however, produce tears while eating (the gusto-lacrimal reflex) only after pathologic repair with misdirected recovery in the seventh cranial nerve. Crocodile tears are associated with facial nerve injury either traumatic, idiopathic, or with associated brain stem pathologies. This gusto-lacrimal reflex is seen with signs of facial nerve damage and repair, hypothetically the consequence of misdirection or ephaptic transmission. Isolated acquired gusto-lacrimation without any sign of associated neural motor fiber involvement is virtually unique. We report such a case.

Description of Case(s):
A 67-year-old man reported moisture and eventual tearing in his right eye while eating over a two-year period. There was neither symptom nor sign or facial nerve dysfunction otherwise. Neurologic exam revealed no sign of facial nerve weakness; nor evidence of synkinetic regeneration confirmed by video analysis. High resolution repeated MRI scans over a six-month period showed no evidence of brain stem or facial nerve lesions. Schirmer's test confirmed excessive tearing only during a period of mastication.

Conclusions, including unique features of the case(s):
The present case is unique in the absence of associated pathology. The site of injury in this case remains uncertain and speculative. Historic literature review of other cases with unusual facial nerve features and crocodile tears will be discussed.

References: None.

Keywords: Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 42
Perineural Spread of Head and Neck Cancer

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Introduction:
Perineural spread is a rare means of tumor extension in head and neck malignancy. Ophthalmic findings may be the first clue to the presence of perineural neoplasia, but can be easily missed if suspicion is not high.

Description of Case(s):
73-year-old man with 18-month history of progressive right sided facial numbness and pain was managed as sinusitis for several months ineffectively. An MRI brain done in 2017 was read as negative. Four months prior to referral, he developed right sided facial nerve palsy followed by binocular horizontal diplopia worse on right gaze. His past medical history includes hypertension, shingles, basal cell carcinoma left cheek, melanoma in situ and actinic keratosis. On examination, his visual acuity was 20/30 OD 20/40 OS. Right eye pertinent findings: trace APD, ISH 6/8, lower lid ectropion, restricted abduction, mild optic disc pallor; decreased sensation over V1- V3 on the right side. Left eye was normal. Laboratory testing: CSF: elevated protein, normal glucose, no malignant cells on cytology. Serum ACE, ANA, paraneoplastic panel, IGG subclass 4, VZV IgM, Lyme – all negative. Chest CT and PET scan - normal. Re-review of MRI brain showed enhancement of right Meckel's cave, facial nerve and enhancing soft tissue in the right pterygopalatine fossa. Skin biopsy of suspicious lesion on the right medial malar region was consistent with invasive squamous cell carcinoma, confirming the diagnosis of perineural spread of skin cancer.

Conclusions, including unique features of the case(s):
Patients presenting with progressive facial numbness and pain should be investigated carefully for head and neck cancer. Skull based MRI with thin sections and contrast enhanced T1-weighted MR imaging with fat suppression is widely used to increase the conspicuity of the enhancing tumor infiltrated nerve by nulling the signal of the surrounding fat.

References: 1. Ableman, Newman, Perineural Spread of Head and Neck Cancer: Ophthalmic Considerations, J Neurol Surg B ;77:131-139,2016 2. Valenzuela, Byrd, Palmer,Osborn, An 82-Year-Old Man with Diplopia ;Clinical-Pathological case study: Journal of Neuro-Ophthalmology ,Vol 36,Number 4, 448-451 December 2016.

Keywords: Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 43
Reversible homonymous quadrantanopsia and subcortical T2 hypointensity in nonketotic hyperglycemia

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Introduction:
Nonketotic hyperglycemia (NKH) is a clinical syndrome comprising hyperglycemia, serum hyperosmolarity, and intracellular dehydration with little or no ketoacidosis. NKH has been associated with various neurological manifestations. We report a case of occipital lobe seizure and subcortical T2 hypointensity associated with NKH.

Description of Case(s):
A 56-year-old man with a history of diabetes mellitus presented with visual impairment characterized by recurrent episodes of flashing colorful lights in his left visual field. He had no headache or ocular pain. On examination, he had a left homonymous superior quadrantanopsia, which confirmed by Humphrey field analyzer. Other abnormal findings were not found. Laboratory evaluation showed severe hyperglycemia, normal osmolarity and negative ketones, consistent with NKH. T2-weighted brain MRI revealed subcortical hypointensity within right occipital lobe. Gadolinium-enhanced T1-weighted images showed no enhancement of the corresponding areas. Electroencephalography performed during interictal period, did not show any epileptiform discharges. With a suspicion of occipital lobe seizure associated with NKH, we started intensive insulin therapy, hydration, and low dose of anti-epileptic drug. As the patient's blood glucose became stable, visual seizure lessened and disappeared 3 days after initiation of treatment. A follow-up Humphrey field test and MRI scan showed disappearance of homonymous quadrantanopsia and subcortical T2 hypointensity.

Conclusions, including unique features of the case(s):
A reversible subcortical T2 hypointensity in NKH may be ascribed to transient free radical accumulation during seizure or intracellular shrinkage resulting from NKH.

References: None.

Keywords: Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 44
Longest Involvement of Visual Pathway in Neuromyelitis Optica Spectrum Disorder

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Introduction:
Neuromyelitis optica spectrum disorder (NMOSD) is an inflammatory demyelinating disease of central nervous system. Patients typically present with optic neuritis (ON) or transverse myelitis. Characteristic MRI findings include extensively long lesions affecting optic nerve. We report a very long involvement of the visual pathway caused by NMO.

Description of Case(s):
A 31-year-old woman presented with progressive painful visual loss in her right eye for 3 days. Ophthalmic examination revealed visual acuity of no light perception in the right eye and 20/20 in the left eye with right RAPD. Anterior segment, posterior segment, and neurologic examination were unremarkable. Static perimetry showed generalized depression in the right eye and incomplete temporal hemianopia in the left eye. MRI of the brain and orbits demonstrated abnormal T2 hyperintensity with enhancement involving proximal right optic nerve, right optic chiasm, right optic tract, and right lateral geniculate body. There was no hallmark white matter lesions of demyelinating disease elsewhere. She had positive ANA, anti-Ro antibody and NMO-IgG. She was diagnosed with NMOSD associated with Sjögren's syndrome. The patient was treated with 1g intravenous methylprednisolone for five days followed with tapered dose oral prednisolone along with azathioprine. Four months after the onset, visual acuity was counting fingers in the right eye and 20/20 in the left eye.

Conclusions, including unique features of the case(s):
The case report highlights the longest involvement of visual pathway inflammation in NMOSD, extending from intraorbital optic nerve to ipsilateral lateral geniculate body.

References: None.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 45
Accidental ophthalmic artery Onyx embolisation for meningioma-Vision lost in an attempt to preserve

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Introduction:
Presurgical embolization of vascular tumors is relatively common. Embolization via the ophthalmic artery carries risk of blindness from iatrogenic ophthalmic or retinal arterial occlusion. We report a case of visual loss following embolization to devascularize a meningioma via the ophthalmic artery; describe key clinical and radiographic features; and review considerations for prevention of potential visual complications of the procedure.

Description of Case(s):
A 40 year old male presented with headache and chronic progressive visual deterioration in the right eye (OD). MRI brain with contrast revealed a right sphenoid wing/petroclival meningioma with right optic nerve compression. The hypervascular mass was devascularised via endovascular embolization prior to surgical resection. During catheter angiography, a microcatheter was advanced via the middle meningeal artery and Onyx-18 liquid embolic material was injected into the feeding vessels to the tumor. After procedure, patient noted vision loss OD. On examination visual acuity was 20/800 OD worsening progressively to light perception. Right pupil was 5 mm and poorly reacted to light with RAPD, the left was 3 mm. He had 10 prism diopter exotropia. Rest of right eye exam and left eye was normal. Ophthalmoscopy revealed retinal artery occlusion OD. The combination of efferent (anisocoria) and afferent (RAPD) findings suggested ophthalmic artery occlusion. Post-procedure CT scans demonstrated linear hyperdensities in the orbit consistent with Onyx in ophthalmic artery OD. Patient vision remains LP.

Conclusions, including unique features of the case(s):
To avoid inadvertent ophthalmic artery embolisation, the microcatheter can advanced to a “safe position” beyond central retinal artery origin and angiographic confirmation of a preserved “choroidal blush” before slow, intermittent, infusion of embolic material to avoid reflux into the ophthalmic artery.2,3 Although ophthalmic and branch occlusions have been described after endovascular embolization, this is the first case in the English literature to demonstrate the orbital CT findings of ophthalmic artery embolization presenting with an isolated ipsilateral afferent/efferent pupillary defect.

References: 1.Oka H, Kurata A, Kawano N, Saegusa H. Preoperative superselective embolization of skull-base meningiomas: indications and limitations. J Neurooncol. 1998 Oct;40(1):67-71. 2.Terada T, Kinoshita Y, Yokote H, Tsuura M. Preoperative embolization of meningiomas fed by ophthalmic branch arteries.Surg Neurol. 1996 Feb;45(2):161-6. 3.Trivelatto, G.S. Nakiri, M. Manisor, R. Riva, M. Al-Khawaldeh, Preoperative Onyx Embolization of Meningiomas Fed by the Ophthalmic Artery: A Case Series. American Journal of Neuroradiology October 2011, 32 (9) 1762-1766.

Keywords: Neuroimaging, Tumors, Skull Base, Vascular disorders, Interventional neuroradiology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 46
Substantia Nigra Hyperintensities leads to diagnosis of Leber's Hereditary Optic Neuropathy

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Introduction:
Leber's hereditary optic neuropathy (LHON) commonly presents with acute or subacute central vision loss mimicking optic neuritis. We describe a young man who presented with bilateral sequential optic neuropathy concerning for retrobulbar optic neuritis. His MRI head, however, revealed bilateral symmetric substantia nigra hyperintensities, unusual in a demyelinating disorder. This finding, along with positive family history, led to further work-up disclosing a diagnosis of LHON.

Description of Case(s):
A 29-year-old alcoholic man with family history of multiple sclerosis presented with sudden painless central visual loss in the right eye. His visual acuity was 20/300 OD, and 20/20 OS. There was right afferent pupillary defect. Fundus revealed bilateral hyperemic optic discs without edema. Retrobulbar optic neuritis in the right eye was suspected. VEP revealed delayed p100 latency in the right eye. MRI head and orbits showed bilateral symmetric T2 hyperintensities in the substantia nigra, without enhancement or restricted diffusion. There was no involvement of the optic nerves. He was given a 3 day course of intravenous methylprednisolone together with intravenous thiamine, but failed to improve. Lumbar puncture was unrevealing. Neuromyelitis optica antibody returned negative. He subsequently lost vision in the left eye within 6 weeks. Interestingly, his maternal uncle had been diagnosed with bilateral optic neuritis in his mid-twenties. Given this family history and imaging concerning more for a metabolic than demyelinating etiology, genetic testing for Leber's Hereditary Optic Neuropathy was performed finding a point mutation (m.11778G>A) in mitochondrially-encoded NADH dehydrogenase.

Conclusions, including unique features of the case(s):
In LHON, MRI typically reveals involvement of the optic nerve, chiasm, and tract. But LHON may involve the brainstem as illustrated by this case suggesting that genetic testing for LHON should be undertaken in cases of optic neuropathy with substantia nigra T2 hyperintensities. Diffuse intracranial lesions with cerebellar atrophy, striatal lesions, hypothalamic lesions, and periventricular lesions have also been described.

References: 1. La Morgia C, Caporali L, Gandini F, Olivieri A, Toni F, Nassetti S, Brunetto D, Stipa C, Scaduto C, Parmeggiani A, Tonon C, Lodi R, Torroni A, Carelli V.Association of the mtDNA m.4171C>A/MT-ND1 mutation with both optic neuropathy and bilateral brainstem lesions. BMC Neurol. 2014 May 28;14:116. 2. Chen YT, Chen WL, Chen SN, Liu CS. Brain stem lesion in mitochondrial DNA G11778A mutation of Leber's hereditary optic neuropathy. J Formos Med Assoc. 2015 Jul;114(7):668-9. 3. Funalot B, Ranoux D, Mas JL, Garcia C, Bonnefont JP. Brainstem involvement in Leber's hereditary optic neuropathy: association with the 14,484 mitochondrial DNA mutation. J Neurol Neurosurg Psychiatry. 1996 Nov;61(5):533-4. 4. Matthews L, Enzinger C, Fazekas F, Rovira A, Ciccarelli O, Dotti MT, FilippiM, Frederiksen JL, Giorgio A, Küker W, Lukas C, Rocca MA, De Stefano N, Toosy A, Yousry T, Palace J; MAGNIMS Network. MRI in Leber's hereditary optic neuropathy: the relationship to multiple sclerosis. J Neurol Neurosurg Psychiatry. 2015 May;86(5):537-42.

Keywords: Genetic Disease, Optic neuropathy, Neuroimaging, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 47
True Foster Kennedy Syndrome Induced by Invasive Anaplastic Meningioma

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Introduction:
Foster Kennedy syndrome is well delineated in the textbook, However, this syndrome is rarely seen clinically. This time, we reported a classic case of true Foster Kennedy Syndrome caused by invasive anaplastic meningioma.

Description of Case(s):
This 44-year-old male patient had experienced left progressive visual loss for 1 week, accompanied with right headache with right hand tremor. The best corrected visual acuity was 20/25 OD and CF/30cm OS. Left relative afferent pupillary defect was impressed. Funduscopic examination revealed right papilledema (Fig A); left optic disc temporal pallor with superior wedge-shaped nerve fiber layer defect (Fig B). Brain magnetic resonance imaging (MRI) demonstrated ill-defined huge mass over the left frontal lobe, and the arrow pointed local invasion of left optic nerve (Fig D, T1 enhancement). Mass compressive effect triggered increased intraocular pressure with right midline shift, and the arrow pointed sheath widening of right optic nerve (Fig C, T2-weighted). Subsequently, the patient received frontotemporal craniectomy. The results of histologic pathology showed that neoplastic meningothelial and spindle cells with marked anaplasia, focal necrosis and increased mitotic activity (> 20 per 10 HPFs) (Figure E). Meanwhile, immunohistochemistry (Ki -67 up to 50 % cells+ (Figure F), EMA(+), Vimentin(+), S-100(-), GFAP(-)) were compatible with anaplastic meningioma.

Conclusions, including unique features of the case(s):
This is a rare case of true Foster Kennedy syndrome that clinical presentation and funduscopic photos thoroughly matched the finding of brain MRI images. The simple test of relative afferent pupillary defect is always the most important clue for diagnosing neurological diseases.

References: None.

Keywords: Neuroimaging, High intracranial pressure/headache, Skull Base, Tumors, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 48
Multifocal Stroke from Ozone Gas Emboli

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Introduction:
A 34-year-old male with cervical radiculopathy had been receiving intramuscular ozone injections into right arm and cervical paravertebral spaces for chronic pain. He was previously treated with C6-C7 anterior cervical decompression and fusion but continued to suffer from chronic pain. As a result, he sought out alternative therapies and had undergone 13 treatments with ozone injections wherein he received approximately 15 injections of ozone per visit.

Description of Case(s):
At his most recent visit, he lost consciousness immediately after the last paravertebral injection of ozone and, on awakening, had obvious dysarthria, aphasia, right-sided weakness, and horizontal diplopia. Urgent CT/CTA of the brain and neck demonstrated intra-arterial air within the right vertebral artery and multiple foci of gas throughout the fascial planes in the posterior neck. Brain MRI demonstrated multiple punctate foci of restricted diffusion involving both cerebellar hemispheres, cerebellar vermis, left pons, midbrain, thalami, and occipital lobes, all within the posterior circulation. Neurological examination demonstrated right hemiparesis, right-sided sensory impairments, left-sided ataxia, dysarthria, dysphagia, left cranial nerve VI palsy with mild left VII nerve palsy, and cognitive impairment. He was treated with hyperbaric oxygen therapy and physical therapy.

Conclusions, including unique features of the case(s):
Prolotherapy is an alternative treatment modality consisting of injections of non-pharmacologic agents, such as ozone gas, for the treatment of chronic pain. Oxygen-ozone gas injections are proposed to generate anti-inflammatory effects, activate neutrophils and cytokine production, and increase perfusion by activating endothelial nitric oxide pathways. Ozone autohemotransfusion and intradiscal injections have been implicated in case reports of acute death, vertebrobasilar strokes, and bilateral preretinal hemorrhages. To our knowledge, this is the first case where presence of intra-arterial ozone after prolotherapy injections was confirmed with a CT-A imaging. Neuro-ophthalmologists should be aware of this treatment modality for chronic pain as it can cause significant morbidity and present with neuro-ophthalmic manifestations.

References: None.

Keywords: Stroke Trauma, Ocular Motility, Miscellaneous

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Poster 49

Single-photon emission computerized tomography (SPECT) in MRI negative Cortical Blindness Post Anoxic Brain Insult

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Introduction:
Herein, we present a case of anoxic brain injury characterized by cortical blindness despite a normal Brain MRI. SPECT imaging used to evaluate regional cerebral profusion, showed moderately diminished activity in bi-occipital lobes. There was additionally mild diminished activity in the posterior frontal and parietal lobes.

Description of Case(s):
This is a 23 year- old male presented with PMH of anoxic/hypoxic ischemic encephalopathy presented with vision loss OU. He was seen by multiple eye care providers and was thought to have functional vision loss, Neuro-ophthalmological exam showed 20/300-1 and 20/400, with brisk pupillary reactions, no RAPD or light near dissociation. The posterior pole was normal as was the rest of his exam including slit lamp exam and motility Humphrey Visual Field (HVF) testing with size V target showed Inferior altitudinal visual field defects OU which were similar in both eyes. OCT showed normal thickness of peripapillary retinal nerve fiber OU and the retinal ganglion cell layer was normal OU. MRI of the brain with and without contrast was negative. SPECT showed diminished activity in bilateral occipital lobes, posterior frontal and parietal lobes. Imaging techniques for patients with presumed cortical blindness and normal MRI's from several disease states, will be reviewed as well as how timing of testing the testing may influence the results.

Conclusions, including unique features of the case(s):
In cases of cortical blindness when the MRI does show occipital pathology, SPECT imaging can confirm regional bi-occipital lobe hypoperfusion, confirming the clinical impression of bilateral occipital disease.

References: None.

Keywords: Neuroimaging, Higher visual functions, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 51
External Carotid-Facial Vein Fistula Masquerading as Carotid-Cavernous Fistula

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Introduction:
Carotid-cavernous sinus fistulas(CCFs)are abnormal communications between the internal or external carotid arteries and the cavernous sinus, and are typically classified as direct(high flow) or indirect(low flow) Here we describe a patient whose presentation mimicked an indirect CCF(connection between pericavernous dural arterial branches and cavernous venous plexus), but instead was found to have a fistula between both the facial and internal maxillary arteries and his facial vein.

Description of Case(s):
An 82 year old male with a history of right carotid endarterectomy presented with 9 months history of right eye pain, periorbital swelling, and blurred vision. On exam, his visual acuity was 20/70 OD, 20/40 OS. He had diffuse injection, conjunctival congestion and proptosis with limited abduction in OD. His intraocular pressure was 26 mm Hg OD & 14 mm Hg OS. Fundus showed healthy optic discs. MRI orbit showed dilated right superior ophthalmic vein and enlargement of right sided extraocular muscles. Due to suspicion for CCF, cerebral angiography was performed. Surprisingly it showed a fistula between branches of the external carotid artery (facial and maxillary) and the facial vein, leading to retrograde filling of the right angular and superior ophthalmic veins. Surgical clips from the endarterectomy were visualized near fistula. The fistula was repaired with partial transarterial Onyx 18 embolization, and subsequent n-Butyl cyanoacrylate embolization, leading to improvement in symptoms.

Conclusions, including unique features of the case(s):
While the presenting clinical picture and the neuroimaging was concerning for an arterial connection to the cavernous sinus, conventional angiography surprisingly revealed an arteriovenous fistula(AVF) from the external carotid artery branches to the facial vein. We strongly suspect that the previous carotid endartectomy had a role in the etiology of this delayed AVF. This case highlights how other fistulas may mimic CCF and how angiography plays a vital role in the diagnosis and management.

References: Ellis JA, Goldstein H, Connolly ES, Meyers PM. Carotid-cavernous fistulas, Neurosurg Focus; 32(5):1–11; 2012. Chaudhry IA, Elkhamry SM, Al-Rashed W, Bosley TM. Carotid cavernous fistula: Ophthalmological implications. Middle East Afr J Ophthalmol;16:57-63; 2009 Cagatay HH, Ekinci M, Sendul SY, Uslu C, Demir M, Ulusay SM, et al. Elevated Intraocular Pressure due to Arteriovenous Fistula between External Carotid Artery and Facial Vein. Case Rep Ophthalmol Med; 2014:897928; 2014.

Keywords: Vascular disorders, Interventional neuroradiology, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 52
Atypical Ectopic Choroid Plexus Papilloma - Not so Benign

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Introduction:
Choroid plexus papillomas (CPP) are rare neoplasms (0.4-0.6% of all brain tumors) arising from cuboidal epithelial cells of the choroid plexus. We describe an adult with a rare atypical ectopic choroid plexus papilloma in the cerebellopontine angle with several neuro-ophthalmic features manifesting slowly over time.

Description of Case(s):
A 56-year-old woman developed vertigo, sensorineural hearing loss, imbalance, and headaches. MRI head showed a right cerebellopontine angle tumor mistaken for an acoustic or glossopharyngeal schwannoma. Despite gamma knife radiation, tumor enlarged leading to worsening symptoms. Subsequent partial tumor resection complicated by CSF leak disclosed it to be an atypical ectopic choroid plexus papilloma. She already had leptomeningeal seeding involving multiple cranial nerves and spinal cord. Patient underwent radiation treatment. Slowly she developed vitreous hemorrhage, papilledema while maintaining 20/25 vision OU, and vertical diplopia from skew deviation. CSF diversion was not possible for the obstructive hydrocephalus, hence was placed on acetazolamide. Overtime she developed right sixth nerve palsy, right facial palsy, right internuclear ophthalmoplegia, and vertical nystagmus. MRI revealed stable tumor with leptomeningeal tumor spread and new patchy enhancement along the right middle cerebellar peduncle and right dorsal pons (intraparenchymal tumor spread versus radiation necrosis). She was placed on chemotherapy bevacizumab (discontinued due to uncontrolled hypertension) and later temozolamide. Diplopia improved with prisms. For lagophthalmos and corneal exposure, she underwent right lower lid ectropion repair, right lateral permanent tarsorrhaphy, gold weight placement, a right temporalis tendon transfer, a right static facial sling, and bilateral rhytidectomies. Her tumor looks stable on serial imaging.

Conclusions, including unique features of the case(s):
Atypical choroid plexus papilloma has been recognized as a distinct and rare entity characterized by increased mitotic activity and can have metastasis even at diagnosis. The cerebellopontine angle location is rare. Our patient's myriad neuro-ophthalmic features could be from the leptomeningeal and intraparenchymal spread besides radiation necrosis.

References: 1. Sethi, Divya et al. "Choroid Plexus Papilloma." Asian Journal of Neurosurgery 12.1 (2017): 139–141. PMC. Web. 16 June 2018. 2. Bahar, Michal, et al. "Choroid plexus tumors in adult and pediatric populations: the Cleveland Clinic and University Hospitals experience." Journal of neuro-oncology 132.3 (2017): 427-432. 3. Safaee, Michael, et al. "Choroid plexus papillomas: advances in molecular biology and understanding of tumorigenesis." Neuro-oncology 15.3 (2012): 255-267. 4. Wolff, Johannes EA, et al. "Choroid plexus tumours." British Journal of Cancer 87.10 (2002): 1086.

Keywords: Tumors, Ocular Motility, High intracranial pressure/headache, Nystagmus, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 53
Pseudo-Internuclear Ophthalmoplegia as the Presenting Sign of Giant Cell Arteritis

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Introduction:
Giant Cell Arteritis is the most common vasculitis in adults, its incidence increases with age, permanent visual loss is the most feared complication, so prompt diagnosis and treatment is of paramount importance. Usual symptoms at presentation are headache, jaw claudication, scalp tenderness, blurring of vision, anorexia, weight loss and fatigue. Here we report a case of GCA who presented with an apparent internuclear ophthalmoplegia (INO).

Description of Case(s):
A 62 year old white male presented with diplopia. Past medical history was significant for hypertension, Polymyalgia rheumatica, and hypercholesterolemia. Outside eye exam showed an adduction deficit in the left eye with a horizontal dissociated abduction nystagmus in the right eye suggestive of an INO. He was admitted to the outside hospital for evaluation of possible ischemic stroke. MRI and MRA Head were unremarkable. A C-reactive protein (CRP) was mildly elevated at 2.7 mg/dL. The vision measured 20/25 OD and 20/30 OS and there was a trace relative afferent pupillary defect OS. A temporal artery biopsy showed transmural inflammatory infiltrate, disruption of the internal elastic lamina and aneurysmatic dilatation of the artery consistent with GCA. The patient symptoms and INO completely resolved after corticosteroid therapy.

Conclusions, including unique features of the case(s):
To our knowledge this is the 8th case of INO as the presenting sign of GCA in the English language literature. Clinicians should consider GCA in the differential diagnosis of INO (or pseudo-INO) in elderly patients.

References: 1) Kawasaki, A., & Purvin, V. (2009). Giant cell arteritis: an updated review. Acta Ophthalmol, 87(1), 13-32. Doi:10.1111/j.1755-3768.2008.01314.x 2) Patil, P., Karia, N., Jain, S., & Dasgupta, B. (2013). Giant cell arteritis: a review. Eye Brain, 5, 23-33. Doi:10.2147/EB.S21825 3) Ahmad, I., & Zaman, M. (1999). Bilateral Internuclear Ophthalmoplegia: An Initial Presenting Sign of Giant Cell Arteritis. Journal of the American Geriatrix Society, 47(6), 734-736. Doi:10.1111/j.1532-5415.1999.tb01600.x.

Keywords: Neuro-ophth & systyemic disease (eg. MS, MG, thyroid), Orbit/ocular pathology, Miscellaneous

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Grant Support: None.

Poster 54
A Case of Neuromyelitis Optica Presenting with Orbital Inlammation

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Introduction:
We present a case of neuromyelitis optica presenting with signs and symptoms of orbital inflammation.

Description of Case(s):
A 45-year-old African-American man with no medical history experienced acute onset of eye pain OD associated with vision loss followed by double vision and subjective bulging OD following 2 months of intermittent eye soreness OD. He presented to the emergency department where visual acuity was counting fingers OD and 20/20 OS. The right pupil was minimally reactive with a relative afferent pupillary defect. He was found to have a partial, right, pupil-involving cranial nerve (CN) III palsy with normal motility OS. IOP was normal OU. Dilated fundus exam showed 360-degree optic disc edema and tortuous vessels OD and was normal OS. Magnetic resonance imaging (MRI) of the orbits with and without contrast showed increased T2 signal with tortuosity and thickening of the retrobulbar optic nerve OD from the globe to the optic canal with posterior globe flattening. There was associated restricted diffusion and enhancement of the optic nerve OD, with enhancement of the orbital fat adjacent to the optic nerve sheath with relative proptosis OD. Brain MRI showed no other lesions. Magnetic resonance angiography showed no vascular anomalies, and cervical spine MRI was unremarkable. RPR, ACE, ANCA, ANA, IgG4, RF, anti-CCP, SPEP, and MOG were negative. Neuromyelitis optica antibody was elevated at 15.3 unit/mL (normal <3.0). Cerebrospinal fluid analysis was normal. He received 5 days of intravenous solumedrol and was discharged on a tapering course of oral prednisone. He experienced improvement in his proptosis and ocular motility with stable vision.

Conclusions, including unique features of the case(s):
Our patient presented with signs and symptoms of orbital inflammation with optic neuritis and after extensive workup was found to have neuromyelitis optica. To our knowledge, this is the first reported case of neuromyelitis optica presenting with orbital inflammatory syndrome.

References: None.

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

Financial Disclosures: The authors had no disclosures.

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Poster 55
Marginal Zone Lymphoma Causing Superior Sagittal Sinus Stenosis and Intracranial Hypertension

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Introduction:
Dural Lymphomas (DL) are a rare type of primary CNS lymphoma, with typical pathology consistent with marginal zone B cell lymphoma (MZL)2. The most common presenting symptoms of DL are seizures (41%), headaches (33%) and cranial nerve palsies (30%)1. We present a case of dural lymphoma causing intracranial hypertension due to critical stenosis of the superior sagittal sinus.

Description of Case(s):
A 32-year-old man who presented for evaluation of incidental bilateral optic disc edema, allegedly for over one year, reporting transient vision obscuration in the left eye and rare headaches. On examination there was bilateral papilledema Frisén Grade 2 and 4, right and left eye, respectively, with normal afferent and efferent visual function. The contrast-enhanced MRI brain/orbits and MRV head revealed dural based enhancement along the left frontal and parietal convexity extending to the posterior falx cerebri with severe critical stenosis of the superior sagittal sinus. Subsequent spinal tap was unrevealing for malignant cells or signs of inflammation/infection but showed expected elevated opening pressure at 32cm H2O. Craniotomy for biopsy provided the diagnosis of MZL. The patient had history of MZL on cervical lymph node diagnosed and resected two years prior. He was prescribed acetazolamide and completed 14 sessions of radiation therapy over a period of one month. He continued with follow-up neuro-ophthalmic examinations and MRI/MRV head, with progressive resolution of the papilledema and radiological findings.

Conclusions, including unique features of the case(s):
The present case illustrates the indolent nature of DL1 with essentially asymptomatic bilateral papilledema for one year before diagnosis. Cerebral venous sinus stenosis by DL should be suspected in patients with prior history of systemic MZL presenting with bilateral papilledema.

References: 1. Macarena I. de la Fuente, Aya Haggiagi, Adrienne Moul, Robert J. Young, Charif Sidani,et.al ,Marginal zone dural lymphoma: the Memorial Sloan Kettering Cancer Center and University of Miami experiences, 58:4, 882-888, DOI: 10.1080/10428194.2016.1218006,2016 2. Bayraktar S, Stefanovic A, Montague N, Davis J, Murray T, et.al, Central nervous system manifestations of marginal zone B-cell lymphoma, Ann Hematol ,Oct;89(10):1003-9, 2010 3. Fabio M. Iwamoto, MD; Lisa M. DeAngelis, MD; and Lauren E. Abrey, MD, Primary dural lymphomas: A clinicopathologic study of treatment and outcome in eight patients, NEUROLOGY ;66:1763–1765, 2006 4. Wajeeha Razaq, Anupama Goel, Ali Amin, Michael L. Grossbard, Primary Central Nervous System Mucosa-Associated Lymphoid Tissue Lymphoma: Case Report and Literature Review, Clinical Lymphoma & Myeloma, Vol. 9, No. 3, E5-E9, 2009 5. Joon Young Choi, Ji Hwan Chung, Young Jun Park, Geun Yong Jung, Tae Wook Yoon, et.al ,Extranodal Marginal Zone B-Cell Lymphoma of Mucosa-Associated Tissue Type Involving the Dura. Cancer Res Treat;48(2):859-863,2016.

Keywords: Tumors, High intracranial pressure/headache, Optic neuropathy

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Poster 56
Ipilimumab and Nivolumab associated VKH like Immune Related Adverse Events

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Introduction:
Ipilimumab and nivolumab are becoming increasingly common drugs in oncology. The associated immune related adverse events can have varying ophthalmic presentations. The author presents two cases of patients on nivolumab and ipilimumab for metastatic melanoma, with Vogt-Koyanagi-Harada like presentations. First, a 61 y.o. female with 20/20 in OU without an RAPD. Humphrey visual field showed enlargement of the blindspot in the OS and was full in the OD. She had bilateral +1 cell in the anterior segment. Dilated fundus exam (DFE) showed deep yellow lesions in the peripapillary choroid in OU, and multiple yellow deep ovoid scattered lesions throughout the macula in the OS with mild optic disc edema in OU. OCT showed thickening of the RNFL in the OU. Macular OCT showed pigment epithelial detachments underlying the yellow ovoid lesions. She underwent an MRI orbits and brain with and without contrast, which was unremarkable. She was treated with oral prednisone with significant improvement in her condition. Secondly, a 49 y.o. male with decreased vision to 20/100 OD and 20/200 OS, without an RAPD. Goldmann visual field showed bilateral cecocentral scotomas. DFE showed large cystic pockets of subretinal fluid. OCT showed large petalloid areas of subretinal and intraretinal fluid. IVFA showed leakage into the numerous intraretinal and subretinal cystic spaces. He was treated with oral prednisone with significant improvement. Both patients had a negative RPR, quantiferon gold, ANA, ANCA, ACE, lysozyme, and a normal CBC.

Description of Case(s):
The author presents two cases of VKH like immune related adverse events in associated with ipilimumab and nivolumab treatment for metastatic melanoma. Both patients improved with oral prednisone.

Conclusions, including unique features of the case(s):
As check point inhibitors are increasingly used in oncology, it is important for the neuro-ophthalmologist to recognize the varying presentation of associated immune related adverse events.

References: Treatment of Ipilimumab-Induced Vogt-Koyanagi-Harada Syndrome With Oral Dexamethasone. Witmer MT. Ophthalmic Surg Lasers Imaging Retina. 2017 Nov 1;48(11):928-931. doi: 10.3928/23258160-20171030-09. PMID:29121363.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 57
A Diagnostically Challenging Case of Neurosarcoidosis in the Era of Highly Sensitive Tests

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Introduction:
Neurosarcoidosis can present a diagnostic challenge in indolent, relapsing cases when ancillary testing is normal. Manifestations confined to the CNS are rare and definitive diagnostic efforts made by brain biopsies would put the patient at great risk.

Description of Case(s):
A 55 yo Caucasian woman presented with 1 week of decreased vision and ache on abduction OD. She had decreased hearing and tinnitus OD, a moderate right-sided frontal headache and unsteady gait without diplopia, facial numbness or paresthesias. She has a history of stage IV BRCA treated with chemotherapy after mastectomy 5 years prior. BCVA was 20/50 OD, 20/25 OS with dyschromatopsia and rAPD OD. EOMs were full. DFE demonstrated a pale right optic nerve. Brain MRI, initially reported as normal, demonstrated thickening and enhancement of both optic nerves, CN III OD, CN V bilaterally, pituitary infundibulum, hypothalamus and adjacent cavernous sinuses, upon our review. Leptomeningeal thickening on the anterior frontal lobes was also evident. CSF contained CD4+, CD8+ T-cells and a small population of polyclonal CD19+ B cells. An extensive inflammatory, infectious and autoimmune work-up was normal. CT thorax and full-body PET revealed no abnormalities. Clinically, she initially responded to corticosteroids. Over the ensuing 5 years, she had multiple similar presentations with facial pain and paresthesias. She developed a chronic small-fiber periphery neuropathy and was treated with mycophenolate mofetil, cyclophosphamide and IVIG. She remained clinically stable for 4 years and returned with similar symptoms. A repeat MRI, PET CT and tissue biopsies were diagnostic.

Conclusions, including unique features of the case(s):
The clinician should maintain a high index of suspicion for neurosarcoidosis despite a negative work-up. It is imperative to review neuroimaging yourself and not rely on the neuro-radiology report. Repeating initially negative studies when new symptoms manifest is necessary.

References: None.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 58
Anti-NMDA Receptor Encephalitis: An Atypical Presentation

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Introduction:
Anti-NMDA receptor encephalitis can present a diagnostic and management challenge for the clinician due to its subtle and relapsing nature and its association with other demyelinating disorders which may require intensive treatment.

Description of Case(s):
A 17-year-old, right-handed Caribbean-African man with history of amblyopia OD, Asperger's syndrome, ADHD and transient chorea of unclear etiology developed bizarre behavior and severe depression that progressed to a catatonic state that was treated with electroshock therapy. MRI showed non-enhancing increased T2 cerebral white matter abnormalities. A few months later, right eye "drifting" and left sided mouth drooping were noted. Visual acuity was 20/125 OD and 20/25 OS, without a rAPD. There was conjugate gaze palsy to the left, a left internuclear ophthalmoplegia, upbeat nystagmus on upgaze, and left facial nerve palsy. MRI showed a T2 hyperintense lesion in left facial colliculus. A lumbar puncture showed 80 lymphocytes and 20 monocytes with a protein level of 13 mg/dl. He was treated with intravenous corticosteroids and IVIG and discharged on mycophenolate mofetil with presumed Hashimoto encephalitis. He was readmitted a few months later with new onset ataxia, optic neuropathy OD and new abduction deficit OD. MRI showed non-enhancing cerebral white matter lesions and a two segment long spinal cord lesion. Three consecutive CSF samples were tested negative for NMDA receptor antibodies and a positive result was found almost one year after the initial presentation. The patient has been on chronic Rituximab for anti-NMDA receptor encephalitis with gradual improvement of his mood, ophthalmoplegia, facial palsy and optic neuropathy.

Conclusions, including unique features of the case(s):
This case supports the growing evidence that anti-NMDA receptor encephalitis can overlap with other demyelinating diseases and the wider than previously described clinical spectrum. The clinician should maintain an index of suspicion especially in young adults even when NMDA receptor antibodies are negative.

References: [1] Antonio Sanz-Clemente, Roger A. Nicoll and Katherine W. Roche, 'Diversity in NMDA Receptor Composition: Many Regulators, Many Consequences', Neuroscientist, 2013 <http://dx.doi.org/10.1177/1073858411435129>. [2] Josep Dalmau and others, 'Clinical Experience and Laboratory Investigations in Patients with Anti-NMDAR Encephalitis', The Lancet Neurology, 2011 <http://dx.doi.org/10.1016/S1474-4422(10)70253-2>. [3] H. Barry and others, 'Anti-N-Methyl-D-Aspartate Receptor Encephalitis: Review of Clinical Presentation, Diagnosis and Treatment', BJPsych Bulletin, 2015 <http://dx.doi.org/10.1192/pb.bp.113.045518>. [4] Sarosh R. Irani and Angela Vincent, 'NMDA Receptor Antibody Encephalitis', Current Neurology and Neuroscience Reports, 2011 <http://dx.doi.org/10.1007/s11910-011-0186-y>.

Keywords: Neuro-ophth & systyemic disease (eg. MS, MG, thyroid), Pediatric neuro-ophthalmology, Demeylinating disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 59
Appearance and Disappearance of Callosal Lesions in Susac Syndrome

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Introduction:
Susac Syndrome (SS) is a B cell mediated endotheliopathy associated with vision loss, hearing loss, and encephalopathy. Common sites of involvement are the very small arterioles such as those in the corpus callosum and retinal arterioles. The diagnosis can be confirmed either by central callosal lesions on magnetic resonance imaging (MRI) or fluorescein angiographic (FA) staining remote from branch retinal artery occlusion. The pathophysiology in these cases is likely due to antibody deposition on endothelial cells resulting in infarction. It is unknown if all acute callosal lesions will cavitate into callosal holes but this is a common belief. We describe 3 patients who had acute callosal lesions at first examination that resolved without sequelae of hole development on subsequent neuroimaging.

Description of Case(s):
Three women aged 27, 26, and 55 suffered from branch retinal artery occlusion and the diagnosis was confirmed via typical MRI and FA findings. They were treated for their syndrome and recovered and all went into remission. Initial MRI showed, in each subject, central callosal lesions and follow up MRI revealed near complete resolution of the callosal lesions without cavitary hole development.

Conclusions, including unique features of the case(s):
Many case reports in the literature document hole formation in the corpus callosum in the description of the neuroimaging findings which has lead to the common belief that most if not all patients with SS will develop callosal holes. These three cases demonstrate that the areas of infarction in the callosum do not necessarily progress to hole development and may disappear over time. The mechanism of action is unknown but it is possible that this occurs in more mildly affected subjects such as these presented since none of them had more than mild encephalopathy which is typically associated with a larger central nervous system lesion load.

References: None.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 60
New biomarkers in inflammatory demyelinating diseases of the central nervous system (CNS)

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Introduction:
The myelin oligodendrocyte glycoprotein (MOG) is a membrane protein expressed on the outmost surface of the myelin sheath in the central nervous system (CNS). Generally, the diagnostic, prognostic and therapeutic implications of anti-MOG-IgG in inflammatory demyelinating diseases in the CNS are unexplained.

Description of Case(s):
Here is a case report presented with a 19-year-old Danish girl with recurrent episodes of idiopathic Optic Neuritis (rON) on both eyes (previously thoroughly investigated for Multiple Sclerosis (MS), but with negative findings). The patient was suspected of having new symptoms of MS and magnetic resonance (MRT) scan (1.5T Siemens) detected a cervical demyelinating lesion extending over C3 and down to C6 / C7. No changes in cerebrum or cerebellum. Radiological diagnosis: acute transverse myelitis. X-ray of the thorax was normal and at lumbar puncture (made before steroid treatment) showed normal conditions in spinal fluid (including cells, protein, glucose, oligoclonal bands, immunoglobulin G index, borrelia and herpes viruses). An extensive examination of blood (all the following tests within normal range) was made to exclude differential diagnoses (e.g. full blood count, liver count, platelet count, glucose, folate, cobalamin, vitamin D thyroid stimulating hormone (TSH), immunoglobulins, P-ANA,P-ANCA, Ig-M Rheum factor, Sjogren syndrome B-antibody,serum-ACE test to exclude sarcoidosis.
Negative test for AQP4, but weak positive test for anti-MOG IgG.The patient was diagnosed with Neuromyelitis Optica Spectrum Disorder (NMOSD) based on the history of rON, tranversel myelitis, normal CSF and normal MR of cerebrum, and negative AQP4 IgG status for demyelinating disease in the CNS.

Conclusions, including unique features of the case(s):
In situations where the diagnosis of MS is less likely it is important to test for both AQP4 and MOG antibodies and have in mind NMOSD/ Neuromyelitis Optica (NMO) and rON. This is may be of great importance to diagnose and assess prognosis and choose treatment in cases of NMOSD / NMO.

References: None.

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

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Grant Support: None.

Poster 61
The Optic Nerve Between a Rock and a Hard Place - Neuro-Ophthalmologic Complications of Osteopetrosis

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Introduction:
16 year old female presented with episodes of "blacking out" with positional changes, along with daily headaches and a recent history of acne, for which she was started on doxycycline. In the past year, she had also been diagnosed with early osteopetrosis; a condition her father had been diagnosed with as well.

Description of Case(s):
At presentation, patient had grade II disc edema by the Frisén scale and Goldmann visual field testing revealed bilateral enlarged blind spots. MRI orbits demonstrated dilated optic nerve sheaths bilaterally with prominence of CSF spaces at the central skull base. Lumbar puncture demonstrated an elevated opening pressure of 37 cm H2O with normal CSF constituents. Patient was advised to discontinue doxycycline, and was started on acetazolamide. The disc edema and headaches improved, but the patient self-discontinued acetazolamide as she left for college because she was bothered by the paresthesias and dysgeusia. After college graduation, patient presented to the neuro-ophthalmology clinic with worsening headaches. Her visual acuity was 20/20 in both eyes, visual field testing demonstrated enlarged blind spots she again had grade II disc edema bilaterally. CT Orbits demonstrated profound osteopetrosis-related changes: bilateral optic canal stenosis with diffuse calvarial thickening. Neurosurgical evaluation determined the patient's complex skull abnormalities precluded ventriculoperitoneal shunt placement and proceeded with lumboperitoneal shunt placement.

Conclusions, including unique features of the case(s):
Osteopetrosis is a rare disease affecting around 1250 patients in the US. Improper functioning of osteoclasts and bone resorption results in unopposed bone growth; in the orbit, this can precipitate worsening papilledema and ultimately compressive optic neuropathy. Very little published data is available regarding optimal treatment. A few case reports discuss success with optic nerve sheath fenestration; others mention extensive optic nerve decompression for compressive optic atrophy. We are following our patient closely; she has been stable with a functioning lumboperitoneal shunt.

References: Al-Mefty O, Fox JL, Al-Rodhan N, Dew JH. Optic nerve decompression in osteopetrosis. J Neurosurg. 1988 Jan;68(1):80-4 Allen RC, Nerad JA, Kattah JC, Lee AG. Resolution of optic nerve edema and improved visual function after optic nerve sheath fenestration in a patient with osteopetrosis. Am J Ophthalmol. 2006 May;141(5):945-7 Alshowaeir D, Ajlan A, Hussain S, Alsuhaibani A. Visual Function Improvement After Optic Nerve Sheath Fenestration in Osteopetrosis Patients with Optic Canal Stenosis: A Report of Two Cases. Neuroophthalmology. 2017 Sep 8;42(3):164-168. doi: 10.1080/01658107.2017.1367011 Hwang JM, Kim IO, Wang KC. Complete visual recovery in osteopetrosis by early optic nerve decompression. Pediatr Neurosurg. 2000 Dec;33(6):328-32 Bollerslev J. Osteopetrosis. A genetic and epidemiological study. Clin Genet. 1987 Feb;31(2):86-90 Wu CC, Econs MJ, DiMeglio LA, et al. Diagnosis and Management of Osteopetrosis: Consensus Guidelines From the Osteopetrosis Working Group. J Clin Endocrinol Metab. 2017;102(9):3111-3123. doi:10.1210/jc.2017-01127.

Keywords: Genetic Disease, Skull Base, High intracranial pressure/headache, Optic nerve trauma and treatment, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 62
Isolated inferior rectus palsy due to orbital lymphoma

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Introduction:
Acquired isolated inferior rectus (IR) palsy is rare and mostly occurs with brainstem or orbital lesion. The most common causes are vascular disorders and trauma. We report a patient presenting with isolated IR palsy due to orbital lymphoma.

Description of Case(s):
A previously healthy 54-year-old woman presented with insidious onset of vertical diplopia for several months. She had no headache or ocular pain. The diplopia was aggravated while looking leftward and downward. Ocular motor examination showed depression deficit of the left eye in the left downward gaze, and Hess test disclosed the isolated inferior rectus palsy of the left eye. Other neuro-ophthalmological examinations were normal. MRI scan of the orbit revealed thickening and enhancement of the left inferior rectus muscle. Results of complete blood count, serum biochemistry profiles, thyroid function, autoimmune antibody screening and serum IgG4 were normal. Anterior orbitotomy and incisional biopsy was performed for the inferior rectus muscle lesion. Histopathologically, atypical lymphoid infiltrates were present between scattered, degenerated muscular bundles. The cells were positive for CD3, CD20 and BCL2, consistent with extra-nodal marginal zone lymphoma. A FDG-PET scan showed hypermetabolism in left inferior rectus muscle and left pectoralis muscle. She was treated with radiation therapy, and the diplopia began to improve.

Conclusions, including unique features of the case(s):
Our case shows that orbital lymphoma can present with isolated involvement of extraocular muscle. Thus, we should be aware of unusual causes of isolated IR palsy.

References: None.

Keywords: Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 63
Masqueraders of common Neuro-Ophthalmologic disease

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Introduction:
We present two distinct cases in which the initial symptoms mimicked the 'classic' presentation of another neuro-ophthalmic disease.

Description of Case(s):
Case 1: 71-year-old male presented to the Neuro-Ophthalmology clinic for evaluation of two weeks of progressive binocular horizontal diplopia, six months of persistent jaw pain, and a year of intractable headaches. His review of system was remarkable for dysphagia, dyspnea and a twenty-pound weight loss. Examination revealed weakness of the right lateral rectus. Constellation of symptoms along with elevated ESR and CRP was concerning for giant cell arteritis (GCA). Bilateral temporal artery biopsies were negative. Neurovascular imaging was unremarkable. Patient had slight improvement of symptoms with oral corticosteroids, and the possibility of a neuromuscular junction disorder was entertained next. He was ultimately found to have positive acetylcholine receptor (Ach-R) blocking and modulating antibodies. Final diagnosis: myasthenia gravis. Initiation of pyridostigmine improved symptoms further, and he did well after steroid taper. Case 2: 69-year-old male with a history of migraines presented with recurrent left-sided scintillating scotoma that had begun three weeks prior and was not associated with headache. Episodes lasted fifteen minutes before gradual resolution. Neuro-ophthalmologic examination and a review of systems were negative. Presentation was classic for ophthalmic migraine and his migraine treatment was escalated. Unfortunately, symptoms were refractory to therapy and further work-up including imaging of the brain and orbits provided no additional information. Carotid Doppler revealed no significant stenosis. Laboratory testing including inflammatory markers, CBC and CMP was normal except for a mildly elevated ESR. The possibility of an atypical presentation of GCA was entertained given non-response to migraine treatment. Temporal artery biopsy was found to be positive, and symptoms improved with initiation of prednisone.

Conclusions, including unique features of the case(s):
These two cases illustrate the complexities of neuro-ophthalmic disorders and showcase atypical presentations of common diseases.

References: Richard J. Caselli, Gene G. Hunder, Jack P. Whisnant. Neurologic disease in biopsy-proven giant cell (temporal) arteritis. Neurology Mar 1988, 38 (3) 352; DOI: 10.1212/WNL.38.3.352 Marshal, Megan et al. "Misdiagnosis of myasthenia gravis presenting with tongue and palatal weakness" Oxford medical case reports vol. 2018,8 omy052. 11 Aug. 2018, doi:10.1093/omcr/omy052 Rana AQ, Saeed U, Khan OA, et al. Giant cell arteritis or tension-type headache?: a differential diagnostic dilemma. J Neurosci Rural Pract 2014;5:409–11. doi:10.4103/0976-3147.140005.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 64
Atypical Saccadic Oscillations In Multiple System Atrophy

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Introduction:
Ocular flutter mostly occurs in the horizontal plane and may evolve into opsoclonus. We describe here a unique pattern of saccadic oscillations and modulation of these eye movements by head shaking in a patient with multiple system atrophy (MSA).

Description of Case(s):
A 63-year-old man with a previous diagnosis of MSA was evaluated. There was no spontaneous or gaze-evoked nystagmus in light with a visual target. Smooth pursuit was impaired in both horizontal directions, and saccades were hypermetric to the right. Head impulse tests were normal, but visual cancellation of the vestibulo-ocular reflex was impaired. In darkness without visual fixation, the patient showed spontaneous downbeat nystagmus that evolved into vertical saccadic oscillations. These vertical ocular flutter-like eye movements disappeared immediately with a presentation of a visual target in darkness, and evolved into oblique and then horizontal oscillation after horizontal head-shaking. Vertical head-shaking realigned the oscillation into the vertical plane. Horizontal and vertical saccades or smooth pursuit to visual or imaginary targets did not provoke these ocular oscillations.

Conclusions, including unique features of the case(s):
The modulation of saccadic oscillations by head shaking may indicate an erroneous interaction between the saccadic and vestibular pathways in MSA.

References: None.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 65
Tuberculous Pachymeningitis presenting as Retrobulbar Optic Neuropathy

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Introduction:
We describe a case of tuberculous pachymeningitis in a patient who presented with painless retrobulbar optic neuritis and was completely asymptomatic for meningeal disease. Meningeal involvement was only evident by magnetic resonance imaging (MRI) of the brain.

Description of Case(s):
A 52 year old female presented with painless right retrobulbar optic neuropathy and no constitutional symptoms. Initial diagnosis was optic neuropathy associated with neuromyelitis optica due to the severe visual loss. MRI revealed enhancement and swelling of the intracanalicular and prechiasmatic segment of the right optic nerve. In addition there was nodular thickening and enhancement in the posterior parietal regions bilaterally, left temporal and left inferior cerebellar region. Computer Tomography of the thorax revealed calcified lymph nodes in the mediastinum, axilla and supraclaavicular region. The differentials included tuberculosis (TB), sarcoidosis, IgG 4 related disease, carcinomatous meningitis as well as lymphoma. Besides a positive TB Tspot , other non-invasive test, including polymerase chain reaction (PCR) and examination of the cerebrospinal fluid examination were negative for TB. Biopsy the supraclavicualr nodes revealed caseating necrosis (typical for TB) and PCR from the tissue was positive for TB. Although not directly diagnostic of TB pachymeningitis and related optic neuropathy, response to treatment and the fact that it has not recurred after the steroids have been stopped does support our diagnosis.

Conclusions, including unique features of the case(s):
Tuberculous pachymeningitis can mimic retrobulbar optic neuritis and present in a patient who is completely asymptomatic for meningeal diseasse. In such cases, non- invasive test may not yield a definitive diagnosis and biopsy is required. From the Optic Neuritis Treatment Trial, MRI was useful as it could prognosticate the development of multiple sclerosis. MRI is also useful to exclude infections as in our case, particularly in atypical optic neuiritis.

References: 1) Tuberculous cranial pachymeningitis. Thurtell MJ, Keed ABR, M Yan, Gottlieb Y, et al. Neurology 2007, 68(4);298-300. 2) Clinical spectrum of tuberculous optic neuropathy. Davis EJ, Rathinam SR, Okada AA, Tow SL, et al. J Ophthalmol Inflamm Infect 2012, 2:183-189. 3) Hypertrophic cranial pachymeningitis in countries endemic for tuberculosis: Diagnostic and therapeutic dilemmas. Shobha N, Nahadevan A, Taly AB, Sinna S, et al. J Clin Neuroscience. 2008, 15(4), 418-427.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 66
Papilledema due to Cryptococcal Meningitis in Immunocompetent Patients

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Introduction:
Infectious meningitis often produces an increase in intracranial pressure (ICP) and severe papilledema. Visual loss from unrecognized papilledema is a common cause of nonreversible visual loss in meningitis. Cryptococcal meningitis is one of the most frequently cause. Herein, we report two cases of papilledema associated with cyptococcal meningitis in immunocompetent patients.

Description of Case(s):
Case 1: A 20 year-old female admitted with headache, vomiting, and photophobia for 3 days, was diagnosed with cryptococcal meningitis and treated with antifungal therapy. She was referred for ophthalmological examination presenting with decreased vision in both eyes (OD 0.2, OS count fingers) and left relative afferent pupillary defect. Funduscopy revealed bilateral papilledema. Cranial MRI showed diffuse leptomeningeal enhancement, as well as enhancement over bilateral basal ganglia and chiasma area. A ventriculoperitoneal shunt was placed for refractory intracranial hypertension. Following treatment for 3 months, her headaches had completely cleared, and visual acuity was remained 0.2 OD and count fingers OS. Case 2: A 56-year-old male with headache, visual hallucination, and diplopia for 3 weeks, was diagnosed with cryptococcal meningitis and treated with antifungal therapy and serial lumbar punctures. After stabilize of his general condition 2 months later, he was referred for ophthalmological examination due to decreased vision in the left eye (OS count fingers). Funduscopy revealed papilledema in the right eye and optic atrophy in the left eye.

Conclusions, including unique features of the case(s):
These two cases highlights papilledema is a common cause of nonreversible visual loss in cryptococcal meningitis. Papilledema accounts for most of the visual loss, but direct infectious, inflammatory, or infiltrative optic neuropathy followed by optic atrophy may occur with or without ICP-related papilledema. Some authors have suggested that visual loss may also occur from optic nerve compartmentation and secondary optic atrophy from increased ICP even without papilledema. Timely diagnosis and effective antifungal therapy as well as intracranial pressure control are crucial.

References: None.

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 67

Papilledema and bilateral optic neuropathy: dual mechanism for visual loss in patient with leptomeningeal carcinomatosis

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Introduction:

Leptomeningeal carcinomatosis (LC) is rare complication of cancer involving spread of cancer cells into central nervous system via cerebrospinal fluid (CSF). Diagnosis can be difficult with contrast-enhanced magnetic resonance imaging (MRI) and cytological analysis of CSF for cancer both not sensitive enough to permit quick detection.

Description of Case(s):

We present a rare case of patient with gastric adenocarcinoma with severe bilateral optic nerve head swelling. Two contrast-enhanced brain MRIs and two CSF analyses were non-diagnostic. Third brain MRI was initially interpreted as normal. Third CSF analysis revealed elevated opening pressure (28 cm of water) and extremely elevated protein levels but normal cytological analysis. MRI of the spine demonstrated diffuse leptomeningeal thickening and enhancing. When third brain MRI was reformatted, enhancement around both optic nerves and thickening of optic nerve sheaths was seen bilaterally which was felt to be compatible with carcinomatous seeding.

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

Our case illustrates that patients with systemic malignancies presenting with bilateral optic nerve head edema might have both papilledema as well as bilateral optic neuropathy responsible for optic nerve swelling. It is also instructive in that despite very high disease load seen on spine MRI, two high volume CSF samples failed to demonstrate presence of malignant cells.

References: None.

Keywords: Tumors, Neuroimaging, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 68
Bilateral optic perineuritis secondary to giant cell arteritis

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Introduction:
Giant cell arteritis is a systemic vasculitis affecting large and medium-sized arteries. It can produce a variety of ocular manifestations including ischemic optic neuropathy and central retinal artery occlusion. We report a patient who developed a progressive bilateral optic perineurits due to giant cell arteritis.

Description of Case(s):
An 81-year-old woman presented with progressive bilateral visual loss for 1 month. She also had jaw claudication and sharp pain in the left temporoparietal region of the scalp. Neurological examination showed bilateral mydriasis and absence of the pupillary reflexes. Visual acuity was no light perception in both eyes. Ophthalmoscopy demonstrated bilateral swelling of the optic disc, cherry red spot, and cotton-wool spots in the posterior pole. The erythrocyte sedimentation rate was 55mm/hr, but other laboratory and CSF analysis were unremarkable. MRI scans of the orbit showed an enhancement along the bilateral optic nerve sheath. She underwent a biopsy of the left temporal artery and histopathology revealed a fragmentation of the elastic membranes together with multinucleated giant cells within the wall and organized thrombus occluding the lumen, consistent with giant cell arteritis. She received high dose pulses of systemic corticosteroids, followed by tapering doses of oral prednisolone, but failed to recover her visions.

Conclusions, including unique features of the case(s):
This case illustrates that optic perineuritis may represent the manifestation of giant cell arteritis.

References: None.

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

Financial Disclosures: The authors had no disclosures.

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Poster 69
LHON-MS patient with long-term non-response to Idebenone shows improvement after 4-AP Usage

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Introduction:
Leber's hereditary optic neuropathy (LHON) is a maternally inherited mitochondrial disorder with a poor visual prognosis due to the loss of retinal ganglion cells and degeneration of the optic nerve head. There are 3 primary mutations: m.11778A>G, m.3460A>G, and m.14484T>C(ordered from worst to best prognosis). VA is primarily affected with a concordant decrease in central vision. Multiple sclerosis is a multisystem immune-mediated process in which an abnormal response of the body's immune system is directed toward the central nervous system. Although there is no direct connection between LHON and MS, if they cooccur there may be utility in the use of adjunctive therapy.

Description of Case(s):
Patient was a 37-year-old male at the time of diagnosis. The patient initially presented with blurred vision OD resulting in 20/100 vision and was treated with steroids for presumed optic neuritis due to multiple sclerosis. His VA decreased further to 20/400 OU and the patient discovered a maternal cousin with m.14484T>C. He came to our clinic and was diagnosed with LHON m.14484T>C after genetic analysis. Patient was treated with Idebenone TID 600mg and vitamin C 500mg. 6 months later, his VA decreased to 20/800 OU. Idebenone was increased to 800mg total. When returning, the patient had been on idebenone for 1.5 years without improvement. He was started on 4-AP 10mg TID. After six months the patient had improvement in color vision, VA and he was able to take a stim III HVF whereas previously he was limited to stim V.

Conclusions, including unique features of the case(s):
This patient had a lack of improvement after prolonged use of Idebenone which is unusual for a patient with the 14484 mitochondrial mutation. The unusual lack of improvement with initial treatment may have been due to concurrent MS. 4-AP may provide a mechanism for improvement in patients with LHON-MS, in this case, with the simultaneous use of idebenone.

References: None.

Keywords: Genetic Disease, Demeylinating disease, Neuro-ophth & systyemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 70
Erdheim-Chester Disease Presenting with Diplopia; A Challenging Diagnosis and Effective Treatment

Mehdi Tavakoli[1], Shiva Roghaee[1], Manasa Gunturu[1], Armando Garcia[1], Sander Dubovy[1], Byron Lam[1], Antonio Omuro[1], Carlos Mendoza-Santiesteban[1]

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Introduction:
Erdheim-Chester Disease (ECD) is an infiltrative disease which can involve the CNS and presents with different symptoms. Herein, we present a patient with ECD who presented with sixth nerve palsy, with a challenging course of diagnosis and successful treatment with two specific protein-targeting agents.

Description of Case(s):
Patient was a 51-year-old man who presented to emergency room with worsening diplopia from right sixth nerve palsy associated with gait ataxia. Brain MRI revealed multifocal FLAIR hyperintensities in the posterior fossa involving several structures. All relevant blood work and CSF analyses were negative. The patient underwent two stereotactic biopsies which were non-diagnostic, then underwent a third, and this time open brain biopsy from the cerebellum that sampled the lesion. At this time his balance has worsened, and he was unable to work because of his fatigue, diplopia, and gait instability. Pathology review revealed non-specific inflammatory changes with no granuloma. Immunohistochemistry studies showed scattered histiocytes positive for langerin and CD1a, but these did not mark the majority of the cells, and BRAF V600E staining was negative. The genetic study revealed BRAF V600E mutation which in conjunction with sclerosis of bilateral distal tibiae in PET body imaging and perinephric fat stranding were indicative of ECD. The patient underwent treatment with Dabrafenib-Trametinib, and after three months his symptoms significantly improved, and he was able to return to work. There was also a significant improvement in the size of the lesions in brain MRI.

Conclusions, including unique features of the case(s):
ECD may be a challenging disorder to diagnose. All blood and investigations were negative, and several brain biopsies and subsequent histologic studies were either non-contributory or non-diagnostic. The genetic study was the key point in this patient to diagnosis. Also, the FDA-approved combination of Dabrafenib and Trametinib showed an effective treatment in brainstem ECD with improving the clinical and radiological involvements.

References: None.

Keywords: Neuro-ophth & systyemic disease (eg. MS, MG, thyroid), Genetic Disease, Neuroimaging, Adult strabismus with a focus on diplopia, Paraneoplastic syndromes

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 71
Ocular Manifestation of Systemic Disease

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Introduction:
Malabsorption of various etiologies, including bowel resection and bariatric surgery, can lead to deficiencies of essential vitamins. We report a case of reversible nyctalopia secondary to vitamin A deficiency in a patient with Crohn's disease.

Description of Case(s):
A 63-year-old high school bus driver who had undergone multiple bowel resections, greater than 20 years from current presentation, for Crohn's disease presented with progressive night blindness over the previous 3 months. No family history of retinitis pigmentosa or other ocular diseases. He was receiving Vitamin B12 injections every 2 weeks. On examination, his visual acuity was 20/25 OD 20/30 OS; pupil, color and fundus were normal OU; mild cataract OU. Humphrey visual field showed generalized depression OU. OCT showed mild thinning of the temporal quadrant OU. Full Field Flash ERG showed predominately rod abnormality OU. Labs: Free retinol (Vitamin. A): 5.5 ug/dl (reference range: 32.5-78 ug/dl), Vitamin. E: 1.9 ug/mL (reference range 5.5-17ug/mL), Vitamin K1 S: 0.03ng/mL(reference range 0.1-2.2 ng/mL). Low levels of Vitamin A confirmed the diagnosis. Patient was started on oral supplementation with Vitamin A 8000 IU/day. Nyctalopia resolved within a week per patient report. In 1 month follow up, HVF returned to normal, and ERG showed improved amplitude though not completely normal. Vitamin A level was 17.7ug/dl (reference range: 32-78 ug/dl). Even though the lab values were not yet back to normal range, our patient's symptoms improved dramatically within a month of initiating oral supplementation without residual deficits, and he was able to resume his job.

Conclusions, including unique features of the case(s):
This case serves as a reminder of Vitamin A deficiency in patients with malabsorption conditions like Crohn's disease and also a warning that its incidence may be on the rise in the developed countries as the popularity of bariatric surgery increases. Early recognition and treatment is critical in reversing visual symptoms and preventing permanent loss.

References: 1. Privett B, Mahajan VB. Vitamin A Deficiency and Nyctalopia: 55-year-old male with gradual onset of night blindness. EyeRounds.org. February 22, 2011; Available from: http://EyeRounds.org/cases/130-vitamin-a-deficiency.htm 2. Clifford, Turnbull, and Denning : Title:Reversible night blindness – A reminder of the increasing importance of vitamin A deficiency in the developed world, J Optom. 2013 Jul; 6(3): 173–174. 3.Chae T., Foroozan R. Vitamin A deficiency in patients with a remote history of intestinal surgery. Br J Ophthalmol. 2006;90:955–956.[PubMed].

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 72
Bilateral Uveitis Presentation in a Patient with Giant Cell Arteritis

Nagham Al-Zubidi[1], Jaspreet Jakhu[2], Moe Ameri[2], May Al-Ameri[3], Rosa Tang[1], Jade Schiffman[2]

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Introduction:
In GCA, it is a critical that a timely diagnosis to avoid permanent blindness. It is very rare for GCA to presents as uveitis. There are only few reported cases with anterior uveitis as the clinical presentation.

Description of Case(s):
A 71- yof presented with acute onset of progressive sudden vision loss OD, red eyes and headache of one week's duration. Neuro-ophthalmologic exam showed visual acuity CF @ 4 feet OD and 20/20 OS. Pupil right RAPD 0.6 - 0.9 log. SLE: bilateral conjunctival hyperemia, anterior chamber reaction, keratic precipitates. OS Vitreous positive for flare,no cells. HVF: generalized depression with superior altitudinal visual field defect OD MD -7.77. OCT: GCL OD 54 and 74 um OS, RNFL OD at 85 and 78 um lOS. Funduscopy showed pale swelling. ESR and CRP were elevated. TAB was positive for smouldering arteritis. We describe the mechanisms that may be operating to cause uveitis due to GCA. Although ischemia may involve the anterior segment, an active anterior uveitis with KP is usually not how that presents, but rather flare out of proportion to cell, as a response to anterior segment ischemia. The vessels involved with GCA are thought to be in the orbit and not ocular and therefore the ischemia does not occur within the iris vessels themselves. Were that the case, inflammation could easily diffuse into the anterior segment. Although, we have always associated ocular manifestations with GCA as opposed to PMR, a recent report describes patients presenting with anterior segment inflammation related to PMR, without manifestations of GCA, that were responsive to low dose of steroids and once tapered, a couple of the cases recurred. This suggests other mechanisms, aside from ischemia, could contribute to the anterior uveitis presentation.

Conclusions, including unique features of the case(s):
GCA rarely present with an anterior uveitis and we discuss potential mechanisms of its occurrence.

References: None.

Keywords: Optic neuropathy, Orbit/ocular pathology, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 73

Atypical presentations of intracranial dysgerminoma mimicking central nervous system inflammatory or demyelinating disease

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Introduction:

Germinomas are the most common type of germ cell tumors and clinical presentation predominantly depends on tumor location and neuro-ophthalmic presentations are common in the pineal (e.g., dorsal midbrain syndrome) and suprasellar (e.g., visual loss) regions. Intracranial dysgerminoma can be focal or multifocal. Thus, multifocal lesions can produce neurologic and radiographic signs and symptoms that appear to be "separated in time and space" and can mimic the clinical and radiographic presentations of CNS inflammatory or demyelinating disease (e.g., multiple sclerosis).

Description of Case(s):

A 23-year old Hispanic male presented with subacute painless binocular diplopia. Past medical history was significant for hyperthyroidism, which was previously treated medically, and the patient remained euthyroid. Past ocular, surgical, family, and social histories were unremarkable, and he was taking no medications. The patient's visual acuity was 20/20 OU. Examination showed light-near dissociation of the pupils OU, right hypertropia, and a 5-degree head tilt to the right. Ductions and versions were full and no convergence nystagmus, lid retraction, papilledema, or optic atrophy was noted. Lumbar puncture showed the presence of seven white blood cells and five oligoclonal bands within the patient's CSF. Both serum and CSF were negative for AFP and beta-HCG. Initial MRI of the brain showed lesions within the left thalamo-mesencephalic region, periaqueductal midbrain, and right cerebellar peduncle. Subsequent serial cranial MRI showed an interval increase in the size of enhancing lesions with new hydrocephalus, worsening vasogenic edema centered in the bilateral thalamus, right midbrain and right superior cerebellar peduncles with new bilateral forniceal hyperintense and optic chiasm lesions. Subsequent brain biopsy showed findings consistent with dysgerminoma.

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

Atypical clinical (dorsal midbrain syndrome, bilateral optic neuropathy) or atypical radiographic features (mass effect, hydrocephalus) should prompt consideration for repeat imaging and possible biopsy even if serum or CSF tumor markers (B-hCG and AFP) are negative for dysgerminoma.

References: None.

Keywords: Tumors, Demeylinating disease, Neuro-ophth & systyemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 74
Hereditary Endotheliopathy with Retinopathy, Nephropathy and Stroke (HERNS)

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Introduction:
Hereditary endotheliopathy, retinopathy, nephropathy, and stroke (HERNS) is a genetic disease that affects the endothelial lining of small vessels. We describe a case of a patient who presents with blurred vision and stroke, and similar findings among several family members.

Description of Case(s):
A 49-year-old hypertensive, Hispanic female presents to an ophthalmologist with subacute blurred vision in the left eye. Dilated fundus examination showed branch retinal vascular occlusions bilaterally with macular edema and optic nerve pallor. She was diagnosed with hypertensive retinopathy and treated with intravitreal anti-VEGF injections (Bevacizumab), before being lost to follow up. A year later, she presented to neuro-ophthalmology with right-sided facial numbness and ipsilateral hemiplegia. On inquiry, several family members had presented with hypertension and strokes under the age of 60. MRI of the brain with contrast revealed an ischemic stroke of the Left Inferior Middle Cerebral Artery. There were cerebral microvasculopathic enhancing lesions in the white matter with surrounding edema. A biopsy of these lesions presented with distinct multi-laminated basement membranes that were typical in tissue examinations among patients with HERNS. Genetic testing showed frame-shift mutations in the carboxyl-terminus of three prime exonuclease 1 (TREX 1), which has been attributed as a causative factor in the disease. As there is no effective treatment for the disease, she was given steroids for her cerebral edema, physical therapy for her neurologic deficits, and anti-hypertensive medications for hypertension secondary to renal disease.

Conclusions, including unique features of the case(s):
This is a case of a patient who presented with hypertension, bilateral retinal vascular disease, optic nerve pallor, and stroke at a young age. Multiple members of her family have presented similarly with hypertension and strokes before the age of 60. These findings in a relatively young patient with a familial nature to the disease should prompt further workup with MRI for potential secondary causes such as HERNS.

References: Jen, J., Cohen, A. H., Yue, Q., Stout, J. T., Vinters, H. V., Nelson, S., Baloh, R. W. Hereditary endotheliopathy with retinopathy, nephropathy, and stroke (HERNS). Neurology 49: 1322-1330, 1997. Kavanagh, D., Spitzer, D., Kothari, P., Shaikh, A., Liszewski, M., Richards, A., Atkinson, P. New roles for the major human 3'-5' exonuclease TREX1 in human disease. Cell Cycle.15; 7(12): 1718 - 1725. 2008 Jun. Seifried, C., Sitzer, M., Jen, J. et al. Neurologist 76: 1191. 2005.

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

Financial Disclosures: The authors had no disclosures.

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Poster 75
Sequential Bilateral Vision Loss due to Lymphomatous Infiltration of the Anterior Optic Pathways

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Introduction:
Lymphomatous infiltration of the orbit and optic nerves is a rare cause of vision loss. Here, we present a case of sequential vision loss secondary to lymphomatous optic nerve infiltration spreading to the optic chiasm.

Description of Case(s):
71 year-old man with peritoneal and bone marrow diffuse large B-cell lymphoma presented with vision loss and painful periorbital swelling in his left eye. His visual acuity was no light perception (NLP) in the left eye. Examination showed complete external ophthalmoplegia, optic disc edema, and a central retinal artery occlusion. MRI showed fat stranding in the left orbit and enhancement along with restricted diffusion in the left optic nerve. CSF flow cytometry confirmed CNS lymphoma. He was treated with dexamethasone and systemic chemotherapy (MTR) with improvement in his periorbital edema and ophthalmoplegia, but no improvement in vision. Two months later, he represented with vision loss in his right eye. His first evaluation showed mild reduction in visual acuity with normal examination of the right eye. His visual acuity further declined to NLP in the right eye. Repeat examination showed normal posterior segment in the right eye. MRI showed new enhancement and thickening of the intracranial right optic nerve and pituitary stalk. CSF cytology showed malignant cells consistent with his lymphoma. He was treated with external-beam whole-brain radiation with improvement of the visual acuity in his right eye to 20/50. However, his left eye remained NLP.

Conclusions, including unique features of the case(s):
Orbital and optic nerve infiltration by lymphoma can cause vision loss by different mechanisms and therefore can present with different clinical and imaging manifestations. The clinicians should have a high index of suspicion, as timely radiation therapy can result in regression of lymphomatous infiltration of the optic nerve, improvement of vision, and, thus, improvement in quality of life for the patient.

References: 1. Rubin, Rumelt, Central retinal artery occlusion due to rapidly expanding orbital lymphoma, Eye, volume 12, 159-161 (1998). 2. Fierz, Sartoretti,Thoelen, Adelheid, Optic Neuropathy and Central Retinal Artery Occlusion in Non-Hodgkin Lymphoma, Journal of Neuro-Ophthalmology: June 2001 - Volume 21 - Issue 2 - p 103-105 3. Sudhakar, Rodriguez, Francisco, Trobe, MRI Restricted Diffusion in Lymphomatous Optic Neuropathy, Journal of Neuro-Ophthalmology: December 2011 - Volume 31 - Issue 4 - p 306–309.

Keywords: Optic neuropathy, Neuroimaging, Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 76

A Chronic Progressive Optic Neuropathy in a Patient with Anti-Myelin-Oligodendrocyte Glycoprotein (MOG) Antibodies

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Introduction:
Anti-MOG antibodies have been described in idiopathic inflammatory optic neuritis, such as aquaporin4-IgG seronegative neuromyelitis optica spectrum disorders and chronic relapsing inflammatory optic neuropathy, among others. Visual symptoms are typically characterized by acute onset vision loss and pain with monophasic or relapsing courses. Some cases of optic neuritis are associated with acute disseminated encephalomyelitis or follow it years later. We present a patient with progressive optic neuropathy and anti-MOG antibodies.

Description of Case(s):
A 32-year-old man presented with right eye "haziness" and "itching" but no abnormality on ophthalmologic exam was found. Two years later, symptoms progressed and he was found to have right optic nerve pallor. Neurological examination was otherwise normal. MRI brain demonstrated few nonspecific white matter changes. Serum studies were negative for inflammatory or infectious etiologies. Lumbar puncture was negative for oligoclonal bands. VEP showed prolonged latency on the right. One year later, he reported continued worsening. On neuro-ophthalmologic examination, visual acuity was (VA) 20/30 OD with reduced color vision. There was a 2+ right afferent pupillary defect (APD) and diffuse pallor of the optic disc. Visual fields (VF) showed an inferior nasal and temporal field defect OD. Optical coherence tomography (OCT) demonstrated thinning of the retinal nerve fiber layer (RNFL) in the right eye. Over the next year, vision deteriorated to 20/40 with worsened color vision OD and remained normal OS. His APD worsened to 3+ and the VF deficit enlarged. OCT demonstrated progressive RNFL thinning in the right eye: initial presentation average thickness 57 microns decreased to 52 microns- most pronounced loss superiorly and inferiorly. Left eye remained stable. MOG testing returned positive at 1:100.

Conclusions, including unique features of the case(s):
This case represents an unusual clinical phenotype in the anti-MOG spectrum of disease: a slow, progressive painless vision loss with progressive thinning on OCT in the absence of other neurologic symptoms and without relapses.

References: Chalmoukou et al, Anti-MOG antibodies are frequently associated with steroid-sensitive recurrent optic neuritis, Neurol Neuroimmunol Neuroinflamm, 2e131, 2015. Chen et al, Myelin Oligodendrocyte Glycoprotein Antibody-Positive Optic Neuritis: Clinical Characteristics, Radiologic Clues, and Outcome, Am J Ophthalmol, July 2018. Epub ahead of print. Havla et al, Myelin-oligodendrocyte-glycoprotein (MOG) autoantibodies as potential markers of severe optic neuritis and subclinical retinal axonal degeneration, J Neurol, 264,139-151, 2017. Jarius et al, MOG-IgG in NMO and related disorders: a multicenter study of 50 patients. Part 2: Epidemiology, clinical presentation, radiological and laboratory features, treatment responses, and long-term outcome, J Neuroinflammation, 13:280, 2016. Jurynczyk et al, Clinical presentation and prognosis in MOG-antibody disease: a UK study, Brain, 1;140(12), 3128-3138, 2017.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 77
A Case of Candida Dubliniensis Meningitis with Associated Vision Loss

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Introduction:
Candida dubliniensis is a rare cause of meningitis [1-3], with only four previously published cases [3]. We present a case of chronic C. dubliniensis meningitis – the first reported with associated vision loss.

Description of Case(s):
A 27-year-old white woman with a history of intravenous drug abuse presented with left monocular vision loss and headache. Over 10 months, the patient developed daily frontal headaches with progressive left eye vision loss. Visual acuity in the left eye was light perception only. There was a left RAPD, bilateral optic disc pallor, and bilateral disc edema without chorioretinal lesions. MRI revealed leptomeningeal enhancement extending from the brainstem to cauda equina. Motion artifact limited evaluation of the left optic nerve on MRI, but there was suspected enhancement of the optic sheath on T1 coronal post-contrast images. CSF demonstrated hypoglycorrhachia, sterile polymorphonuclear pleocytosis and an opening pressure of 35 cm H2O. Repeat CSF fungal cultures were positive for C. dubliniensis and CSF beta-D-glucan was significantly elevated. Systemic fungal cultures remained negative. The patient received 2 weeks of IV amphotericin and 6 weeks of fluconazole. Following amphotericin treatment, CSF cultures demonstrated no growth and there was significant improvement of leptomeningeal enhancement on MRI. Her headaches resolved without perceived visual improvement. Potential mechanisms of the patient's vision loss include optic nerve and/or sheath infiltration, optic nerve infarction and chronically elevated intracranial pressure.

Conclusions, including unique features of the case(s):
While C. dubliniensis infections are rare, diagnostic delay can lead to significant morbidity. A high level of suspicion should be maintained for at risk patients, as initial cultures can be negative. Beta-D-glucan may be a useful screening test in at-risk patients [4-6]. Future advancements in diagnostic testing, such as metagenomic next-generation sequencing [3], may facilitate the diagnosis of C. dubliniensis meningitis and familiarity with its presenting signs and symptoms has the potential to further reduce diagnostic delay.

References: 1. Andrew NH, Ruberu RP, Gabb G. The first documented case of Candida dubliniensis leptomeningeal disease in an immunocompetent host. BMJ Case Rep. 2011 Aug 4, 2011. 2. Yamahiro A, Lau KH, Peaper DR, Villanueva M. Meningitis Caused by Candida Dubliniensis in a Patient with Cirrhosis: A Case Report and Review of the Literature. Mycopathologia. 181(7-8):589-93, 2016. 3. Wilson MR, O'donovan BD, Gelfand JM, et al. Chronic Meningitis Investigated via Metagenomic Next-Generation Sequencing. JAMA Neurol. 75(8):947-955, 2018. 4. Farrugia MK, Fogha EP, Miah AR, Yednock J, Palmer HC, Guilfoose J. Candida meningitis in an immunocompetent patient detected through (1→3)-beta-D-glucan. Int J Infect Dis. 51:25-26, 2016. 5. Litvintseva AP, Lindsley MD, Gade L, et al. Utility of (1-3)-β-D-glucan testing for diagnostics and monitoring response to treatment during the multistate outbreak of fungal meningitis and other infections. Clin Infect Dis. 58(5):622-30, 2014. 6. Lyons JL, Thakur KT, Lee R, et al. Utility of measuring (1,3)-β-D-glucan in cerebrospinal fluid for diagnosis of fungal central nervous system infection. J Clin Microbiol. 53(1):319-22, 2015.

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Optic neuropathy, Skull Base, High intracranial pressure/headache

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Poster 78
First case of melanoma-associated retinopathy with conjunctival melanoma

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Introduction:
Melanoma-associated retinopathy (MAR) is characterized by the presence of antiretinal antibodies, reacting mainly with retinal bipolar cells.

Description of Case(s):
A 63-year-old man was referred to the neurology clinic with a few months history of right monocular vision loss. He was complaining of phosphenes with eye closure but denied nyctalopia. The patient had noticed a brown mass in the conjunctiva of his left eye, possibly increasing in size over the last two years with a tendency to bleed. On presentation, best-corrected visual acuity was 6/9 OD and 6/6 OS, with a relative afferent pupillary defect OD. Color vision testing with HRR was 8/10 OD and 10/10 OS. His Goldmann visual field testing showed severe contraction with central 5 degrees preservation in the right eye, while left eye testing was normal. Slit lamp exam revealed a voluminous hyperpigmented lesion of the inferior bulbar conjunctiva in the left eye Ocular motility testing, funduscopic exam, OCT and fluorescein retinal angiography were unremarkable. Based on patient's history and clinical findings, MAR with conjunctival melanoma was suspected. The electroretinogram showed b-wave loss with rod-cone dysfunction (negative waveform) OU, but OD affected more than OS . The patient tested positive for antiretinal autoantibodies, which confirmed the diagnosis The patient was treated with prednisone 60 mg daily, with subsequent improvement of vision.

Conclusions, including unique features of the case(s):
This case is unique and interesting for several reasons. To the best of our knowledge, this is the first case of MAR associated with conjunctival melanoma. The fact that vision loss was clinically isolated to the contralateral eye made the decision about optimal treatment complex. Indeed, exenteration would have made the patient severely visually impaired, making this option less attractive. Finally, the spectacular response to treatment with steroids was unexpected and much more favorable than in previous medical literature.

References: 1.Keltner JL, Thirkill CE, Yip PT. Clinical and immunologic characteristics of melanoma-associated retinopathy syndrome: eleven new cases and a review of 51 previously published cases. J Neuroophthalmol. 2001;21(3): 173-187. 2.Rush JA. Paraneoplastic retinopathy in malignant melanoma. Am J Ophthalmol 1993:115:J 90–1. 3.Ko MW, Dalmau J, Galetta SL. Neuro-ophthalmologic manifestations of paraneoplastic syndromes. J Neuroophthalmol. 2008;28(1):58. 4.Larsen, A et al. A Retrospective Review of Conjunctival Melanoma Presentation, Treatment, and Outcome and an Investigation of Features Associated With BRAF Mutations. JAMA Ophthalmol. 2015;133(11):1295-1303. 5.Shields CL. Conjunctival melanoma: risk factors for recurrence, exenteration, metastasis, and death in 150 consecutive patients. Trans Am Ophthalmol Soc. 2000;98:471-492.

Keywords: Paraneoplastic syndromes, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Visual fields, Tumors

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Poster 79
Myelin Oligodendrocyte Glycoprotein Antibody-Associated Optic Neuritis with Sjögren's Syndrome

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Introduction:
The association between optic neuritis and demyelinating and inflammatory conditions is well established; however, optic neuritis as a presenting sign of Sjögren's Syndrome is rare. We present a case of anti-Myelin Oligodendrocyte Glycoprotein (MOG) optic neuritis with Sjögren's Syndrome.

Description of Case(s):
A 32-year-old African-American woman with no autoimmune history presented with 3 days of left-sided headache, progressive vision loss, and pain with eye movements. Visual acuity was 20/20 OD and Counting Fingers OS (6 feet). She had a left relative afferent pupillary defect. Automated perimetry was full OD with complete depression OS. Ophthalmoscopy showed left optic disc edema with scattered intraretinal hemorrhages throughout the posterior pole without vascular sheathing. Fluorescein angiography showed left optic disc leakage with delayed arteriovenous transit and no vasculitis. Orbital magnetic resonance imaging (MRI) demonstrated left retrobulbar optic nerve and sheath enhancement and intraconal fat. Brain and cervical spine MRI were unremarkable. Workup showed ESR of 75, positive ANA with 1:80 titer, and positive anti-Ro antibody. She was diagnosed with optic neuritis with central retinal vein occlusion from underlying Sjogren's Syndrome and was treated with 3 days of intravenous solumedrol followed by oral prednisone taper. She experienced visual improvement to 20/20 with persistent scattered, nonspecific visual field depression OS. Disc edema and retinopathy resolved. She was followed regularly without relapse, and 4 years later was found to have positive anti-MOG antibody with 1:100 titer. Anti-aquaporin-4 was negative. She has not experienced other manifestations of anti-MOG disease and has retained 20/20 vision OU on hydroxychloroquine.

Conclusions, including unique features of the case(s):
To our knowledge, anti-MOG-associated disease has not been described in the setting of Sjogren's Syndrome. As the clinical profile of anti-MOG disease is being elucidated, testing for lupus-associated antibodies will help to further delineate the marker's associations.

References: None.

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

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Poster 80
Bilateral Optic Neuropathy associated with Wilson's disease

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Introduction:
Kayser-Fleischer ring is the well known ocular manifestation of Wilson's disease (WD), which is a rare autosomal recessive condition characterized by hepatic and neurologic manifestations. Optic neuropathy is very rarely reported with WD, but has been reported with penicillamine therapy. We report the case of a 19-year-old male presenting with advanced cirrhosis secondary to WD, and a rapid onset bilateral optic neuropathy. We discuss the possible association of WD and optic neuropathy.

Description of Case(s):
A 19-year-old male developed symptoms of episodes of blackouts lasting a few seconds, abdominal pain, headaches, bilateral blurred vision and yellow vision around May 2018. He had normal visual function post-LASIK in December 2017. In August 2018, he was noted with best corrected visual acuity of 20/50 OD and 20/25 OS with moderately reduced color vision OU. Kayser-Fleischer ring and bilateral optic disc pallor were noted. OCT RNFL of 70 µm OD and 69 OS. Macular ganglion cell layer thickness 53 µm OD and 52 OS. Broad differential diagnosis for bilateral optic neuropathy was considered. Orbital MRI negative. Heavy metal screen was negative. Serum ACE elevated. Serum copper 7 mcg/dL (normal 70-140). Serum retinol reduced at 0.11 mg/L (normal 0.3-1.2). Serum B6 low at 12 nmol/L (normal 20-125). He had several gastrointestinal abnormalities: transaminitis, cholestasis, thrombocytopenia, splenomegaly and portal hypertension. Hepatic copper at 371 mcg/g dry weight, normal 10-35. Liver biopsy consistent with WD. He did not tolerate chelation and is awaiting liver transplantation.

Conclusions, including unique features of the case(s):
Wilson's disease is rarely reported to be associated with optic neuropathy. Previous reports of optic neuropathy in WD did not find the possible cause of optic neuropathy. Vitamin A deficiency, pyridoxine deficiency and relative copper deficiency were noted in our patient.

References: 1. Goldstein NP, Hollenhorst RW, Randall RV, Gross JB. Possible relationship of optic neuritis, Wilson's disease, and DL-Penicillamine therapy. JAMA 1966; 196: 146–7. 2. Tu J, Blackwell RQ, Lee P. DL-Penicillamine as a cause of optic axial neuritis. JAMA 1963; 185: 83–6. 3. Rossa V. Retinal changes in Wilson's disease. Fortschr. Ophthalmol. 1991; 88: 230–2.

Keywords: Neuro-ophth & systyemic disease (eg. MS, MG, thyroid), Optic neuropathy, Genetic Disease, Pediatric neuro-ophthalmology, Miscellaneous

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Poster 81
Rapidly progressing retinal dystrophy in Spinocerebellar Ataxia 7 (SCA7): A case report of three brothers

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Introduction:
SCA7, an autosomal dominant neurodegenerative disorder with retinal degeneration, is caused by CAG repeat expansion usually >36 in the ATXN7gene1,2. The ATXN7, normally <17 repeats, is responsible for chromatin remodeling through deubiquination to enhance transcription. Aggregates of expanded ATXN7complexes decrease deubiquination and create toxicity, leading to early cell death affecting retinal photoreceptors and cerebellum. These abnormal repeats show anticipation with the potential for marked expansion in subsequent generations, leading to severe disease. We present a family with SCA7 in whom very slight variations in expansion lead to devastating phenotypes.

Description of Case(s):
A 10-year-old boy was evaluated for clumsiness, intellectual disability and failed vision screen. Initial ophthalmologic exam showed vertical nystagmus, color blindness, failed stereo test. Electroretinogram responses were consistent with cone-rod dystrophy. Neurologic exam revealed dysmetria and difficulty with tandem. Rapidly progressive visual loss, ataxia, and failure to thrive ensued. Five years from initial presentation, the patient had light perception vision and was wheelchair bound. His younger brother, at 7 years of age, showed visual decline with loss of independent ambulation and pseudobulbar dysfunction. The youngest brother presented with hypotonia and dysarthria at 2 years of age. Genetic testing of the 10-year-old proband showed 70 / 12 CAG repeats in ATXN7and testing of the 7-year-old brother showed 71/10 CAG repeats. Testing of the youngest brother was declined by guardian and their mother was not tested because of underlying psychiatric condition.

Conclusions, including unique features of the case(s):
SCA7 is a devastating neurodegenerative disease. Classically thought to involve mainly the retinal and cerebellar tissue, our case shows the expanded phenotype including early hypotonia, pseudobulbar symptoms, and psychiatric disease affecting many of these patients. Early diagnosis is key for appropriate counseling about the natural history and genetics of the disease, establishment of rehabilitation services to maximize quality of life and preventing early death from complications such as falls, aspiration and malnutrition.

References: 1. Donis KC, Mattos EP, Silva AA, et al. Infantile spinocerebellar ataxia type 7: Case report and a review of the literature. J Neurol Sci. 2015;354(1-2):118-121. 2. McLaughlin ME, Dryja TP. Ocular findings in spinocerebellar ataxia 7. Arch Ophthalmol. 2002;120(5):655-659.

Keywords: Pediatric neuro-ophthalmology, Ocular manifestations of vestibular disorders, Genetic Disease, Orbit/ocular pathology

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Poster 82

Case of Heidenhain Variant Creutzfeldt-Jakob Disease Presenting with Homonymous Quadrantanopia and Corresponding Nuclear Imaging Findings

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Introduction:
Sporadic Creutzfeldt-Jakob disease (sCJD) belongs to a class of prion diseases in which prion protein forms abnormal and pathological folds. In the Heidenhain variant of Creutzfeldt-Jakob disease (HvCJD), patients present with early, prominent visual complaints prior to the onset of more typical features of sCJD. MRI brain is commonly normal, making early diagnosis of this variant particularly challenging. We present a case of a patient with impaired depth perception and homonymous inferior quadrantanopia with normal MRI, in contrast to marked focal FDG-PET and SPECT abnormalities providing clinical-anatomical correlate.

Description of Case(s):
A 77-year-old man presented with two weeks of impaired depth perception, blurred vision on the right and falls. On initial exam, he had a dense right inferior quadrantanopia and no cognitive deficits. The general neurologic and ophthalmologic exam were otherwise unremarkable. MRI brain and EEG were non-revelatory. Over the following month, the patient developed right-sided sensory neglect, bilateral right>left dysmetria, a mild right hemiparesis and brisker reflexes on the right. FDG-PET brain revealed striking asymmetric hypometabolism in the left frontal.

Conclusions, including unique features of the case(s):
HvCJD is a clinical variant sCJD with predominant, early visual symptoms heralding disease later characterized by rapid cognitive decline, movement abnormalities and incipient death. Early diagnosis of HvCJD is hindered by isolated visual signs and symptoms, and often normal ancillary testing including MRI brain and EEG. Nuclear imaging including FDG-PET and SPECT brain demonstrate striking focal abnormalities that correspond to exam findings and may aide in earlier diagnosis and prognostication of this devastating disease.

References: None.

Keywords: Visual fields, Neuroimaging, Higher visual functions, Neuro-ophth & systyemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 83
Vertical Gaze Palsy with Bilateral Third Nerve Palsy and Contralateral Hemiparesis

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Introduction:
Vertical gaze palsy with bilateral third nerve palsy is a rare neurological finding. We present a case of a 62- year-old male with unilateral mid-brain bleed, who presented with vertical gaze palsy and bilateral partial third nerve palsy with contra-lateral hemiparesis.

Description of Case(s):
62-year-old hypertensive male presented with a history of diplopia and sudden-onset weakness of right upper and lower limbs. He sought treatment at a local clinic, where he was recorded to have a blood pressure of 210/120, and the hypertensive crisis was managed. Patient was then referred to our centre for ophthalmic evaluation. On ocular examination, visual acuity was 6/6 OU. Ptosis was absent. Extra-ocular movement examination showed bilateral limitation of elevation and mild limitation of depression. Vestibulo-ocular reflex(VOR) was normal for elevation bilaterally but slightly impaired for depression OU. Bell's reflex was good bilaterally.There was left eye exotropia and right eye hypertropia in primary gaze with increase in vertical deviation on dextroversion. Anisocoria was noted with pupil measuring 2 mm OD and 4 mm OS under moderate illumination. Pupillary reaction was brisk OD and sluggish OS. Fundus showed signs of hypertensive retinopathy. Physical examination revealed right sided hemiparesis with right UMN facial palsy. Contrast-enhanced MRI axial, sagittal and coronal, T2-weighted images showed an area of focal bleed in the tectum of midbrain. The patient was advised to continue anti-hypertensive medications. At 3 months of follow-up, his hemiparesis had improved remarkably but the gaze palsy and diplopia persisted.

Conclusions, including unique features of the case(s):
Unilateral mid brain bleeds are known to cause VGP. But bilateral partial third nerve palsy has never been reported in combination with vertical gaze palsy and hemiparesis. This case report highlights a unique presentation of unilateral mid-brain lesions.

References: None.

Keywords: Neuro-ophth & systyemic disease (eg. MS, MG, thyroid), Adult strabismus with a focus on diplopia, Vascular disorders, Ocular Motility, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 84
Optic Neuritis and Intracranial Hypertension caused by Chronic Lymphocytic Leukemia

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Introduction:
Cases of CLL with optic infiltration have been reported with good response to intrathecal methotrexate and/or systemic chemotherapy when ICP is normal. However, concomitant intracranial hypertension is unusual and poses treatment challenge. We present an unusual case of chronic lymphocytic leukemia (CLL) causing infiltrative /optic neuritis and intracranial hypertension.

Description of Case(s):
A 53-year-old woman with history of untreated CLL (RAI stage III) presented with blurry vision, morning headaches, pulsatile tinnitus and transient visual obscurations. Eye examination was pertinent for 20/20 visual acuity (VA), full color vision, 0.3 log unit APD left eye and bilateral severe optic disc edema. MRI orbits showed findings consistent with increased intracranial pressure and mild enhancement of the left optic nerve. Lumbar puncture revealed opening pressure of 47 cm H2O, protein of 67.5 mg/dl and 7 WBCs. Left eye VA continued to deteriorate with persistent disc edema, despite maximizing acetazolamide (4000mg daily) and furosemide. Repeat lumbar puncture revealed opening pressure of 36 cm H2O, 38 WBCs with 95% lymphocytes, and protein of 110.5 mg/dl. Flow cytometry showed monoclonal B-cell population with CD19+ B-cells (27.1%). CSF studies for infectious and inflammatory conditions were negative. Repeat MRI orbit showed intense enhancement of intracanalicular and proximal intraorbital segment of left optic nerve. She was treated with high dose IV methylprednisolone, intrathecal cytarabine (6 doses), and systemic chemotherapy with fludarabine, cyclophosphamide and rituximab. Disc edema improved bilaterally but she developed optic atrophy in left eye.

Conclusions, including unique features of the case(s):
1. Co-existence of the two conditions explained by either: Primary idiopathic intracranial hypertension complicated by spread of CLL intracranially, or intracranial leukostatis from CLL leading to secondary intracranial hypertension. 2. Co-existence of intracranial hypertension and optic infiltration in CLL patients raises diagnostic and treatment challenge. 3. Efficacy and safety of Intrathecal cytarabine vs methotrexate in the presence of papilledema requires further studies.

References: 1. Saenz-Frances, Calvo-Gonzalez, Garcia-Feijoo, Bilateral papilledema secondary to Chronic lymphocytic leukemia, ARCH SOC ESP OFTALMOL 2007; 82: 303-306 2. Wilson I. Gonsalves, Clive S. Zent, Jose S. Pulido, and Mrinal M. Patnaik, Visual loss in early stage chronic lymphocytic leukemia, VOLUME 31 NUMBER 17 JUNE 10 2013 3. Khan K , Malik AI, Almarzouqi SJ, Morgan ML, Yalamanchili S, Chevez-Barrios P, Lee AG, Optic Neuropathy Due to Chronic Lymphocytic Leukemia Proven With Optic Nerve Sheath Biopsy, J Neuroophthalmol. 2016 Mar;36(1):61-6.

Keywords: High intracranial pressure/headache, Optic neuropathy, Neuro-ophth & systyemic disease (eg. MS, MG, thyroid), Neuroimaging, Chemotherapy and radiation injury

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Poster 85
Optic Nerve: A window to Neurosyphilis

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Introduction:
Syphilis is a multisystem chronic infection caused by Treponema Pallidum that progresses into four stages if untreated. Primary syphilis: typical painless syphilitic ulcer (chancre at the inoculation region) (incubation period lasting for 2-3 weeks). Secondary syphilis: weeks or months later in nearly 25% of untreated patients, lymphadenopathy, gastrointestinal abnormalities and CNS alterations. Tertiary syphilis: 1-30 years after primary infection – end of latent period – (25% of untreated) progresses slowly as neurosyphilis or gummatous syphilis.

Description of Case(s):
68 year old man with 1 month history of bilateral decreased vision acuity (VA). Medical history: arterial hypertension. He referred progressive weakness, paresthesias and pain of the lower extremities. Corrected VA OD 2/10 (PH 4/10) OS 1/10 (PH 4/10). Altered visual field: OD supero-temporal scotoma, OS central relative scotoma. Optic nerve: head diffuse pallor OU. Light near dissociation was detected in both eyes. MRI show subcortical and periventricular white matter high signal intensity T2/flair images without gadolinium enhance. MRI angiography revealed a 7x6mm dissecting pseudo-aneurysm in the cervical segment of the left internal carotid artery. Test for serum shown: ESR 93 mm; VDRL: 1/1024; FTA-ABS+. The patient refused the lumbar puncture although infectologist and neurologist also strongly recommended it. He was treated with Penicillin G 4 intravenously for 14 days. 3D-Angiography was performed for diagnosis and treatment of carotid pseudo-aneurism. VA and visual field restituted ad integrum a month after the end of the treatment and serum antibodies progressively decreased.

Conclusions, including unique features of the case(s):
Neurosyphilis is still a significant medical problem in developing countries and syphilitic ocular manifestations are often not diagnosed due to the lack of typical characteristics. This case shows an unusual early ocular involvement. We also support the view that the presence of ocular involvement in syphilitic patients is suggestive of involvement of the CNS and should be considered synonymous with neurosyphilis.

References: 1. Bharucha NE. Infections of the nervous system. In: Bradley WG, Daroff RB, Fenichel GM, editors. Neurology in Clinical Practice. 3th edition. London: Butterworth-Heinemann; 2000. pp. 1334–5. 2. Adams RD, Victor M, Ropper AH. Principles of Neurology. 7th edition. New York: Mc Graw-Hill Companies; 2000. pp. 722–8. 3. Schmidt RP. Neurosyphilis. In: Joynt RJ, editor. Clinical Neurology. Revised edition. Vol. 2. Philadelphia: Lippincott Williams & Wilkins; 1992. pp. 1–23. 4. Berger JR. Neurosyphilis in human immunodeficiency virus type 1-seropositive individuals. A prospective study. Arch Neurol. 1991;48:700–2. [PubMed] 5. Birnbaum NR, Goldschmidt RH, Buffett WO. Resolving the common clinical dilemmas of syphilis. Am Fam Physician. 1999;59:2233–46. [PubMed] 6. Polsky I, Samuels SC. Neurosyphilis. Screening does sometimes reveal an infectious cause of dementia. Geriatrics. 2001;56:60–2. [PubMed] 7. Merritt HH, Adams RD, Solomon HC. Neurosyphilis. Oxford, New York: 1946. 8. Stokes JH, Beerman H, Ingraham NR. Modern Clinical Syphilology:Diagnosis, Treatment, Case Study.3rd ed. Philadelphia: WB Saunders; 1944.

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

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Poster 86
Cobalt-chromium toxicity and late-onset disease conversion in LHON – is there a causal link?

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Introduction:
Lebers hereditary optic neuropathy (LHON, OMIM 535000) is the most common primary mitochondrial DNA disease in the population with the marked gender bias (male predominance) and the peak age of onset is in the second and third decades of life. However, presentation has been reported in patients from 2 to 87 years of age. There is increasing evidence that mitochondrial dysfunction can be influenced by environmental factors such as smoking, heavy drinking and particular drug agents. In addition, cobalt has been linked to mitochondrial dysfunction and ocular cobalt toxicity has been reported in the context of cobalt-chromium ions released from a metal hip prosthesis. The measurement of cobalt-chromium ions blood level is helpful in confirming the diagnosis, but there are challenges related to the laboratory methods used and the threshold level deemed to be toxic. We report a case, where cobalt-chromium ions leak possibly have contributed to disease conversion in late-onset LHON.

Description of Case(s):
An 84-year-old female with a family history of LHON (m.11778G>A) presented with subacute bilateral visual blurring and bilateral central scotomas. The patient underwent a comprehensive neuro-ophthalmological examination, including ocular imaging, where no optic disc or retinal abnormalities were noted. Visual electrophysiological assessment was performed to ISCEV standards at around 4 and 10.5 (follow-up) months after symptoms onset, which revealed bilateral severe macular and optic nerve dysfunction, which showed deterioration with the disease duration. The patient had previously undergone four hip arthroplasties, with the most recent prosthesis known to have cobalt-chromium components. As the age of presentation was highly atypical for LHON, the possibility of cobalt-chromium toxicity was considered and ion levels were tested in blood.

Conclusions, including unique features of the case(s):
The visual electrophysiological findings of dual macular and optic nerve pathology raise the possibility of cobalt-chromium toxicity, which in turn may have contributed to the relatively late onset of LHON in our patient.

References: Sadun AA et al. Leber's Hereditary Optic Neuropathy. Curr Treat Options Neurol. 2011;13(1):109-117. Yu-Wai-Man P, et al. Treatment strategies for inherited optic neuropathies: past, present and future. Eye. 2014;28(5):521-537. Fraser JA, et al. The neuro-ophthalmology of mitochondrial disease. Surv Ophthalmol. 2010;55(4):299-334. Lambertini L, Byun HM. Mitochondrial Epigenetics and Environmental Exposure. Curr Env Heal Rep. 2016;3(3):214-224. Kirkman MA, et al. The clinical spectrum of mitochondrial genetic disorders. Clin Med. 2008;8(6):601-606. Kikuchi S, et al. Cobalt inhibits motility of axonal mitochondria and induces axonal degeneration in cultured dorsal root ganglion cells of rat. Cell Biol Toxicol. 2018;34(2):93-107. Valko M, et al. Metals, toxicity and oxidative stress. Curr Med Chem. 2005;12(10):1161-1208. Grillo LM, et al. Cobalt-Chromium Metallosis With Normal Electroretinogram. J Neuroophthalmol. 2016;36(4):383-388. Lim CA, et al. The effect of cobalt on the human eye. Doc Ophthalmol. 2015;130(1):43-48. Apel W, et al. Cobalt-chromium toxic retinopathy case study. Doc Ophthalmol. 2013;126(1):69-78.

Keywords: Optic neuropathy, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Genetic Disease, Miscellaneous

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Poster 87
Diagnostic of micro adenoma pituitary in patients pediatric

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Introduction:
The micro adenoma pituitary has an incidence in pediatrician of 0.1-4.1/100,000 cases per year. The visual compromise is the main cause of consultation. Generally it is represented as a defective visual field, specifically with temporary superior quadrantopsia and temporary hemianopsia.

Description of Case(s):
A 9 year old girl calls to the ophthalmologist in March 2017 for bilateral blurry vision progressive since 1 year, without previous checking diagnosed with ametropia (myopia) and family history of medulloblastoma (sister). She calls on to a second opinion with the following findings: visual acuity 20/20, eye sight color test 8/8, fundus with papillary excavation of .4, perimetry for confrontation reports mayor bi temporal hemianopsia of LE(left eye). Older age is apparently obtained to the chronology by Tanner IV. Pituitary disorder is suspected so visual fields are requested. Visual field superotemporal frank decrease and lack of island of temporary vision. A Humphrey perimetry is accomplished and reports reliable bi temporal hemianopsia plus a temporary decrease 50^{o} and superior of 40^{o} in LE, decrease of 20^{o} in RE(right eye). In October of 2018, a reliable control of perimetry is accomplished and reports in LE a temporary scotoma >50º, RE inferotemporal scotoma of >60º. Symmetric pupillary reflexes lightly decreased. It is sent to research for the endocrine and pediatric neurosurgery for magnetic resonance.

Conclusions, including unique features of the case(s):
Nowadays the gold standard in pediatrician for the diagnosis of micro adenoma pituitary is the magnetic resonance; even so the use of Humphrey campimetry should not be rejected, since it can be a great diagnostic tool by expert hands.

References: Gracia, Patología del tallo. Tumores adenohipofisarios, Revista Española Endocrinologica Pediatrica., 1, pp 56-66, Noviembre 2010. Castaño, Martínez, Portillo, Rica. Adenomas hipofisarios: Impacto clínico de los hallazgos moleculares. Revista Española Endocrínologia de Pedíatria; 8: pp 36-45. 2017. Castaño, Fernández, Galano, Gómez. Confiabilidad de la campimetría manual por confrontación para detectar defectos de campos visuales en patologías neurológicas Reliability of confrontation testing of visual fields in neurological diseases. Revista Neuro-psiquiatra Chilena; 2: pp. 73-80, 2014. Patel, Cumberland, Walters, Russell-Eggitt, Rahi, OPTIC study group Study of Optimal Perimetric Testing in Children (OPTIC): Feasibility, Reliability and Repeatability of Perimetry in Children. PLoS ONE 10(6), 2015.

Keywords: Pediatric neuro-ophthalmology, Perimetry

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Poster 88
Ophthalmoparesis and Optic Neuropathy in a Woman with Catastrophic Antiphospholipid Syndrome

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Introduction:
Antiphospholipid syndrome (APS), presence of antiphospholipid antibodies, is characterized by hypercoagulability and diverse related clinical manifestations. Here we showed a case to remind ophthalmologists to screen for this disease especially for patients with underlying risk.

Description of Case(s):
A 40 years old woman presented with intermittent blurred vision in left eye and diplopia for 2 weeks. She was admitted in hospital a few days ago because of left limbs and face numbness for 2 months. She had peripheral artery occlusion and coronary artery disease, and underwent percutaneous transluminal angioplasty a few months prior. Her best corrected vision was 20/20 in both eyes, and normal pupillary reaction. Eye position was parallel with moderate deficiency in adduction and abduction in left eye. Fundus examination, confrontation and color test were unremarkable. Prolong and reduced waveform in left eye was detected by visual evoked potential. Brain MRI showed no recent infarction. Blood test found anti-nuclear antibody titer 320x and lupus anticoagulant ratio 2.1. During admission, she received antiplatelet and anticoagulant oral medications. She lost follow-up after discharge, so no visual field data available. Unfortunately, she passed away 3 months later at a local hospital.

Conclusions, including unique features of the case(s):
The most common ocular finding of APS is retinal vasculitis (approximately 60% according to literature review). Although our patient did not have retinal vascular occlusion, small vessels thrombosis might contribute to her ophthalmoparesis and ischemic optic neuropathy. Catastrophic APS is generalized intravascular thrombosis leading to multiorgan ischemia and failure. It is a rare, but life-threatening. Therefore, ophthalmologists should be familiar with this disease in order to save patient's vision and life.

References: None.

Keywords: Neuro-ophth & systyemic disease (eg. MS, MG, thyroid), Adult strabismus with a focus on diplopia, Optic neuropathy, Vascular disorders, Ocular Motility

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Poster 89
A Case of an Esophageal Adenocarcinoma Causing Infiltrative Optic Neuropathy and Carcinomatous Meningitis

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Introduction:
Gastroesophageal junction adenocarcinoma is known as one of the most difficult malignancies to treat. The development of carcinomatous meningitis from it is extremely rare and indicates poor prognosis. This case report describes diagnostic challenges in a patient with an esophageal adenocarcinoma causing infiltrative optic neuropathy and carcinomatous meningitis.

Description of Case(s):
A 58-year-old man with a history of stage IIIC esophageal adenocarcinoma in remission with minimal residual nodal disease, enrolled in a trial of nivolumab versus placebo at the time of presentation (arm unknown at presentation, subsequently found to be in the placebo arm), reported blurred vision OS. His afferent visual function and automated perimetry demonstrated signs of left optic neuropathy and funduscopy revealed markedly asymmetric disc edema. MRI revealed left optic nerve head and bilateral optic nerve sheath enhancement. Extensive serological testing was unrevealing. Lumbar puncture demonstrated an elevated opening pressure, CSF pleocytosis with cytology showing “metastatic carcinoma consistent with the patient’s known esophageal adenocarcinoma”.

Conclusions, including unique features of the case(s):
The initial differential was broad and included newly-recognized disorders (checkpoint inhibitor complications), infiltrative optic neuropathy which is rare with esophageal adenocarcinoma, papilledema due to elevated intracranial pressure, ischemic optic neuropathy, immune-mediated etiologies, and infectious optic neuropathies. This patient disc edema reflects two processes: locally invasive disease of the optic nerve head and sheath as well as elevated intracranial pressure. This case illustrates the need to maintain a high index of suspicion for multiple etiologies of neuro-ophthalmic dysfunction in cancer patients. Marked asymmetry in disc edema, uncommon in elevated ICP, raised suspicion for direct infiltration. Recognition of both processes is critical in developing an optimal treatment strategy. MRI of the brain may be inadequate to diagnose leptomeningeal disease and multiple lumbar punctures are often required to establish the diagnosis. Gastroesophageal junction adenocarcinoma is difficult to treat and the development of carcinomatous meningitis from it indicates poor prognosis.

References: 1. Wall M, White WN II. Asymmetric papilledema in idiopathic intracranial hypertension: prospective interocular comparison of sensory visual function. Invest Ophthalmol Vis Sci; Vol. 39, pp. 134-142, 1998. 2. Straathof CSM, De Bruin HG, Dippel DWJ, Vecht CJ. The diagnostic accuracy of magnetic resonance imaging and cerebrospinal fluid cytology in leptomeningeal metastasis. Journal of Neurology, Vol. 246, No. 9, pp. 810–814, 1999 3. Wasserstrom WR, Glass JP, Posner JB. Diagnosis and treatment of leptomeningeal metastases from solid tumors: experience with 90 patients. Cancer, Vol. 49, No. 4, pp. 759–772, 1982 4. Giglio P, Weinberg JS, Forman AD, Wolff R, Groves MD. Neoplastic meningitis in patients with adenocarcinoma of the gastrointestinal tract. Cancer, Vol. 103, No. 11, pp. 2355–2362, 2005.

Keywords: Optic neuropathy, High intracranial pressure/headache, Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 90
A Case of Posterior Reversible Encephalopathy Syndrome Presenting as Obstructive Hydrocephalus

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Introduction:
Posterior reversible encephalopathy syndrome (PRES) is a clinico-radiographic disorder classically consisting of subcortical edema bilaterally in the cerebral hemispheres. Extensive white matter hyperintensities are observed typically in the occipital and parietal regions on T2 weighted imaging without diffusion restriction (1). Cases of predominant brainstem involvement, without the classic aforementioned subcortical involvement, are uncommon (2,3) with one study estimating it to comprise 4% of those diagnosed with PRES (2). We present a rare case of brainstem PRES who presented with obstructive hydrocephalus and signs of raised intracranial pressure (4, 5).

Description of Case(s):
A 33 year old Caucasian female with a history of poorly controlled hypertension, cocaine abuse, chronic kidney disease, and pre-eclampsia, presented with recurrent headaches and papilledema. Her BMI was 22. Initial MRI brain demonstrated isolated edema of the pons with narrowing of the fourth ventricle and dilation of the lateral and third ventricles consistent with obstructive hydrocephalus. This was initially mistaken for a pontine glioma, but subsequently diagnosed as PRES. She improved with control of blood pressure, but two years later she presented with recurrence of papilledema and sixth nerve palsy with recurrence of PRES secondary to uncontrolled hypertension. At this time, BP was 156/123 and brain MRI demonstrated recurrent pontine and midbrain edema but now with extension into the cerebellar hemispheres, basal ganglia bilaterally, and some subcortical edema with signs of obstructive hydrocephalus. Lumbar puncture opening pressure was 27. The patient improved on Diamox and optimization of BP.

Conclusions, including unique features of the case(s):
PRES can occur with isolated or predominant brainstem involvement yet without clinical features of brainstem pathology, but rather symptoms of raised intracranial pressure due to obstructive hydrocephalus.

References: 1. Hinchey J, Chaves, C, Appignani B, et al. A reversible posterior leukoencephalopathy syndrome. N Engl J Med. 334: 494-500, 1996. 2. McKinney AM, Jagadeesan BD, Truwit CL, et al. Central-variant posterior reversible encephalopathy syndrome: brainstem or basal ganglia involvement lacking cortical or subcortical cerebral edema. AJR Am J Roentgenol. 201:631–8, 2013. 3. Cruz-Flores S, de Assis Aquino Gondim F, Leira EC. Brainstem involvement in hypertensive encephalopathy: clinical and radiological findings. Neurol. 62(8):1417-9, 2004. 4. Grossbach AJ, Abel TJ, Hodis B, et al. Hypertensive posterior reversible encephalopathy syndrome causing posterior fossa edema and hydrocephalus. J Clin Neurosci. 21:207–211, 2014. 5. Li D, Lian L, Zhu S. Isolated cerebellar involvement in posterior reversible encephalopathy syndrome. J Neurol Sci. 357:101-105; 2015.

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

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Grant Support: None.

Poster 91

Delayed Development of a Dural AV Fistula and PTEN Hamartoma Syndrome in Pseudo-Idiopathic Intracranial Hypertension

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Introduction:
DAVF is a known IIH masquerader that can take time to manifest fully on neuroimaging. Mutations in the tumor suppressor gene PTEN on chromosome 10 are described in Cowden and Bannayan-Riley-Ruvalcaba syndromes and rarely manifest as DAVF.

Description of Case(s):
A 31-year-old woman presented with headache, pulsatile tinnitus, postural tunnel vision, and papilledema. Brain MRI and MR Venography (MRV) were normal. Lumbar puncture revealed opening pressure with normal cerebrospinal fluid. She was diagnosed with IIH and started on acetazolamide 3,000 mg daily. Optic disc swelling improved but did not resolve. VF worsening often accompanied dose reductions. At age 33, she underwent nephrectomy for clear cell renal carcinoma. She lost 40 pounds; however IIH symptoms persisted. Repeat imaging showed distal transverse sinus stenosis. At age 38, she remained acetazolamide-dependent and had a progressive visual field deficit in the left eye. Repeat MRI and MRV raised concern for a DAVF, confirmed by conventional angiography, that was embolized with reduction in intracranial pressure. Within two weeks, symptoms and signs of increased intracranial pressure improved. Genetic workup given personal and family histories of malignancy was positive for the PTEN+ p. R130* mutation. She was ultimately diagnosed with the PTEN Hamartoma Syndrome.

Conclusions, including unique features of the case(s):
Persistent dependence on high doses of acetazolamide for years in a patient with presumed IIH should lead to constant re-evaluation of the underlying cause for raised intracranial pressure. The presence of malignancy and a DAVF may suggest a PTEN mutation.

References: -Cognard et al, Dural arteriovenous fistulas as a cause of intracranial hypertension due to impairment of cranial venous outflow, J Neurol Neurosurg Psychiatry, 65:308-316, 1998. -Eng, C, PTEN: One Gene, Many Syndromes, Human Mutation, 22:183-198, 2003. -Lok et al, Brain Magnetic Resonance Imaging in Patients With Cowden Syndrome, Medicine, 84(2): 129-136, 2005. -Tan et al, The spectrum of vascular anomalies in patients with PTEN mutations: implications for diagnosis and management, J Med Genet, 44: 594-602, 2007. - Torres et al, Dural AVM (dAVM) in Cowden disease, Interdisciplinary Neurosurgery, 10: 155-158, 2017.

Keywords: Genetic Disease, High intracranial pressure/headache, Neuroimaging

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Poster 92
Case Presentation of Relapse of Acute Lymphoblastic Leukemia with Optic Nerve Infiltration

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Introduction:
Knowledge of ocular involvement in leukemia is important for detecting either relapse or initial presentation of the entity, given that the eye is one of the only sites where the leukemic involvement of the nerve and blood vessels can be observed directly. Prior studies have shown that the incidence of ocular involvement in acute lymphoblastic leukemia (ALL) is about ~5%. Here, we present a case of relapse of a patient with (ALL) identified by visual complaints and abnormalities on dilated fundoscopic exam.

Description of Case(s):
A 37-year-old male with past medical history notable for B-cell (ALL) post treatment with allogenic bone marrow transplant and bilateral history of bacterial endophthalmitis presented with progressively worsening right eye pain for five days. Visual acuity was 20/400 in the right eye (worse from 20/150 one month prior) and stable visual acuity of 20/40 in the left eye. Dilated fundus examination was notable for stable scars but new disc fullness in the right eye as compared to the left eye, which was seen on optical coherence tomography (OCT) imaging. The patient was sent for emergent MRI which showed abnormal thickening and enhancement of the right optic nerve sheath with associated perineural enhancement. The patient was admitted where lumbar puncture (LP) revealed relapse of B cell lymphoblastic leukemia. He underwent intrathecal chemotherapy and steroids with radiotherapy to the brain and optic nerve sheath. Visual acuity improved to 20/100 in the right eye with no evidence of disease seen on LP and bone marrow biopsy 2 months after.

Conclusions, including unique features of the case(s):
This case represents a novel presentation of relapse of a patient with acute lymphoblastic leukemia identified by decreased vision and optic nerve fullness.This highlight the urgency of imaging and prompt treatment in suspected nerve infiltration by leukemic process, which can lead to improvement in visual outcomes.

References: None.

Keywords: Orbit/ocular pathology, Optic neuropathy, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Neuroimaging

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Grant Support: None.

Poster 93
Cerebellar Stroke and Prostaglandin

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Introduction:
Misoprostol is a synthetic analog of PGE1 (Prostaglandin). It is formerly used to treat stomach and duodenum ulcers or to prevent or treat gastritis due to non steroidal anti-inflammatory therapy. In France (and elsewhere in the world) this molecule is widely used to cause medical abortions.

Description of Case(s):
A 30-year-old woman with no known risk factors for cerebro vascular events, is hospitalized in December 2017 for dizziness. Brain MRI revealed an acute left cerebellar ischemic zone. An extensive workup for possible etiologies was negative , except Misoprostol. After a review of the relevant literature, pathophysiological mechanism is explained.

Conclusions, including unique features of the case(s):
Misoprostol, widely used in many countries to induce medical abortion, can, in addition to harmful uterine effects, provoke ischemic stroke.

References: None.

Keywords: Vascular disorders, Vestibular, Neuroimaging, Higher visual functions, Skull Base

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Poster 94
Spontaneous Superior Ophthalmic Vein Thrombosis

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Introduction:
Superior ophthalmic vein thrombosis (SOVT) is a rare entity. We report a case of SOVT in a patient without any underlying risk factors.

Description of Case(s):
A 68-year-old white woman with myasthenia gravis and a remote history of migraine headaches presented to the emergency department with an ongoing headache for 2 weeks. The headache was right sided, retro-orbital, throbbing, and progressively getting worse. She also had photophobia and intermittent binocular horizontal diplopia. There was no history of fever or sinus infection. Physical examination was pertinent for proptosis of the right eye, adduction deficiency right eye due to third nerve palsy, and normal visual acuity and fundus. There was no anisocoria present. No sign of infection was noted on exam. Laboratory tests were unremarkable. MRI of brain with contrast revealed right SOVT. Heparin drip was initiated and bridged to Coumadin on discharge. Hypercoagulable work up was sent prior to initiating anticoagulants returned unremarkable. The patient's proptosis and horizontal diplopia was resolved after treatment.

Conclusions, including unique features of the case(s):
In patients with opthalmoplegia, painful proptosis , and periorbital edema , the diagnosis of SOVT should be considered to prevent potentially serious sequela such as cavernous sinus thrombosis. The patient had history of migraine headaches and myasthenia Gravis, which confused the picture of the newly acquired disease and delayed the diagnosis. The patient developed thrombosis without having any history of trauma, infection, vasculitis, autoimmune disease or having any blood clothing disorders. The extensive blood work and coagulative tests did not reveal any offending cause.

References: 1. Lim, Scawn, Whipple, et al. Spontaneous superior ophthalmic vein thrombosis: a rare entity with potentially devastating consequences. Eye (London, England), 28:348-351, 2014 2. Choi, Jung, Baik, Park, Choi. Restricted diffusion in isolated superior ophthalmic vein thrombosis. Journal of neuro-ophthalmology : the official journal of the North American Neuro-Ophthalmology Society ,34:98-99, 2014 3. Kim, Cho. Superior ophthalmic vein thrombosis in a patient with adenoid cystic carcinoma in middle meatus. Canadian journal of ophthalmology Journal canadien d'ophtalmologie, 48:e12-14, 2013 4. Akiyama, Karaki, Samukawa, Mori. Blindness caused by septic superior ophthalmic vein thrombosis in a Lemierre Syndrome variant. Auris, nasus, larynx, 40:493-496, 2013 5. Cumurcu, Demirel, Keser, et al. Superior ophthalmic vein thrombosis developed after orbital cellulitis. Seminars in ophthalmology, 28:58-60, 2013 6. Coban, Cetinkaya, Karalezli, Donmez, Ozbek. Unilateral superior ophthalmic vein thrombosis in a neonate. Ophthalmic plastic and reconstructive surgery, 29:e154-156, 2013.

Keywords: Neuro-ophth & systyemic disease (eg. MS, MG, thyroid), Neuroimaging, Ocular Motility, Vascular disorders, Orbit

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Poster 95
Neurosarcoidosis Masquerading as Cavernous Sinus Meningioma

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Introduction:
Neurosacroidosis can mimic intracranial tumors resulting in a diagnostic and therapeutic challenge 1-4. We present a case of right cavernous sinus and superior orbital fissure sarcoidosis masquerading as meningioma on MRI and associated with bilateral optic neuropathy that caused serious vision loss.

Description of Case(s):
A 65-year-old African American man with a past medical history of diabetes and hypertension presented with bilateral acute vision loss for 2 weeks and intermittent bitemporal headaches. At presentation, his visual acuity was CF OD and HMOS with no RAPD and an otherwise unremarkable neuro-ophthalmic exam. His ESR was high, and he was admitted for 3-day course of IVMP, temporal artery biopsy, and diagnostic evaluation. MRI showed a small focus of enhancement in the right paracavernous sinus region, suggestive of meningioma. LP showed slight CSF protein elevation. Otherwise, his extensive labs were unremarkable. He was discharged on prednisone 60 mg pending biopsy results, which returned negative. His vision recovered to 20/20 on a 3-week tapering prednisone course, with full color and visual fields OU. His steroid course was complicated by hyperglycemia and thoracic shingles treated with oral acyclovir. The patient re-presented 2 months later with severe bilateral loss of vision down to CFOU.He also had a forehead skin rash, which crossed the midline, and had been treated in the interval as another zoster lesion by his PCP. Repeat MRI showed interval increase in the size of the presumed meningioma and bilateral optic nerve enhancement. Steroids were re-initiated. Chest CT showed hilar lymphadenopathy and perichondrovascular pulmonary nodules. Biopsy of the forehead lesion showed granulomatous inflammation, consistent with sarcoidosis. Vision improved in the left eye to 20/25 after restarting oral 60 mg prednisone therapy; however, vision for the right eye remained at CF at 1ft.

Conclusions, including unique features of the case(s):
Neurosarcoidosis can mimic meningioma. Consideration of steroid trial may be prudent in atypical meningioma.

References: 1. Rodriguez F, Link MJ, Driscoll CL, Giannini C. Neurosarcoidosis Mimicking Meningioma. Arch Neurol.2005;62(1):148–149. 2. Tan, L.A., Kasliwal, M.K., Wewel, J. et al. Neurosarcoidosis mimicking bilateral posterior fossa tentorial meningiomas. J Neurooncol (2015) 125: 435. 3. Wang K, He X, Wang W, et al. Isolated neurosarcoidosis mimicking multifocal meningiomas: a diagnosis pitfall: A case report. Medicine (Baltimore). 2016;95(46):e4994. 4. Pollock JM, Greiner FG, Crowder JB, Crowder JW, Quindlen E. Neurosarcoidosis mimicking a malignant optic glioma. J Neuroophthalmol. 2008 Sep;28(3):214-6.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 96
A Case of Villaret Syndrome due to Aspergillus in an Immunocompromised Host

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Introduction:
A 61-year-old male with history of diabetes, hypertension, and ischemic cardiomyopathy status post heart transplant on tacrolimus presented with 2 weeks of dysphonia and dysphagia.

Description of Case(s):
Three months before presentation, the patient developed bilateral facial pain and was treated with antibiotics for presumed sinusitis and had some improvement. Two weeks prior to presentation, he developed hoarseness of voice and difficulty swallowing. He also had 20 pounds of unintentional weight loss in the preceding three months. He presented to an outside hospital and there had an MRI brain without contrast, read as normal. He was transferred to our hospital for further management. Vital signs were normal at arrival. Examination was notable for left ptosis (more evident in darkness), miosis, decreased elevation of the palate and trapezius on the left, and tongue deviation to the right. Laboratory studies showed leukocytosis of 13.6 × 103/µL (79% neutrophils), glucose 98, hemoglobin A1c of 7.6, ESR 86, and CRP of 12.6. Lumbar puncture including gram stain, bacterial/fungal culture, viral PCRs, and paraneoplastic assay was unrevealing. MRI skull base showed soft tissue thickening and post-contrast enhancement involving the nasopharynx, the clivus, and left jugular foramen. There was also enhancement of the left pterygopalatine fossa, left inferior orbital fissure, and Meckel's cave. Nasopharyngoscopy with biopsy revealed osteomyelitis with necrotic tissue due to Aspergillus flavus and MRSA. Nerve function improved slightly after debridement and intravenous antimicrobials.

Conclusions, including unique features of the case(s):
In this case, re-imaging with dedicated skull based MRI was essential in reaching diagnosis in a timely manner. This case highlights a rare constellation of symptoms known as Villaret syndrome, in this case due to invasive Aspergillus in an immunocompromised host. It is essential to have a broad differential in immunocompromised hosts and to include fungal infections high in the differential, especially given comorbid diabetes. Early recognition and surgical management may improve outcomes.

References: None.

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

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Poster 98
The Treatment of Chronic Papilledema Secondary to a Dural Arteriovenous Fistula

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Introduction:
Dural arteriovenous fistulas (dAVFs) are known to cause elevated intracranial pressure (ICP) and papilledema. Delays in appropriate treatment can lead to severe vision loss and blindness.

Description of Case(s):
A 30 year-old man with a history of Factor V Leiden Deficiency and previously treated venous sinus thromboses presented to the emergency department for seizures, chronic headaches, and bilateral disc edema. On evaluation his distance vision was counting fingers bilaterally. There was no relative afferent pupillary defect and color vision was control plate only bilaterally. Dilated exam was significant for pale, gliotic nerves with mild disc edema. MR Venogram demonstrated a right dAVF and filling defects in the superior sagittal sinus (SSS). Cerebral angiogram demonstrated a right transverse-sigmoid sinus dAVF supplied by multiple branches derived from the right ICA, ECA, vertebral artery and AICA with cortical venous reflux (CVR) into the right superior petrosal sinus. Lumbar puncture and ventriculoperitoneal shunt were considered but deferred given concern for developing melting brain syndrome. Anticoagulation was not thought to be integral to the treatment because the elevation in ICP was being driven by the dAVF, which required embolization for definitive treatment. Urgent bilateral optic nerve sheath fenestrations (ONSFs) were recommended as a temporizing measure to treat the end-stage papilledema. He underwent right ONSF, followed by transvenous coil embolization of the dAVF, and left ONSF. On subsequent neuro-ophthalmic evaluation his vision remained stable and there was resolution of the papilledema. Follow-up cerebral angiogram demonstrated complete obliteration of CVR with persistence of type I (benign) right transverse sinus dAVF and no progression of thrombotic disease.

Conclusions, including unique features of the case(s):
For chronic papilledema secondary to a dAVF with associated CVR, treatment with embolization of the dAVF is important for preventing further vision loss. ONSF may be utilized as a temporizing measure to stabilize the vision while awaiting resolution of the elevated ICP.

References: None.

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

Financial Disclosures: The authors had no disclosures.

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Poster 99
Disseminated Adult Atypical Teratoid Rhabdoid Tumor causing Dorsal Midbrain Syndrome

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Introduction:
A 36-year-old woman with no significant past medical history presented with 1 month of severe headaches and vomiting associated with abnormal eye movements. MRI demonstrated an enhancing mass along the splenium of the corpus callosum and in the pineal region extending towards the right thalamus with a necrotic center. Her vision was 20/25 OU, and pupils were round and slowly reactive to light without relative afferent pupillary defect. Extraocular movements revealed -4 upgaze deficits bilaterally, partially overcome by oculocephalic maneuvering. Convergence retraction nystagmus and light-near dissociation were present. Dilated fundus exam was unremarkable OU.

Description of Case(s):
She initially underwent stereotactic biopsy. The results, limited by a small tissue specimen, were consistent with a glioneuronal tumor. Final pathology from a larger specimen showed a high-grade tumor with chordoid architecture and rhabdoid cytologic features. The tumor was positive for epidermal growth factor receptor (EGFR) and SMARCB1 mutations. Mutation and inactivation of SMARCB1 have been identified as the underlying mechanism in the development of Malignant Rhabdoid and Atypical Teratoid/Rhabdoid Tumors. Postoperative imaging demonstrated residual tumor that was not amenable to resection, and adjuvant external beam radiation was performed.

Conclusions, including unique features of the case(s):
Based on clinical and radiographic evidence, the patient initially appeared to have an aggressive pineal region meningeal tumor with metastasis. However, initial pathology showed a benign glioneuronal tumor. She deteriorated rapidly from progressive tumor growth and venous obstruction causing hydrocephalus. Final pathology ultimately revealed an adult Atypical Teratoid Rhabdoid Tumor (ATRT) with leptomeningeal spread along the biopsy and shunt tracts. A combined approach of whole spine radiation and intrathecal chemotherapy was planned. Molecular testing revealed an activation of the EGFR pathway that would be sensitive to the tyrosine kinase inhibitor osimertinib. She underwent whole spine radiation and intrathecal chemotherapy; however, she ultimately developed widespread CNS metastasis with involvement of the spinal cord and multiple cranial nerves bilaterally.

References: Kim EY, Weon, Kim ST, Kim HJ, Byun et al. Rhabdoid meningioma: clinical features and MR imaging findings in 15 patients. AJNR Am J Neuroradiol. 28(8), 1462-5, 2007. Rogerio, De araújo zanardi, Ribeiro de menezes netto, De souza queiroz. Meningioma with rhabdoid, papillary and clear cell features: case report and review of association of rare meningioma variants. Clin Neuropathol, 30(6), 291-6, 2011. Wu, Ho, Lin YJ, Lin JW. Rhabdoid papillary meningioma: a clinicopathologic case series study. Neuropathology, 31(6): 599-605, 2011. Sangoi, Dulai, Beck, Brat, Vogel. Distinguishing chordoid meningiomas from their histologic mimics: an immunohistochemical evaluation. Am J Surg Pathol, 33(5), 669-81, 2009. Darr, Klochendler, Isaac, Geiger, Eden. Phosphoproteomic analysis reveals Smarcb1 dependent EGFR signaling in Malignant Rhabdoid tumor cells. Mol Cancer, 14, 167, 2015.

Keywords: Ocular Motility, Higher visual functions, Neuroimaging, Interventional neuroradiology, Tumors

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Poster 100

Unusual Presentation of Convergence insufficiency in Parkinsons' Disease patient stimulated by Deep Brain Stimulation

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Introduction:

To report CI (convergence insufficiency) in PD (Parkinsons' disease) patient stimulated by DBS (deep brain stimulation).

Description of Case(s):

72 y.o. man with PD and hypertension presenting for the evaluation of blurry vision at near and mid distance that started after activation of an implanted DBS. Physical exam with DBS turned off showed BCVA 20/20, normal pupil exam, VF and DFE. Motility was full and eyes straight at distance and near. Following this examination, the DBS was turned on and reevaluation showed same findings except for a 6 prism diopter XT at near consistent with CI. Following our evaluation a set of +3 diopters base-in prisms were added to near glasses with total relief of symptoms. The patient didn't need to have the electrodes of the DBS re-implanted.

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

The Basal Ganglia are reported to have an important role in the control of eye movements. In PD, the DBS electrodes are implanted to target the GPi (Globus Pallidus internus) and STN (Sub Thalamic Nuclei) located in close proximity to the convergence center in the pretectal area dorsal to the third nerve nuclei. We believe that the location of the electrodes of the DBS and their proximity to the convergence center were probably the reason behind this patient's findings. This is the first report of CI caused by activation of DBS in a patient with PD. We report this case to stress the importance of a full neuro-ophthalmic evaluation in patients with neuro-degenerative diseases complaining of blurry vision prior to any surgical intervention.

References: [1] Antoniades CA, Buttery P, FitzGerald JJ, Barker RA, Carpenter RHS, et al. (2012) Deep Brain Stimulation: Eye Movements Reveal Anomalous Effects of Electrode Placement and Stimulation. PLoS ONE 7(3): e32830. doi:10.1371/journal.pone.0032830 [2] Catherine Cho, Ron Alterman, Tiffany Morris, Steven Moore, JanetRucker Convergence Insufficiency Responsive to Bilateral Subthalamic Nucleus Deep Brain Stimulation in Parkinson's Disease (P02.257) Neurology Apr 2012, 78 (1 Supplement) P02.257;) [3] Erlick AC Pereira, Alexander L Green, Dipankar Nandi & Tipu Z Aziz (2014) Deep brain stimulation: indications and evidence, Expert Review of Medical Devices, 4:5, 591-603, DOI: 10.1586/17434440.4.5.591 [4] Matthew D. Johnson, Cameron C. McIntyre, Jerrold L. Vitek. Deep Brain Stimulation. Mechanisms of Action. https://clinicalgate.com/deep-brain-stimulation-2/ [5] Purves , Dale et al. Neuroscience I edited 5th ed. [6] Sharma R, Hicks S, Berna CM, Kennard C, Talbot K, Turner MR. Oculomotor Dysfunction in Amyotrophic Lateral SclerosisA Comprehensive Review. Arch Neurol. 2011;68(7):857–861. doi:10.1001/archneurol.2011.130.

Keywords: Ocular Motility

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Grant Support: None.

Poster 101
Unusual presentations of anti-MuSk-antibody-positive ocular myasthenia gravis

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Introduction:
Myasthenia gravis is an autoimmune disease that affects the neuro-muscular junction resulting in variable muscle weakness and fatigability. Antibodies to a muscle-specific receptor tyrosine kinase (MuSK) have been found in approximately 40% of patients with generalized myasthenia gravis who are seronegative for the antiacetylcholine receptor antibody1 but anti-MuSK antibodies where never detected in seropositive myasthenia gravis2.

Description of Case(s):
The most prominent manifestations of myasthenia gravis patients with antibodies to a muscle-specific receptor tyrosine kinase include bulbar and neck weakness associated with respiratory complications3,4. Only few cases of anti-MuSK antibodies have been reported in purely ocular myasthenia gravis 5. We would like to address two rare cases of pure ocular myasthenia who presented with positive Anti-MuSK antibodies. The first patient presented initially with double vision and almost complete horizontal ophthalmoplegia. Electromyogram was reported as normal and he was seronegative for antiacetylcholine receptor antibodies. Anti-MuSk antibodies were later tested in this patient and he was seropositive. He was very responsive to oral steroids, but was later switched to azathioprine because he became steroid dependent. The second patient presented with intermittent ptosis and double vision. Interestingly, this patient had positive titers for Acetylcholine receptor antibodies as well as Anti-MuSK antibodies.

Conclusions, including unique features of the case(s):
Anti-MuSK antibodies can be found in pure ocular myasthenia having diplopia without ptosis Double seropositive antibodies can be found in ocular maysthenia.

References: 1. Caress, James B., Christopher H. Hunt, and Sat Dev Batish. "Anti-MuSK myasthenia gravis presenting with purely ocular findings." Archives of neurology 62.6 (2005): 1002-1003. 2. Bennett, D. L. H., et al. "Anti-MuSK antibodies in a case of ocular myasthenia gravis." Journal of Neurology, Neurosurgery & Psychiatry 77.4 (2006): 564-565. 3. Sanders D B, El-Salem K, Massey J M. et al Clinical aspects of MuSK antibody positive seronegative MG. Neurology 2003601978–1980 4. Evoli A, Tonali P A, Padua L. et al Clinical correlates with anti-MuSK antibodies in generalized seronegative myasthenia gravis. Brain 20031262304–2311 5. Caress J B, Hunt C H, Batish S D. Anti-MuSK myasthenia gravis presenting with purely ocular findings. Arch Neurol 2005621002–1003.

Keywords: Myasthenia, Adult strabismus with a focus on diplopia

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 102
Fisher Variant of Guillain-Barre Syndrome Following a Viral Illness

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Introduction:
Fisher Syndrome is an autoimmune-mediated peripheral neuropathy. The constellation of findings in this disease process include the classic triad of ophthalmoplegia, ataxia, and areflexia. We report a case of an anti-GQ1b neuronal antibody positive patient in the setting of recent viral prodrome.

Description of Case(s):
A 42-year-old male presented in January 2018 with binocular diplopia, photophobia, ataxia, and peripheral paresthesias. He initially presented to the emergency department where CT and subsequently MRI were found to be unremarkable. Ophthalmologic exam revealed excellent visual acuity with diffuse restriction in extraocular motility, especially in horizontal gaze with a resultant moderate angle esotropia. Of note, he also had bilateral nonreactive pupils to light. Lumbar puncture revealed albuminocytologic dissociation with two well-defined oligoclonal bands that are non-specific but associated with Guillain-Barre syndrome. His serum sample was found to be positive for anti-GQ1b IgG antibody which is present in the majority of patients with the Fisher variant of Guillain-Barre. The patient was started on IV corticosteroids and received a course of IVIG. He was found to have significant improvement in his extraocular motility with some residual diplopia. Overall his ataxia had greatly improved in the following two weeks. The patient continued to be seen throughout the course of this year. The last visit in September of 2018 showed complete resolution of ataxia and diplopia with minor residual left arm paresthesia.

Conclusions, including unique features of the case(s):
This case highlights the importance of identifying the associated findings of ophthalmoplegia, ataxia, and areflexia in the setting of the characteristic ascending paralysis of Guillain-Barre syndrome. Most patients have a recent history of viral illness preceding symptoms, and a high suspicion for this disease entity should be maintained. Anti-GQ1b antibodies are present in the majority of cases and can aid in confirming the clinical diagnosis.

References: Berlit P, Rakicky J. The Miller Fisher syndrome. Review of the literature. J Clin Neuroophthalmol 1992; 12:57–63. Chiba, A., Kusunoki, S., Obata, H., Machinami, R. and Kanazawa, I., Serum antibody against ganglioside GQ1b is associated with ophthalmoplegia in Miller Fisher syndrome and Guillain-Barré syndrome: Clinical and immunohistochemical studies, Neurology, 43 (1993) 1911–1917. Mori M, Kuwabara S, Fukutake T, et al. Clinical features and prognosis of Miller Fisher syndrome. Neurology 2001;56:1104–1106. Mori M, Kuwabara S, Fukutake T, et al. Intravenous immunoglobulin therapy for Miller Fisher syndrome. Neurology 2007;68:1144–1146. Mori M, Kuwabara S, Fukutake T, Hattori T. Plasmapheresis and Miller Fisher syndrome: analysis of 50 consecutive cases. Journal of Neurology, Neurosurgery, and Psychiatry. 2002;72(5):680.

Keywords: Ocular Motility, Demeylinating disease, Neuro-ophth & systyemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 103
Look Mobius syndrome, but is "bilateral" Millard–Gubler syndrome

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Introduction:
Paresis of the sixth or seventh cranial nerve becomes the distinguishing criterion for Mobius síndrome. Moebius syndrome is usually bilateral, however, it could be unilaterally; in opposition with Millar Gubler syndrome, which is usually unilateral and associated with contralateral hemiparesis. We report the case of a young patient with paralysis of VI and VII bilateral nerve with bilateral hemiplegia (bilateral Gluber Millar Syndrome) secondary a tumor lesion. Apparently bilateral Gubler Millard syndrome has not been previously reported.

Description of Case(s):
A 19 years old man developed nausea, vomiting, dizziness (signs of intracranial hypertension) due to compressive tumor. The magnetic resonance imagen demonstrates a compressive lesión at the pontomedullary level. The patient underwent surgery (partial exeresis of the tumor) and placement of ventriculoperitineal shunt. As a consequence it presents bilateral palsies of the VII and VII bilateral nerve with bilateral hemiplegia. The biopsy resulted in oligodendroglioma.

Conclusions, including unique features of the case(s):
Millard-Gubler syndrome, Millard-Gubler- Foville syndrome, Raymond-Cestan syndrome is usually manifested by classical crossed syndromes consist of ipsilateral peripheral cranial VI and VII nerve palsies and contralateral hemiparesia.The more common etiology is ischemic, and less frequent is tumor like the case presented. The extension of the lesion in the pontine area probaby caused the bilateral VI and VIII facial nerve with bilateral hemiparesia. In young patients with bilateral VI and VII bilateral nerves paralysis suggests Mebiues Syndrome; however, this condition is usually congenital, not progressive. It is typically attributed to agenesis of the abducens and facial cranial nerves. Rarely has it been associated with neurological deficit. Both entities have similar characteristics but the clinical history allows the diagnosis. Until now, bilateral Millard Gubler Syndrome had not been previously reported.

References: Rucker JC, Webb BD, Frempong T, et al: Characterization of ocular motor deficits in congenital facial weakness: Moebius and related syndromes. Brain ;137(Pt 4):1068-79. 2014 Prasad K, Kappor K,Srivastava A, et al: Neurocysticersosis presenting as a Millar Gubler syndrome. J Neurosci Rural Pract; 3(30): 375-7. 2012.

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Neuroimaging, Adult strabismus with a focus on diplopia, Ocular Motility, Miscellaneous

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Grant Support: None.

Poster 104

HaNDL Syndrome (Headache, Neurologic Deficits And CSF Lymphocytosis) With Intracranial Hypertension And Abducens Palsy

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Introduction:
HaNDL syndrome is a disorder characterized by recurrent headache, neurologic deficits and CSF lymphocytosis. HaNDL cases with documented intracranial hypertension, papilledema, and abducens nerve palsy have been reported (1-3). We present a case of HaNDL with intracranial hypertension and unilateral abducens palsy and review similar cases in the English language literature.

Description of Case(s):
A 32-year-old male presented to the emergency department with recurrent profound headache and intermittent confusion. Brain imaging was normal. Lumbar puncture opening pressure was 41 cm of CSF. CSF WBC 222 (94% lymphocytes) and CSF protein was 139 mg/dL. He was treated with IV antibiotics and antivirals until CSF gram stain, HSV 1 and 2 PCR and cryptococcal AG returned normal. Within a week he developed pulse synchronous tinnitus and binocular horizontal diplopia. Neuro-ophthalmologic exam found 20/20 acuity OU, normal confrontational visual fields, Frisen grade 2 papilledema and abduction deficit left eye consistent with abducens palsy. Follow up lumbar puncture opening pressure was 16 cm CSF with CSF WBC 108 (97% lymphocytes) and CSF protein 91 mg/dL. At that point he was started on topiramate 25 mg/day and verapamil for headache management. Within 2 months all symptoms resolved and his neuro-ophthalmologic exam normalized. Previously reported cases of HaNDL plus documented intracranial hypertension and abducens palsies were treated for intracranial pressure (acetazolamide, furosemide, serial LP). Outcomes varied between complete recovery and persistent deficits. In this case, therapy was not required to lower intracranial pressure and subsequently normalize.

Conclusions, including unique features of the case(s):
HaNDL syndrome can be associated with intracranial hypertension and abducens palsy. Previously reported cases describe patients who were treated with therapies to lower intracranial pressure with mixed results. The case we present is unique as this patient did not require therapy to lower his intracranial pressure. Treatment for intracranial hypertension is appropriate in some cases but may not be necessary in all cases.

References: 1. Ophthalmology 2003; 110: 115-118 2. Eye (2010) 24, 198-199 3. Neurology Jul 1998, 51(1) 313-314

Keywords: High intracranial pressure/headache, Ocular Motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 105
Giant cell arteritis mimicking orbital apex syndrome: A case report

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Introduction:
Giant cell arteritis (GCA) is a large-vessel vasculitis in elderly Caucasian. Arteritic anterior ischemic optic neuropathy (AAION) is the most common ophthalmic manifestation. We report unilateral visual loss with complete ophthalmoplegia, mimicking orbital apex syndrome as a rare presentation of GCA.

Description of Case(s):
A 77-year-old Thai man presented with gradual visual loss in his right eye for 7 hours. He reported preceding severe headache at bilateral temporal regions for 1 month, then developed horizontal binocular diplopia and right ptosis 3 weeks later. Best corrected visual acuity was no light perception in the right eye and 20/40 in the left eye. There was complete ophthalmoplegia with ptosis in the right eye. Anterior segment examination revealed severe corneal edema with Descemet's fold, and 4+ cellular reaction in the right anterior chamber. Right pupil was sluggish with relative afferent pupillary defect. Right eye was hypotonic. Fundus examination could not be visualized in the right eye due to ocular media opacity. He also had cord-like temporal arteries with tenderness. The presumptive diagnosis of orbital apex syndrome was made but MRI and MRA of the brain and orbits were unremarkable. Transcranial doppler ultrasonography was performed and failed to identify right ophthalmic artery. Laboratory investigations showed increased ESR and CRP. He was then diagnosed as suspected GCA with ophthalmic arteritis. Intravenous methylprednisolone (1g) was administered for 4 days then switched to oral prednisolone. Right temporal artery biopsy was performed, and pathologic examination confirmed the diagnosis of GCA. His eye movements improved after treatment but visual acuity remained no light perception in the right eye. He developed AAION in the other eye 15 months later.

Conclusions, including unique features of the case(s):
GCA should be considered as a cause of complete ophthalmoplegia and ocular ischemia in elderly patient. Early diagnosis and prompt treatment may help preserve vision in some patients.

References: None.

Keywords: Vascular disorders, Ocular Motility, Orbit

Financial Disclosures: The authors had no disclosures.

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Poster 106
Ophthalmic manifestations and diagnostic of Friedreich Syndrome

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Introduction:
Ataxia of Friedreich is caused by a mutation in the gene Frataxin located in the chromosome 9q13. It occurs 1 in 30,000 cases in Caucasian population. The symptoms are progressive and start between 7 and 25 years of age. The ocular manifestations are a sign of progression in the disease.

Description of Case(s):
A 61 year old male with ataxia of Friedreich since 7 years old and antecedent of mellitus diabetes 2 since 20 years ago, he calls on ophthalmology for referring progressive decrease of the visual field. In November of 2017, it is found in the exploration RE(right eye) 20/30, IOP(intraocular pressure) 14 and LE(left eye) 20/50, IOP 12. It is found in ocular exploration a transparent cornea, formed camera grade IV, crystalline opacity, and reactive circular papillary. Fundus RE, slight pale papillary and excavation of 0.85 nasalized vessels; fundus of LE, yellow papillary and excavation of 0.9 diminished edges. Non reliable perimetry is reported, a loss of central vision, absolute concentric scotomas and isle of central bilateral vision. The Optical Coherence Tomography reports a frank damage and decrease of retinal nerve fiber layer, only normal in right nasal quadrant and M5, M7 in LE.

Conclusions, including unique features of the case(s):
The decrease of secondary visual acuity to the ataxia of Frederich has a direct relation with of the time evolution of the disease. It is important to highlight that the visual symptoms are not the primary manifestations. The OCT is the used method to evaluate the progression and answer to the treatment.

References: Noval, Contreras, Sanz-Gallego, Manrique, Arpa,. Ophthalmic features of Friedreich ataxia. Nature,26: pp. 315-320, 2012. Anheim, Tranchant, Koenig, The Autosomal Recessive Cerebellar Ataxias. New England Journal,7: pp.636-646, Feb 16, 2012 Reetz, Dogan, Hohenfeld, Didszun, Giunti. The EFACTS Study Group. Nonataxia symptoms in Friedreich Ataxia. Neurology. 10: pp. 917-930, 2018.

Keywords: Ocular manifestations of vestibular disorders, Ocular Motility

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Grant Support: None.

Poster 107
A Case of Miller Fisher Syndrome After Exposure To A North Korean Vaccine

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Introduction:
This report presents a rare case of Miller Fisher syndrome after inoculation with a proprietary North Korean vaccine.

Description of Case(s):
A 33-year-old Asian male presented to the Ophthalmology clinic with a sudden onset binocular, horizontal diplopia that began 3 days prior. He was in excellent health otherwise and stated his symptoms began 24 hours after arriving from Mongolia. Past ocular history was negative. He denied taking any medications, however he had recently received a series of injections of a vaccine made in North Korea. He reported dizziness and generalized weakness, but denied any significant change in visual acuity, headache, pain, or other ocular and systemic complaints. Visual acuity was 20/25 in both eyes (OU). Pupils were 8 mm OU and sluggish. IOP and confrontation visual field were within normal limits. Extra-ocular movement testing revealed bilateral abduction deficits with negative forced-duction but otherwise full. The remainder of his ophthalmic exam was unremarkable. He was subsequently sent for emergent neuro-imaging and referred to neurology for likely admission. Imaging, CSF serology and initial blood work were all unremarkable. Neurology evaluation was remarkable for absent deep tendon reflexes and ataxia, suggesting a diagnosis of the Miller Fisher syndrome. Anti-GQ1b IgG titers were requested and found to be significantly elevated, confirming the diagnosis.

Conclusions, including unique features of the case(s):
Miller Fisher Syndrome occurs after exposure to a pathogen that is capable of molecular mimicry. This is the first reported case that has occurred after exposure to Kumdang-2, a vaccine manufactured in North Korea. According to the manufacturer's website and online articles from a number of news outlets, Kumdang-2 contains various "rare Earth metals", ginseng, and other unknown ingredients harvested directly from North Korean soil and has recently grown in popularity in countries such as Russia, China, and Mongolia due to its purported healing properties.

References: None.

Keywords: Ocular Motility, Neuro-ophth & infectious disease (eg, AIDS, prion), Neuro-ophth & systyemic disease (eg. MS, MG, thyroid), Non-organic visual disorders,

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 108
Multi-modal Imaging of Retinal Capillary Hemangioblastoma

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Introduction:
Retinal capillary hemangioblastoma is the most frequent and earliest manifestation of Von Hippel Lindau disease, though they can be an isolated finding without systemic involvement. Although peripheral lesions are most common, juxtapapillary lesions are found in 11 to 15% of cases and can mimic pseudopapilledema, papillitis, or choroidal neovascular membrane. Here we present a case of retinal capillary hemangioblastoma masquerading as pseudopapilledema.

Description of Case(s):
A 53-year-old Thai male was referred for evaluation of asymptomatic right optic disc swelling. Visual acuity of the right eye was 20/20 and intraocular pressure was normal. There was no APD and color testing was normal. Posterior examination of the right optic nerve revealed blurring and elevation of the temporal margin with a well-defined nasal border. OCT demonstrated an elevated mass temporal to disc with corresponding nasal defects on visual field. Fluorescein angiography revealed a 0.75DD juxtapapillary vascular lesion with early leakage, marked hyperfluorescence, and delineation of vasculature within the lesion, confirming our suspicion of juxtapapillary capillary hemangioblastoma. The patient is currently undergoing a MRI/MRA of the brain, and renal ultrasound for suspected Von Hippel Lindau disease. Genetic testing is pending the results of these studies.

Conclusions, including unique features of the case(s):
This case illustrates the importance of multi-modal imaging for the work-up of pseudopapilledema and the diagnosis of retinal capillary hemangioblastoma. Timely recognition of this lesion is crucial for initiating systemic work-up and referral to appropriate specialists if necessary.

References: None.

Keywords: Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Orbit/ocular pathology, Pupils Retina, Vascular disorders, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 109
Case Report: Idiopathic Presentation of Raeder's Paratrigeminal Neuralgia

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Introduction:
Raeder's Paratrigeminal Neuralgia (RPN) is a rare condition that results from inflammation or compression of the trigeminal nerve and its branches. The purpose of this report is to present a classic idiopathic presentation of this disease, and to contribute to the general understanding and treatment of RPN.

Description of Case(s):
A 70-year-old man initially presented with hypersensitivity in his right periorbital region. His symptoms progressed over the course of a day, resulting in ipsilateral ptosis, miosis, and ocular pain localized to the vicinity of the right supraorbital nerve foramen. Anhidosis was absent. The patient's medical history consisted of well-controlled hypertension, atrial fibrillation and prostate cancer. He had no significant past ocular or neurologic disease. The patient had an emergent chest CTA and an MRI/MRA of the brain and orbits. Carotid dissection was excluded. The Horner's syndrome was confirmed with instillation of 1% apraclonidine, which effectively dilated the affected eye. Additional workup including a chest X ray was insignificant. The patient was diagnosed with idiopathic Group III Raeder's Paratrigeminal Neuralgia. Over the course of 2 months, his symptoms gradually resolved.

Conclusions, including unique features of the case(s):
Raeder's Paratrigeminal Neuralgia is an uncommon condition which can portend a serious neurological diagnosis. Depending on the symptoms experienced, which are derived from the location of compression, RPN can be classified as group I, II, or III. The condition typically presents with a Horner's syndrome – ipsilateral headache or facial pain, miosis, and ptosis; however, anhidrosis is generally absent. The most common causes of RPN are an internal carotid artery dissection, cavernous sinus thrombosis, or head trauma, although other etiologies are not fully understood. Many patients achieve a spontaneous remission of their symptoms. This case report serves to describe a classic presentation of RPN, to detail its ultimate resolution and to illustrate the importance of recognizing and properly evaluating this condition.

References: None.

Keywords: Orbit, Orbit/ocular pathology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 110
Destructive Rhino-Orbital IgG4-Related Disease

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Introduction:
Although IgG4 related disease frequently affects the orbit and paranasal sinuses, extensive destruction is unusual. We present a case of destructive rhino-orbital tissues in a patient whose initial symptom was diplopia.

Description of Case(s):
A 64-year old woman was referred for diplopia on right lateral gaze. Past medical history was significant for hypertension, type 2 diabetes mellitus, dyslipidemia, and right-sided trigeminal neuralgia. Remote intranasal cocaine use 30 years ago with no consumption since. She was initially noted to have right abduction deficit and esotropia with normal visual acuity. An MRI showed destruction of the right-sided turbinates, lateral nasal cavity, and lamina papyracea. There was enhancing tissue lining the right maxillary sinus and a defect in the lamina papyracea with extension into the orbit and inferomedial extraocular muscles. Fiberoptic nasal endoscopy revealed a large cavity on the right side with absent turbinates and absent orbital floor. No necrotic lesions were seen. Biopsy revealed sinonasal mucosa with a dense inflammatory lymphoplasmocytic infiltrate with associated fibrosis. No obliterative phlebitis. There was increased number of IgG4 positive plasma cells (>40/HPF) with a ratio of IgG4 to IgG greater than 40%. No evidence of malignancy or fungal elements. Blood work revealed increased serum IgG4 at 1.56g/L. Negative ANA, ANCA, ACE, and rheumatoid factor. In the meantime, there was worsening diplopia with right eye esotropia and hypotropia. She developed almost complete opthalmoplegia and right eye enophthalmos. She was started on Prednisone 60 mg/day and is now on a tapering schedule. There has been no further clinical/radiological deterioration. We are currently considering using steroid-sparing agents.

Conclusions, including unique features of the case(s):
Although nasal and paranasal sinus involvement has been previously reported in IgG4 related disease, the occurrence of extensive destruction of these structures is uncommon. It is also unusual that despite extensive nasal-paranasal involvement, diplopia was still the initial symptom.

References: 1. Deshpande V, Zen Y, Chan JK, et al. Consensus statement on the pathology of IgG4-related disease. Mod.Pathol. 2012; 25: 1181-1192 2. Cain RB, Colby TV, Balan V, et al. Perplexing lesions of the sinonasal cavity and skull base: IgG4-related and similar inflammatory diseases. Otolaryngol. Head Neck Surg. 2014 Sep;151(3):496-502

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 111
A case of brainstem infarction diagnosed with ophthalmic findings a day prior to radiopathological evidence

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Introduction:
Although many brainstem infarctions are accompanied by dysarthria and sensory or motor nerve weakness in the face or limbs, some small and localized infarctions occasionally cause vague systemic symptoms or only ophthalmic manifestations. In the present report, we describe a patient diagnosed with a brainstem infarction using an ophthalmic examination within 8 hours of onset and a day before definite radiolpathological evidence.

Description of Case(s):
A 50-year-old male visited the neuro-ophthalmology department with a new-onset binocular diplopia which had started the same day in the morning. His corrected vision, intraocular pressure, and relative afferent pupillary defect were normal. Using the alternate prism cover test, 16 prism diopters (PD) of exodeviation and 4 PD of left hypertropia were detected in all directions. In terms of ocular motility, left medial rectus limitation (-2.5) and inferior rectus limitation (-1) were detected. He did not have his head tilted. Right fundus excyclotorsion and left fundus incyclotorsion were observed. However, the initial DWI taken within 12 hours of the onset of symptoms was negative. The next day, 28 hours after onset, his symptoms had not resolved, and a second brain MRI with enhancement including DWI was performed. The brain MRI showed definite high signal intensity (SI) on DWI, low SI on the apparent diffusion coefficient (ADC), and high SI on the T2 weighted image (T2WI) at the left medial aspect of the midbrain. He was finally diagnosed with a brainstem infarction radiologically, right skew deviation [incomplete ocular tilt reaction (OTR) without head tilt], and left INO.

Conclusions, including unique features of the case(s):
Brainstem infarctions may cause only ophthalmic symptoms; if the symptoms and ophthalmic examination are sufficient to suspect infarction and last for 24 hours after onset, a second brain imaging study including DWI is needed even if the initial brain imaging study within 24 hours of onset was negative.

References: None.

Keywords: Ocular manifestations of vestibular disorders, Ocular Motility, Neuroimaging, Adult strabismus with a focus on diplopia

Financial Disclosures: The authors had no disclosures.

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Poster 112
Anti-Hu associated Gaze Palsy Associated with Recurrent Small Cell Lung Cancer

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Introduction:
Paraneoplastic encephalomyelitis (PEM) is an indirect result of malignancy. In more than 50% of cases, it is associated with small cell lung cancer (SCLC). The majority of patients present with sensory symptoms.Isolated diplopia, nystagmus, opsoclonus and other signs indicative of brain stem pathology are seen in 6-11% of cases and are typically associated with anti-ri or anti-yo antibodies.Treatment for PEM includes immunotherapy, with variable outcomes; in some patients, treatment of the underlying cancer leads to resolution of of the paraneoplastic symptoms.

Description of Case(s):
A 66-year-old female with a past medical history of breast cancer and SCLC, concurrently diagnosed in November 2015, status post chemoradiation presented with several weeks of binocular vertical diplopia and ataxia. Her neuro-ophthalmic examination was significant for normal afferent function with a left gaze palsy and right hypertropia in the pattern of a skew deviation[MD1] .[AT2] MRI brain was negative for any ischemic, infiltrative or compressive lesion, and a lumbar puncture was negative for leptomeningeal disease. CT chest showed a suspicious right upper lobe mass with associated mediastinal adenopathy, positive for small cell carcinoma on fine needle aspiration. Anti-Hu antibody was detected in her serum confirming paraneoplastic disease. Her clinical exam and symptoms were unchanged despite starting treatment with etoposide and carboplatin and 5 days of IVIG therapy.

Conclusions, including unique features of the case(s):
We describe a rare case of a horizontal gaze palsy and skew deviation associated with an anti-Hu PEM. Brainstem involvement is relatively rare in anti-Hu PEM occurring in only 12/200 in one series.1 Horizontal gaze palsies are even scarcer, occurring at presentation in only 1/ 22 in a series of patients with anti-Hu brainstem encephalitis. In patients with gaze palsies or skew deviations and a history of cancer, once metastatic disease has been ruled out, a paraneoplastic brainstem encephalitis should be considered.

References: References 1. Graus F, Keime-Guibert F, Rene R, Benyahia B, Ribalta T, Ascaso C et al. Anti-Hu-associated paraneoplastic encephalomyelitis: analysis of 200 patients. Brain 2001 Jun;124(Pt6):1138-48. 2. Saiz A1, Bruna J, Stourac P, Vigliani MC, Giometto B, Grisold W, Honnorat J, Psimaras D, Voltz R, Graus F. Anti-Hu-associated brainstem encephalitis. J Neurol Neurosurg Psychiatry. 2009 Apr;80(4):404- 3. Mitchell AN, Bakhos CT, Zimmerman EA. Anti-Ri-associated paraneoplastic brainstem cerebellar syndrome with coexisting limbic encephalitis in a patient with mixed large cell neuroendocrine lung carcinoma. J Clin Neurosci. 2015 Feb;22(2):421-3. 4. Muni RH, Wennberg R, Mikulis DJ, Wong AM. Bilateral horizontal gaze palsy in presumed paraneoplastic brainstem encephalitis associated with a benign ovarian teratoma. J Neuroophthalmol. 2004 Jun;24(2):114-8. 5. Dalmau J, Graus F, Rosenblum MK, Posner JB. Anti-Hu—associated paraneoplastic encephalomyelitis/sensory neuronopathy. A clinical study of 71 patients. Medicine (Baltimore)1992 Mar;71(2):59-72.

Keywords: Ocular Motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 113
Paraneoplastic Downbeat Nystagmus Secondary to Metastatic Prostatic Carcinoma

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Introduction:
Acquired downbeat nystagmus (DBN) is commonly caused by lesions involving the cerebellum and the craniocervical junction. The primary causes of DBN are Arnold Chiari malformations and spinocerebellar degenerations. DBN can also be secondary to paraneoplastic syndromes caused by lung and fallopian tube malignancies. We present a patient with DBN and ataxia secondary to a paraneoplastic cerebellar degeneration caused by metastatic prostatic carcinoma. The purkinje cell antibodies were markedly elevated at 1:30720. To our knowledge this the first reported case of paraneoplastic DBN associated with prostate cancer.

Description of Case(s):
A 73 year-old, right-handed male with a history of metastatic stage IV prostatic carcinoma presents with new onset decreased depth perception, disequilibrium and oscillopsia. Initial examination on 10/16/17 showed a best corrected visual acuity of 20/40 OU. Color vision was slightly reduced, 4.5 of 6 HRR plates bilaterally. Flicker fusion was 27 hertz OD and 23 hertz OS. Ocular motility examination showed evidence of moderate DBN in primary gaze which increased on gaze down and to the right and left. There was a small-angle comitant skew deviation. The funduscopic examination was normal. Mental status examination, cranial nerves and motor examination were all normal. Gait testing showed evidence of a wide-based and markedly reduced tandem gait. Cerebellar testing showed normal finger to nose and heel to shin testing bilaterally. The neuroimaging studies showed mild midline cerebellar degeneration. There was no evidence of an Arnold Chiari malformation or posterior fossa mass. The MRI scan of the cervical spine showed mild to moderate degenerative disc disease. Laboratory studies showed evidence of a markedly elevated Purkinje cell cytoplasmic antibody type II at 1:30720! (Reference interval normal range <1:240).

Conclusions, including unique features of the case(s):
This patient has evidence of a paraneoplastic downbeat nystagmus associated with metastatic prostatic carcinoma. The downbeat nystagmus and ataxia clinically improved following treatment with pulse IVIG, gabapentin, and physical therapy.

References: Choi SY, Park SH, Kim HJ, Kim JS. Paraneoplastic downbeat nystagmus associated with cerebellar hypermetabolism especially in the nodulus. J Neurol Sci. 2014;343(1-2):187-191. Bussiere M, Al-Khotani A, Steckley JL, Nicolle D. Paraneoplastic downbeat nystagmus. ICan J Ophthalmol. I2008;43(2):243-245. Igarashi S, Tanaka K, Nakajima T, Yamazaki M, Inuzuka T, Miyatake T. [A case of paraneoplastic cerebellar degeneration—success in early detection of cancer by anti-Purkinje cell antibody}. Rinsho Shinkeigaku. 1992;32(3):309-313. Hong MK, Kong J., Namdarian B, Longano A, Grummet J, Hovens CM, Costello AJ, Corcoran NM. Pareneoplastic syndromes in prostate cancer. NNat Rev Urol. 2010 Dec 7(12):681-92. Wray, SH, Dalmau, J, Chen, A, King, S, Leigh, RJ. Paraneoplastic disorders of eye movements. Annals of the New York Academy of Sciences. (2011) 279-284.

Keywords: Ocular Motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 114
Dissociated Pendular Nystagmus in Oculopalatal Tremor with Bilateral Inferior Olivary Hypertrophy

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Introduction:
Oculopalatal tremor (OPT) is characterized by a synchronous tremor of the palate and eyes that may also involve other muscles from the branchial arches. The nystagmus of OPT may be conjugate, disconjugate or disjunctive. In the previous studies, only symmetric pendular nystagmus was observed in the bilateral hypertrophic changes of inferior olivary nucleus (ION), while dissociated pendular nystagmus was associated with either ipsilateral or bilateral changes. We report a case of dissociated pendular nystagmus in bilateral olivary hypertrophy.

Description of Case(s):
A 47-year-old man visited our clinic, complaining of oscillopsia. According to his past medical history, he had intracerebral hemorrhage in the pontine tegmentum 3 years ago. Initial neuro-ophthalmologic examination and video-oculography revealed medial gaze limitation of the right eye and dissociated pendular nystagmus which were composed of mainly vertical-torsional components in the right eye and horizontal-torsional components in the left eye. Palatal tremor was also observed. These findings were compatible with OPT due to intracerebral hemorrhage in the pontine tegmentum. High signal intensities with hypertrophy of the bilateral ION were seen in T2-weighted and fluid-attenuated inversion recovery MR images.

Conclusions, including unique features of the case(s):
OPT is a delayed complication of damage to the dentato-rubro-olivary pathway (the Guillain- Mollaret triangle) and subsequent hypertrophic olivary degeneration. Bilateral hypertrophic changes of ION have been reported to show symmetrical pendular nystagmus, however, in this case, the pendular nystagmus was asymmetric and dissociated. Similar to our case, a former study reported three patients including literature review who showed dissociated pendular nystagmus in bilateral inferior olivary hypertrophy. We suppose that combined ocular motor deficits due to structural lesions in the pontine tegmentum (i.e., internuclear ophthalmoplegia in this case), or impairments of vestibulo-ocular reflex signal from contralateral vertical semi-circular canals due to medial longitudinal fasciculus lesion may be a causative pathomechanism.

References: None.

Keywords: Nystagmus, Ocular Motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 115
The Use Of Positional Head Impulse Test In Vertical Nystagmus: Evidence For Vestibular Imbalance

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Introduction:
Upbeat (UBN) and downbeat nystagmus (DBN) have been ascribed to an imbalance between circuits generating upward and downward eye movements within either the vestibular (semicircular canals [SCC]- and/or otolith-related pathways), pursuit, or the neural integrator system. Positional modulation of UBN and DBN seems to favour the vestibular imbalance theory. Video-head impulse test (VHIT) is a recent tool that enables us to quantify SCC in the upright position. We used VHIT in a patient evidencing both UBN and DBN to assess SCC function in prone, upright and supine position.

Description of Case(s):
A 37-year-old female presented with a 4-month history of vertical oscillopsia and imbalance after gastric bypass surgery for morbid obesity. Intravenous thiamine replacement for probable thiamine deficiency had already been initiated and provided minimal improvement. General exam revealed limb and gait ataxia. In upright position there was spontaneous UBN, which was more intense in downward gaze. In supine position, UBN showed a similar behaviour. In prone position, there was spontaneous DBN which was more intense in upward gaze while UBN was still present in downward gaze. VHIT in upright position showed hyperactive anterior (1.50) and posterior (1.12) SCC-related gains. In prone position, both vertical SCC-related gains increased, slightly more for the anterior SCC-related gain (1.80; 1.38). In supine position, anterior SCC-related gain normalized (1.0) while posterior SCC-related gain increased (1.25).

Conclusions, including unique features of the case(s):
In our case, UBN and DBN seem to have been generated by hyperactive vestibular neurons conveying anterior and posterior SCC and/or otolith information, lacking normal cerebellar inhibition. Importantly we show that such hyperactivity is modulated by head position and correlates with the positional changes observed in primary gaze nystagmus. Specifically, when compared to upright position, a relative increase in anterior SCC-related gain in prone position causes DBN while a relative increase in posterior SCC-related gain in supine position causes UBN.

References: Hirose G, Kawada J, Tsukada K, Yoshioka A, Sharpe JA. Upbeat nystagmus: clinicopathological and pathophysiological considerations. J Neurol Sci. 1991 Oct;105(2):159-67; Gresty M, Barratt H, Rudge P, Page N. Analysis of downbeat nystagmus. Otolithic vs semicircular canal influences. Arch Neurol. 1986 Jan;43(1):52-5; Chambers BR, Ell JJ, Gresty MA. Case of downbeat nystagmus influenced by otolith stimulation. Ann Neurol. 1983 Feb;13(2):204-7; Mizuno M, Kudo Y, Yamane M. Upbeat nystagmus influenced by posture: report of two cases. Auris Nasus Larynx. 1990;16(4):215-21; Pierrot-Deseilligny C, Milea D, Sirmai J, Papeix C, Rivaud-Péchoux S. Upbeat nystagmus due to a small pontine lesion: evidence for the existence of a crossing ventral tegmental tract. Eur Neurol. 2005;54(4):186-90; Shin BS, Oh SY, Kim JS, Lee H, Kim EJ, et al. Upbeat nystagmus changes to downbeat nystagmus with upward gaze in a patient with Wernicke's encephalopathy. J Neurol Sci. 2010 Nov 15;298(1-2):145-7.

Keywords: Nystagmus, Ocular Motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 116
Exacerbation of Oscillopsia and Nystagmus from Reading Aloud in Superior Semicircular Canal Dehiscence

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Introduction:
Tullio phenomenon consists of dizziness induced by sound. This rare condition is often caused by superior canal dehiscence (SCD), which may present as vertigo, oscillopsia, and nystagmus triggered by sounds or pressure changes [1-3]. We describe a case of SCD and used infrared oculography to measure changes in eye movement control during self-generated sound while performing the King-Devick single-digit number reading test aloud [4].

Description of Case(s):
A 29-year-old woman with a history of migraines headache presented with severe oscillopsia, vertigo, and nausea after a syncopal event. She was diagnosed with SCD, and computed tomography revealed a severely thinned left superior semicircular canal. She underwent successful left trans-mastoid plugging, and post-operatively, her sound induced vertigo improved. However, her oscillopsia remained severe, especially while talking to customers at work. On examination, she exhibited gaze-evoked nystagmus on extreme right gaze and a small 0.5-Hz leftward square-wave jerks in primary gaze. When the patient spoke, her eye movement abnormality was not obviously worse on clinical exam. To better understand the impact of self-generated sound on eye movement, we used 500-Hz 2-dimensional infrared oculography to assess eye movement while performing the King-Devick number reading test aloud vs. silently [5]. While reading aloud, there was an increase in the amplitude of oscillatory eye movement compared with reading silently. She also read 28% slower and made 50% more saccades while reading aloud. With vestibular therapy and treatment with venlafaxine, her symptoms improved over several months, with resolution of gaze-evoked nystagmus on right gaze, although she remained slightly dizzy and sound sensitive.

Conclusions, including unique features of the case(s):
Self-generated sound during King-Devick number reading test can exacerbate symptoms of superior canal dehiscence. Infrared oculography during King-Devick number reading test is an easy way to quantified eye movement disorder while reading aloud in superior canal dehiscence and helped validate patient's symptoms.

References: 1. Edlow JA, Gurley KL, Newman-Toker DE. A New Diagnostic Approach to the Adult Patient with Acute Dizziness. J Emerg Med 2018;54:469-483. 2. Carey JP, Migliaccio AA, Minor LB. Semicircular canal function before and after surgery for superior canal dehiscence. Otol Neurotol 2007;28:356-364. 3. Ward BK, Carey JP, Minor LB. Superior Canal Dehiscence Syndrome: Lessons from the First 20 Years. Front Neurol 2017;8:177. 4. Ventura RE, Balcer LJ, Galetta SL, Rucker JC. Ocular motor assessment in concussion: Current status and future directions. J Neurol Sci 2016;361:79-86. 5. Jehangir N, Yu CY, Song J, Shariati MA, Binder S, Beyer J, Santini V, Poston K, Liao YJ. Slower saccadic reading in Parkinson's disease. PLoS One 2018;13:e0191005.

Keywords: Ocular manifestations of vestibular disorders, Ocular Motility

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Poster 117

Fourteen Syndrome and Fifteen Syndrome: Horizontal Gaze Palsy Plus Unilateral Seventh and Sixth Nerve Paresis

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Introduction:
Horizontal gaze palsy due to lesions of the sixth nerve nucleus is frequently associated with ipsilateral facial nerve palsy. The combination of these findings has recently been termed eight syndrome. If the causative pontine lesion extends to the abducens nerve fascicle, a sixth nerve paresis can be added.

Description of Case(s):
Two patients with pontine hemorrhages presented with combined horizontal eye movement disorders together with unilateral facial nerve paresis: A 34-year old male patient had a left conjugate horizontal gaze palsy combined with an infranuclear sixth nerve paresis and facial weakness on the left side. A 54-year old male patient showed bilateral incomplete horizontal gaze palsy together with an infranuclear sixth nerve paresis and facial nerve palsy on the right side. Vertical eye movements were normal in both patients.

Conclusions, including unique features of the case(s):
The combination of these clinical findings can be described as “14 syndrome” (7 + 6 + 1 = 14) and "15 syndrome" (7 + 6 + 1 + 1 = 15), respectively. Both cases illustrate the close anatomic relationship of the abducens nerve nucleus and fascicle with the intrapontine part of the facial nerve in the lower dorsal pons.

References: Green, Rastall, Eggenberger. Eight Syndrome: Horizontal Gaze Palsy Plus Ipsilateral Seventh Nerve Palsy. Journal of Neuro-Ophthalmology. 38: 347-349. 2018.

Keywords: Ocular Motility, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 118
Traumatic Ophthalmoplegia In A Pediatric Patient

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Introduction:
Approximately 3 to 7% of patients with head injuries have ocular motor palsies, most commonly of the third, fourth, and sixth cranial nerves. Internuclear Ophthalmoplegia (INO) is an uncommon complication from closed head trauma. INO is characterized by a paresis of adduction in lateral gaze and a horizontal jerk nystagmus in the abducting fellow eye. Most often, an INO is caused by a lesion or demyelination in the Medial Longitudinal Fasciculus (MLF). Traumatic INO often results from stretching MLF tract fibers or from shear forces in the brainstem which stretch branches of the basilar artery which leads to ischemia. Prognosis of traumatic INO is typically good but correlation of radiographic evidence to clinical findings is often missing.

Description of Case(s):
A previously healthy 11yo male presented to the emergency department after suffering minor closed head trauma from a fall with transient loss of consciousness & subsequent confusion & diplopia. A CT head was normal. MRI brain w/o contrast was normal. An ophthalmologic examination revealed a near visual acuity sc of 20/20 ou, normally brisk pupils ou, full limitation of adduction OD, an abducting nystagmus OS, an upbeat nystagmus OU on attempted upgaze, and loss of convergence. Given findings of a right internuclear ophthalmoplegia, there was concern for an injury to the rostral midbrain. He was admitted for observation & MRI brain w/ contrast showed “a 3mm focus diffusion restriction along the paramedian aspect of the dorsal pontine tegmentum.” The patient’s neurologic status remained stable & he was discharged. At a 3 week follow-up visit, there was complete resolution of his INO & upbeat nystagmus, which the family reported occurred around 1 week after the initial event.

Conclusions, including unique features of the case(s):
An INO following closed head trauma, should prompt a clinician to obtain a MRI brain with contrast and discuss possible findings with a neuroradiologist.

References: Chan JW. Isolated unilateral post-traumatic internuclear ophthalmoplegia. J Neuroophthalmol. 2001;21:212–213. Rich JR, Gregorius FK, Hepler RS. Bilateral internuclear ophthalmoplegia after trauma. Arch Ophthalmol 1974;92:66-8.

Keywords: Pediatric neuro-ophthalmology, Ocular Motility, Stroke Trauma

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 119
A Case of Pendular Nystagmus: Delayed Onset of Infantile Nystagmus

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Introduction:
Pendular nystagmus (PN) is characterized by quasi-sinusoidal oscillations of the eyes disrupting visual acuity and causing oscillopsia. PN can be classified into congenital and acquired form. Infantile nystagmus (IN) describes a syndrome of involuntary, pathological oscillations of the eyes that are almost invariably conjugate, symmetrical and horizontal. The numerous afferent visual system pathologies associated with IN make it difficult to establish etiology, and furthermore, a sizable proportion of IN cases do not appear to be associated with any ocular pathology whatsoever (these are referred to as 'idiopathic' or 'isolated' IN).

Description of Case(s):
A 33-year-old man presented with binocular horizontal PN, dizziness and oscillopsia. These symptoms have been felt by the patient since the age of 20. In past medical history, the patient had no specific medical or surgical history, and the patient's head was shocked by the traffic accident a few months before he felt the symptoms. The nystagmus was unaffected by convergence, vibration, head shaking, hyperventilation, or changes in body position. Brain MRI and MRA showed normal findings. Despite treatments using various medications including memantine, there were no changes in patient symptoms and nystagmus.

Conclusions, including unique features of the case(s):
The infantile nystagmus (IN) occasionally presents during adult life, when it may create a diagnostic problem, especially if the patient has other symptoms such as headache or dizziness. PN may affect one or both eyes, and can occur in any axis or combination of axes. Although acquired PN may be idiopathic, the most common cause of secondary acquired PN is disorders of central myelin, namely multiple sclerosis (MS). Unfortunately, no abnormal findings were found in this patient, including various genes, blood and imaging studies. In addition, No PN has been reported after head trauma such as concussion. Therefore, the author report a rare case of medication unresponsive PN and suggest that more research is needed.

References: None.

Keywords: Nystagmus, Ocular manifestations of vestibular disorders, Ocular Motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 120
Bilateral abducens palsy in West Nile Meningoencephalitis

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Introduction:
West Nile virus (WNV) is a neurotropic virus, transmitted to humans via an infected mosquito.1 Twenty percent of infected indivuals develop systemic symptoms such as fever, rash and adenopathy. Approximately 0.67% of patients develop associated meningoencephalitis with altered mental status and various sensory and motor deficits, which may be life threatening. Some patients may present with diplopia, as it has have been previously reported, two specifically due to abducens palsy. We present the case of a man presenting with binocular horizontal diplopia due to bilateral abducens palsy.

Description of Case(s):
A 61-year-old male with past medical history of psoriatic arthritis, not on any immunomodulating therapy, who presented to the emergency room with several weeks of worsening fever, malaise, and night sweats and two days of binocular, horizontal diplopia and ataxia. Two weeks prior, he traveled to western Massachusetts but denied any tick bites; he was started on Doxycycline for presumed Lyme disease. His inpatient neuro-ophthalmic examination was significant for normal afferent function with incomitant esotropia, increased in horizontal gazes with bilateral, mild abduction deficits. Contrast enhanced MRI brain was significant only for sinus disease. Lumbar puncture revealed a concerning pleocytosis (280 WBC) and elevated protein (122.6mg/dL) with normal opening pressure (22cmH20). Further workup revealed positive IgG and IgM for WNV with negative Lyme, VDRL and SPEP with normal CSF cytology. He was managed with supportive therapy and experienced progressive improvement of his symptoms. In his outpatient follow-up visit 2 weeks later, there was residual diplopia only in eccentric gaze.

Conclusions, including unique features of the case(s):
The visual manifestations of WNV infection may include uveitis, multifocal choroiditis, and optic disc edema. There are a few reported cases of WNV meningoencephalitis presenting with diplopia, two of which attributed to abducens palsies. We present a third case, in which there was bilateral 6th cranial nerve dysfunction.

References: Chan CK, Limstrom SA, Tarasewics DG, Lin SG. Ocular features of west nile virus infection in North America: a study of 14 eyes. Ophthalmology 2006 Sep;113(9):1539-46 Udip Dahal, Neville Mobarakai, Dikshya Sharma, Bandana Pathak. West Nile virus infection and diplopia: a case report and review of literature. Int J Gen Med. 2013 May 20;6:369-73 Matthew B. Jensen. Diplopia Secondary to West Nile Virus Meningitis. Webmedcentral. 2010 Sep 9; 1(9): 580. Caitlin Pepperell, Neil Rau, Sigmund Krajden, Ralph Kern, Atul Humar, Barbara Mederski, et al. West nile virus infection in 2002: morbidity and mortality among patients admitted to hospital in southcentral Ohio. CMAJ. 2003 May 27; 168(11): 1399–1405. Miller AH1, Liang IE. Diplopia: a focal neurologic presentation of West Nile meningioencephalitis. Ann Emerg Med. 2003 Sep;42(3):413-6.

Keywords: Ocular Motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 121
A Case of Acute Leukemia Presenting as Acute 6th Nerve Palsy

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Introduction:
Acute 6th nerve palsy has been attributed to many etiologies including microvascular insufficiency, neoplasm, trauma, infection, and inflammation. Isolated acute 6thnerve palsy is an uncommon presentation of acute lymphoblastic leukemia.

Description of Case(s):
A 36-year-old apparently healthy man presented with a 5-day history of horizontal, binocular diplopia. Review of systems was significant for a cough about 3 weeks prior to presentation. Examination demonstrated a complete abduction deficit of the left eye. Dilated fundus examination showed 3 retinal hemorrhages in the left eye. Otherwise, neuro-ophthalmic examination, including cranial nerves evaluation and optic disc appearance, was unremarkable. Contrasted high-resolution skull base MRI showed left 6th nerve enhancement involving the cisternal segment and was otherwise unremarkable. CSF analysis showed elevated white blood cells with 77% blasts. Bone marrow biopsy and flow cytometry confirmed acute T-cell lymphoblastic leukemia diagnosis. Other imaging studies reported no additional extramedullary disease.

Conclusions, including unique features of the case(s):
Isolated 6th nerve palsy is an uncommon presentation of acute lymphoblastic leukemia. In young patients and those patients without underlying vascular risk factors, thorough and expedited evaluation of acute cranial nerve palsies, including contrasted MRI, is required to evaluate for life-threatening disease.

References: None.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 122
Tolosa-Hunt Syndrome: A Case Series of Atypical Presentations

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Introduction:
We present three cases of Tolosa-Hunt Syndrome (THS) with atypical clinical symptoms. These varied presentations allow us to expand our diagnostic acumen of this rare disease. THS should be considered in those with unusual disease courses.

Description of Case(s):
Patient #1: 76-year-old male presenting initially with painless binocular oblique diplopia. One week later he developed retro-ocular pain OS. Examination revealed a partial oculomotor nerve palsy OS. Laboratory along with CSF analysis was essentially unrevealing, excluding other diagnoses from our differential. MR imaging showed left cavernous sinus enhancement. He improved after treatment with steroids. This presentation is atypical due to the timeline of onset of the severe peri-orbital headache and pain. Patient #2: 62-year-old male presenting with a pupil sparing oculomotor nerve palsy OD without any associated peri-orbital headache, with MR imaging showing right anterior cavernous sinus enhancement. Other diagnoses excluded. Treatment with steroids resolved his symptoms. This is atypical due to the lack of periorbital headache and pain usually associated with presentation of THS. Patient #3: 61-year-old female presenting with peri-orbital pressure and swelling OS followed by similar symptoms OD about one week later, associated with binocular horizontal diplopia and found to have a partial oculomotor nerve palsy. MR imaging showed enhancement of the bilateral cavernous sinuses with anterior extension into the optic nerve sheath OU. Symptoms improved with steroids treatment. This is atypical because of the bilateral involvement and the anterior involvement along the optic nerves.

Conclusions, including unique features of the case(s):
Although incidence of THS is rare, diagnostic consideration should include those who have uncommon characteristic physical features in their disease course. Treatment should not be delayed in those with atypical clinical features after careful evaluation with physical examination, laboratory analysis and neuroimaging.

References: None.

Keywords: Orbit/ocular pathology, Neuroimaging, Ocular Motility

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Poster 123
Frozen Eye in Gastrointestinal Stromal Tumor (GIST): Who is Guilty? Imatinib or metastasis

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Introduction:
The objectives of the ophthalmological exposure are to present a rare case of progressive oculomotor palsy in a 70 year old Caucasian male patient with a Gastro Intestinal Stromal Tumor (GIST) treated with Imatinib as adjuvant treatment.

Description of Case(s):
The patient began with binocular horizontal diplopia. Physical examination showed an alternating esotropia, periocular edema and lacrimation. As a background, he had a GIST, with metastasis under treatment with Imatinib 800mg that had been increased from 400mg the previous week and 48 hours after the increase in medication, began with diplopia. Different secondary diagnoses of orbital or central cause, metastasis, meningeal carcinomatosis, Lambert Eaton syndrome or pharmacological cause were evaluated. Computed Tomography (CT) scan of orbits that was reported as normal. The dose of Imatinib was decreased to 400 mg/day. On the 6th day, there begins to be a VI nerve palsy. On the 9th day he began with ptosis, and VI nerve palsy. On day 14th he presented a 3rd nerve palsy with pupil spared plus a 6th nerve palsy. Brain Magnetic Resonance Image (MRI) shows an image, located in the left side of clivus, sellar region and ipsilateral cavernous sinus. On day 28th, there was a "Frozen Eye" with pupil.The autopsy confirmed the compromise of part of the sellar, the anterior clinoid process, the sphenoid cleft, the cavernous sinus region, the trigeminal ganglion region, the internal carotid, pituitary gland. Histopathological exam: C-kit was positive, which occurs in 95% of the GIST cases.

Conclusions, including unique features of the case(s):
The investigation of the relevant literature through the publications leads us to believe that this is the first case of frozen eye and GIST, third case of clivus metastasis from GIST reported. Although Imatinib produces diplopia, the cause of diplopia of the patient was a cavernous sinus syndrome due to GIST metastasis in the clivus and cavernous sinus.

References: 1) Barrière J, y col: Diplopia as the first symptom of an aggressive metastatic rectal stromal tumor. Onkologie. 2009 Jun;32(6):345-7 2) Myong Ki Baeg, y col: Diplopia as a Presenting Symptom in a Gastric Gastrointestinal Stromal Tumor. Jpn J Clin Oncol 2011;41(2)265– 268 3) Verweij J, Casali PG, Zalcberg J, LeCesne A, Reichardt P, Blay JY, et al. Progression-free survival in gastrointestinal stromal tumours with high-dose imatinib: randomized trail. Lancet 2004;364:1127–34. 4) Blay JY, Bonvalot S, Casali P, Choi H, Debiec-Richter M, DeiTos AP, et al. GIST consensus meeting panelists. Consensus meeting for the management of gastrointestinal stromal tumors. Report of the GIST Consensus Conference of 20–21 March 2004, under the auspices of ESMO. Ann Oncol 2005;16:566–78. 5) Collin M, Mc CLelland, George J Harocopos, and Philip L Custer. Periorbital edema secondary to imatinib mesylate. Clin Ophthalmol. 2010; 4: 427-431.

Keywords: Neuro-ophth & systyemic disease (eg. MS, MG, thyroid), Ocular Motility, Skull Base, Miscellaneous

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Poster 124
WEBINO and 8-and-a-half in a Young Indian Female

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Introduction:
Wall-eyed bilateral internuclear ophthalmoplegia (WEBINO) and 8-and-a-half syndrome are two uncommon clinical entities that are sometimes harbingers of demyelinating disease. We present a South Asian patient who developed both and was diagnosed with multiple sclerosis (MS).

Description of Case(s):
A previously healthy 12 year old female presented with one day of nausea, vomiting, and binocular oblique diplopia. Her visual acuity was preserved and there was no rAPD nor optic disc edema; however, her motility exam demonstrated a wall-eyed bilateral internuclear ophthalmoplegia (WEBINO). Magnetic resonance imaging (MRI) of the brain showed fifteen patchy areas of demyelination throughout the cortex, with one lesion in the right cerebellum. She was started on 1000 mg intravenous methylprednisolone daily for MS. After initially presenting with a WEBINO, on hospital day four the patient developed a total paralysis of left gaze with continued contralateral internuclear ophthalmoplegia (INO) and an accompanying left seventh nerve palsy- the so called "8-and-a half –syndrome." As of her last follow up she was stable and completing an oral steroid taper before consideration of immunomodulatory therapy.

Conclusions, including unique features of the case(s):
MS is far less prevalent amongst Indians than European and North American patients1; for it to present with two rare but classic clinical pictures in a 12 year old Indian female is notable and serves a strong educational purpose.

References: 1. Bhatia R, Bali P, Chaudhari RM. Epidemiology and genetic aspects of multiple sclerosis in India. Ann Indian Acad Neurol. 2015;18(Suppl 1):S6-S10.

Keywords: Demeylinating disease, Ocular Motility, Pediatric neuro-ophthalmology, Nystagmus

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Poster 125
Titrating the correction angle in modified Harada-Ito procedure in over 15 degree extorsion

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Introduction:
The modified Harada-Ito procedure is known to have excyclotropia correction effect of about 5 to 10 degrees in a unilateral surgery. Although Metz and Lerner proposed adjustable technique, it is based on patients' subjective reports in the adjustment session. Here we propose simple calculation formula to titrate the correction angle of modified Harada-Ito procedure. Furthermore, by resecting the superior oblique tendon, we could achieve correction of more than 15-degree extorsion.

Description of Case(s):
Since the 8mm point of the lateral rectus from insertion lies on near the plane of globe equator, the titration angle per dose millimeter can be calculated as follows: Correction angle (degree)/displacement (mm) = 360 / [axial length (mm) x 3.14] Case presentation A 67-year-old male patient suffering from 15 degree of extortional diplopia underwent an adjustable modified augmented Harada-Ito surgery in his right eye. Before the reattachment, 5mm resection of the superior oblique tendon was done to intort 28 degree for intentional augmentation since the axial length of the patient was 21mm. After the surgery, double Maddox rod test showed 20-degree intorsion. Two days after the operation, 3 mm hangback adjustment was done and the patient showed 3 degree of remaining intorsion. After 1 year, the patient showed no subjective and objective torsion.

Conclusions, including unique features of the case(s):
With our simple calculation formula, one can perform modified Harada-Ito procedure in more predictable manner not only with adjustable technique but also with non-adjustable technique. By resecting the superior oblique tendon, correction of more than 15-degree extorsion is possible.

References: Mets H, Lerner H. The adjustable Harada-Ito procedure. Arch Ophthalmol 1981;99:624-6.

Keywords: Ocular Motility, Adult strabismus with a focus on diplopia

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 126
mTOR Inhibitor Causes Regression of Retinal Hamartomas in Patients with Tuberosclerosis

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Introduction:
Tuberous sclerosis (TS) is a systemic disorder characterized by hamartomas in multiple organs (1), among those the retina. The mutations underlying TS are TSC1 or TSC2, resulting in activation of mTOR which promotes cell proliferation (1). Everolimus, mTOR inhibitor, is a new treatment for TS-related lesions, indicated for the treatment of subependymal giant cell astrocytomas (SEGA) in the brain and renal angiomyolipomas (2). Here we present regress in the size of the retinal hamartomas in a TS patient following systemic treatment with Everolimus.

Description of Case(s):
A 24 years old TS female had multi-organ involvement including rhabdomyoma of the heart, SEGA that was successfully resected, and angiolipomas of the kidney. She was treated by Everolimus 12 mg after failure of recurrent embolization of the kidney, reaching therapeutic blood level. Ocular history included hyperopic anisometropia amblyopia, esotropia and retinal hamartomas. On repeated eye exams she showed stable visual acuity of 20/30 and 20/40 and eye movement, with normal optic nerves function. Fundus exam revealed multiple retinal hamartomas in both eyes, documented since 2006. Fundus photos and repeated retinal OCT measurements showed shrinkage of the hamartomas during the 24 months of treatment.

Conclusions, including unique features of the case(s):
This is the first OCT measurement report of resolving hamartomas in TS- retinas following treatment with mTOR inhibitor. Although retinal hamartomas are not vision-threatening, it might progress. Zhang et al (3) described reduction in size in seven patients treated with Sirolimus. Another report showed response to Everolimus but without objective measurement (4). The visible and measurable response may indicate response in other organs, and OCT might become a valuable tool to monitor the efficacy of the treatment.

References: 1. Curatolo P, Bombardieri R, Jozwiak S. Tuberous sclerosis. Lancet, 372(9639):657-68, 2008. 2. Sasongko TH, Ismail NF, Zabidi-Hussin Z. Rapamycin and rapalogs for tuberous sclerosis complex. Cochrane Database Syst Rev. 7:CD011272, 2016. 3. Zhang ZQ, Shen C, Long Q, Yang ZK, Dai RP, Wang J, Zhang W, Pan Q, Zhu Z, Xu KF. Sirolimus for Retinal Astrocytic Hamartoma Associated with Tuberous Sclerosis Complex. Ophthalmology. 122(9):1947-9, 2015. 4. Zipori AB, Tehrani NN, Ali A. Retinal astrocytoma regression in tuberous sclerosis patients treated with everolimus. J AAPOS. ,22(1):76-79, 2018.

Keywords: Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc), Eyelid & adnexal disease, Genetic Disease

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Poster 127
Superior Ophthalmic Vein Thrombosis from Orbital Cellulitis in Setting of Trauma

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Introduction:
The diagnosis of superior ophthalmic vein thrombosis (SOVT) should be considered in patients who present with painful proptosis, chemosis, periorbital edema, and ophthalmoplegia. Early diagnosis and treatment is crucial to prevent SOVT progression to cavernous sinus thrombosis (CST), which can lead to neurologic deterioration, blindness, or death. It is assessed by imaging, preferably via CT scan or MRI. Both septic and aseptic causes have been implicated in SOVT. The most common cause of septic SOVT is sinusitis, but can also involve other infections of the orbits, teeth, and face. Aseptic causes include anatomic constraints, inflammatory conditions, hematologic abnormalities, and trauma. Once the etiology is determined, the patient can be managed appropriately. If infectious, broad-spectrum antibiotics should be administered. Systemic anticoagulation is recommended, as it not only prevents, but also reduces mortality in CST. Currently, there is not enough data supporting the role of steroids in SOVT. Surgery is indicated when there is an underlying source of infection, such as an abscess, that can be drained.

Description of Case(s):
This is a 12-year-old boy who initially presented with blunt trauma to the right periorbital region. His exam was concerning for decreased visual acuity and motility, proptosis, along with 360 degrees of nonhemorrhagic chemosis in the right eye. CT of the right orbit revealed a dilated superior ophthalmic vein in the setting of pan-sinusitis, with patterns of inflammation classic for orbital cellulitis. He was subsequently started on broad-spectrum antibiotics and systemic anticoagulation.

Conclusions, including unique features of the case(s):
Though SOVT is rare, it is an important diagnosis to consider in patients presenting with typical orbital symptoms. This case highlights both aseptic and septic causes for SOVT that occurred simultaneously. Failure to recognize and treat SOVT early in its course can lead to devastating consequences. The current mainstay of treatment includes broad-spectrum antibiotics, systemic anticoagulation, and surgery.

References: Akingbola, Shar, Singh, Frieberg, Petrescu, Posttraumatic Superior Ophthalmic Vein Thrombosis in a 2 Year Old, Pediatric Emergency Care, Volume 30, Pages 108-110, 2014 Kumar, Colón-Acevedo, Liss, Diagnosis and Management of Superior Ophthalmic Vein Thrombosis, EyeNet Magazine, 2015 Lim, Scawn, Whipple, Oh, Lucarelli, Spontaneous Superior Ophthalmic Vein Thrombosis: A Rare Entity With Potentially Devastating Consequences, Eye, Volume 28, Pages 248-251, 2014 Singh, Gaindh, Mustafa, Kamal, Mowla, Spontaneous Superior Ophthalmic Vein Thrombosis: A Case Report, Neurology, Volume 84, Page 14, 2015 Syed, Bell, Hise, Philip, Spak, Bilateral Cavernous Sinus and Superior Ophthalmic Vein Thrombosis in the Setting of Facial Cellulitis, BUMC Proceedings, Volume 29, Pages 36-38, 2016 van der Poel, de Witt, van den Berg, de Win, Mourits, Impact of Superior Ophthalmic Vein Thrombosis: A Case Series and Literature Review, Orbit, 2018.

Keywords: Vascular disorders, Orbit/ocular pathology, Orbit

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Poster 128
Pseudo von Graefe's Sign following Operative Vaginal Delivery

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Introduction:
To report and review a case of unilateral upper eyelid retraction in downgaze following prolonged and difficult operative vaginal delivery. Its a descriptive case report based on analysis of clinical eye examination, observations and investigations.

Description of Case(s):
A 9-week-old male with birth history of prolonged (16-18 hours) and difficult operative vaginal delivery (use of vacuum and then forceps) presented with right eye opening wider intermittently . Postnatally right eye was noted to be swollen and closed with hematoma and petechiae over right side of the face. One month later, right lagophthalmos and widening of palpebral aperture on downgaze was seen. On eye examination, mild ptosis not covering the visual axis and pseudo von Graefe's sign was present. A limitation of elevation in right eye with right intermittent hypotropia of 6PD for near and distance was measured with Krimsky Test. MRI Brain and Orbit did not reveal any abnormality. Left eye examination was normal. No neurological or developmental abnormality was seen.

Conclusions, including unique features of the case(s):
A trauma to levator palpebral superioris and superior rectus complex due to difficult vaginal delivery followed by cicatricial changes may result in lid retraction in downgaze. This case adds to the literature of possibility of presence of pseudo von Graefe's sign following difficult operative vaginal delivery.

References: None.

Keywords: Ocular Motility, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 129

Bilateral Eyelid Apraxia Secondary to Bilateral Paramedian Mesencephalic Stroke Treated with Botulinum A Toxin Injection

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Introduction:
Eyelid apraxia following cerebral infarction has been reported in the literature. This sequela is rare, and its management remains undefined. We present a case of bilateral complete eyelid apraxia and blepharospasm after bilateral paramedian mesencephalic stroke successfully treated with botulinum A toxin injection.

Description of Case(s):
A 59-year-old man with hypertension, hyperlipidemia, and type 2 diabetes mellitus who sustained a bilateral paramedian mesencephalic stroke in the setting of profound hypertensive urgency one year prior was referred to ophthalmology for evaluation of subsequent bilateral eyelid opening apraxia. Additional sequelae from his stroke included severe diffuse bilateral spasticity, tremor, and rigidity of his body causing quadriparesis. External examination revealed bilateral upper face spasm and tremor. He was able to forcefully close his eyelids but unable to open them despite frontalis activation. His ophthalmic evaluation was limited by orbicularis spasm with attempted forced eyelid opening. He underwent botulinum A toxin injection to bilateral orbital and palpebral orbicularis oculi muscles. At follow-up five weeks after treatment, the patient and his wife reported improved quality of life. He demonstrated reduced periorbital spasms and was able to lift his eyelids 2 mm bilaterally using frontalis activation.

Conclusions, including unique features of the case(s):
Apraxia of eyelid opening is a rare condition that can result from a range of neuromuscular and neurodegenerative disorders and can severely impact a patient's quality of life. Botulinum toxin injection as a treatment modality for eyelid apraxia has been described in literature in the setting of non-infarct etiologies such as congenital myotonia, progressive supranuclear palsy, and parkinsonism. To the best of our knowledge, the present case is the only report of post-cerebral infarction eyelid apraxia successfully treated with botulinum A toxin injection in current literature.

References: 1. Cardoso F. Botulinum toxin in parkinsonism: The when, how, and which for botulinum toxin injections. Toxicon, 147, 107-110, 2018. 2. Fernandez E, Latasiewicz M, Pelegrin L, Romera M, Schellini S, et al. Botulinum toxin for treating unilateral apraxia of eyelid opening in a patient with congenital myotonia. Arq Bras Oftalmol, 80, 330-331, 2017. 3. Kanazawa M, Shimohata T, Sato M, Onodera O, Tanaka K, et al. Botulinum toxin A injections improve apraxia of eyelid opening without overt blepharospasm associated with neurodegenerative diseases. Mov Disord, 22, 597-598, 2007. 4. Myint PK, Anderson KN, Antoun NM, Warburton EA. Eyelid apraxia associated with bilateral paramedian thalamic infarct. Age Ageing, 37, 343-344, 2008.

Keywords: Neuro-ophth & systyemic disease (eg. MS, MG, thyroid), Stroke Trauma, Vascular disorders, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 130
Misdiagnose of Carotid Cavernous Fistulas, who´s to blame?

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Introduction:
We report 4 cases of patients who were misdiagnosed of Carotid Cavernous fistula.

Description of Case(s):
First case: 28 year-old woman who consulted for “chronic conjunctivitis” associated with congestive and exophthalmic OS. She had a history of topic corticosteroid treatments for the last four months, showing no clear improvement in signs and symptoms. The particular precedent in this case was that her symptoms appeared days after the birth of her first child. Disthyroidism was discarded, and the diagnosis of Carotid Cavernous fistula imposed, being positive in the contrasted brain angio-CT. Second case: 72 year-old man who consulted for “chronic asymptomatic 4-month conjunctivitis in OS” associated to vertical diplopia and exophthalmos. Third case: 54 year-old man (with poor controlled diabetes type 2) began with OD exophthalmos and congestion, and as precedent: topic corticosteroids and IM gentamicin for ear infection treatment, and ocular manifestations were associated with this infection at first. Nevertheless, no improvement occurred. Both cases had “normal” neuroimaging, but in the second case the angio-CT was, in fact, clearly positive, and the third case seemed negative in the angioMRI (poor quality) and angiography established the diagnosis. Fourth case: 69 year-old man began with intermittent diplopia, and high IOP in OU associated to intense hyperemia and proptosis, limited bilateral abduction. MRI: extraocular muscles engorgement, and informed “negative” for fistulas in brain MRI and angio- CT (this was clearly positive: bilateral images in cavernous sinuses). Angiography: indirect carotid cavernous fistula.

Conclusions, including unique features of the case(s):
All these patients undergone neurosurgery. Although it’s true that the first differential diagnosis is Graves´ Ophthalmopathy, clinical examination was suspicious of anything else. And it became more difficult because in 3 of the 4 cases neuroradiologists, at first sight, discarded the presence of fistula. Review of images or angiography, based on clinical examination allowed to establish the diagnosis and treatment.

References: None.

Keywords: Orbit, Vascular disorders, Interventional neuroradiology, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 131
Spontaneous dehiscence of the lateral orbital wall

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Introduction:
The lateral wall of the orbit is usually thicker than the floor, roof, or medial wall. Spontaneous bony defects of the lateral wall are extremely rare. We report a case of spontaneous lateral wall defect in a patient with thyroid eye disease, incidentally noted on CT scan and confirmed intraoperatively during orbital decompression. Bony remodeling and "spontaneous decompression" associated with thyroid eye disease has been reported, although it is unclear whether the patient's thyroid eye disease played a role with this osseous defect.

Description of Case(s):
A 58-year old man with history of thyroid eye disease, treated hepatitis C, COPD, and hypertension presented with recurrent diplopia and worsening left-sided proptosis. He had a history of right orbital decompression and multiple strabismus surgeries, but no left-sided orbital surgery or trauma. CT scan for preoperative planning revealed a focal area of thinning of the left lateral orbital wall, as well as evidence of his previous right orbital decompression involving the floor and medial wall. During left orbital decompression, a dehiscence was noted in the lateral orbital wall with buccal fat prolapsing into the orbit once the periosteum was elevated. This osseous defect was separate from the inferior orbital fissure. Some of the buccal fat was removed along with orbital fat and bone from the lateral and medial walls and floor to achieve decompression.

Conclusions, including unique features of the case(s):
Literature review revealed 3 previous cases of anatomic variation causing defects in the lateral orbital wall. Two describe an enlarged inferior orbital fissure with buccal fat prolapse into the orbit and another of bilateral orbital fat herniating into the temporal fossa. In rare cases there may be spontaneous thinning and/or dehiscence of the lateral orbital wall. The pathogenesis of such defects remains unknown, and it is unclear to what extent the patient's thyroid eye disease played a role in this osseous defect.

References: 1. Martinez-Barbero, JP, Bilateral fat herniation of the lateral orbital wall in a patient with Down Syndrome, New Frontiers in Ophthalmology, 3, 1-2, 2017 2. Kakizaki H, Ichinose A, Takahashi Y, Iwaki M. Anomaly of the deep lateral orbital wall in two cases, The Open Ophthalmology Journal, 5, 25-26, 2011. 3. Tan NYQ, Leong YY, Lang SS, Htoon ZM, Young SM, Sundar G, Radiologic Parameters of Orbital Bone Remodeling in Thyroid Eye Disease. Investigative Ophthalmology & Visual Science, 58, 2527-2533, 2017. 4. Kang EM, Yoon JS, Clinical and radiological characteristics of Graves' orbitopathy patients showing spontaneous decompression. Journal of Craniomaxillofacial Surgery, 43, 48-52, 2015. 5. Aldridge T, Thomson A, Ilankovan V, Abnormal anatomy of inferior orbital fissure and herniation of buccal fat pad. British Journal of Oral Maxillofacial Surgery, 53, 92-3, 2015.

Keywords: Graves (systemic disease), Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 132
Pembrolizumab-associated Diplopia Secondary to Orbital Pseudotumor

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Introduction:
57 year-old female presented with acute onset of painful horizontal diplopia on right gaze. Her medical history was notable for metastatic adenocarcinoma (non-small cell lung cancer), treated with radiation therapy as well as pembrolizumab (Keytruda®, Merck). The diplopia started with her fifth cycle of pembrolizumab.

Description of Case(s):
Patient's visual acuities were 20/20 OD, 20/15 OS. There was no RAPD. Motility demonstrated a painful abduction deficit with an incomitant esotropia (12^ in primary gaze, building to 40^ in right gaze; 4^ at near). There was excellent orbicularis strength without fatigable ptosis or variability in extraocular deviations. Anterior and posterior segment examinations were unremarkable. Urgent MRI Orbits and Brain were obtained for concern of metastatic disease. There was new, diffuse enhancement and enlargement of the right lateral rectus muscle that had not been present on imaging six weeks prior. For presumed orbital pseudotumor, patient was started on oral steroid therapy. Inflammatory changes, pain, and diplopia entirely resolved with treatment.

Conclusions, including unique features of the case(s):
Pembrolizumab is an immune checkpoint inhibitor approved in 2014; it is a humanized monoclonal antibody targeting programmed cell death-1 (PD-1). Aside from its excellent efficacy in enhancing the immune system's ability to block cancer cells (approved for non-small cell lung cancer, melanoma, urothelial carcinomas, among others), the T-cell proliferation that results can also lead to autoimmune-related adverse events. Reported ophthalmologic manifestations include myasthenia gravis, uveitis, conjunctivitis, optic neuritis, disc edema, chorioretinal changes, and thyroid eye disease-like changes. We are still learning about other adverse events related to this medication. This seems to be the first reported case of pembrolizumab-induced orbital pseudotumor resulting in diplopia in a patient with lung cancer. Diplopia resolved entirely with oral methylprednisolone administration. It is critical that we remain vigilant to observe for other potentially reversible side-effects that emerge as this treatment becomes so widely used.

References: Antoun J, Titah C, Cochereau I. Ocular and orbital side-effects of checkpoint inhibitors: a review article. Curr Opin Oncol. 2016;28(4):288-294 Mori S, Kurimoto T, Ueda K, Enomoto H, Sakamoto M, et al. Optic Neuritis Possibly Induced by Anti-PD-L1 Antibody Treatment in a Patient with Non-Small Cell Lung Carcinoma. Case Rep Ophthalmol 2018;9:348–356. Park ES, Rabinowitz G, Hamnvik O, Dagi LR. Short Report: A case of Graves' ophthalmopathy associated with pembrolizumab (Keytruda) therapy. J AAPOS. 2018; Aug22(4):310-312. Roberts P, Fishman GA, Joshi K, Jampol LM. Chorioretinal lesions in a case of melanoma-associated retinopathy treated with pembrolizumab. JAMA Ophthalmol, 134 (2016), pp. 1184-1188 Samra A, Valdes-Navarro M, Lee S, Swan R, Foster CS, et al. A case of bilateral uveitis and papillitis in a patient treated with pembrolizumab. Eur J Ophthalmol, 26 (2016), pp. 46-48 Taylor SC, Hrisomalos F, Linette GP, Rao PK. A case of recurrent bilateral uveitis independently associated with dabrafenib and pembrolizumab therapy. Am J Ophthalmol Case Rep. 2016;2:23-25. Published 2016 Apr 13.

Keywords: Orbit, Neuroimaging, Adult strabismus with a focus on diplopia

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 133
Orbital Myositis Triggering Oxygen-responsive Cluster Headache

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Introduction:
We present a case of new onset of headache meeting diagnostic criteria for cluster headache, responsive to oxygen treatment, associated with diplopia and subtle ocular misalignment. This was revealed, by a contrast-enhanced MRI of the orbits, to be secondary to orbital myositis.

Description of Case(s):
A 19-year-old woman presented with new headaches and diplopia. She had a history of migraines with visual auras, usually perimenstrually, characterized by severe bilateral occipital pain and associated with photophobia, phonophobia, nausea and prostration in dark room. These were responsive to NSAIDs. While recovering from an URI and ear infection the patient developed a completely new type of headache: severe right-sided retro-orbital pain occurring in clusters, unrelieved by rest and NSAIDs, with ipsilateral Horner's syndrome, lid edema, miosis, rhinorrhea and unilateral photophobia. Between episodes she had persistent right retro-orbital aching, and noticed binocular vertical diplopia on downgaze. A brain MRI did not reveal any intracranial pathology. Administration of high-flow oxygen immediately relieved the pain. Subsequently, the patient received a brief steroid taper. No recurrence of headaches was reported. Patient continued to have discomfort and diplopia on downgaze. Examination revealed right ptosis and right hypertropia on downgaze. MRI of the orbits with contrast demonstrated T2 hyperintensity and contrast enhancement of the superior rectus and levator palpebrae complex, consistent with orbital myositis. A 30-day course of prednisone 40 mg daily resolved the patient's residual symptoms.

Conclusions, including unique features of the case(s):
The association of unilateral headache or periorbital pain with ipsilateral autonomic features characterizes the trigeminal autonomic cephalalgias (TACs). To our knowledge this is the first case of orbital myositis being described as presenting as an oxygen-responsive headache. In the diagnostic workup of headache and facial pain, the presence of orbital symptoms and signs such as pain with eye movements, diplopia or ptosis should direct attention to the orbit, and appropriate imaging should be considered.

References: None.

Keywords: Orbit, Ocular Motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 134
Walsh to the Rescue: Case of Neurosarcoidosis with Vasogenic Edema and Pachymeningitis

Sravanthi Vegunta[1], Alison Crum[1], Kathleen Digre[1], Bradley Katz[1], Edward Quigley[2], Cheryl Palmer[3], Karen Salzman[2], Meagan Seay[1], Karen Salzman[2]

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Introduction:
A 50-year-old man presented with rapidly progressive painful right eye (OD) vision loss. He developed multiple cranial neuropathies, seizures, pachymeningitis, and vasogenic edema. He was evaluated for inflammatory conditions, infection, and tumor. Many years after presentation, re-review of his dural biopsies revealed noncaseating granulomas, and he was diagnosed with neurosarcoidosis.

Description of Case(s):
At presentation in 2007, our patient had light perception vision OD, right relative afferent pupillary defect, and slight right optic nerve elevation. Brain MRI showed diffuse meningeal thickening of anterior basilar meninges. Work up including CBC, CMP, ESR, CRP, blood cultures, c-ANCA, p-ANCA, PR3 and MPO antibodies, serum and CSF ACE, ANA, HIV testing, CSF studies, and chest imaging were unremarkable. Dural biopsy returned as idiopathic hypertrophic pachymeningitis. In 2008, while on oral prednisone, he developed partial right 3rd nerve palsy. MRI showed worsening pachymeningitis with extension into right orbital apex. Repeat dural biopsy had same results as initial biopsy. In 2010, while on steroids, he returned with seizures. MRI showed new FLAIR and T2 hyperintensity of right frontal lobe, consistent with vasogenic edema. Increased dural and perivascular enhancement were noted without parenchymal enhancement. Glioma and infection were suspected. However the edematous area did not have diffusion restriction, and CSF studies were normal. After attending 2013 Walsh presentations, where a case of IgG-4 disease with pachymeningitis was presented, we re-evaluated the 2009 biopsy. The specimen was not consistent with IgG-4 disease but instead revealed granulomatous inflammation. Our patient was diagnosed with neurosarcoidosis.

Conclusions, including unique features of the case(s):
Optic neuropathy is the second most common cranial neuropathy after 7th nerve palsy in neurosarcoidosis. Enhancing mass lesions in neurosarcoidosis are thought to represent spread of leptomeningeal disease along the perivascular spaces causing defective blood brain barrier. Some invoke phenomenon of pial steal. In cases with no diagnosis, keep a broad differential, revisit the diagnosis, and re-review histology!

References: 1. Joseph FG, Scolding NJ. Neurosarcoidosis: A study of 30 new cases. J Neurol Neurosurg Psychiatry 2009; 80:297-304. 2. Scott TF, et al. Neurosarcoidosis mimicry of multiple sclerosis: Clinical, laboratory, and imaging characteristics. Neurologist 2010; 16:386-9. 3. Stjepanović MI, et al. Radiological presentation of neurosarcoidosis. Med Pregl 2014 Jan-Feb; 67(1-2):24-7. 4. Pickuth D, et al. Role of radiology in the diagnosis of neurosarcoidosis. Eur Radiol 2000;10(6):941-4. 5. Loor RG, et al. Multiple cranial nerve dysfunction caused by neurosarcoidosis. Am J Otolaryngol 2012;33:484-6.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 135
Vertical Diplopia: An Unusual Manifestation of Silent Sinus Syndrome

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Introduction:
Silent Sinus Syndrome (SSS) is a rare, typically unilateral disorder characterized by spontaneous involution and hypoplasia of the maxillary sinus leading to enophthalmos and hypoglobus. We report a case with vertical diplopia as the initial presentation.

Description of Case(s):
A 38-year-old male presented with intermittent vertical diplopia. Strabismus was noted 2 years earlier by optometrist. There was no history of trauma, periocular or sinus surgery, or congenital strabismus. Pertinent exam findings were exophthalmometry measurements of 18 mm OD and 21 mm OS, with hypoglobus OD. Left eye motility was normal. Right eye showed impaired elevation in abduction and adduction. There was overaction of the right SO>SR muscle. Ocular alignment testing showed an incomitant right hypotropia measuring 25 prism diopters (PD) in primary gaze and left gaze, but increasing to 35 PD in right gaze. The 25 PD hypotropia persisted in upgaze and diminished to 16 PD in downgaze. There was exotropia of 12 PD in primary, lateral and downgaze. In upgaze, it measured 20 PD, a mild V pattern. CT scan revealed opacification and hypoplasia of right maxillary sinus, volume expansion of the bony orbit, and a rightward deviation of the nasal septum consistent with right SSS. The patient underwent endoscopic maxillary sinus antrostomy. Postop examinations at 3 and 8 months showed no change in diplopia, motility/alignment, or enophthalmos.

Conclusions, including unique features of the case(s):
Diplopia is an infrequent symptom of SSS. Its optimal treatment is unknown, but methods have included subperiosteal implants along the orbital floor and prisms. In our case, sinus surgery failed to improve the diplopia. We felt that orbital surgery would not predictably correct the strabismus. We propose a staged approach of orbital surgery to correct the enophthalmos and hypoglobus, followed by staged strabismus surgery, as employed in treatment of orbital fractures or thyroid ophthalmopathy, which manifests with a similar pattern of restrictive strabismus.

References: None.

Keywords: Adult strabismus with a focus on diplopia, Ocular Motility, Orbit/ocular pathology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 136

Checkpoint inhibitor associated orbital inflammation masquerading as ocular myasthenia gravis and thyroid eye disease

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Introduction:

We report a case of a 67-year-old woman who presented with double vision and ptosis with clinical findings consistent with ocular myasthenia gravis and imaging findings consistent with thyroid eye disease in the setting of ipilimumab and nivolumab treatment for metastatic melanoma. Ipilimumuab blocks cytotoxic T-lymphocyte–associated antigen 4 and nivolumab blocks programmed death-1 receptors to promote T-cell-mediated response to tumor. [1,2] However, in so doing, these medications can unleash several forms of autoimmune disease affecting the extraocular muscles including myasthenia gravis and thyroid eye disease-like orbital inflammation. [1,3-5]

Description of Case(s):

A 67-year-old woman presented with binocular, oblique diplopia, right sided blepharoptosis, injection of bilateral conjunctiva, periorbital ache and mild blurry vision in the right eye. Her medical history was significant for nasal mucosal melanoma diagnosed 1.5 years prior. Ipilimumab and nivolimumab were initiated 1 month prior to presentation. She subsequently developed hyperthyroidism followed by hypothyroidism. Afferent examination was normal. Efferent examination revealed 1 mm of ptosis of the right upper eyelid with a Cogan eyelid twitch. There was limitation of abduction and adduction in both eyes, as well as a limitation in elevation of the right eye. MRI demonstrated enlargement and enhancement of the extraocular muscles bilaterally. Thyroid peroxidase antibodies were positive and anti-acetylcholine receptor antibodies were negative. She was started on 60 mg of prednisone which resulted in symptomatic improvement and normalization of the extraocular muscle size on imaging.

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

This case highlights the association between checkpoint inhibitors and orbital inflammatory disease, which may present with clinical features of ocular myasthenia gravis and thyroid eye disease. Thyroid eye disease-like orbital inflammation associated with checkpoint inhibitors typically responds to systemic steroids without the need to discontinue the checkpoint inhibitor. [4] Unlike thyroid eye disease not associated with check point inhibitors, the extraocular muscles returned to normal size with corticosteroid treatment in this case.

References: 1. Papavasileiou E, Prasad S, Freitag SK, Sobrin L, Lobo AM: Ipilimumab-induced Ocular and Orbital Inflammation--A Case Series and Review of the Literature. Ocular immunology and inflammation 2016;24:140-146. 2. Baughman DM, Lee CS, Snydsman BE, Jung HC: Bilateral Uveitis and Keratitis Following Nivolumab Treatment for Metastatic Melanoma. Medical case reports (Wilmington, Del) 2017;3 3. Dalvin LA, Shields CL, Orloff M, Sato T, Shields JA: CHECKPOINT INHIBITOR IMMUNE THERAPY: Systemic Indications and Ophthalmic Side Effects. Retina (Philadelphia, Pa) 2018;38:1063-1078. 4. Sagiv O, Kandl TJ, Thakar SD, Thuro BA, Busaidy NL, Cabanillas M, Jimenez C, Dadu R, Graham PH, Debnam JM, Esmaeli B: Extraocular Muscle Enlargement and Thyroid Eye Disease-like Orbital Inflammation Associated with Immune Checkpoint Inhibitor Therapy in Cancer Patients. Ophthalmic Plast Reconstr Surg 2018 5. Johnson DB, Saranga-Perry V, Lavin PJ, Burnette WB, Clark SW, Uskavitch DR, Wallace DE, Dickson MA, Kudchadkar RR, Sosman JA: Myasthenia Gravis Induced by Ipilimumab in Patients With Metastatic Melanoma. J Clin Oncol 2015;33:e122-124.

Keywords: Orbit, Ocular Motility, Myasthenia, Neuro-ophth & systyemic disease (eg. MS, MG, thyroid), Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 137

Relative afferent pupillary defect with contralateral demyelinating midbrain lesion in a patient with Charcot's Triad

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Introduction:
We describe a patient with a left relative afferent pupillary defect secondary to demyelinating lesions in the right optic tract and/or right dorsal midbrain.

Description of Case(s):
A 17-year-old female presented to neuro-ophthalmology clinic for evaluation of nystagmus, ataxia, and white matter brain abnormalities. In March 2018 she developed binocular diplopia for distance that was managed as decompensated strabismus. She was seen by a neurologist who was concerned about gait ataxia. In July 2018 brain and spine MRI showed numerous white matter lesions. She was treated with IV steroids and her double vision improved. On neuro-ophthalmology exam she was noted to have normal vision 20/20 bilaterally with full visual fields. A dense left relative afferent pupillary defect (rAPD) was noted. Eye movements showed a mild left aBduction defect. Jerk nystagmus was noted on both directions of horizontal gaze. Her exam was notable for dysarthria, mild intention tremor, and ataxia. Her symptoms of nystagmus, intention tremor, and dysarthria (Charcot's triad) with brain MRI findings suggest multiple sclerosis. Lesions in the pons and middle cerebellar peduncles are responsible for the left sixth nerve palsy and nystagmus/ataxia respectively. The left rAPD can be explained by lesions in the right optic tract or right dorsal midbrain.

Conclusions, including unique features of the case(s):
The basis of a midbrain relative afferent pupillary defect lies in the nasal-temporal asymmetry of pupillomotor input that is seen when a unilateral post-chiasmal lesion interrupts homonymously paired fibers traveling in the contralateral optic tract or midbrain pathway. The characteristics of a rAPD from a dorsal midbrain or optic tract lesion will resemble that of a rAPD from a pre-chiasmatic lesion but in the opposite eye. Case reports have shown midbrain compression causing a contralateral rAPD however we are reporting a case with a demyelinating lesion in a young female with multiple sclerosis and no visual sensory deficit.

References: 1. Chen C, Scheufele M, Sheth M, Torabi A, Hogan N, Frohman E. Isolated Relative Afferent Pupillary Defect Secondary to Contralateral Midbrain Compression. ARCH NEUROL Sep 2004; Vol 61. 2. Girkin C, Perry J, Miller N. A Relative Afferent Pupillary Defect Without Any Visual Sensory Deficit. ARCH OPHTHALMOL Nov 1998; Vol 116. 3. Kupfer C, Chumbley L, Downer J, Quantitative histology of optic nerve, optic tract and lateral geniculate nucleus of man. J ANAT 1967; 101. 393-401. 4. Ellis CJK. Afferent pupillary defect in pineal region tumor. JOURNAL OF NEUROL, NEUROSURG, PSYCH 1984; 47. 739-741. 5. Kawasaki A, Miller N, Kardon R. Pupillographic Investigation of the Relative Afferent Pupillary Defect Associated with a Midbrain Lesion. OPHTHALMOLOGY 2010.

Keywords: Pupils Retina, Demeylinating disease, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

North American Neuro-Ophthalmology Society

45th Annual Meeting

March 16 – March 21, 2019
Red Rock Casino, Resort & Spa • Las Vegas, Nevada
Program Schedule

Monday, March 18

6:00 am – 6:45 am	**Yoga**	**Veranda DE**
6:30 am – 7:30 am	**Breakfast**	**Charleston Ballroom**
6:30 am – 7:30 am	**Breakfast with the Novices**	**Charleston 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 – 5:00 pm	**Registration/Help Desk**	**5th floor Registration Desk**
6:30 am – 7:30 am	**NOVEL/Editorial Board/Curriculum Committee Meeting**	**Veranda AB**
7:30 am – 9:30 am	**New Information I Should Know** *Moderators: Christian Lueck, PhD, FRACP, FAAN and Claire Sheldon, MD, PhD*	**Red Rock Ballroom**

There have been enormous advances in neuroimmunology over the last two decades relating to both diagnosis and treatment of disease. For example, novel disease entities such as neuromyelitis optica spectrum disorder (NMOSD), chronic ataxic neuropathy, ophthalmoplegia, IgM monoclonal gammopathy, cold agglutinins and disialosyl antibodies (CANOMAD), and various autoimmune encephalitides have been described. Similarly, there has been an explosion of immunomodulatory therapies and monoclonal antibodies for the treatment of many conditions, some of which are autoimmune (e.g. multiple sclerosis and NMOSD), and some which are not (e.g. migraine). This session will provide an update of neuroimmunology as it relates to the practicing neuro-ophthalmologist. Following an introduction with an approach to the developing field of neuroimmunology, particular topics will include: 1) autoimmune encephalopathies 2) peripheral neuropathies 3) new treatments for multiple sclerosis and 4) novel immunomodulatory therapies for migraine.

Upon completion of this session, participants should be able to: 1) formulate a detailed framework of neuro-immunological disease 2) identify and describe neuroimmune diseases and 3) use immunotherapies appropriately.

7:30 am – 7:42 am	**Neuro-Immunology, a New Specialty - Classifications of Disorders**, *Jeffrey Bennett, MD, PhD*
7:42 am – 8:09 am	**Autoimmune Encephalitis: GFAP, DPPX, Other**, *Eric Eggenberger, DO*
8:09 am – 8:36 am	**Ganglioside-Related Disorders (GQ1b; Miller-Fisher Syndrome; CANOMAD)**, *Umapathi Thirugnanam, MBBS*
8:36 am – 9:03 am	**New Treatments for Multiple Sclerosis**, *Sashank Prasad, MD*
9:03 am – 9:30 am	**New Treatments for Migraine**, *Kathleen Digre, MD*

9:30 am – 10:00 am	**Coffee with Exhibitors** (with support from EMD Serono)	**Charleston Ballroom**
10:00 am – 12:00 pm	**Hot Topics: How do I Treat?** *Moderators: Vivek Patel, MD and Klara Landau, MD*	**Red Rock Ballroom**

This session is designed to provide the audience with a practical, evidence-based discussion of how to manage important clinical scenarios, which are of specific and contemporary interest to the neuro-ophthalmic community. Five "hot topics" will be presented by established experts and thought-leaders for the respective conditions. The chosen topics are important clinical scenarios. As a community, our understanding of how to optimally manage these challenging presentations is currently evolving.

Upon completion of this session, participants should be able to: 1) recognize the various etiologies of headache in IIH patients 2) distinguish MOG positive optic neuritis from other forms of optic neuritis and 3) identify possible treatment options for radiation induced optic neuropathy.

10:00 am – 10:24 am	**Ischemic Optic Neuropathy from GCA**, *Fiona Costello, MD, FRCP*
10:24 am – 10:48 am	**Ocular Myasthenia Gravis**, *Michael Lee*, *MD*
10:48 am – 11:12 am	MOG- IgG **Optic Neuritis**, *John Chen, MD, PhD*
11:12 am – 11:36 am	**Headaches in IIH**, *Deborah Friedman, MD, MPH*
11:36 am – 12:00 pm	**Radiation Optic Neuropathy**, *Norah Lincoff, MD*

12:00 pm – 1:00 pm	**Lunch**	**Charleston Ballroom**
12:00 pm – 1:00 pm	**WIN- LeadHERship: A Call to Thought and Action (lunch provided)**	**Pavilion Ballroom**

Please join the Women in Neuro-Ophthalmology (WIN) for an exciting networking event. Dr. Kimberly Winges will share what she learned through the inaugural NANOS Pilot Grant for Leadership Development, followed by small group discussions regarding leadership and empowerment in the workplace. All are welcome!

1:00 pm – 3:00 pm	**Scientific Platform Session I** *Moderators: Melinda Chang, MD and Timothy J. McCulley, MD*	**Red Rock Ballroom**

1:00 pm – 1:15 pm	**An Epidemiological Study of LHON Using a Large International Sample of Affected Individuals**, *Alexander L. Pearson, BA*
1:15 pm – 1:30 pm	**Neuro-Ophthalmic Manifestations of Collapsin Response- Mediator protein-5 (CRMP5) Autoimmune Neuropathy**, *Devon A. Cohen, MD*
1:30 pm – 1:45 pm	**Associations Between Pattern Electroretinogram and Intra-retinal Layer Thicknesses in Patients Multiple Sclerosis***, Hong Jiang, MD, PhD*
1:45 pm – 2:00 pm	**Presentation of NAION in a Global Treatment Trial**, *Mark J. Kupersmith, MD*
2:00 pm – 2:15 pm	**Characterization of Visual Pathway Abnormalities in Infants with Congenital Zika Syndrome Using CT and MRI***, Amanda D. Henderson, MD*

2:15 pm – 2:30 pm	**A Prospective Outcomes Study of Pediatric Optic Neuritis**, *Stacy Pineles, MD, MS*
2:30 pm – 2:45 pm	**Long-term OCT Follow-up in Children with Optic Disc Drusen**, *Lasse Malmqvist, MD, PhD*
2:45 pm – 3:00 pm	**Progressive Neurodegeneration of the Retinal Nerve Fiber Layer in Veterans with Mild Traumatic Brain Injury**, *Randy H. Kardon, MD, PhD*

3:00 pm – 5:00 pm **YONO Forum** **Pavilion Ballroom**

All are welcome to attend this 2 hour session catering to students, residents, fellows and neuro-ophthalmologists in the early years of their career. The first hour will consist of brief 10 minute prepared talks delivered by knowledgeable speakers in the field of neuro-ophthalmology on topics of interest for aspiring neuro-ophthalmologists and young neuro-ophthalmologists. The next hour will include small group discussions led by these same speakers allowing participants more time to ask questions.

3:15 pm **Optional Excursions (advanced registration required)**
3:15 pm **NANOS Race Car Experience Fundraiser (advanced registration required)**

A once-in-a-lifetime opportunity to ride in a Porsche GT3 Cup race car at the Las Vegas Motor Speedway. Powered by Dr. Preston Calvert, Neuro-Ophthalmologist and professional race car driver. Funds raised at this event will support NANOS educational offerings.

NEURO-IMMUNOLOGY: A NEW SPECIALTY – CLASSIFICATION OF DISORDERS

Jeffrey L. Bennett, MD, PhD
University of Colorado School of Medicine
Denver, CO

LEARNING OBJECTIVES

1. Formulate a schema for categorizing central and peripheral neuro-immunologic disorders.
2. Describe data supporting the roles of cellular and humoral immunity in neuro-inflammatory and neuro-degenerative disorders
3. Enumerate and distinguish treatment strategies for acute and prophylactic therapy of neuro-immunologic disease.

CME QUESTIONS

1. Autoimmune responses in demyelinating and encephalopathic disorders of the nervous system have been described against all of the following except:
    A. synaptic proteins
    B. ion channels
    C. transcription factors
    D. gangliosides
    E. myelin proteins

2. Mechanisms of immunopathology in neuro-immunologic disorders include all of the following except:
    A. complement-mediated cytotoxicity
    B. enhanced synaptic vesicle release
    C. receptor internalization
    D. cell-mediated cytotoxicity
    E. nerve conduction block

3. Prophylactic treatment strategies for neuro-immunologic disorders include all of the following except:
    A. programmed cell death ligand-1 pathway inhibition
    B. B cell depletion
    C. sphingosine 1-phosphate receptor agonists
    D. lymphocyte depletion
    E. complement inhibition

KEYWORDS

1. Neuro-immunology
2. Demyelinating disease
3. Autoimmune encephalopathy
4. Peripheral neuropathy
5. Immunotherapeutics

HIGHLIGHTS

Introduction

Neuro-immunology began as scientific discipline devoted to the study of the intersection of neuroscience and immunology during development, health, and disease. Due to scientific advances, neuro-immunology has also developed into a new neurologic subspecialty dedicated to understanding, diagnosing, and treating patients with immunologic disorders of the central and peripheral nervous systems. Interest in neuro-immunology has been spurred by a new appreciation for immunopathology in degenerative disorders such as Alzheimers disease, Lewy-Body Disorders, amyotrophic lateral sclerosis, and age-related macular degeneration, and the advancement of immunotherapeutics for neurologic disorders. Neuro-immunologic disorders have been classically organized by a combination of clinical, imaging, electrophysiologic, and histopathologic criteria; however, recent advances in auto-antigen discovery have identified disease-specific targets in an expanding array of nervous system disorders. As a result, physicians have gained a new perspective on the clinical presentation, immunopathology, and immunotherapy.

Pathogenic Autoantigens

Initial studies of paraneoplastic neurologic encephalitides identified auto-antibodies against intracellular (onconeural) antigens.[1] Histopathology characteristically shows evidence of T cell cytotoxicity: elevated CD8/CD3 T cell ratios and CD8 T cells adjacent to neurons.[2] In passive transfer animal models, these onconeural autoantibodies fail to produce encephalitis or neuronal destruction. Recently, an increasing number of antibody-associated encephalitides, demyelinating disorders, and peripheral neuropathies have been identified. Autoantibodies in these disorders are targeted against neuronal or glial cell-surface antigens and directly mediate tissue injury through activation of antibody effector function,[3] internalization of cell-surface targets,[4] or disruption of protein interactions.[5] In contrast to onconeural antigens, cell-surface antigens recognized by pathogenic autoantibodies provide potential novel therapeutic targets for non-immunosuppressive therapeutics[6] and immune tolerance.[7,8]

Antigenic Classification of Neuro-immunologic Disorders

The pathogenicity of cell-surface autoantibodies has generated renewed interest in classifying neuro-immunologic disorders based on their antigenic target. This nosologic strategy is supported on clinical, diagnostic, immunologic, and therapeutic grounds.

Clinical Syndromes

Antigen-specific disorders affecting multiple levels of the nervous system tend to have syndromic presentations that facilitate diagnosis. Autoantibodies targeted against the N-methyl-d- aspartate receptor (NMDAR) typically present with the acute onset of neuropsychiatric symptoms.[9] As disease progresses, seizures, dyskinesias, altered consciousness, and autonomic instability emerge. In limbic encephalitides, autoantibody syndromes commonly present with behavioral changes, seizures, and impaired memory formation.[10] Individual anti-neuronal autoantibodies, however, manifest unique constellations of symptoms such as myoclonus, tremors, and hyperekplexia (dipeptidyl-peptidase–like protein 6 [DPPX]), status epilepticus (GABA type A receptor [$GABA_AR$]), and insomnia, ataxia, peripheral nerve hyperexcitability, and neuropathic pain (contactin-associated protein–like-2 [CASPR2]). In demyelinating disorders, clinical presentations such as optic neuritis and transverse myelitis are common; however, protracted nausea, vomiting and hiccups is syndromic of aquaporin-4 autoantibody (AQP4-IgG) seropositive neuromyelitis optica spectrum disorders (NMOSD),[11] whereas acute disseminated encephalomyelitis is pathognomonic for myelin oligodendrocyte glycoprotein autoantibody (MOG-IgG) seropositive encephalomyelitis.[12] Peripheral neuropathy associated with

neuromyotonia, dysautonomia, and pain are syndromic of Morvans syndrome and CASPR2 autoantibodies.[13] And, at the neuromuscular junction, muscle-specific tyrosine kinase (MUSK) antibody-associated myasthenia gravis frequently presents with prominent bulbar and facial weakness, and rarely manifests with ocular myasthenia gravis.[14]

Diagnosis

In most cases, antibody-mediated neuro-immunologic disorders are highly specific. For instance, APQ4-IgG seropositive NMOSD patients are not MOG-IgG seropositive. Similarly, autoimmune encephalitides rarely demonstrate autoantibodies against multiple neuronal surface proteins outside of the setting of paraneoplastic disease where autoantibodies against intracellular onconeural antigens (e.g., Hu, Ma2, GAD65) are commonly observed.[10] On rare occasions, autoimmune demyelinating disorders will develop in association with anti-NMDAR encephalitis resulting in a mixed clinical picture.[15] As a result of their disease specificity, assays to detect anti-neuronal, anti-glial, and anti-ganglioside autoantibodies often yield significant diagnostic power. Assays for many autoantibodies are commercially available; however, there are important considerations to address in assay design, use, and interpretation. Cell binding assays are considered the gold standard for detection of autoantibodies against cell-surface neuronal and glial proteins; nevertheless, many labs perform enzyme-linked immunosorbent assays (ELISA), radioimmunoprecipitation assays (RIPA), or fluorescence immunoprecipitation assays (FIPA) for certain targets. For certain antigens, such as AQP4, ELISA, RIPA, and FIPA assays may have reduced sensitivity and specificity.[16] CSF should be examined for autoantibodies in all cases of presumed encephalitis, especially anti-NMDAR encephalitis, where some patients may have exclusively CSF autoantibodies.[10] In patients with mixtures of autoantibodies, the antigen targeted in the CSF typically determines the clinical presentation. Low positive assays for voltage-gated potassium channels are notoriously non-specific and should be confirmed with testing for antibodies against CASPR2 and leucine-rich glioma-inactivated-1 (LGI1); in general, titers are non-informative for anti-neuronal and anti-glial autoantibodies. Assays for anti-ganglioside antibodies may pose additional concerns due to antigen purity, assay methods (individual gangliosides vs. complexes), and variability in normal ranges.[17]

Immunology

There are multiple mechanisms through which autoantibodies may contribute to neurologic injury: complement-mediated cytotoxicity (CDC), antibody-dependent cell-mediated cytotoxicity (ADCC), antibody-dependent cell-mediated phagocytosis (ADCP), cross-linking and internalization of receptors, disruption of protein-protein interaction, and receptor blockade.[2,3,17,18] The pathologic mechanisms are determined by the nature of the target antigen, organization of the target antigen within the cell membrane, epitope specificity, and access to complement factors and effector cells. For instance, AQP4 is organized into large membrane arrays that are ideal for CDC; whereas NMDAR dissociated from ephrin-B2 receptors are rapidly internalized resulting in disrupted neuronal transmission. Voltage-gated calcium channel antibodies block signaling in presynaptic neurons resulting in diminished synaptic vesicle release in Lambert-Eaton myasthenic syndrome, and GABA type B receptor ($GABA_BR$) autoantibodies block ligand binding causing limbic encephalitis. In demyelinating polyneuropathies, nerve biopsies have revealed immune cell infiltration as well as immunoglobulin and complement deposition, suggestive of ADCC/ADCP and CDC, respectively. In myasthenia gravis (MG), membrane attack complexes resulting from CDC are deposited at the neuromuscular junction. In some disorders with neurologic and neuro-ophthalmologic injuries, the role of autoantibodies remains uncertain. Amongst these conditions, cerebral amyloid angiopathy related inflammation (CAA-RI) is particularly intriguing. Histopathology in CAA-RI may demonstrate perivascular inflammation (inflammatory CAA) or transmural granulomatous destruction (amyloid-beta-related angiitis).[19] In amyloid-beta-related angiitis, amyloid-β deposits co-localize with areas of inflammation suggesting a targeted immune response.[19]

Therapeutics

Identifying the role of specific autoantibodies in various neuro-immunologic disorders has allowed investigators to begin to model the immunopathology driving neuronal injury. Plasma exchange (PLEX) has emerged as an important intervention in the acute care of autoimmune encephalopathies, NMOSD, MG, and severe demyelinating lesions due to MOG encephalomyelitis. In addition to depleting the titer of pathogenic autoantibodies, PLEX may reduce circulating proinflammatory cytokines and thereby alter immune cell phenotypes.[20] The prominent role of CDC in MG and NMOSD injury has led to clinical trials of eculizumab, a humanized monoclonal antibody that inhibits the cleavage of complement C5 into C5a and C5b, blocking both the classical and alternative pathways (NCT01892345). Eculizumab has already been approved by the FDA for treatment of refractory MG,[21] and is under review for use in NMOSD. The clinical success of IVIg in treating neurologic injury in MG, acute inflammatory demyelinating polyneuropathies, and NMOSD may be due in part to its inhibition of ADCC and ADCP.[22] A common immunotherapeutic employed for the care of patients with antigen-targeted neuro-immunologic disorders is rituximab, an anti-CD20 monoclonal antibody targeting mature B cells from the transitional to plasmablast stage. While the intended strategy was to reduce circulating autoreactive antibodies, the efficacy of rituximab may likely lie with its ability to modulate other pro-inflammatory B cell activities.[23]

SUMMARY

As we begin to understand the immunopathologies driving disease activity in acute and chronic neuro-immunologic disorder, we are likely to have a panoply of agents to interrupt key steps in neuro-immunologic disease: antigen presentation, immune cell signaling, immune cell trafficking to the central nervous system, blood-brain barrier derangement, autoantigen engagement, cytotoxic injury, and antibody-mediated effector functions. With these goals in mind, targeted immunotherapeutics are already in clinical trials or approved for use in disorders as varied as migraine and multiple sclerosis. Enhancing immune activity for therapeutic purposes, however, may have unintended consequences, such as autoimmunity with immune checkpoint inhibitors (antibodies to programmed death-1, PD-ligand-1, and cytotoxic T lymphocytes-associated antigen 4)[24] and amyloid angiitis with amyloid-β immunotherapies.[25]

CME ANSWERS

1. C
2. B
3. A

REFERENCES

1. Darnell RB, Posner JB. Paraneoplastic syndromes involving the nervous system. N Engl J Med 349:1543-1554, 2003
2. Bien CG, Vincent A, Barnett MH, et al. Immunopathology of autoantibody-associated encephalitides: clues for pathogenesis. Brain 135: 1622-1638, 2012
3. Ratelade J, Asavapanumas N, Ritchie AM, Wemlinger S, Bennett JL, Verkman AS. Involvement of antibody-dependent cell-mediated cytotoxicity in inflammatory demyelination in a mouse model of neuromyelitis optica. Acta Neuropathol 126: 699-709, 2013
4. Hughes EG, Peng X, Gleichman AJ, et al. Cellular and synaptic mechanisms of anti-NMDA receptor encephalitis. J Neurosci 30: 5866-5875, 2010

5. Ohkawa T, Fukata Y, Yamasaki M, et al. Autoantibodies to epilepsy-related LGI1 in limbic encephalitis neutralize LGI1-ADAM22 interaction and reduce synaptic AMPA receptors. J Neurosci 33: 18161-18174, 2013.
6. Tradtrantip L, Zhang H, Saadoun S, et al. Anti-aquaporin-4 monoclonal antibody blocker therapy for neuromyelitis optica. Ann Neurol 71: 314-322, 2012
7. Bar-Or A, Steinman L, Behne JM, et al. Restoring immune tolerance in neuromyelitis optica: Part II. Neurol Neuroimmunol Neuroinflamm 3: e277, 2016
8. Steinman L, Bar-Or A, Behne JM, et al. Restoring immune tolerance in neuromyelitis optica: Part I. Neurol Neuroimmunol Neuroinflamm 3: e276, 2016
9. Titulaer MJ, McCracken L, Gabilondo I, et al. Treatment and prognostic factors for long-term outcome in patients with anti-NMDA receptor encephalitis: an observational cohort study. Lancet Neurol 12: 157-165, 2013.
10. Graus F, Titulaer MJ, Balu R, et al. A clinical approach to diagnosis of autoimmune encephalitis. Lancet Neurol 15: 391-404, 2016
11. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology 85: 177-189, 2015.
12. Jarius S, Paul F, Aktas O, et al. MOG encephalomyelitis: international recommendations on diagnosis and antibody testing. J Neuroinflammation 15: 134, 2018
13. Irani SR, Pettingill P, Kleopa KA, et al. Morvan syndrome: clinical and serological observations in 29 cases. Annals of neurology 72: 241-255, 2012
14. Lavrnic D, Losen M, Vujic A, et al. The features of myasthenia gravis with autoantibodies to MuSK. J Neurol Neurosurg Psychiatry 76: 1099-1102, 2005
15. Titulaer MJ, Hoftberger R, Iizuka T, et al. Overlapping demyelinating syndromes and anti-N-methyl-D-aspartate receptor encephalitis. Annals of neurology 75: 411-428, 2014
16. Waters P, Pittock S, Bennett J, Jarius S, Weinshenker B, Wingerchuk D. Evaluation of aquaporin-4 antibody assays. Clin Exp Neuroimmunol doi: 10.1111/cen3.12107, 2014
17. Willison HJ, Yuki N. Peripheral neuropathies and anti-glycolipid antibodies. Brain 125: 2591-2625, 2002
18. Dalmau J, Graus F. Antibody-Mediated Encephalitis. N Engl J Med 378: 840-851, 2018
19. Moussaddy A, Levy A, Strbian D, Sundararajan S, Berthelet F, Lanthier S. Inflammatory Cerebral Amyloid Angiopathy, Amyloid-beta-Related Angiitis, and Primary Angiitis of the Central Nervous System: Similarities and Differences. Stroke 46: e210-213, 2015
20. Reeves HM, Winters JL. The mechanisms of action of plasma exchange. British journal of haematology 164: 342-351, 2014
21. Howard JF, Utsugisawa K, Benatar M, et al. Safety and efficacy of eculizumab in anti-acetylcholine receptor antibody-positive refractory generalised myasthenia gravis (REGAIN): a phase 3, randomised, double-blind, placebo-controlled, multicentre study. Lancet neurology 16: 976-986, 2017
22. Anthony RM, Wermeling F, Ravetch JV. Novel roles for the IgG Fc glycan. Annals of the New York Academy of Sciences 1253: 170-180, 2012
23. Bennett JL, O'Connor KC, Bar-Or A, et al. B lymphocytes in neuromyelitis optica. Neurol Neuroimmunol Neuroinflamm 2: e104, 2015
24. Michot JM, Bigenwald C, Champiat S, et al. Immune-related adverse events with immune checkpoint blockade: a comprehensive review. Eur J Cancer 54: 139-148, 2016
25. Boche D, Zotova E, Weller RO, et al. Consequence of Abeta immunization on the vasculature of human Alzheimer's disease brain. Brain 131: 3299-3310, 2008

AUTOIMMUNE ENCEPHALITIS: GFAP, DPPX, OTHER NEW AUTOIMMUNE SYNDROMES

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LEARNING OBJECTIVES

1. Distinguish the newly-described varieties of autoimmune encephalitis
2. Describe and evaluate the role of antibodies in the diagnosis of autoimmune encephalitis in clinical practice
3. Recognise the clinical features and apply appropriate treatment options for autoimmune encephalitis

CME QUESTIONS

1. Clinical features of anti-NMDA receptor antibody syndrome include which of the following:
    A. Psychiatric symptoms, alterations in consciousness and dyskinesia
    B. INO, Ptosis, diplopia, facial palsy and myoclonus
    C. Memory deterioration, faciobrachial dystonic, psychiatric symptoms and hyponatremia
    D. GI symptoms with weight loss, cognitive change, and CNS hyperexcitability
    E. Urticaria, epilepsy and visual loss

2. Clinical features of DPPX (dipeptidyl-peptidase-like protein 6) antibody syndrome include which of the following:
    A. Psychiatric symptoms, alterations in consciousness and dyskinesia
    B. Memory deterioration, faciobrachial dystonic, psychiatric symptoms and hyponatremia
    C. Urticaria, epilepsy and visual loss
    D. GI symptoms with weight loss, cognitive change, and CNS hyperexcitability
    E. Gait apraxia, incontinence and myoclonus

3. LGI1-antibody syndrome typically presents with which of the following clinical features:
    A. Psychiatric symptoms, alterations in consciousness and dyskinesia
    B. Dysarthria, dysphasia and dementia
    C. Memory deterioration, faciobrachial dystonic, psychiatric symptoms and hyponatremia
    D. INO, Ptosis, diplopia, facial palsy and myoclonus
    E. GI symptoms with weight loss, cognitive change, and CNS hyperexcitability

KEYWORDS

1. Autoimmune encephalitis
2. NMDA receptor
3. LGI1
4. DPPX
5. Herpes simplex

HIGHLIGHTS

Paraneoplastic (classic) vs autoimmune encephalitis

Paraneoplastic (classic) encephalitis syndromes are commonly associated with, but often present before the diagnosis of, an underlying neoplasm, most commonly small cell lung cancer (SCLC), lymphoma, thymoma or various other neoplasms. These are T-cell medicated diseases that rapidly produce neuronal dysfunction that is usually irreversible; the syndromic antibody is typically not pathogenic. In contrast, the more recently described autoimmune encephalitis syndromes are associated with pathogenic antibodies that target cell surface or synapse proteins, are less commonly associated with an underlying neoplasm, and are much more treatment-responsive than the "paraneoplastic" category. The rate of these autoimmune encephalitidies appears to be increasing over time.

Specific syndromes and antibodies

N-methyl-D-aspartate (NMDA)

Ab: IgG antibody to GluN1 (AKA NR1) subunit of NMDA receptor
Symptoms: NMDA Ab syndrome is the prototype for the newer neuronal surface autoimmune encephalitis group. NMDA Ab syndrome presents with *neuropsychiatric* behavioral symptoms including psychosis and cognitive decline, progressing to *autonomic* features, frequent *dyskinesia* commonly involving *oral-facial movements*, seizures, autonomic instability, language change, and, potentially coma. The syndrome is most common in woman and younger children, with some patients presenting in infancy.
Neuro-ophthalmic interest: In a case series, Brandt et al. noted mild reduction in visual acuity among patients after NMDA encephalitis compared to controls (logMAR 0.02 vs -0.09); however, there was no difference in OCT measures. The opsoclonus-myoclonus syndrome has rarely been described.
Ancillary: CSF usually has a lymphocytic pleocytosis. CSF anti-NMDA antibodies are highly sensitive and specific. EEG may document epileptic activity, and MRI may be normal or show transient FLAIR or non-enhancing cortical abnormalities in varied locations.
Association: ovarian teratoma (50% of adult females with NMDA Ab syndrome)
Treatment: methylprednisone + IVIG or PLEX

DPPX

Ab: antibody to dipeptidyl-peptidase-like protein 6 (DPPX6) (previously thought to be VGKC Ab)
Symptoms: Rapid *encephalopathy* with cognitive dysfunction, *CNS hyperexcitability* manifest as agitation, myoclonus and seizures; although the disease commonly causes GI symptoms including diarrhea with attendant *weight loss*, it is not associated with underlying cancer in most patients.

GFAP

Ab: glial fibrillary acidic protein (GFAP)
Symptoms: Meningo-encephalomyelitis with headache, optic disc edema, postural tremor and cerebellar ataxia with a distinct MRI appearance including linear perivascular radial enhancement extending peripherally from the ventricles or cerebellum. Approximately 30% of patients have an underlying neoplasm, potentially involving ovary, prostate or gastrointestinal tract.

Leucine rich glioma inactivated 1/LGI1

Ab: previously this was attributed to voltage gated potassium channel Ab (VGKC)
Symptoms: Patients with anti-leucine-rich glioma inactivated 1 limbic encephalitis present with a classic limbic encephalitis picture; many patients also experience distinct, short faciobrachial dystonic seizures.

Associated features may include hyponatremia and REM behavioral disorders. The MRI picture often demonstrates mesial temporal hyperintensity, and most patient do not harbor an underlying neoplasm.

GAD

Ab: glutamic acid decarboxylase (GAD) Ab
Symptoms: This syndrome is associated with varied phenotypes, including stiff person syndrome, cerebellar ataxia, seizures, limbic encephalitis, in addition to the common linkage with diabetes type 1.

Pathogenesis of autoimmune encephalitis

Although a post-infectious pathophysiology has been suspected, it was not until the report of the Spanish Herpes Simplex Encephalitis Study Group that more firm evidence in this regard came to light. These authors reviewed the data from 51 cases of herpes simplex encephalitis and found that 27% of this cohort developed symptomatic anti-neuronal antibodies with autoimmune encephalitis within approximately 1 month of their original illness. This included 64% anti-NMDA and 36% other neuronal antibodies. It appears very likely that many such clinical relapses are misdiagnosed as viral in origin

SUMMARY

Management

Evaluation. A thorough search for autoimmune antibodies in serum and CSF is mandatory. This is an ever-increasing, dynamic field, and clinicians should review the specific list of antibodies contained within their institution's panel surveys to be sure that all possible syndromes of interest are interrogated.

MRI brain and EEG are often obligatory components of evaluation depending upon the presentation.

Treatment. Appropriate therapy for any underlying neoplasm if applicable is important – the association between NMDA receptor Ab syndrome and teratoma is a classic example. Immunotherapy should be initiated at diagnosis rather than waiting for confirmation of an underlying neoplasm. This usually takes the form of corticosteroids and either IVIG or plasma exchange. Second line therapy may consist of rituximab or cyclophosphamide.

CME ANSWERS

1. A
2. D
3. C

REFERENCES

1. Hara M, Arino H, Petit-Pedrol M, et al. DPPX antibody-associated encephalitis. Main syndrome and antibody effects. Neurology 88: 1340-1348, 2017
2. Brandt AU, Oberwahrenbrock T, Mikolajczak J, et al. Visual dysfunction, but not retinal thinning, following anti-NMDA receptor encephalitis. Neurol Neuroimmunol Neuroinflamm 3: 198, 2016
3. Gelfand J. Autoimmune encephalitis after herpes simplex encephalitis: insights into pathogenesis. Lancet Neurology 17; 733-5, 2018

4. Armangue T, Spatola M, Vlagea A, et al. Frequency, symptoms, risk factors and outcomes of autoimmune encephalitis after herpes simplex encephalitis: a prospective observational study and retrospective analysis. Lancet Neurology 17: 760-72, 2018
5. Dubey D, Pittock SJ, Kelly CR, et al. Autoimmune encephalitis epidemiology and a comparison to infectious encephalitis. Ann Neurol 83: 166-177, 2018
6. Pittock SJ, Yoshikawa H, Ahlskog E, et al. Glutamic acid decarboxylase autoimmunity with brainstem, encephalitis, and spinal cord dysfunction. Mayo Clin Proc 81: 1207-1214, 2006

GANGLIOSIDE-RELATED DISORDERS (GQ1b; MILLER FISHER SYNDROME; CANOMAD)

(A Kabuki dance of masked microbiological villains, deceptions, mistaken identities and fratricide)

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LEARNING OBJECTIVES

1. Explain the role of ganglioside-related antibodies in the pathogenesis of peripheral neuropathies
2. Describe the immunopathology of the paranodal ion channels in peripheral nerves
3. Describe and differentiate the treatment options available for these conditions

CME QUESTIONS

1. Anti-GQ1b antibody is associated with all of the following syndromes EXCEPT:
    A. Acute inflammatory demyelinating polyneuropathy
    B. Acute ophthalmoplegia
    C. Bickerstaff encephalitis
    D. CANOMAD
    E. Miller Fisher syndrome

2. Each of the following "clinical pearls" related to Miller Fisher syndrome is true EXCEPT:
    A. Being a limited form of Guillain-Barre syndrome, Miller Fisher syndrome is not associated with a significant risk of respiratory compromise.
    B. Gaze-evoked horizontal nystagmus is not a prominent sign in Miller Fisher syndrome.
    C. In a patient with acute complex ophthalmoplegia without an apparent cause, it is reasonable to consider a *forme fruste* of Miller Fisher syndrome and check for the presence of anti-GQ1b antibody.
    D. In a patient with Miller Fisher syndrome resulting in complete III, IV, VI ocular motor palsies, there may be no associated pupillary involvement.
    E. In the diagnosis of Miller Fisher syndrome, the presence of anti-GQ1b antibody is a more sensitive and specific test than either nerve conduction study or spinal fluid analysis.

3. Antibodies against the paranodal-juxtaparanodal antigens are associated with all the following conditions EXCEPT:
    A. Chronic inflammatory demyelinating polyneuropathy
    B. Morvan's syndrome
    C. Neuromyotonia (Isaac's syndrome)
    D. Stiff person syndrome
    E. Voltage-gated K-channel antibody-associated limbic encephalitis

KEYWORDS

1. Demyelinating peripheral neuropathy
2. Miller Fisher syndrome
3. Guillain-Barré syndrome
4. CANOMAD

5. Anti-ganglioside antibodies

HIGHLIGHTS

Molecular mimicry between microbiologic agents and endogenous antigens that triggers dysimmunity has been well delineated in Guillain–Barré syndrome (GBS).[1] The lipopolysaccharide (LPS) capsule of *Campylobacter jejuni* carries moieties that resemble gangliosides that are enriched in the nodal regions of nerves. The LPS configuration of the infecting bacteria and the immune constitution of the host determine the type of anti-ganglioside antibodies that are produced. The patients develop different subtypes of GBS contingent on the target of these antibodies. Miller Fisher syndrome and acute ophthalmoparesis are both associated with anti-GQ1b antibody. GQ1b is strongly expressed in the oculomotor, trochlear and abducens nerves, as well as muscle spindles in the limbs (the latter explaining the limb ataxia).[2,3] Likewise, the acute motor axonal neuropathy form of GBS is associated with antibodies against GM1 and GD1a, antigens found in motor and sensory nerves. The immune attack, directed at the gangliosides in the nodal region, causes collateral damage to nearby sodium channels that are responsible for generating the current required for node–to-node saltatory conduction.[4] The patient recovers quickly if this conduction failure is reversed promptly. If the immune injury is severe and the axolemma is damaged, Wallerian degeneration occurs with attendant poor and delayed recovery. Treatment with immunoglobulins and plasma exchange hastens recovery. Not surprisingly, since complement activation plays an important role in GBS immunopathology, the complement inhibitor, eculizumab, has recently been shown to have adjunctive effects in its treatment.[5]

Other paranodal and juxtaparanodal antigens include contactin 1 (CNTN1), and contactin-associated protein 1 (Caspr1). Non-complement binding IgG4 antibodies against these antigens have recently been implicated in the pathogenesis of subgroups of chronic inflammatory demyelinating polyneuropathy (CIDP).[6] These patients often do not respond to standard immunotherapy, but respond well to B-lymphocyte depleting therapy, namely Rituximab.

SUMMARY

The elucidation of immunopathology at the nodal and paranodal regions of peripheral nerves, so called nodopathy-paranodopathy,[7] is likely to open up new avenues of investigation into other immunological diseases[8] linked to similar antibodies. Examples include autoimmune limbic encephalitis and epilepsy (both associated with leucine-rich glioma inactivated 1protein, LGI1, of the voltage-gated potassium channel complex, VGKC), Morvan's syndrome (associated with Caspr2 antibody), Isaacs' syndrome-neuromyotonia (associated with VGKC antibody), Bickerstaff encephalitis (associated with GQ1b antibody) and CANOMAD (chronic, ataxia, neuropathy, ophthalmoplegia, M protein, agglutination, and associated with disialosyl GD1b ganglioside antibodies). Neuro-ophthalmologists may well encounter these conditions so it is helpful to have some familiarity with them.

<u>A Haiku in a Kabuki</u>
Kabuki (歌舞伎) dance
Sing (歌), dance (舞), skill (伎), masked villain
Seduced to fratricide.

Sialated ganglioside,
NOT LPS armoured C-jejuni
Halt antibodies!

CME ANSWERS

1. A
2. A
3. D

REFERENCES

1. Yuki, N. Ganglioside mimicry and peripheral nerve disease. Muscle Nerve 35: 691–711, 2007.
2. Chiba A, Kusunoki S, Obata H, et al: Serum anti-GQ1b IgG antibody is associated with ophthalmoplegia in Miller Fisher syndrome and Guillain-Barré syndrome:clinical and immunohistochemical studies. Neurology 43:1911-7, 1993.
3. Liu JX, Willison HJ, Pedrosa-Liu JX, et al: Immunolocalization of GQ1b and related gangliosides in human extraocular neuromuscular junctions and muscle spindles. Invest Ophthalmol Vis Sci 50:3226-32, 2009
4. Susuki, K., Rasband, M.N., Tohyama, K., et al.: Anti-GM1 antibodies cause complement-mediated disruption of sodium channel clusters in peripheral motor nerve fibers. J. Neurosci. 27, 3956–3967, 2007.
5. Davidson AI, Halstead SK, Goodfellow JA, et al: Inhibition of complement in Guillain-Barré syndrome: the ICA-GBS study. J Peripher Nerv Syst. 22:4-12, 2017.
6. Querol L, Devaux J, Rojas-Garcia R et al.:Autoantibodies in chronic inflammatory neuropathies: diagnostic and therapeuticimplications. Nat Rev Neurol.13:533-547, 2017.
7. Uncini A, Vallat J-M.Autoimmune nodo-paranodopathies of peripheral nerve: the concept is gaining ground. J Neurol Neurosurg Psychiatry 89:627–635, 2018
8. Graus F, Titulaer MJ, Balu R, et al: A clinical approach to diagnosis of autoimmune encephalitis. Lancet Neurol. 15:391-404, 2016

NEW TREATMENTS FOR MULTIPLE SCLEROSIS

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LEARNING OBJECTIVES

1. Describe and evaluate the new, highly-effective infusion therapies for MS, including rituximab, ocrelizumab, and alemtuzumab
2. Appraise therapies in development, including cell-based therapies and siponimod
3. Describe and compare recent developments in neuroprotection, including anti-Lingo, clemastine, and high-dose biotin

CME QUESTIONS

1. True or False: Rituximab currently has US FDA approval for treatment of MS?
2. True or False: No disease-modifying therapy currently has US FDA approval for the treatment of primary-progressive MS?
3. True or False: No disease-modifying therapy currently has US FDA approval for the treatment of secondary-progressive MS?

KEYWORDS

1. Multiple Sclerosis
2. Rituximab
3. Alemtuzumab
4. Siponimod
5. Ocrelizumab

HIGHLIGHTS

1. Ocrelizumab is a fully humanized anti-CD20 monoclonal antibody approved for RRMS and PPMS.
2. Siponimod is a sphingosine 1 receptor antagonist, like fingolimod, that is under investigation and may show benefit in SPMS.
3. Other immunomodulatory treatments that have been recently evaluated include alemtuzumab, cladribine, and stem cell transplantation.
4. In addition to immunomodulatory disease modifying drugs other 're-myelination' strategies including opicinumab, clemastine, and high dose biotin, have been recently studied.

SUMMARY

The era of disease modifying therapy for Multiple Sclerosis (MS), which began with ACTH in the 1950s, has truly accelerated in the past 2 decades. Neuro-ophthalmologists should be aware of the important recent therapeutic advances that will impact their patients with MS.

Ocrelizumab is a recently approved drug for the treatment of relapsing remitting MS (RRMS), based on results from a placebo-controlled trial and a head-to-head trial with injectable interferon beta-1a.[1,2] Ocrelizumab became the first drug to obtain FDA approval for primary progressive MS (PPMS) as well, where it is probably most effective in younger patients with active enhancing MRI lesions. It is a fully humanized anti-CD20 monoclonal antibody that depletes B cells. It is related to rituximab, which is a murine antibody with the same target that has also shown efficacy in treatment of MS but is used off-label in the US without regulatory approval.

Alemtuzumab is another MS treatment that has been recently developed.[3]It is an anti-CD52 antibody that depletes T and B cells, and it has been used in the treatment of CLL and other hematologic malignancies. In the past 5 years, it became approved for treatment of MS in both Europe and the US. Its use is limited by toxicities that include immune-mediated thrombocytopenia, thyroiditis, and nephritis.

Several other disease-modifying treatments may also emerge soon. Cladribine is a purine analogue that targets B cells more than T cells. It is an oral formulation taken for short durations that is currently approved in Europe, but not in the US.[4] Cell-based therapy for MS, such as stem cell transplantation, is a treatment offered in some centers, but the associated mortality has generally prevented wider acceptance.[5] Siponimod is a sphingosine 1 receptor antagonist, like fingolimod, that has shown promising data that may lead to regulatory approval soon.[6] Of note, it may show benefit in secondary progressive MS (SPMS), which is a stage of the disease that has been very challenging to treat effectively.

In addition to long-term disease-modifying therapies and acute treatments for relapses, other drugs have been developed with the aim of so-called 'neuroprotection.' The potential effects of opicinumab (anti-LINGO-1) have been difficult to fully assess in existing trials[7] and further studies are ongoing. Clemastine is an older molecule that has shown some positive effects after acute optic neuritis relating to MS.[8] Finally, high dose biotin has reportedly shown significant improvement of deficits in a subgroup of patients.[9]

There is a long tradition of neuro-ophthalmologists playing an important role in the field of MS. As treatment strategies for MS continue to evolve quickly, it is as important as ever for neuro-ophthalmologists to contribute their expertise evaluating the visual system to judge the effects of newer drugs, both in in the care of individual patients and in the context of clinical trials for the MS population in general.

CME ANSWERS

1. False
2. False
3. True

REFERENCES

1. Hauser SL Bar-Or A, Comi G, et al. Ocrelizumab versus Interferon Beta-1a in Relapsing Multiple Sclerosis. N Engl J Med 376(3): 221-234, 2017
2. Montalban X, Hauser SL, Kappos L. Ocrelizumab versus Placebo in Primary Progressive Multiple Sclerosis. N Engl J Med 376(3): 209-220l, 2017

3. CAMMS223 Trial Investigators. Alemtuzumab vs. interferon beta-1a in early multiple sclerosis. N Engl J Med 359(17): 1786-801, 2008
4. Giovannoni G, Comi G, Cook S, et al. A placebo-controlled trial of oral cladribine for relapsing multiple sclerosis. N Engl J Med 362(5): 416-26, 2010
5. Scolding NJ, Pasquini M, Reingold SC, et al. Cell-based therapeutic strategies for multiple sclerosis. Brain 140(11): 2776-2796, 2017
6. Kappos L, Bar-Or A, Cree BAC, et al. Siponimod versus placebo in secondary progressive multiple sclerosis (EXPAND): a double-blind, randomised, phase 3 study. Lancet 391(10127): 1263-1273, 2018
7. Cadavid D, Balcer L, Galetta S. Safety and efficacy of opicinumab in acute optic neuritis (RENEW): a randomised, placebo-controlled, phase 2 trial. Lancet Neurol 16(3):189-199, 2017
8. Green AJ, Gelfand JM, Cree BA, et al. Clemastine fumarate as a remyelinating therapy for multiple sclerosis (ReBUILD): a randomised, controlled, double-blind, crossover trial. Lancet 390(10111): 2481-2489, 2017
9. Tourbah A, Lebrun-Frenay C, Edan G, et al. MD1003 (high-dose biotin) for the treatment of progressive multiple sclerosis: A randomised, double-blind, placebo-controlled study. Mult Scler 22(13): 1719-1731, 2016

NEW TREATMENTS FOR MIGRAINE

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LEARNING OBJECTIVES

1. Describe current concepts of migraine pathophysiology
2. Describe and distinguish the role of CGRP receptor antagonists and monoclonal anti-CGRP and PACAP receptor antibodies in the treatment of migraine
3. Review the role of devices in the treatment of migraine

CME QUESTIONS

1. True or False: CGRP is the only neuropeptide released in significant quantities during the headache phase of migraine attacks.

2. Which of the following was the first non-peptide CGRP receptor antagonist to be discovered?
    A. Atogepant
    B. Olcegepant
    C. Sumatriptan
    D. Telcagepant
    E. Ubrogepant

3. Which of the following is an antibody directed against the CGRP receptor?
    A. Eptinezumab
    B. Erenumab
    C. Fremanezumab
    D. Galcanezumab
    E. Ocrelizumab

KEYWORDS

1. Migraine
2. Calcitonin gene-related peptide
3. CGRP receptor antagonists
4. CGRP monoclonal antibodies
5. Device therapies for migraine

HIGHLIGHTS

Migraine is very common—more common than diabetes and asthma combined. It affects almost 20% of women and 10% of men, and will make up a large number of people visiting a neuro-ophthalmology clinic. The World Health Organization has listed migraine in the top 10 most disabling conditions. Keeping up with advances in migraine pathophysiology and treatment is almost a full-time job, but every

neuro-ophthalmologist must know about these new advances in treatment since individuals will be requesting medication or presenting with migraine in the neuro-ophthalmology clinic.

1. Introduction: migraine and some of the current concepts of pathophysiology and therapeutic targets.

Migraine has a complex pathophysiology which most believe involves both central and peripheral nervous systems. There appears to be a physiology for each phase of a migraine attack: prodrome, acute aura and/or headache, and postdrome. The trigeminal vascular system is activated in an acute migraine attack. This system includes the trigeminal nuclei in the brain stem, the trigeminal ganglia and especially the ophthalmic division of V that innervates blood vessels and subserves pain in the meninges. When this pathway is activated it releases neuropeptides such as Calcitonin Gene-Related Peptide (CGRP), substance P, and pituitary adenylate cyclase-activating peptide (PACAP). Levels of CGRP and PACAP are increased during a migraine attack and both of these peptides can cause a migraine-like headache.

One of the most important advances in the last 10 years is the focus on CGRP—an important neurotransmitter which is involved in the migraine process. CGRP is expressed in neurons in both central and peripheral nervous systems and is dispersed widely in the nervous system (e.g. cortex, hippocampus, cerebellum, thalamic nuclei, brain-stem nuclei). CGRP is also released when the trigeminal nerve is activated.

What is the evidence that CGRP is involved in migraine? First, infusing CGRP can precipitate a migraine in those with migraine. Blocking CGRP can relieve a migraine. CGRP is released by stimulating the trigeminal ganglion and there are elevated blood levels during an attack. The receptor for CGRP is located in all sites that have been implicated in migraine pathogenesis, including: cortex, thalamus, brain stem, nucleus tractus solitarius, and trigeminal and dorsal root ganglia among others. CGRP itself is a vasodilator.

The CGRP receptor was characterized by Lars Edvinsson and Peter Goadsby who recognized the importance of the CGRP receptor and molecule.

The CGRP receptor antagonists that were studied were olcegepant (really the first to be studied, given IV, and found to work as well as triptans), and then telcagepant (an oral preparation)—hence the 'Gepants' were born. They were found to not have significant adverse events like vasoconstriction. In the early studies done in 2004 (mainly in Europe) telcagepant was found to be both very effective and without many side effects. However, due to liver toxicity further studies of telcagepant were aborted for a period of time. It was subsequently found that the medication itself was not toxic but that its metabolites were.

The Gepants are now being developed as acute migraine therapies for treatment of episodic migraine. The benefit of the Gepants over the triptans include: no evidence of any vasoconstriction—though they can prevent vasodilation. They are also very well tolerated. They are all oral formulations. All trials are monitoring for elevated liver function tests. The problem in the liver is related to the metabolism of the molecule and not related to direct toxicity of the drug itself.

2. Advances in acute migraine therapy

Acute treatment of migraine includes ergots, triptans, and nonsteroidal anti-inflammatory drugs. Triptans have been the evidence-based acute therapy for migraine for the last 20 years. They include: sumatriptan, naratriptan, rizatriptan, zolmitriptan, eletriptan almotriptan, and frovatriptan. These FDA-

approved drugs affect serotonin and have proven efficacy in the acute treatment of migraine. Each medication has various formulations—all are tablets, but some are injectable (sumatriptan), nasal spray (sumatriptan, zolmitriptan), or melt (rizatriptan). Most are short acting, while naratriptan and frovatriptan are longer acting. All are contraindicated in coronary artery disease, uncontrolled hypertension and Prinzmetal's angina because of their unwanted vasoconstrictive properties. The triptans also inhibit CGRP by inhibiting release of the chemical.

The Gepants, which have not yet been released, will likely play a major role in the acute treatment of migraine since there is no evidence that they cause vasoconstriction so they can probably be used in the groups that cannot use triptans, or do not respond to triptans.

Gepant	**Studies done (phase)**	**Reported efficacy (pain freedom (PF)/most bothersome symptom (MBS)**	**Side-effects reported**
Ubrogepant 50mg, 100 mg (acute treatment of migraine)	Phase 2, phase 3 (x2 studies) ACHIEVE 1 study	50 mg 19.2% PF at 2 hours; 100 mg 21.2% PF vs placebo 11.8% MBS: 50 mg 27.8% , 100 mg 38.6% vs placebo 37.7%	Nausea, somnolence, dry mouth in less than 5%
Rimegepant 75 mg (acute treatment of migraine)	Phase 2, phase 3	Pain free 75 mg 19.2 % vs placebo 14.2% MBS 36.6% vs placebo 27.7% PF: 66% vs 47% placebo Sustained PF: 52.9% rimegepant vs 36.1%placebo	Nausea less than 2%
Telcagepant 300 mg (acute treatment of migraine)	Randomized trials in Europe; First GEPANT in phase 3 trials but liver toxicity led to its being abandoned	PF 2 hours: 26% vs 10% placebo	
Atogepant (also being studied for migraine prevention)	Trials underway		

3. **Advances in Migraine Prevention**

This is really important. When migraines are too frequent, or too severe for treatment, prevention is indicated. Many medications have been used to prevent migraine including beta-blockers, calcium channel blockers, tricyclic antidepressants, and anti-convulsants (notably topiramate and valproate). Onabotulinum toxin was approved for prevention of chronic migraine and this really was the first drug approved for that disorder.

Onabotulinum toxin was approved by the FDA for chronic migraine in 2010 based on two randomized phase 3 trial--PREEMT. The drug was not effective for episodic migraine but received approval for chronic migraine. Onabotulinum toxin may affect the release of many different neurotransmitters: CGRP, substance P, serotonin, glutamate, gamma-aminobutyric acid (GABA), noradrenaline, dopamine, encephalin, and glycine It may also affect pain receptors like TRPV1, TRP1a, GABA A, and even opioid

receptors. The major study that showed that Botulinum was better than placebo was the PREEMPT study. Adverse events were mild—including neck pain, injection site pain. It was not effective in tension type headache or episodic migraine.

With the advent of monoclonal antibodies for disease modification, CGRP monoclonal antibodies were developed as the first "designer drug" for the prevention of migraine. While there is good evidence that many classes of drugs (beta-blockers, calcium channel blockers, tricyclic antidepressants and anti-convulsants) are useful in the prevention of migraine, these monoclonal antibodies represent a specific therapy. The monoclonal antibodies do not cross the blood-brain barrier, are metabolized by the reticuloendothelial system, and are not associated with liver problems. They are given parenterally (IM and IV) and have a long-half life—so they are administered monthly or quarterly.

MONOCLONAL ANTIBODY	**TARGET**	**Phase 3 results**	**Side effects**	**Other comments**
Erenumab (fully human antibody) 70 mg and 140 mg; Monthly self-injection SQ Episodic and chronic migraine Half-life 21 days FDA-approved Trade name: Aimovig	CGRP receptor; IgG 2;	Phase 3: STRIVE Trial: Episodic prevention: Primary outcome: Reduction of headache days/month -1.8 days placebo -3.2 days 70 mg -3.7 days 140 mg 50% responder rate 70 mg: 43% vs 140 mg: 50%; 26.6% placebo ARISE Trial: episodic migraine prevention: Similar to STRIVE TRIAL LIBERTY Trial—prevention of episodic migraine refractory to previous treatments 50% reduction end-point: 13.7% placebo 140 mg 30.3%	Nasopharyngitis symptoms, constipation Injection site redness Neutralizing antibodies 0.2%	Approved and available; Trials with those who have failed 3 other preventives Successful for some Studied in individuals with coronary artery disease and thought to be safe

Fremanezumab (95% humanized) Monthly (self-injector) SQ 225 mg (monthly) and 675 mg (quarterly) Episodic and chronic migraine Half-life: 31 days FDA-approved Trade Name: Ajovy	CGRP peptide (ligand); IgG 2	Phase 3 trials: HALO trial: episodic migraine Reduction in migraine days Monthly: -3.7 vs -2.2 placebo Quarterly: -3.4 days Halo Chronic migraine Placebo: -2.5 days Quarterly: -4.3 days Monthly -4.6 days	Injection site redness Respiratory symptoms, fatigue, dizziness	Approved and available Also being studied for episodic and chronic cluster
Galcanezumab SQ (90% humanized) 120 mg 240 mg Monthly SQ injection Episodic and chronic migraine Half-life 28 days FDA-approved Trade name Egality	CGRP peptide or ligand; and; IgG 4	Phase 3: EVOLVE 1 and 2: 120 mg -4.73 days 240 mg –4.57 days vs placebo -2.81 days REGAIN study: (Chronic migraine—with 63% Medication overuse) -4.83 120 mg -4.62 240 mg -2.74 placebo	Respiratory symptoms, fatigue,	Also studied for episodic cluster—efficacious but not chronic cluster
Eptinezumab 90% humanized antibody IV administration quarterly 100 mg and 300 mg Episodic and chronic migraine Half-life 32 days	CGRP peptide/ligand; IgG1; N-linked carbohydrate removed (reduces immune activity)	Phase 3: PROMISE-1 trial (episodic migraine): 30 mg: -4 days 100 mg -3.9 days 300 mg -4.3 days Placebo -3.2 Promise-2: chronic migraine Reduction of migraine days -5.6 placebo -7.7 100 mg -8.2 300 mg	Respiratory infection Nasopharyngitis, fatigue, dizziness,	

4. Advances in Neuro-modulation for migraine: DEVICES

The other area of development in the field of migraine is new devices. Three devices have been FDA-approved for the treatment of migraine: vagal nerve stimulator, transcranial magnetic stimulation, and supraorbital stimulation (Cefaly Device).

Device	FDA approved indication	Believed mechanism of action	Trials	Side-effects/ contraindications
Vagus Nerve Stimulator (nVNS) GammaCore	Acute migraine Chronic migraine Cluster Acute	Block connections from vagus nerve to trigeminal system and possibly lower glutamate levels	EVENT: chronic migraine patient reduced headache/month by 8.	Paresthesiae; vasovagal syncope Contraindicated with other implanted devices (e.g pacemaker, cochlear implant)
Transcranial Magnetic Stimulation Single pulse/ Repetitive pulse (Cerena/Spring)	Acute treatment of migraine and chronic migraine Prevention of migraine (ESPOUSE trial)	May block cortical spreading depression	ESPOUSE: reduction of 3 days in episodic and 8 days in chronic migraine	Transient and mild dizziness, light headedness Contraindicated in implanted devices—pacemaker defibrillator; epilepsy
Supraorbital Stimulator (Cefaly Device)	Acute Prevention—20 minutes daily	Like TENS units and other similar devices may change signals peripherally	ACME trial: PREMICE trial: found reduction in mean headache days: 6.9 migraine days to 4.8 days vs sham 6.4 to 6.2	Paresthesiae Contraindicated with skin abrasion forehead

There are other stimulators that are still being investigated. For example, the percutaneous mastoid electrical stimulator (PMES)—surface electrode behind the ear. This device showed a reduction in migraine days per month in a randomized controlled trial.

The Caloric vestibular stimulation (which we use to assess brainstem function) is also non-invasive by using a thermoelectric stimulation. Used daily for 3 months, subjects had a reduction in migraine days by month 3 compared to placebo. There were no serious adverse events. Side-effects included dizziness and nausea. The authors propose the mechanism of action is modulating brainstem centers.

Occipital nerve stimulation is a more invasive neuro-modulation with an implantable device. Initial studies did not improve chronic intractable migraines. There are other studies still on-going.

Sphenopalatine ganglion blockade with lidocaine has been reported to abort migraine attacks. Several devices have been invented to deliver lidocaine to the ganglion. In addition, more invasive

sphenopalatine ganglion stimulators have been tested, but have not been found to be efficacious at present.

SUMMARY

So why does a neuro-ophthalmologist need to know about these medications and devices in migraine? First, migraine is common: you will see it every day in clinic and we may be able to guide our patients to better treatments of this disabling condition. Second, eye pain and orbital pain can be migraine—we need to know how to treat it. Third, these new developments may help reduce the visual disability associated with migraine and other related conditions such as idiopathic intracranial hypertension. Finally, every neuro-ophthalmologist wants to be up on any field that touches our speciality—migraine is certainly one of those fields!

CME ANSWERS

1. False
2. B
3. B

REFERENCES

Pathophysiology of Migraine

1. Puledda F, Messina R, Goadsby PJ. An update on migraine: current understanding and future directions. J Neurol 264(9): 2031-2039, 2017
2. Goadsby PJ, Holland PR, Martins-Oliveira M, Hoffmann J, Schankin C, Akerman S. Pathophysiology of Migraine: A Disorder of Sensory Processing. Physiol Rev 97; 553-622, 2017
3. Charles A. The pathophysiology of migraine: implications for clinical management. Lancet Neurol 17(2):174-182, 2018

CGRP Inhibitors, Gepants, Monoclonal Antibodies

1. Edvinsson L. The Trigeminovascular Pathway: Role of CGRP and CGRP Receptors in Migraine. Headache 57 Suppl 2: 47-55, 2017
2. Edvinsson L. The CGRP Pathway in Migraine as a Viable Target for Therapies. Headache 58 Suppl 1: 33-47, 2018
3. Deen M, Correnti E, Kamm K, Kelderman T, Papetti L, Rubio-Beltrán E, Vigneri S, Edvinsson L, Maassen Van Den Brink A; European Headache Federation School of Advanced Studies (EHF-SAS). Blocking CGRP in migraine patients - a review of pros and cons. J Headache Pain 18(1):96, 2017
4. Russo AF. Calcitonin gene-related peptide (CGRP): a new target for migraine. Annual Rev Pharmacol Toxicol 55: 533-52, 2015
5. Hay DL, Walker CS. CGRP and its receptors. Headache 57(4): 625-636, 2017
6. Tepper SJ. History and Review of anti-Calcitonin Gene-Related Peptide (CGRP) Therapies: From Translational Research to Treatment. Headache Sep 22 (ePub ahead of print) doi:10.111/head.13379, 2018
7. Holland PR, Goadsby PJ. Targeted CGRP Small Molecule Antagonists for Acute Migraine Therapy. Neurotherapeutics 15(2): 304-312, 2018
8. Taylor FR. Antigens and Antibodies in Disease With Specifics About CGRP Immunology. Headache Sep 5 (ePub ahead of print) doi:10.111/head.13409, 2018.
9. Edvinsson L, Haanes KA, Warfvinge K, Krause DN. CGRP as the target of new migraine therapies - successful translation from bench to clinic. Nat Rev Neurol 14(6): 338-350, 2018

10. Israel H, Neeb L, Reuter U. CGRP Monoclonal Antibodies for the Preventative Treatment of Migraine. Curr Pain Headache Rep ; 22(5):38, 2018
11. Raffaelli B, Reuter U. The Biology of Monoclonal Antibodies: Focus on Calcitonin Gene-Related Peptide for Prophylactic Migraine Therapy. Neurotherapeutics 15(2): 324-335, 2018

Clinical Trials

1. Grimsrud KW, Halker Singh RB. Emerging Treatments in Episodic Migraine. Curr Pain Headache Rep 22(9): 61, 2018
2. Dodick DW, Goadsby PJ, Silberstein SD, *et al.* Safety and efficacy of ALD403, an antibody to calcitonin gene-related peptide, for the prevention of frequent episodic migraine: a randomised, double-blind, placebo-controlled, exploratory phase 2 trial. *Lancet Neurol* 13 :1100-1107, *2014*
3. Sun H, Dodick DW, Silberstein S, *et al.* Safety and efficacy of AMG 334 for prevention of episodic migraine: A randomised, double-blind, placebo-controlled, phase 2 trial. *Lancet Neurol* 15: 382-390, *2016*
4. Tepper S, Ashina M, Reuter U, *et al.* Safety and efficacy of erenumab for preventive treatment of chronic migraine: A randomised, double-blind, placebo-controlled phase 2 trial. *Lancet Neurol* 16: 425-434, *2017*
5. Goadsby PJ, Reuter U, Hallström Y, *et al.* A controlled trial of fr for episodic migraine. *N Engl J Med* 377: 2123--132, *2017*
6. Ashina M, Dodick D, Goadsby PJ, *et al.* Erenumab (AMG 334) in episodic migraine: Interim analysis of an ongoing open-label study. *Neurology* 89: 1237-1243, *2017*
7. Bigal ME, Dodick DW, Rapoport AM, *et al.* Safety, tolerability, and efficacy of TEV-48125 for preventive treatment of high-frequency episodic migraine: A multicentre, randomised, double-blind, placebo-controlled, phase 2b study. *Lancet Neurol* 14: 1081-1090, *2015*
8. Bigal ME, Edvinsson L, Rapoport AM, *et al.* Safety, tolerability, and efficacy of TEV-48125 for preventive treatment of chronic migraine: a multicentre, randomised, double-blind, placebo-controlled, phase 2b study. *Lancet Neurol* 14: 1091-1100, *2015*
9. Silberstein SD, Dodick DW, Bigal ME, *et al.* Fremanezumab for the preventive treatment of chronic migraine. *N Engl J Med* 377**:** 2113-2122, *2017*
10. Dodick DW, Goadsby PJ, Spierings EL, Scherer JC, Sweeney SP, Grayzel DS. Safety and efficacy of LY2951742, a monoclonal antibody to calcitonin gene-related peptide, for the prevention of migraine: A phase 2, randomised, double-blind, placebo-controlled study. *Lancet Neurol* 13: 885-892, *2014*
11. Skljarevski V, Oakes TM, Zhang Q, *et al.* Effect of different doses of galcanezumab vs placebo for episodic migraine prevention: A randomized clinical trial. *JAMA Neurol* 75: 187-193, *2018*
12. Voss T, Lipton RB, Dodick DW, Dupre N, Ge JY, Bachman R, Assaid C, Aurora SK, Michelson D. A phase IIb randomized, double-blind, placebo-controlled trial of ubrogepant for the acute treatment of migraine. Cephalalgia 36(9): 887-98, 2016
13. Ho TW, Ho AP, Ge YJ, Assaid C, Gottwald R, MacGregor EA, Mannix LK, van Oosterhout WP, Koppenhaver J, Lines C, Ferrari MD, Michelson D. Randomized controlled trial of the CGRP receptor antagonist telcagepant for prevention of headache in women with perimenstrual migraine. Cephalalgia 36(2): 148-61, 2016
14. Ho TW, Connor KM, Zhang Y, Pearlman E, Koppenhaver J, Fan X, Lines C, Edvinsson L, Goadsby PJ, Michelson D. Randomized controlled trial of the CGRP receptor antagonist telcagepant for migraine prevention. Neurology 83(11): 958-66, 2014

Onabotulinum Toxin

1. Do TP, Hvedstrup J, Schytz HW. Botulinum toxin: A review of the mode of action in migraine. Acta Neurol Scand 137(5): 442-451, 2018

2. Chiang CC, Starling AJ. OnabotulinumtoxinA in the treatment of patients with chronic migraine: clinical evidence and experience. Ther Adv Neurol Disord 10(12): 397-406, 2017
3. Dodick DW, Turkel CC, DeGryse RE, Aurora SK, Silberstein SD, Lipton RB, Diener HC, Brin MF; PREEMPT Chronic Migraine Study Group. OnabotulinumtoxinA for treatment of chronic migraine: pooled results from the double-blind, randomized, placebo-controlled phases of the PREEMPT clinical program. Headache 50(6): 921-36, 2010
4. Aurora SK, Dodick DW, Turkel CC, DeGryse RE, Silberstein SD, Lipton RB, Diener HC, Brin MF; PREEMPT 1 Chronic Migraine Study Group. OnabotulinumtoxinA for treatment of chronic migraine: results from the double-blind, randomized, placebo-controlled phase of the PREEMPT 1 trial. Cephalalgia 30(7): 793-803, 2010
5. Diener HC, Dodick DW, Aurora SK, Turkel CC, DeGryse RE, Lipton RB, Silberstein SD, Brin MF; PREEMPT 2 Chronic Migraine Study Group. OnabotulinumtoxinA for treatment of chronic migraine: results from the double-blind, randomized, placebo-controlled phase of the PREEMPT 2 trial. Cephalalgia 30(7): 804-14, 2010
6. Aurora SK, Dodick DW, Diener HC, DeGryse RE, Turkel CC, Lipton RB, Silberstein SD. OnabotulinumtoxinA for chronic migraine: efficacy, safety, and tolerability in patients who received all five treatment cycles in the PREEMPT clinical program. Acta Neurol Scand 129(1): 61-70, 2014

Devices

1. Juan Y, Shu O, Jinhe L, Na Y, Yushuang D, Weiwei D, Lanying H, Jian W. Migraine prevention with percutaneous mastoid electrical stimulator: A randomized double-blind controlled trial. Cephalalgia 37(13): 1248-1256, 2017
2. Black RD, Rogers LL, Ade KK, Nicoletto HA, Adkins HD, Laskowitz DT. Non-invasive neuromodulation using time varying caloric vestibular stimulation. IEEE J Transl Eng Health Med 4:2000310, 2016
3. Tassorelli C, Grazzi L, de Tommaso M, Pierangeli G, Martelletti P, Rainero I, Dorlas S, Geppetti P, Ambrosini A, Sarchielli P, Liebler E, Barbanti P; PRESTO Study Group. Noninvasive vagus nerve stimulation as acute therapy for migraine: The randomized PRESTO study. Neurology 91(4): e364-e373, 2018
4. Lipton, RB, Dodick DR, Silberstein SD, et al. Single-pulse transcranial magnetic stimulation for acute treatment of migraine with aura: A randomized, double blind, parallel-group, sham-controlled trial. Lancet Neurol 4: 373-380, 2010
5. Starling AJ. A multicenter, prospective, single arm, open label, post-market, observational study to evaluate the use of TMS in reduction of migraine headache (ESPOUSE Study). Neurology 88 (16 Supp), 2017
6. Schoenen J, Vandersmissen B, Jeangette S, et al. Prevention of migraine by supraorbital transcutaneous neurostimulation using the Cefaly device (PREMICE): A multi-centre, randomized, sham-controlled trial. J Headache Pain 14 (Suppl 1):184, 2013
7. Schoenen J, Vandersmissen B, Jeangette S, Herroelen L, Vandenheede M, Gérard P, Magis D. Migraine prevention with a supraorbital transcutaneous stimulator: a randomized controlled trial. Neurology 80(8): 697-704, 2013
8. Puledda F, Goadsby PJ. An Update on Non-Pharmacological Neuromodulation for the Acute and Preventive Treatment of Migraine. Headache 57(4): 685-691, 2017
9. Miller S, Sinclair AJ, Davies B, Matharu M. Neurostimulation in the treatment of primary headaches. Pract Neurol 16(5): 362-75, 2016
10. Robbins MS, Lipton RB. Transcutaneous and Percutaneous Neurostimulation for Headache Disorders. Headache 57 Suppl 1: 4-13, 2017
11. Goadsby PJ, de Coo IF, Silver N, Tyagi A, Ahmed F, Gaul C, Jensen RH, Diener HC, Solbach K, Straube A, Liebler E, Marin JC, Ferrari MD; ACT2 Study Group. Non-invasive vagus nerve stimulation for the

acute treatment of episodic and chronic cluster headache: A randomized, double-blind, sham-controlled ACT2 study. Cephalalgia 38(5): 959-969, 2018
12. Wilkinson D, Ade KK, Rogers LL, Attix DK, Kuchibhatla M, Slade MD, Smith LL, Poynter KP, Laskowitz DT, Freeman MC, Hoffer ME, Saper JR, Scott DL, Sakel M, Calhoun AH, Black RD. Preventing Episodic Migraine With Caloric Vestibular Stimulation: A Randomized Controlled Trial. Headache 57(7): 1065-1087, 2017
13. Cadalso RT Jr, Daugherty J, Holmes C, Ram S, Enciso R. Efficacy of Electrical Stimulation of the Occipital Nerve in Intractable Primary Headache Disorders: A Systematic Review with Meta-Analyses. J Oral Facial Pain Headache. Winter 32(1): 40–52, 2018
14. Vukovic Cvetkovic V, Jensen RH. Neurostimulation for the treatment of chronic migraine and cluster headache - a review article. Acta Neurol Scand Oct 6 (ePub ahead of print) doi:10.1111/ane.13034, 2018
15. Cady RK, Saper J, Dexter K, Cady RJ, Manley HR. Long-term efficacy of a double-blind, placebo-controlled, randomized study for repetitive sphenopalatine blockade with bupivacaine vs. saline with the Tx360 device for treatment of chronic migraine. Headache 55(4): 529-42, 2015
16. Cady R, Saper J, Dexter K, Manley HR. A double-blind, placebo-controlled study of repetitive transnasal sphenopalatine ganglion blockade with tx360(®) as acute treatment for chronic migraine. Headache 55(1): 101-16, 2015
17. Tepper SJ, Rezai A, Narouze S, Steiner C, Mohajer P, Ansarinia M. Acute treatment of intractable migraine with sphenopalatine ganglion electrical stimulation. Headache 49(7): 983-9, 2009

ISCHEMIC OPTIC NEUROPATHY FROM GIANT CELL ARTERITIS

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LEARNING OBJECTIVES

1. Discuss acute management of arteritic ischemic optic neuropathy (ION) using a case-based format and discussion
2. Review current challenges in the management of giant cell arteritis (GCA)
3. Highlight emerging treatment options for GCA patients with reference to the published literature

CME QUESTIONS

1. Do visual manifestations of GCA warrant a more aggressive approach to acute management?
2. What percentage of GCA patients experience complications from long-term corticosteroid use?
3. In the GiACTA trial, did GCA patients receive standard steroid doses typically used in the treatment of arteritic ION?

KEYWORDS

1. Ischemic optic neuropathy (ION)
2. Giant Cell Arteritis (GCA)
3. Corticosteroids
4. Steroid Sparing Therapies
5. Tocilizumab

HIGHLIGHTS

Giant cell arteritis (GCA) is a challenging condition to manage. Patients presenting with ION warrant special consideration, because their vision loss is often irreversible. In general terms, the neuro-ophthalmic care of these patients is governed by several universal goals, namely: preserving or improving the visual status of the patient; protecting the patient from non-visual consequences of the diagnosis; and, ameliorating the inevitable effects of high-dose, long term corticosteroid therapy. Yet, for any given patient there are also challenges that are case specific. Clinicians caring for these individuals must consider the relative frailty of the patient, and anticipate what co-morbidities may be unveiled or exacerbated by treatment. Moreover, the severity of the patient's vision loss, and presence or absence of non-visual manifestations also impact management decisions. Therefore in the approach of the GCA patient with ION it is helpful to prioritize the goals of care, by posing a series of questions:

- How severe is the visual deficit?
- Does the patient have extra-cranial GCA manifestations that may be life threatening in nature?
- What are the patient-specific issues that may complicate therapy?
- When should I seek help from other specialists and/or allied health care professionals?

High dose corticosteroids remain the mainstay of treatment for GCA patients presenting with acute ION. While there is a paucity of clinical trials comparing different steroid regimens in GCA, the British Society of Rheumatology (1, 2) has published recommended guidelines regarding the treatment of GCA and polymyalgia rheumatica patients, based predominantly on level 3 evidence:

- Prednisolone 40–60 mg daily for "uncomplicated" GCA (no vision loss)
- IV methylprednisolone 500–1000 mg for 3 days prior to initiating oral steroids for evolving visual loss
- Prednisolone 60 mg daily for cases of established visual loss, to protect the contralateral eye

Some published reports have demonstrated visual improvement with corticosteroid treatment, with more robust results noted in patients treated initially with intravenous corticosteroids versus oral steroids (2). In clinical practice, the initial high dose of steroids is often maintained for 3–4 weeks and tapered if there are no ongoing clinical symptoms or laboratory evidence of active disease (2). While most GCA patients are able to taper or discontinue steroids after 1–2 years of treatment, the duration of therapy is variable (2). Long-term corticosteroid therapy causes adverse side effects that affect up to 86% of patients (2). Accordingly, refractory GCA manifestations and challenges with weaning steroid dosage often prompt consideration of steroid-sparing, adjunctive therapies. Methotrexate is sometimes used as a safe, and modestly effective steroid-sparing drug for patients with refractive symptoms (2,3). Alternatively, azathioprine or leflunomide may be considered for GCA patients with difficult to treat, steroid-resistant disease (2). Biologic agents have also been trialed in the treatment of GCA patients, with variable results. Anti-tumor necrosis factor-alpha therapy with infliximab has not been proven effective, whereas etanercept has shown inconclusive results (2, 3). B-cell depletion by rituximab has been used as a steroid-sparing strategy in GCA, with evidence from positron emission tomography scanning after several months of resolved disease (2). A small randomized placebo-controlled trial of abatacept, a CTLA-4 inhibitor used in GCA patients was published in 2017 (4). All patients were given an 8-week induction course and a 28-week prednisone taper. The abatacept treatment group had a small but statistically significantly higher rate of relapse-free survival at 12 months (4). Ustekinumab, an IL12/23 inhibitor is a monoclonal protein that is thought to suppress both Th1 and Th17 lymphocytes (3,4). This agent has helped facilitate prednisone dose reduction in a case series of refractory GCA patients. A prospective open label study is currently underway (ClinicalTrials.gov Identifier: NCT02955147) (4). Tofacitinib and baracitinib are both Janus kinase inhibitors that suppress a range of inflammatory cytokines and proteins. An open label trial of baracitinib, is ongoing in patients with refractory GCA (ClinicalTrials.gov Identifier: NCT03026504) (4). Anakinra, an IL-1-receptor antagonist, has shown benefit in several GCA cases, albeit no recommendation regarding use of anakinra can be made at this time (3). Stone et al reported the results of a randomized, double blind, placebo-controlled, phase 3 trial, the Giant-Cell Arteritis Actemra (GiACTA) trial, which was designed to investigate whether tocilizumab, an IL-6 inhibitor, resulted in higher rates of sustained corticosteroid-free remission in GCA patients relative to placebo through a period of 52 weeks (2-6). Although the weekly tocilizumab group had no vision-related flare events, there were two vision events in the tocilizumab group receiving treatment every two weeks (4). Furthermore, in the GiACTA trial, the use of intravenous methylprednisolone at doses greater than 100 mg daily within 6 weeks before baseline was not permitted (6). This dosing regimen would not be considered standard of care for GCA patients presenting with ION (5). Other adjunctive therapies considered in the care of GCA patients include aspirin, which has been shown to suppress proinflammatory cytokines in vascular lesions in giant cell arteritis. In a recent Cochrane review, it was concluded that there is currently no evidence from randomized controlled trials to determine the safety and efficacy of low-dose aspirin as an adjunctive treatment in GCA (5). There has been recent interest in the potential role of anti-viral treatment for GCA

because analysis of temporal artery specimens from biopsy positive and negative GCA patients has revealed the presence of varicella zoster virus antigen, particularly in “skip” areas that correlate with adjacent pathology (3,5). No trials have been conducted to determine whether combination therapy with antiviral agents (oral or intravenous) and corticosteroids provides any additional benefit to GCA patients as compared to corticosteroids alone (5).

SUMMARY

There have been recent advancements in the management of GCA patients. Longitudinal follow up will determine how emerging therapies can be best implemented in clinical practice.

CME ANSWERS

1. Yes. The British Society of Rheumatology recommends IV methylprednisolone 500–1000 mg for 3 days prior to initiating oral steroids for GCA cases complicated by vision loss.
2. A significant percentage of GCA patients (86%) experience corticosteroid related side effects.
3. No, doses exceeding 100mg of daily prednisone were not permitted in the first 6 weeks of treatment.

REFERENCES

1. Dasgupta B. Concise guidance: diagnosis and management of giant cell arteritis. Clin Med August 1, 2010
2. Patil P, Karia N, Jain S, Dasgupta B. Giant cell arteritis: a review. Eye and Brain 5, 23–33, 2013
3. Roberts J, Clifford A. Update on the management of giant cell arteritis. Ther Adv Chronic Dis, 8(4-5), 69-89, 2017
4. Sammel AM, Fraser CL. Update on giant cell arteritis. Curr Opin Ophthalmol 29, 520 – 527, 2018
5. Palkovacs EM, Costello F, Golnik KC. Treatment of Giant Cell Arteritis. Neuro-Ophthalmology, Springer Nature, 2018
6. Stone JH, Tuckwell K, Dimonaco S, et al. Trial of Tocilizumab in Giant-Cell Arteritis. NEJM, 77:317-28, 2017

TREATMENT OF OCULAR MYASTHENIA GRAVIS

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LEARNING OBJECTIVES

1. Compare the evidence for treating ocular myasthenia gravis with early high-dose vs. early low-dose prednisone
2. Identify alternative non-medical therapies in the treatment of double vision from ocular myasthenia
3. Determine when strabismus surgery and ptosis repair are indicated in ocular myasthenia
4. Review the evidence of thymectomy without thymoma for the treatment of ocular myasthenia gravis

CME QUESTIONS

1. True or False: Thymectomy in the absence of a thymoma has been shown to be safe and effective for ocular myasthenia gravis
2. True or False: Treating ocular myasthenia gravis with corticosteroids has been proven to reduce the risk of progression to generalized disease.
3. True or False: Before starting mycophenolate mofetil, the patient should be tested for thiopurine methyltransferase activity

KEY WORDS

1. Ocular myasthenia
2. Treatment
3. Therapy
4. Pyridostigmine
5. Corticosteroids
6. Thymectomy
7. Azathioprine
8. Mycophenolate mofetil

INTRODUCTION

Myasthenia gravis is caused by pathogenic autoantibodies to the postsynaptic neuromuscular junction. Clinically, this may affect any of the skeletal muscles causing variable weakness, which worsens with continued muscle activity. Ocular myasthenia gravis (OMG) may affect the levator palpebrae superioris, extraocular muscles, and orbicularis oculi causing ptosis and diplopia. Meanwhile, generalized myasthenia gravis (GMG) refers to involvement of the non-ocular skeletal muscles. This talk will focus on treatment strategies for OMG. Discussion of the diagnosis of OMG and the treatment of GMG is beyond the scope.

NON-MEDICAL THERAPY

Ptosis

Spectacle-mounted eyelid crutches help raise the eyelids above the visual axis while allowing the patient to blink. Historically, these are permanently welded to a metal-framed pair of eyeglasses by an experienced optician. However, recently, an open-source, 3D printed ptosis crutch has been developed. These crutches can be attached to spectacle frames by a clip and then adjusted up and down to fit the patient. They may be removed from the glasses at any time. (Saidi)

Diplopia

There are a variety of ways to manage binocular diplopia, which is not unique to OMG. Since OMG causes variable diplopia throughout the day, Fresnel and ground-in prisms are typically not recommended. If diplopia becomes chronic and stable despite treatment, then prisms can be considered. The easiest and cheapest ways to manage diplopia include patching or placing a sleeve/tape on spectacles. Sleeves for amblyopia are widely available on the internet. I have also had patients sew themselves one. Scotch giftwrap tape placed on the inside surface of the glasses represents a fairly unobtrusive way to "patch", however some patients cannot tolerate the partial blur (De Poole). Patients can also consider putting other kinds of tape on one lens. Presbyopic patients may be able to manage diplopia using monovision with a +3.00 add (Bujak). Each eye is sufficiently blurred to improve symptomatic diplopia. We have had great success with black contact lenses that completely cover the pupil and result in a nice cosmetic outcome. To some extent, it reduces the effective peripheral visual field. To mitigate this, Robert et al reported a scotogenic contact lens with an area of central blur and a gradual reduction of blur eccentrically (that matches the reduction of visual acuity eccentrically) to allow an individual to have improvement in peripheral visual field but eliminate diplopia (Robert).

MEDICAL THERAPY

Alpha adrenergic receptor agonists

Naphazoline is a nonspecific alpha 1 and alpha 2 agonist used for the treatment of allergy. In an open-label trial, Nagane et al enrolled 60 individuals with MG and 10 healthy volunteers to determine the effect of 0.05% naphazoline for the treatment of ptosis in MG. MG patients could use the naphazoline as needed and the controls used it twice daily for a month. There was a significant improvement in ptosis in 63% of eyes. Controls had no change in their eyelid height. I have tried this in several patients, and only one has noted significant improvement in their ptosis, but it is noninvasive with little risk, so it may be worth trying temporarily.

Pyridostigmine

Pyridostigmine inhibits the action of cholinesterase and this reduces the breakdown of acetylcholine in the synaptic cleft. It facilitates neuromuscular transmission but does not alter the autoimmune process. Dosing starts at 60 mg three times daily and can escalate to 180 mg every 4 hours. A sustained release form of pyridostigmine is also available and is taken at a dose of 180-540 mg once or twice daily. Side effects most often include GI cramping and diarrhea, which can be mitigated to some extent with loperamide (2 mg four times daily as needed) or glycopyrrolate (1 mg three times a day as needed). Relative contraindications to pyridostigmine may include severe COPD/asthma or symptomatic bradycardia. Pyridostigmine tends to improve ptosis to a greater extent than ophthalmoplegia or diplopia (Kupersmith 1996). Caution must be used to avoid over-treatment with pyridostigmine, as this can result in a cholinergic crisis. Persistent or worsening weakness in association with cholinergic side

effects may be a sign of over-treatment. I usually start at 60 mg three times a day, but I usually do not go over 120 mg four times a day.

Oral corticosteroids

Oral corticosteroids are commonly used for the treatment of OMG because they are widely available, widely prescribed by nearly all providers, inexpensive, and effective. The beneficial effects of prednisone often occur within a few weeks (Kupersmith 2005), unlike other immunosuppressive agents, which can take months to show improvement. In the absence of clear treatment guidelines, controversy exists regarding the starting dose and how to manage increases and decreases in dose. The treatment regimens basically fall into two established paradigms: 1) Increase prednisone to 60 mg daily within a week then slowly taper over a few months to a dose below 7.5 mg daily (Kupersmith 2005); 2) Start at a low dose of 10-20 mg and slowly increase until symptoms resolves, then taper back down to a dose below 7.5 mg daily (EPITOME). Comparing the two paradigms, the overall prednisone dose generally appears lower in the first regimen compared to the second one. Alternate day dosing has a reported failure rate of 27% (Evoli 1988). I generally start patients on 10 mg/d for two days then increase to 60 mg/d x 1 week. I slowly taper them by 10 mg/d each week until I reach 30 mg/d and then taper by 5 mg/d each week until I reach 15 mg/d then reduce by 2.5 mg/d until I get to 7.5 mg/d. At that point, I try to keep them at that dose or reduce them by 1 mg/d each month.

Lee and Kim gave oral methylprednisolone (16-32 mg (prednisone equivalent = 20-40 mg) to 29 patients with OMG with positive AchR binding antibodies. When patients became symptom free they were tapered by 8 mg/d each week. By 2 weeks of treatment, 43% showed resolution of symptoms and, by 8 weeks, 83% of patients were symptom free and remained so at 6 months. Four of 23 patients that completed follow up never achieved symptom resolution. They suggest that moderate doses of oral corticosteroids may represent a compromise between the two commonly above-used strategies.

Approximately 50-60% of those who present with ocular symptoms of MG will go on to develop GMG (Benatar 2012) and the majority will do so within 2 years. There has been a suggestion that oral corticosteroids may also reduce the risk of OMG converting to GMG (Kupersmith 2003). Kupersmith reported that 4/58 (7%) of prednisone treated and 13/36 (36%) of patients not treated with prednisone developed GMG within 2 years of onset of OMG. Meanwhile, Nagia et al performed a retrospective chart review of 158 patients with OMG. They divided them into two groups: 1) immunosuppression (corticosteroids, azathioprine, mycophenolate mofetil, methotrexate, cyclosporine, plasmapheresis, or IVIG) and 2) no immunosuppression (predominantly pyridostigmine). They found that 8/76 in group 1 vs. 15/82 in group 2 converted to GMG at 2 years with no significant differences in conversion rates (Nagia)

Mycophenolate mofetil

Mycophenolate mofetil (MMF) depletes guanosine and deoxyguanosine on both T and B lymphocytes leading to reduced proliferation of these cell lines. Although it is rarely used as a first-line agent, some advocate for its use among those who fail or have contraindications to prednisone therapy (Cornblath). The typical starting dose is 1000 twice mg daily. Adverse effects include gastrointestinal upset, increase risk of lymphoma, teratogenicity, bone marrow suppression, increase risk of infection. Disadvantages of MMF also include cost and the longer time to improvement with MMF compared to prednisone. To that end, MMF is often given with prednisone, which is tapered off later. Unlike azathioprine, prior to starting MMF, patients do not require any testing of thiopurine methyltransferase activity.

There have been two double-blind, placebo-controlled clinical trials of MMF (2.5 g/d and 2g/d) in **GMG** (Muscle Study Group, Sanders). Neither showed a benefit of MMF compared to prednisone alone or

placebo plus prednisone. In an open-label study without controls, Chan gave 31 patients MMF 1g/d to patients with OMG after a steroid initiation and found that 93% showed a positive effect with a mean of 4.2 years of followup (Chan).

Azathioprine
Azathioprine inhibits synthesis of DNA and cell proliferation by blocking purine metabolism. It is used for the treatment of **GMG** and, given the effectiveness in **GMG**, it follows that patients with OMG would benefit from treatment with azathioprine. Studies that have looked at patients with OMG have focused on the conversion rates to GMG showing some reduction in risk. There are no randomized controlled trials (RCT) studying the effect of azathioprine in OMG. Unfortunately, azathioprine takes 6-12 months to note an effect in OMG and is often initiated along with prednisone. There is a risk of leukopenia and hepatotoxicity. Patients should be tested for low thiopurine methyltransferase activity, because they are at increased risk for toxicity.

Other medical therapies
Other therapies that have shown benefit in patients with **GMG** include cyclosporine A, tacrolimus, methotrexate, rituximab, and cyclophosphamide. These treatments may also have some benefit in patients with OMG, but data are lacking. Plasmapheresis and IVIG are also used frequently in the treatment of GMG. There are no RCT of plasmapheresis in OMG. In one randomized, placebo-controlled trial of IVIG for MG, there were 17 patients with OMG (7 received IVIG, 10 received placebo). There were no significant differences in outcome for OMG patients (Zinman) but the numbers were small. In general, plasmapheresis and IVIG have been used in OMG on a case by case basis.

SURGICAL THERAPY

Ptosis
Surgical repair of ptosis is not advised unless the patients are symptomatic, stable for at least several months to years, and have failed other medical therapy. Brogan et al. performed external levator advancements on 9 patients with MG (5 GMG, 4 OMG). Of the 4 OMG patients, medical treatment before surgery was 23-100 months with a mean of 60 months. All patients were treated with pyridostigmine. One was treated with prednisone plus azathioprine and one with prednisone. Only one underwent repeat surgery. Depending on the orbicularis oculi strength, one may try to target just above the visual axis to avoid exposure keratopathy.

Strabismus surgery
Similar to ptosis, patients with variable eye misalignment are not candidates for strabismus surgery. There have been several reports of strabismus surgery in patients with stable ocular misalignment from OMG. Success defined as < 10 PD of strabismus or free from diplopia ranged from 44 – 75% but these were small case series (n=4-9). All of the patients underwent surgery with an adjustable suture and only one study included botulinum toxin injections. Factors that seemed to correlate with poor outcome included older patients, seropositivity, and GMG. Interestingly, duration of preoperative stability was not predictive (range = 6 weeks to 8 years).

Thymectomy
Thymectomy without thymoma has been shown effective for the treatment of **GMG**, but improvement and remission can take years to realize. (Wolfe, Cataneo) Controversy exists on whether a therapeutic benefit exists for thymectomy without thymoma in OMG. Studies by Kawaguchi 2004 and Papatestas 1987 did not show improvement in ocular symptoms but also did not show progression to GMG. Liu et

al retrospectively reviewed 115 patients with OMG who underwent extended transsternal thymectomy. Eighty-four percent showed significant improvement in signs and symptoms (Liu). A European task force suggested that thymectomy is considered in the treatment of a patient with refractory OMG. (Kerty)

SUMMARY

The treatment of OMG has advanced considerably over time, but this disease still lacks randomized clinical trials to define safety and efficacy. Early on, most patients might benefit from some type of occlusion therapy for diplopia. One could consider alpha adrenergic receptor agonists for ptosis, but I have not seen significant improvement with this therapy. Initial therapy often includes pyridostigmine alone or pyridostigmine plus oral corticosteroids. While some controversy exists on initial dosing, I favor higher doses initially. If that is not beneficial or contraindicated, then either azathioprine or mycophenolate mofetil could be considered. Thymectomy is indicated if a thymoma is present. However, in the absence of a thymoma, it is not clear that thymectomy is beneficial and should be decided on a case by case basis. Finally, ptosis repair and strabismus surgery could be considered if OMG therapy has been maximized and the measurements are repeatedly stable for several months to years.

CME ANSWERS

1. False
2. False
3. False

REFERENCES

1. Benatar M, Kaminski H. Medical and surgical treatment for ocular myasthenia: Review. Cochr Database Syst Rev 2012
2. Brogan K, Farrugia ME, Crofts K. Ptosis Surgery in Patients with Myasthenia Gravis: A Useful Adjunct to Medical Therapy, Seminars in Ophthalmology 33:3, 429-434
3. Bujak MC, Leung AK, Kisilevsky M, Margolin E. Monovision correction for small-angle diplopia. Am J Ophthalmol. 2012 Sep;154(3):586-592.
4. Cataneo AJM, Felisberto G Jr, Cataneo DC. Thymectomy in nonthymomatous myasthenia gravis - systematic review and meta-analysis. Orphanet J Rare Dis. 2018;13:99.
5. Chan JW. Mycophenolate mofetil for ocular myasthenia. J Neurol. 2008 Apr; 255(4):510-3.
6. De Pool ME, Campbell JP, Broome SO, et al. The dragged-fovea diplopia syndrome: clinical characteristics, diagnosis, and treatment. Ophthalmology. 2005 Aug;112(8):1455-62.
7. Evoli A, Batocchi AP, Minisci C, et al. Clinical characteristics and prognosis of myasthenia gravis in older people. J Am Geriatr Soc. 2000 Nov;48(11):1442-8.
8. Gilhus NE, Verschuuren JJ. Myasthenia gravis: subgroup classification and therapeutic strategies. Lancet Neurol 2015;14:1023-36.
9. Kawaguchi N, Kuwabara S, Nemoto Y, et al. Treatment and outcome of myasthenia gravis: retrospective multi-center analysis of 470 Japanese patients, 1999-2000. Journal of the Neurological Sciences 2004;224(1-2):43–7.
10. Kerty E, Elsais A, Argov Z, Evoli A, Gilhus NE. EFNS/ENS Guidelines for the treatment of ocular myasthenia. Eur J Neurol. 2014 May;21(5):687-93.
11. Kupersmith MJ, Moster M, Bhuiyan S, et al. Beneficial effects of corticosteroids on ocular myasthenia gravis. Arch Neurol 1996;53:802–4.

12. Kupersmith MJ, Ying G. Ocular motor dysfunction and ptosis in ocular myasthenia gravis: effects of treatment. Br J Ophthalmol. 2005 Oct;89(10):1330-4.
13. Kupersmith MJ. Ocular myasthenia gravis: treatment successes and failures in patients with long-term follow-up. J Neurol. 2009 Aug;256(8):1314-20.
14. Lee YG, Kim US. Efficacy and safety of low-to-moderate dose oral corticosteroid treatment in ocular myasthenia gravis. J Pediatr Ophthalmol Strabismus. In press.
15. Liu Z, Feng H, Yeung SC, et al. Extended transsternal thymectomy for the treatment of ocular myasthenia gravis. Ann Thorac Surg 2011; 92: 1993–1999.
16. Muscle Study Group. A trial of mycophenolate mofetil with prednisone as initial immunotherapy in myasthenia gravis. Neurology. 2008 Aug 5; 71(6):394-9.
17. Nagane Y, Utsugisawa K, Suzuki S, et al. Topical naphazoline in the treatment of myasthenic blepharoptosis. Muscle Nerve. 2011 Jul;44(1):41-4. doi: 10.1002/mus.22002. Epub 2011 Apr 12.
18. Nagia L, Lemos J, Abusamra K, et al. Prognosis of ocular myasthenia gravis: Retrospective multicenter analysis. Ophthalmology 2015;122:1517-22.
19. Oosterhuis HJ. Observations of the natural history of myasthenia gravis and the effect of thimectomy. Ann N Y Acad Sci. 1981;377:678–90.
20. Papatestas AE, Genkins G, Kornfeld P, et al. Effects of thymectomy in myasthenia gravis. Annals of Surgery 1987;206(1):79–88.
21. Peragallo JH, Velez FG, Demer JL, Pineles SL. Long-term follow-up of strabismus surgery for patients with ocular myasthenia gravis. J Neuroophthalmol. 2013 Mar;33(1):40-4.
22. Robert MP, Bonci F, Pandit A, et al. The scotogenic contact lens: a novel device for treating binocular diplopia. Br J Ophthalmol. 2015 Aug;99(8):1022-4.
23. Robertson NP, Deans J, Compston DAS. Myasthenia gravis:a population based epidemiological study in Cambridgeshire, England. J Neurol Neurosurg Psychiatry. 1998;65:492–6.
24. Saidi T, Sivarasu S, Douglas TS. Open source modular ptosis crutch for the treatment of myasthenia gravis. Expert Review Med Devices 2018;15:137-143.
25. Sanders DB, Hart IK, Mantegazza R, et al. An international, phase III, randomized trial of mycophenolate mofetil in myasthenia gravis. Neurology. 2008 Aug 5; 71(6):400-6.
26. Sommer N, Sigg B, Melms A, et al. Ocular myasthenia gravis: response to long term immunosuppressive treatment. Journal of Neurology, Neurosurgery and Psychiatry 1997;62(2):156–62.
27. Wolfe GI, Kaminski HJ, Sonnett JR, Aban IB, Kuo HC, Cutter GR. Randomized trial of thymectomy in myasthenia gravis. J Thorac Dis. 2016 Dec;8(12):E1782-E1783.
28. Zinman L, Ng E, Bril V. IV immunoglobulin in patients with myasthenia gravis: a randomized controlled trial.
Neurology. 2007 Mar 13;68(11):837-41.

TREATMENT OF MOG-IgG OPTIC NEURITIS

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LEARNING OBJECTIVES

1. Recognize common presentations of MOG-IgG optic neuritis
2. Describe the acute treatment options for MOG-IgG optic neuritis
3. Discuss the indications for chronic treatment for MOG-IgG optic neuritis

CME QUESTIONS

1. True or False: MOG-IgG is a good marker for multiple sclerosis.

2. Which of the following would be suggestive of MOG-IgG optic neuritis?
   A. No optic disc edema at onset
   B. Periventricular white matter lesions
   C. Enhancement of both the optic nerve and sheath
   D. Oligoclonal bands in the cerebral spinal fluid

3. True or False: Disease modifying medications for multiple sclerosis are effective in preventing MOG-IgG recurrent demyelinating attacks.

KEYWORDS

1. Myelin oligodendrocyte glycoprotein (MOG)-IgG
2. Optic neuritis
3. chronic relapsing inflammatory optic neuropathy
4. neuromyelitis optica spectrum disorder (NMOSD)
5. demyelinating disease

HIGHLIGHTS

<u>INTRODUCTION TO MOG-IgG OPTIC NEURITIS</u>

Optic neuritis is the most common cause of optic neuropathy in young patients, which can cause debilitating vision loss and blindness. Two novel glial autoantibodies have been discovered that better characterize a subset of patients with optic neuritis. In 2004, antibodies against an astrocytic water channel, aquaporin-4 (AQP4) were discovered,[1] which greatly improved our understanding and detection of the clinical entity neuromyelitis optica spectrum disorders (NMOSD).[2] More recently, antibodies specific for myelin oligodendrocyte glycoprotein (MOG-IgG), have been found in a subset of patients with optic neuritis and other demyelinating phenotypes. Although initially erroneously associated with multiple sclerosis in early literature with use of solid-phase assays,[3] newer live transfected cell-based assays have shown MOG-IgG to be a reproducible marker for a subset of patients with optic neuritis,[4] AQP4-IgG seronegative inflammatory CNS demyelinating disorders with NMOSD-like phenotype, and acute disseminated encephalomyelitis (ADEM).[5,6] MOG-IgG is not typically found in

patients with classic multiple sclerosis or in patients positive for AQP4-IgG.[5,7-9] While there is some clinical overlap with other demyelinating disease processes, MOG-IgG-associated demyelinating disease is now becoming recognized as its own disease entity, distinct from classic MS and AQP4-IgG-positive NMOSD.[7,10]

There are some characteristics of MOG-IgG that should alert the clinician to the possibility of MOG-IgG demyelinating disease. The most common phenotype of MOG-IgG disease is optic neuritis. MOG-IgG-positive optic neuritis have a higher likelihood of being recurrent, bilateral, and associated with disc edema than other forms of demyelinating optic neuritis. Recurrent optic neuritis is seen in between 50-80% of cases of MOG-IgG-positive optic neuritis.[6,11,12] It can sometimes be steroid responsive and dependent, thus meeting the criteria for chronic relapsing inflammatory optic neuropathy (CRION).[12-14] Bilateral simultaneous optic neuritis occurs in almost half of cases of MOG-IgG-positive optic neuritis.[6,11,12,15,16] Optic disc edema at onset is present in up to 86% of cases,[9,10,12,15-17] and can be severe with peripapillary hemorrhages, which is a feature that is rarely seen in other forms of demyelinating optic neuritis. The vision loss is usually severe at the nidus, but recovery is typically better than seen with AQP4-IgG-postive optic neuritis.[6,12] On MRI, there is often longitudinally extensive enhancement of the optic nerve.[9,10,12,18,19] Perineural enhancement of the optic nerve sheath and peribulbar structures is seen in up to 50% of cases, which is a fairly specific sign of MOG-IgG-positive optic neuritis.[12,17,18,20,21]

Accompanying longitudinally extensive transverse myelitis (≥ 3 contiguous vertebral segments) that is negative for AQP4-IgG should be tested for MOG-IgG, which accounts for ~1/3 of AQP4-IgG-seronegative NMOSD. Transverse myelitis involves the conus medullaris in MOG-IgG disease more commonly than other demyelinating diseases, including AQP4-IgG-positive transverse myelitis.[6,10,22] In MOG-IgG transverse myelitis, the T2-signal abnormality is often restricted to the grey matter forming a hallmark "H-sign" on axial images.[22]

Accompanying brainstem encephalitis and/or an ADEM-like presentation should also raise the suspicion for MOG-IgG disease since these are less commonly seen with AQP4-IgG or classic MS.

ACUTE TREATMENT OPTIONS

Because MOG-IgG-positive optic neuritis is a newly described entity, the optimal treatment has yet to be established. Overall the outcomes of MOG-IgG optic neuritis are better than AQP4-IgG optic neuritis and therefore may not require as aggressive treatment as AQP4-IgG-mediated disease. However, some patients can end up with severe vision loss after MOG-IgG optic neuritis.[6,12,21] At the Mayo Clinic, we typically treat acute MOG-IgG optic neuritis with intravenous methylprednisolone for 5 days followed by an oral prednisone taper over 6-12 weeks because of the higher propensity to relapse than other forms of optic neuritis (see treatment algorithm). Some practitioners will treat early with plasma exchange if the vision loss is severe. The addition of plasma exchange is based on retrospective studies suggesting that plasma exchange may improve outcomes of NMOSD demyelinating attacks, especially if given early.[24-26] However, it is still unclear whether these findings will apply to MOG-IgG-positive optic neuritis. We typically add plasma exchange (7 treatments every other day) if the patient has severe vision loss and does not show demonstrable improvement within 1-2 weeks (see treatment algorithm). Future randomized, prospective trials comparing plasma exchange and IV methylprednisolone are required to determine the best treatment and timing of the treatment for MOG-IgG optic neuritis. Occasionally, patients will have rapid recovery during the IV methylprednisolone treatment, which is faster than the delayed recovery of several weeks typically seen with MS-related optic neuritis. The patients that are exquisitely responsive to steroids may also be more prone to be steroid dependent and follow a CRION-like phenotype. These patients need to be monitored for relapse and often need a longer oral prednisone taper. If they continue to relapse and cannot be tapered to a prednisone dose of 10 mg or less, a chronic immunosuppression is typically required (see below).

CHRONIC TREATMENT

Unlike AQP4-IgG disease, which is associated with poor outcomes if left untreated and therefore almost universally requires chronic immunosuppression, the necessity for chronic treatment of MOG-IgG disease is less clear. MOG-IgG positive demyelinating disease is highly associated with recurrent severe attacks, with relapse occurring in 50-80% of patients.[6,12] However, patients tend to recover better from each attack than with AQP4-IgG.[6,12] On the other hand, recurrent attacks can lead to significant morbidity and permanent vision loss with poor visual outcomes reported as high as 26%,[21] although other studies suggest a lower percentage.[6,12] In addition to recurrent optic neuritis attacks, there is also the risk of other demyelinating attacks, such as transverse myelitis, that can lead to significant morbidity.[6,15,21]

Because of the high likelihood of recurrent attacks, our group advises treatment with a chronic immunosuppressive agent if a patient has an optic neuritis with incomplete recovery (see treatment algorithm). If a patient has complete recovery from a demyelinating attack, they could be observed because there are patients with MOG-IgG autoimmunity who only have a single demyelinating attack without any relapses, especially in children. If a patient has 2-3 attacks, we typically recommend a chronic immunosuppressive agent because of the concern for future permanent morbidity from the accumulation of attacks. Patients also require a steroid sparing agent if they have a CRION-like phenotype with consistent relapses when tapered off prednisone.

The choice of the chronic immunosuppression is still unclear. Disease modifying agents used to treat MS are not effective in preventing relapse in MOG-IgG disease.[21,27,28] It has yet to be determined if they exacerbate attacks as has been suggested for AQP4-IgG-mediated disease, but regardless should not be used in a patient that is positive for MOG-IgG. Prednisone is effective and it has been shown that MOG-IgG demyelinating attacks rarely relapse when on prednisone.[15] However, patients often require higher doses of prednisone than can be tolerated long term and therefore many will require a steroid sparing agent. The most commonly used medications are mycophenolate, azathioprine, rituximab, and IVIG. All have been found to have breakthrough attacks despite proper dosing, but all likely do decrease the relapse rate.[15,21] A recent multicenter study has suggested that rituximab reduces relapse rates in MOG-IgG disease, but potentially not as effectively as it does with AQP4-IgG-positive NMOSD.[29] In reviewing our data on MOG-IgG relapsing disease, we found that relapse occurred in about 50% of patients treated with a chronic immunosuppression. This cohort was a selective group of MOG-IgG patients that presented with a high relapse rate and therefore a 50% relapse rate reflects a significant reduction in attacks. Interestingly, six patients were treated with IVIG and only one patient had a relapse while on treatment. Future prospective randomized clinical trials will be required to determine the best chronic immunotherapy for MOG-IgG disease.

Lastly, the importance of MOG-IgG titer and persistence has yet to be established. While the titer unlikely has an impact on clinical outcomes and relapse, the persistence may suggest a higher propensity toward recurrent attacks. A recent study on MOG-IgG positive ADEM patients showed that patients with persistent MOG-IgG-seropositivity were more likely to have recurrent demyelinating attacks than those with transient MOG-IgG seropositivity.[30] This trend of higher relapse in patients with persistent MOG-IgG was also seen in a prospective UK cohort.[6] However, not all patients with persistent MOG-IgG will develop recurrent attacks.[6] Further prospective studies on MOG-IgG titers are warranted to determine their role in predicting disease.

SUMMARY

MOG-IgG disease is becoming recognized as its own distinct demyelinating process primarily associated with recurrent optic neuritis. MOG-IgG is not found in patients with classic MS or in patients positive for AQP4-IgG. The optimal treatment of MOG-IgG is still being elucidated. Acute attacks are typically treated with IV methylprednisolone for 3-5 days followed by a PO prednisone taper. Plasma exchange can be

considered for severe attacks that do not show demonstrable improvement in 1-2 weeks. Chronic immunosuppression is recommended for patients with MOG-IgG attacks with incomplete recovery, relapsing disease, and steroid dependent optic neuritis. Commonly used chronic immunosuppressive agents include mycophenolate, azathioprine, rituximab, and IVIG. MS disease modifying agents are not effective in preventing future attacks. Ultimately, prospective randomized clinical trials comparing acute treatment for severe optic neuritis and chronic treatment modalities will be required to determine the best treatments for MOG-IgG disease.

Figure 1. Treatment algorithm for MOG-IgG optic neuritis
*Duration of prednisone taper depends on history of steroid dependence. For a first attack, consider a prednisone taper over 6-12 weeks. **No significant improvement: <20/200 with ≤2 line improvement.

CME ANSWERS

1. False
2. C
3. False

REFERENCES

1. Lennon VA, Wingerchuk DM, Kryzer TJ, et al. A serum autoantibody marker of neuromyelitis optica: distinction from multiple sclerosis. Lancet 2004;364:2106-12.
2. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology 2015;85:177-89.
3. Berger T, Rubner P, Schautzer F, et al. Antimyelin antibodies as a predictor of clinically definite multiple sclerosis after a first demyelinating event. N Engl J Med 2003;349:139-45.
4. Jarius S, Ruprecht K, Kleiter I, et al. MOG-IgG in NMO and related disorders: a multicenter study of 50 patients. Part 2: Epidemiology, clinical presentation, radiological and laboratory features, treatment responses, and long-term outcome. J Neuroinflammation 2016;13:280.
5. Ramanathan S, Mohammad S, Tantsis E, et al. Clinical course, therapeutic responses and outcomes in relapsing MOG antibody-associated demyelination. J Neurol Neurosurg Psychiatry 2017.
6. Jurynczyk M, Messina S, Woodhall MR, et al. Clinical presentation and prognosis in MOG-antibody disease: a UK study. Brain 2017;140:3128-38.
7. Weber MS, Derfuss T, Metz I, Bruck W. Defining distinct features of anti-MOG antibody associated central nervous system demyelination. Ther Adv Neurol Disord 2018;11:1756286418762083.
8. Jarius S, Ruprecht K, Stellmann JP, et al. MOG-IgG in primary and secondary chronic progressive multiple sclerosis: a multicenter study of 200 patients and review of the literature. J Neuroinflammation 2018;15:88.
9. Ramanathan S, Prelog K, Barnes EH, et al. Radiological differentiation of optic neuritis with myelin oligodendrocyte glycoprotein antibodies, aquaporin-4 antibodies, and multiple sclerosis. Mult Scler 2016;22:470-82.
10. Jarius S, Paul F, Aktas O, et al. MOG encephalomyelitis: international recommendations on diagnosis and antibody testing. J Neuroinflammation 2018;15:134.
11. Jarius S, Ruprecht K, Kleiter I, et al. MOG-IgG in NMO and related disorders: a multicenter study of 50 patients. Part 1: Frequency, syndrome specificity, influence of disease activity, long-term course, association with AQP4-IgG, and origin. J Neuroinflammation 2016;13:279.

12. Chen JJ, Flanagan EP, Jitprapaikulsan J, et al. Myelin Oligodendrocyte Glycoprotein Antibody (MOG-IgG)-Positive Optic Neuritis: Clinical Characteristics, Radiologic Clues and Outcome. Am J Ophthalmol 2018.
13. Ramanathan S, Reddel SW, Henderson A, et al. Antibodies to myelin oligodendrocyte glycoprotein in bilateral and recurrent optic neuritis. Neurol Neuroimmunol Neuroinflamm 2014;1:e40.
14. Chalmoukou K, Alexopoulos H, Akrivou S, Stathopoulos P, Reindl M, Dalakas MC. Anti-MOG antibodies are frequently associated with steroid-sensitive recurrent optic neuritis. Neurol Neuroimmunol Neuroinflamm 2015;2:e131.
15. Ramanathan S, Mohammad S, Tantsis E, et al. Clinical course, therapeutic responses and outcomes in relapsing MOG antibody-associated demyelination. J Neurol Neurosurg Psychiatry 2018;89:127-37.
16. Zhao Y, Tan S, Chan TCY, et al. Clinical features of demyelinating optic neuritis with seropositive myelin oligodendrocyte glycoprotein antibody in Chinese patients. Br J Ophthalmol 2018.
17. Akaishi T, Sato DK, Nakashima I, et al. MRI and retinal abnormalities in isolated optic neuritis with myelin oligodendrocyte glycoprotein and aquaporin-4 antibodies: a comparative study. J Neurol Neurosurg Psychiatry 2016;87:446-8.
18. Zhou L, Huang Y, Li H, et al. MOG-antibody associated demyelinating disease of the CNS: A clinical and pathological study in Chinese Han patients. J Neuroimmunol 2017;305:19-28.
19. Akaishi T, Nakashima I, Takeshita T, et al. Lesion length of optic neuritis impacts visual prognosis in neuromyelitis optica. J Neuroimmunol 2016;293:28-33.
20. Kim SM, Woodhall MR, Kim JS, et al. Antibodies to MOG in adults with inflammatory demyelinating disease of the CNS. Neurol Neuroimmunol Neuroinflamm 2015;2:e163.
21. Jarius S, Ruprecht K, Kleiter I, et al. MOG-IgG in NMO and related disorders: a multicenter study of 50 patients. Part 2: Epidemiology, clinical presentation, radiological and laboratory features, treatment responses, and long-term outcome. J Neuroinflammation 2016;13:280.
22. Dubey D, Pittock SJ, Krecke KN, et al. Myelin Oligodendrocyte Glycoprotein Autoantibody Myelitis; Clinical characteristics, MRI clues and discriminators from other demyelinating myelitis etiologies. In: Clinic M, ed.2018.
23. Chen JJ, Tobin WO, Majed M, et al. Prevalence of Myelin Oligodendrocyte Glycoprotein and Aquaporin-4-IgG in Patients in the Optic Neuritis Treatment Trial. JAMA Ophthalmol 2018;136:419-22.
24. Bonnan M, Valentino R, Debeugny S, et al. Short delay to initiate plasma exchange is the strongest predictor of outcome in severe attacks of NMO spectrum disorders. J Neurol Neurosurg Psychiatry 2018;89:346-51.
25. Magana SM, Keegan BM, Weinshenker BG, et al. Beneficial plasma exchange response in central nervous system inflammatory demyelination. Arch Neurol 2011;68:870-8.
26. Merle H, Olindo S, Jeannin S, et al. Treatment of optic neuritis by plasma exchange (add-on) in neuromyelitis optica. Arch Ophthalmol 2012;130:858-62.
27. Hacohen Y, Wong YY, Lechner C, et al. Disease Course and Treatment Responses in Children With Relapsing Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease. JAMA Neurol 2018;75:478-87.
28. Spadaro M, Gerdes LA, Krumbholz M, et al. Autoantibodies to MOG in a distinct subgroup of adult multiple sclerosis. Neurol Neuroimmunol Neuroinflamm 2016;3:e257.
29. Whittam D, Cobo-Calvo A, Lopez-Chiriboga AS, et al. Treatment of MOG-IgG-associated demyelination with Rituximab: a multinational study of 98 patients. Neurology 2018;90.
30. Lopez-Chiriboga AS, Majed M, Fryer J, et al. Association of MOG-IgG Serostatus With Relapse After Acute Disseminated Encephalomyelitis and Proposed Diagnostic Criteria for MOG-IgG-Associated Disorders. JAMA Neurol 2018.

HEADACHES IN IDIOPATHIC INTRACRANIAL HYPERTENSION

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LEARNING OBJECTIVES

1. Establish the headache phenotype using ICHD-3 criteria
2. Devise a headache management plan incorporating acute and preventive headache treatments
3. Describe the effectiveness of treatments directed at lowering CSF pressure in the management of IIH-related headaches

CME QUESTIONS

1. What percentage of patients with IIH continue to experience headaches after their CSF pressure normalizes?
   A. 33%
   B. 50%
   C. 67%
   D. 80%

2. The most common headache phenotype at baseline in the IIH Treatment Trial was:
   A. migraine without aura
   B. probable migraine without aura
   C. tension-type headache
   D. probable tension-type headache
   E. unclassifiable

3. The most likely explanation for persistent headaches in IIH is:
   A. persistent intracranial hypertension
   B. overuse of acute medications
   C. ongoing central sensitization
   D. venous sinus stenosis

KEYWORDS

1. Idiopathic intracranial hypertension
2. Pseudotumor cerebri
3. Headache

HIGHLIGHTS

- The most common headache phenotypes in the IIHTT were migraine and probable migraine, tension-type and probable tension-type headaches. Only 8% were not classifiable.
- Headache disability in active IIH is severe a major contributor to reduced general quality of life.

- Acetazolamide treatment had no more benefit than placebo in reducing headache disability in the IIHTT.
- About two-thirds of patients with IIH continue to have headaches after their CSF pressure is controlled.
- The headache phenotype drives the therapeutic plan.
- Both acute and preventive treatments are needed, avoiding overuse of acute medications.
- Preventive treatments are selected based on efficacy, cost, possible drug interactions, desirable and undesirable side effects and co-existing medical conditions.
- Procedures to lower ICP frequently only yield short-term benefit.

SUMMARY

Background:
Headache is the most frequent initial symptom and most common symptom of Idiopathic Intracranial Hypertension (IIH). 84% of participants in the Idiopathic Intracranial Treatment Trial (IIHTT) had headache at baseline; values over 90% have been reported in more heterogeneous population including patients with more severe visual loss.[1,2] Careful phenotyping of the headache characteristics in IIHTT participants using the International Classification of Headache Disorders (ICHD-3B) descriptive criteria revealed that the headache most commonly resembled migraine without aura/probable migraine (67%) or tension type/probable tension type headache (25%) with 8% being unclassifiable.[2,3] Common headache-associated symptoms in this cohort include photophobia (70%), phonophobia (52%), nausea (47), vomiting (17%) and worsening with routine physical activity (50%). The pain was constant and daily in 23% of participants with a mean frequency of 12 headache days monthly. Headache disability, as determined by the Headache Impact Test (HIT-6) questionnaire, was severe and headache was a major contributing factor to overall quality of life.[4] Overuse of symptomatic pain relievers was common.[2]

Although headache generally improved in IIHTT participants during the 6 months of randomized treatment, there was no statistical difference in mean HIT-6 scores at 6 months between the acetazolamide group and the placebo group. A small number of enrolees were treated with preventive headache medications, most commonly amitriptyline or nortriptyline (topiramate was an excluded medication). The average HIT-6 score in each group was about 51, reflecting “some impact” on the ability to function. However, over 30% of participants in each treatment group indicated that their headaches had substantial to severe impact at month 6. Headache disability scores did not correlate with cerebrospinal fluid pressure, BMI or visual parameters.[2]

Headaches in patients with IIH often persist after their CSF pressure normalizes, their papilledema resolves and they are elsewise remission. Two independent studies found that about 2/3 of patients continue to experience headaches following otherwise successful treatment.[5,6] It is noteworthy that 41% of the IIHTT participants had a prior history of migraine, which is over twice the prevalence in the general population (18% of women have migraine).[2] The high rate of persistent headaches in IIH may due be to a process similar to chronic migraine and related to central sensitization of the trigeminal system, lowering the threshold for generating headache and perpetuating the pain process.

In summary, experience in clinical trials and in clinical practice underscores the need for effective headache treatment for patients with IIH both during the active phase of the disorder and, in many cases, beyond.

Considerations for Headache Treatment

1. Establish the Phenotype

Headache disorders are classified based on their clinical characteristics: Location, character of the pain, duration, severity, and the presence of associated symptoms (e.g., nausea, vomiting, photophobia, phonophobia, osmophobia).[3]

2. Acute Treatments

Most patients need acute treatment for severe headaches. Acute treatment is appropriately used no more than 2-3 days weekly. More frequent use of many acute treatments may produce medication overuse ("rebound") headache, which can potentially worsen the headache over time. As caffeine can increase intracranial pressure, it should be avoided or minimized (including beverages, over-the-counter and prescription medications containing caffeine); many patients and providers do not consider this simple intervention. Medication overuse is associated with acetaminophen, caffeine, NSAIDs with a short half-life (e.g., ibuprofen), triptans, opioids and butalbital. Corticosteroids should be reserved for "dire straits" situations as their side effects are detrimental and counterproductive (e.g., weight gain, fluid retention).

Acute treatment options: migraine specific therapies (triptans, ergots, isometheptene), NSAIDs, muscle relaxants, antiemetics, non-pharmacologic and complementary/alternative treatments.

3. Preventive Treatments

Indications for prevention are: (1) Four or more moderate to severe headache days monthly; (2) fewer than 4 monthly headache days if associated with significant disability; (3) use of acute treatment more than 2-3 days weekly; (4) patient preference.

Commonly used preventives: topiramate, zonisamide, tricyclic antidepressants, indomethacin, naproxen, onabotulinumtoxinA (chronic migraine phenotype), beta blockers, calcium channel blockers, SSRI/SNRI, gabapentin, riboflavin.[7,8] All have advantages and disadvantages that need to be taken into account. The role of neuromodulation devices, anti-GCRP monoclonal antibodies and cannabinoids is uncertain.

4. Intracranial Pressure Lowering Treatments

The IIHTT suggests that lowering intracranial pressure is not enough. Patients and providers often get fixated with treating the opening pressure measurement which often does not improve the headache. Options: Medical (acetazolamide, methazolamide, other diuretics, octreotide), surgical (shunting)[9], procedural (stenting)[10]

CME ANSWERS

1. C
2. A
3. C

REFERENCES

1. NORDIC Idiopathic Intracranial Hypertension Study Group Writing Committee, Wall M, McDermott MP, et al. Effect of acetazolamide on visual function in patients with idiopathic intracranial hypertension and mild visual loss: The Idiopathic Intracranial Hypertension Treatment Trial. JAMA, 311:641-51, 2014.

2. Friedman DI, Quiros PA, Subramanian PS, et al. Headache in idiopathic intracranial hypertension: findings from the Idiopathic Intracranial Hypertension Treatment Trial. Headache, 57:1195-1205, 2018
3. Headache Classification Committee of the International Headache Society. The international classification of headache disorders, 3rd edition. Cephalalgia 38:18-40, 2018
4. Digre KB, Bruce BB, McDermott MP, et al. Quality of life in idiopathic intracranial hypertension at diagnosis: IIH Treatment Trial results. Neurology 84:2449-56, 2015
5. Friedman DI, Rausch EA. Headache diagnoses in patients with treated idiopathic intracranial hypertension. Neurology 58:1551-3, 2002
6. Yri HM, Rönnbäck C, Wegener M, et al. The course of headache in idiopathic intracranial hypertension: a 12 month prospective follow-up study. Eur J Neurol 21:1458-64, 2014
7. Silberstein SD, Holland S, Freitag F, et al. Evidence-based guidelines update: pharmacologic treatment for episodic migraine prevention in adults. Report of the Quality Standards Committee of the American Academy of Neurology and American Headache Society Neurology 78:1335-45, 2012
8. Holland S, Silberstein SD, Freitag F et al. Evidence-based guideline update: NSAIDs and other complementary treatment for episodic migraine prevention in adults. Report of the Quality Standards Committee of the American Academy of Neurology and American Headache Society. Neurology 78:1346-53, 2012
9. McGirt MJ, Woodworth G, Thomas G, et al. Cerebrospinal fluid shunt placement for pseudotumor cerebri-associated headache: predictors of treatment response and an analysis of long-term outcomes. J Neurosurg 101:627-32, 2004
10. Teleb MS, Cziep ME, Lazzaro MA, et al. Idiopathic intracranial hypertension: A systematic analysis of transverse sinus stenting. Interv Neurol 2:132-43, 2013

HOW IS RADIATION OPTIC NEUROPATHY TREATED?

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LEARNING OBJECTIVES

1. Review diagnostic Criteria for RON
2. Discuss treatment of Radiation Optic Neuropathy (RON) in the ophthalmologic literature
3. Report treatment of Radiation Necrosis in the oncologic literature

CME QUESTIONS

1. True or False: To date, there are less than 500 cases of RON reported in the literature.

2. Treatment modalities considered for RON include all of the following except
    A. Zinc infusions
    B. Vitamin E and Pentoxifylline
    C. Hyperbaric Oxygen
    D. Anticoagulation
    E. Anti VEGF agents
    F. Steroids

3. Pathologic RON specimens have shown presence of:
    A. Areas of necrosis with fibrin exudate
    B. Reactive astrocytosis
    C. Myelin and axonal cylinder loss
    D. Obliterative endarteritis from vascular endothelial injury
    E. All of the above

4. True or False: Concurrent use of chemotherapies such as Vincristine, Temozolomide and Cisplatin can cause radio-sensitization of tissues, placing tissues at higher risk of radiation necrosis.

KEY WORDS

1. Radiation
2. Optic neuropathy
3. Treatment
4. Radio-sensitization
5. Hyperbaric oxygen
6. Bevacizumab

SUMMARY

Diagnostic criteria for RON (Kline L et al, RON, Ophthalmology- 1985) (1,2)

1. Acute visual loss whether monocular or binocular
2. Visual field loss indicating optic nerve or chiasmal dysfunction
3. Absence of optic disc edema
4. Onset within three years of therapy, typically months to years
5. No imaging evidence of visual pathway compression

Radiation optic neuropathy is a devastating late complication of radiotherapy to the anterior visual pathway, first reported in the literature in 1930. In approximately 25% of cases both optic nerves are affected. Effort is usually made to protect the visual pathways with shields, careful radiation dosing protocols, and more precise radiation modalities, and yet RON continues to be reported in the literature. Cases have been seen following external beam radiation, stereotactic radiosurgery, proton beam radiotherapy and whole brain radiation in patients who have been treated with concomitant chemotherapy (Vincristine, Temozolomide and Cisplatin).

Because radiation dose is the primary risk factor for radiation necrosis, retrospective studies have been done to clarify what is a safer dose. In the case of external beam radiation it is found that <50Gy (in fx<2Gy) is the safest, and >70Gy leads to up to a 16% incidence of RON (Ferguson B et al) (16). In the case of stereotactic single fraction radiosurgery it is felt that the risk is <1% if treated with <10Gy (Leavitt J et al)(8).

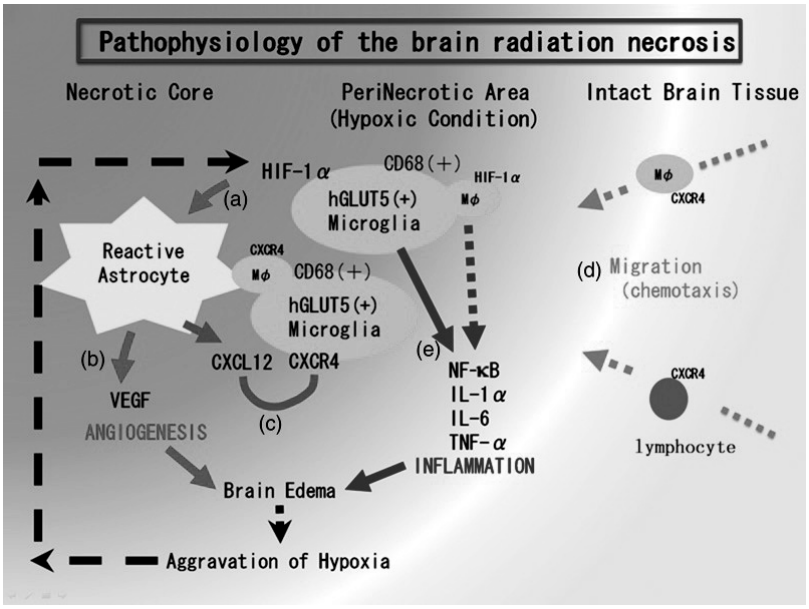
The majority of cases receive IV steroids close to the onset of visual symptoms in hope of reducing swelling in the area of necrosis. Surgical resection of the necrotic tissue is unfortunately not an option with necrosis of the anterior visual pathway. In the oncologic literature radiation necrosis of other areas of the CNS can be considered for resection in selected cases. In the innumerable case reports and retrospective case series, regarding treatment of radiation necrosis, treatments for this condition have included anticoagulation with heparin and warfarin, combination treatment with Vitamin E and Pentoxifylline, hyperbaric oxygen treatment, ACE Inhibitors and IV Bevacizumab (monoclonal antibody against VEGF). The presumed effect and dosing of each treatment will be summarized below. The results have been extremely variable, and often the visual prognosis overall has been poor in one or both eyes. The literature seems to still be grasping for straws. Physicians are often happy to save one eye in the case of RON. What has come out of all of these case reports, and is felt to be of utmost importance, is that diagnosis and treatment needs to be swift in hope of a more positive outcome. Treatment should be started within 24-48 hours of the onset of visual symptoms. Understanding how to use imaging to differentiate necrosis from tumor is therefore essential when presented with a case of presumed RON.

In the ophthalmologic literature there are no prospective, randomized controlled trials that exist regarding any treatments of RON. In the oncologic treatment there is only **one** regarding CNS necrosis. Levin VA et al conducted a randomized double-blind placebo-controlled trial of Bevacizumab therapy for radiation necrosis of the CNS. This is the only Class 1 evidence study regarding available treatment for CNS necrosis, and it was a positive outcome study (14). Why are there so few good studies? The reason is fortunately because though the cases are often devastating, they are fairly rare at any one institution.

In conclusion, when brain lesions are treated with radiation there is always a risk of delayed radiation induced necrosis of healthy brain tissue including the optic nerves and chiasm. The prognosis for

preservation of vision unfortunately remains grim. When choosing a treatment, we must not rely only on the literature that we are comfortable with. There are many more case reports of treating CNS necrosis with Bevacizumab than our ophthalmologic literature suggests. The oncology world does use hyperbaric oxygen treatment as well in select cases, when it is available. This treatment is expensive, not readily available, very time consuming for patients and their family, and the outcomes are not better than with Bevacizumab. Chamberlain et al. reassures naysayers of Bevacizumab in a large case review, that it is safe and is rarely a proven cause of optic neuropathy. They found 0/200 cases of optic neuropathy in patients treated with Bevacizumab and RT for metastatic CNS disease (12,13). Treatment of suspected cases of RON should be started quickly with whichever treatment modality your department is most comfortable with.

Figure 1. Pathophysiology of brain radiation necrosis (from Yoritsune E et al)



Treatments for CNS Radiation Necrosis in the literature:

1. Surgical resection
2. Corticosteroids: 1gm/day for 5 days followed by a long oral prednisone taper
3. Therapeutic anticoagulation for 3-6 months
4. Hyperbaric 0xygen 2-2.4 atmospheres (90-120 minutes/20-30 sessions)
5. IV Bevacizumab 5-7.5 mg/kg every 2-3 weeks for 4-8 cycles
6. Vitamin E 1000mg/day in combination with Pentoxifylline (800mg/day)
7. ACE Inhibitor Ramipril 5-10mg/day

Presumed effect of medications on radiation necrosis:

1. **Corticosteroids**: 1st treatment line since 1984 because of its anti-inflammatory effect. It also moderates vasodilation, and inhibits/downregulates VEGF-induced vascular leakage (as commonly used in the treatment of retinal edema).

2. **Anticoagulation**: Heparin augments activity of antithrombin III and prevents conversion of fibrinogen to fibrin. It inhibits further thrombogenesis in tissues. Warfarin decreases the body's ability to form blood clots by blocking the formation of vitamin K dependent clotting factors.
3. **HBO2**: promotes tissue healing and improves angiogenesis, reduces edema, helps restore normal cellular function in ischemic tissue, enhances VEGF. Also can enhance collagen synthesis for healing. Helps reduce steroid dose. Symptom and imaging improvement has been found. Stabilizes vision in many cases, and in some cases vision improved.
4. **Bevacizumab**: blocks vascular endothelial growth factor (VEGF) from reaching damaged leaky capillaries, reducing edema in tissues. Improvement noted in post gadolinium and FLAIR images on MRI). Since 2007, 22 papers have reported 126 patients with neurologic improvement in 115 patients. There is Class I data/Cleveland Clinic Experience: Levin-2011: evidence showed that 14/14 pts with decrease in T2 FLAIR and T1 weighted gadolinium enhanced volumes**.** All patients showed improvement in neurological symptoms and signs. Boothe D et al studied 11 patients treated with Bevacizumab; decrease in the radiation necrosis volume was seen on T1 post gadolinium and FLAIR MRI by 64% (18).
5. **Vitamin E**: fat soluble vitamin which is a biologic antioxidant that protects cells by scavenging free radicals that cause cell damage. Causes volume reduction of edema in RN.
6. **Pentoxiphylline**: Improves blood flow in ischemic tissue by decreasing the viscosity. It increases red cell flexibility.
7. **ACE inhibitor Ramipril**: anti-hypertensive agent that has angiogenic properties and reduces stromal fibrosis, potentially leading to improved perfusion of hypoxic tissues. It suppresses the renin-angiotensin system.

Managing my next patient with acute Radiation Optic Neuropathy:

1. Hear words "tumor treated and blindness", add the case on to your already busy schedule -**Timing** is likely the essence for all treatments available (within 72 hours of vision loss)
2. Imaging looking for classic enhancement with expansion of the posterior optic nerves on T1/T2 images. Metabolic and perfusion scans can be useful to differentiate from tumor
3. Initiate IV steroids
4. Contact oncologist involved or new oncologist who is comfortable with IV Bevacizumab
5. If cardiac risk factors too large, initiate HBO protocol
6. Need to consider/study the use and safety of IV Bevacizumab and Hyperbaria in combination

CME ANSWERS

1. True
2. A
3. E
4. True

REFERENCES

1. Arnold AC. Radiation optic neuropathy, NANOS Meeting Syllabus 1995; 217-21, Tucson AZ..
2. Kline LB, Kim JY, Ceballos R. Radiation optic neuropathy. Ophthalmology 1985; 92:1118-26.

3. Guy J, Schatz NJ. Hyperbaric oxygen in the treatment of radiation-Induced optic neuropathy. Ophthalmology 1986; 93: 1083-88..
4. Borruat FX, Schatz NJ, Glaser JS, et al Visual recovery from radiation-induced optic neuropathy. J Clin Neuroophthalmol 1993;13:98-101.
5. Lessell S. Friendly fire: Neurogenic visual loss from radiation therapy. J Neuroophthalmol 2004; 24: 243-50.
6. Levy RL, Miller NR. Hyperbaric oxygen therapy for radiation-induced optic neuropathy. Annals of the Academy of Medicine 2006;35(3):151-7.
7. Girkin CA, Comey CH, Lunsford LD, Goodman ML, Kline LB, Radiation optic neuropathy after stereotactic radiosurgery, Ophthalmology 1997; 104:1634-43.
8. Leavitt JA, et al. Long-term evaluation of radiation induced optic neuropathy after single-fraction stereotactic radiosurgery. Int J Radiat Oncol Biol Phys 2013; 87: 524-7.
9. Farooq O, Lincoff NS, et al. Novel treatment for radiation optic neuropathy with intravenous Bevacizumab. J Neuroopthalmol 2012; 32(4):321-4.
10. Archer EL, Liao EA, Trobe JD. Radiation-induced optic neuropathy: Clinical and imaging profile of twelve patients. J Neuroophthalmol 2018.
11. Sherman JH, Aregawi DG, et al. Optic neuropathy in patients with glioblastoma receiving Bevacizumab. Neurology 2009; 73(22): 1924-26.
12. Chamberlain MC. Emerging clinical principles on the use of bevacizumab for the treatment of malignant gliomas. Cancer 2010; 116(17): 3988-99.
13. Chamberlain MC, Raizer J, et al. Optic neuropathy in patients with glioblastoma receiving Bevacizumab. Neurology 2010; 75(3): 289-90.
14. Levin VA, Bidaut L, et al. Randomized double-blind placebo-controlled trial of bevacizumab therapy for radiation necrosis of the CNS. Neuro Onc 2013; 15(9): 1257-63.
15. Leber KA, Bergloff J. Dose-response tolerance of the visual pathways and cranial nerves of the cavernous sinus to stereotactic radiosurgery. J Neurosurg 1998; 88(1): 43-50.
16. Ferguson BA, Huecker MS, Van Stavern G, et al. Risk factors for radiation-induced optic neuropathy: a case control study. Clin Exp Ophthalmol 2017; 45(6): 592-7.
17. Doroslovacki P, Liu GT, et al. Factors associated with occurrence of radiation-induced optic neuropathy at “safe” radiation dosage. Semin Opthalmol 2018; 33(4): 581-8.
18. Boothe D et al. Bevacizumab as a treatment for radiation necrosis for brain metastases post stereotactic radiosurgery. Neuro Oncol 2013; 15(9): 1257-63.
19. Yoritsune E, Furuse M, et al. Inflammation as well as angiogenesis may participate in the pathophysiology of brain radiation necrosis. J Rad Res 2014; 55: 803-11.

SCIENTIFIC PLATFORM SESSION I

Monday, March 18, 2019 - 1:00 pm – 3:00 pm
Red Rock Ballroom
Moderators: Melinda Chang, MD and Timothy J. McCulley, MD

Monday, March 18th from 1:00 - 1:15 pm
An Epidemiological Study of LHON Using a Large International Sample of Affected Individuals

Alexander Pearson[1], Lissa Poincenot[2], Rustum Karanjia[1]

[1]University of Ottawa, Toronto, Canada, [2]LHON Project at www.LHON.org, San Diego, California, USA

Introduction:
Leber's hereditary optic neuropathy (LHON) is the most common inherited mitochondrial disease. It results in acute/subacute, painless, profound loss of central and color vision. The current literature reports males as 4-5 times more likely than females to be affected by LHON, and that symptom onset occurs during late teen/young adult life. As a result, LHON is usually called a "young man's disease." However, this may be a self-fulfilling prophecy, with underdiagnosis of females, older adults and children. We analyzed the epidemiology of LHON using a large international database of people affected by LHON.

Methods:
People with a diagnosis of LHON confirmed by genetic testing provided self-reported data, which was compiled and analyzed.

Results:
Over 1,450 people affected by LHON were included. Only 45% of our data set consisted of "young men". Unlike the traditional 5:1 male to female ratio, we found a 3:1 M:F ratio. The commonly reported peak in symptom onset (ages 14-26) was found only in males. 10.4% of those affected had LHON onset after age 50, whereas the current literature states only 5%. Below the age of 5 and after 45, the M:F ratio of conversion was approximately 1:1. As per the literature, we found that the m.11778 (69%), m.14484 (17%) and m.3460 (13%) were the most common mutations.

Conclusions:
This is the largest epidemiological study of LHON to date. It suggests that females, older adults and children carrying a LHON mutation are at higher risk of losing vision than is generally expected. Contrary to the existing literature, LHON affects females and males of all ages, rather than just young men. This should prompt physicians to conduct genetic testing for LHON in patients who meet the clinical criteria, regardless of whether they fit the traditional demographics.

References: None.

Keywords: Optic neuropathy, Genetic Disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Monday, March 18th from 1:15 - 1:30 pm
Neuro-ophthalmic manifestations of collapsin response-mediator protein-5 (CRMP5) autoimmune neuropathy

Devon Cohen[1], Divyanshu Dubey[1], Jose Pulido[1], Eoin Flanagan[1], Andrew McKeon[1], Sean Pittock[1], Christopher Klein[1], Tariq Bhatti[1], John Chen[1]

[1]Mayo Clinic, Rochester, Minnesota, USA

Introduction:
Collapsin response-mediator protein-5 (CRMP5)-IgG has been associated with paraneoplastic optic neuritis and/or retinitis, but there are only a few case series reporting these findings. To further characterize its neuro-ophthalmic phenotype, we reviewed the neuro-ophthalmic findings and visual outcomes of a large series of patients with CRMP5-IgG.

Methods:
Retrospective chart review of 76 CRMP5-IgG positive patients (defined by serum titer >1:240) seen at the Mayo Clinic from 2001-2017.

Results:
Twenty-nine of 76 (38%) patients had neuro-ophthalmic manifestations. The median age was 67 years (range 33-88) and 20 (69%) were women. Cancer was diagnosed in 67% (small cell carcinoma in 83%). Neuro-ophthalmic symptoms occurred before cancer diagnosis in 65%. Seventeen of 76 (22%) patients had ocular (i.e. anterior visual pathway or intraocular) manifestations. Among these patients, the presenting median visual acuity was 20/50 (range 20/20 – Count Fingers) and the median final visual acuity was 20/40 (range 20/20 – Hand Motion). Fourteen of 17 (82%) had an optic neuropathy. Optic neuropathy was isolated in 6%, associated with retinitis, vitritis, or iritis in 71%, while retinitis, vitritis, or iritis occurred without optic neuropathy in 18%. Among the 12 patients with an optic neuropathy and a documented fundus examination at visual symptom onset, all had optic disc edema. No patient had optic nerve enhancement on magnetic resonance imaging (MRI). Twelve of 76 (16%) had ocular motility manifestations consisting of central nystagmus and diplopia. The predominant neurologic manifestations were neuropathy (75%) and cerebellar ataxia (59%). Coexisting neural autoantibodies were present in 69%, with ANNA1 in 14%. Immunosuppressants, received by 84%, resulted in ocular symptom improvement in 44%.

Conclusions:
Within these CRMP5-IgG positive patients, optic neuropathy was most consistent with a papillitis, often associated with vitritis and/or retinitis. Papillitis was rarely present in isolation, and was not found to be associated with MRI optic nerve enhancement.

References: Cross SA, Salomao DR, Parisi JE, et al. Paraneoplastic autoimmune optic neuritis with retinitis defined by CRMP-5-IgG. Ann Neurol 2003;54:38–50. Dubey D, Lennon VA, Gadoth A, et al. Autoimmune CRMP5 neuropathy phenotype and outcome defined from 105 cases. Neurology 2018;90:e103–10. Pulido J, Cross SA, Lennon VA, et al. Bilateral autoimmune optic neuritis and vitreitis related to CRMP-5-IgG: intravitreal triamcinolone acetonide therapy of four eyes. Eye (Lond) 2008;22:1191–1193. Yu Z, Kryzer TJ, Griesmann GE, Kim K, Benarroch EE, Lennon VA. CRMP-5 neuronal autoantibody: marker of lung cancer and thymoma-related autoimmunity. Ann Neurol 2001;49:146–154.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Monday, March 18th from 1:30 - 1:45 pm

Associations between Pattern Electroretinogram and Intra-retinal Layer Thicknesses in Patients Multiple Sclerosis

Hong Jiang[1], Giovana Gameiro[1], Huiling Hu[1], Vittorio Porciatti[1], Pedro Monsalve[1], Jeffrey Hernandez[1], Siliva Delgado[1], Jianhua Wang[1]

[1]*University of Miami, Miami, USA*

Introduction:

Previous studies (1-4) showed that impaired retinal ganglion cell function associated with thinning of peripapillary retinal nerve fiber layer (RNFL) and combined ganglion cell and inner plexifrom layer (GCIPL) in patients with multiple sclerosis (MS). As multiple intra-retinal layers may be affected in MS, studying the associations between Pattern Electroretinogram (PERG) and various intra-retinal layer thicknesses may provide a better understanding of the PERG measurements and their applications in monitoring disease progression.

Methods:

A total of 140 eyes of 70 relapsing-remitting MS patients were studied using PERG and ultrahigh resolution OCT (UHR-OCT), and compared with 126 eyes (HC) of 63 age- and sex-matched healthy subjects. Of MS eyes, there were 30 eyes with optic neuritis (MSON), and 22 non-ON fellow eyes (MSFE), in addition to 88 non-ON MS eyes (MSNON). A steady-state PERG was concurrently recorded from each eye. Volumetric data of the various intra-retina layers centered on the fovea acquired using UHR-OCT were segmented to obtain the thickness maps of six intra-retinal layers.

Results:

The average PERG amplitude and latency in MS eyes (MSON, MSFE, and MSNON) were significantly lower compared to HC eyes (post hoc, $P < 0.05$) after age and sex adjustment. Also, PERG amplitude and latency in MSON eyes were significantly lower than in other MS groups ($P < 0,05$), however, there were no significant differences of the amplitude and latency between MSFE and MSNON ($P > 0.05$). Both the amplitude and latency in the MS eyes were significantly correlated to the annular thickness of the macular RNFL and GCIPL (r range from 0.36 to 0.42, $P < 0.05$).

Conclusions:

This study reveals impaired ganglion cell function in patients with multiple sclerosis regardless of optic neuritis, which were mostly related to macular RNFL and GCIPL. It appears that generalized subclinical ganglion cell dysfunction occurs in MS.

References: 1. Monsalve P, Ren S, Jiang H, et al. Retinal ganglion cell function in recovered optic neuritis: Faster is not better. Clin Neurophysiol. 2018;129:1813-1818. 2.Rodriguez-Mena D, Almarcegui C, Dolz I, et al. Electropysiologic evaluation of the visual pathway in patients with multiple sclerosis. J Clin Neurophysiol. 2013;30:376-381. 3. Almarcegui C, Dolz I, Pueyo V, et al. Correlation between functional and structural assessments of the optic nerve and retina in multiple sclerosis patients. Neurophysiol Clin. 2010;40:129-135. 4. Parisi V, Manni G, Spadaro M, et al. Correlation between morphological and functional retinal impairment in multiple sclerosis patients. Invest Ophthalmol Vis Sci. 1999;40:2520-2527.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: The work has been supported by the National Multiple Sclerosis Society (RG-1506-04890), NIH Center Grant P30 EY014801, and a grant from Research to Prevent Blindness (RPB).

Monday, March 18th from 1:45 - 2:00 pm
Presentation of NAION in a Global Treatment Trial

Mark Kupersmith[1], Neil Miller[2], Mays El-Dairi[3], Leonard Levin[4], Sharon Klier[5]

[1]Icahn School of Medicine at Mount Sinai and New York Eye and Ear Infirmary, New York, New York, USA, [2]Wilmer Eye Institute at Johns Hopkins, Baltimore, Maryland, USA, [3]Duke University School of Medicine, Durham, North Carolina, USA, [4]McGill University School of Medicine, Montreal, Canada, [5]Quark Pharmaceutical, Fremont, California, USA

Introduction:
Knowledge of presenting features and systemic factors associated with acute NAION is based predominantly on retrospective reports and one prospective treatment trial, with only 258 participants. The Quark / NORDIC NAION treatment trial will recruit 800 participants and the features of the first 400 enrolled provides the largest prospectively uniformly collected dataset on NAION from multiple sites in 8 countries.

Methods:
We report screening and enrollment data for participants with acute symptomatic NAION in a multi-country multi-site clinical trial including detailed medical history, laboratory studies, EKG, extensive evaluation including optical coherence tomography (OCT) and 24-2 threshold perimetry with use of spot III for screening and spot V as an outcome for the first time in a clinical trial.

Results:
Of the 121 women and 279 men, average age 61 years, 46% had hypertension, 24% diabetes, 46% hyperlipidemia, 25% cardiac disease, 2.5% ischemic brain disease (all of which varied widely by country). 18% had prior fellow eye NAION. With a mean separation of 1.9±2.0 days for screen and day 1, visual acuity (r=0.90) and the average visual field threshold (r=0.89) strongly correlated. Retinal nerve fiber layer (NFL) thickening had a mild correlation with the average threshold for spot 3(r= 0.24) and spot 5 (r=0.27) but not with visual acuity.

Conclusions:
Our data corroborate the prior described associations for systemic factors but show that hyperlipidemia is more frequent and cerebrovascular disease is less common than previously recognized. RNFL thickening correlated better with visual field threshold than with visual acuity.

References: None.

Keywords: Optic neuropathy, Vascular disorders, Visual fields

Financial Disclosures: Consultant Quark Pharmaceutical.

Grant Support: Quark Pharmaceutical Sponsored clinical trial.

Monday, March 18th from 2:00 - 2:15 pm
Characterization of Visual Pathway Abnormalities in Infants with Congenital Zika Syndrome using CT and MRI

Amanda Henderson[1], Thierry A. G. M. Huisman[2], Avner Meoded[3], Adriano Hazin[4], Vanessa van der Linden[5], William May[1]

[1]Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA, [2]Johns Hopkins University School of Medicine; Texas Children's Hospital, Baltimore, Maryland, USA, [3]Johns Hopkins University School of Medicine, Baltimore, Maryland, USA, [4]Instituto de Medicina Integral Professor Fernando Figueira, Recife, Brazil, [5]Barão de Lucena Hospital, Recife, Brazil

Introduction:
Congenital malformations related to Zika virus infection were first described in 2015 among infants born in the Pernambuco state of Brazil. The congenital Zika syndrome since has been further characterized to include microcephaly, ocular abnormalities, arthrogryposis, and spinal cord thinning. Additionally, severe visual impairment has been demonstrated in affected infants, often in the absence of ocular abnormalities. However, to our knowledge, there has not been a comprehensive characterization of visual pathway abnormalities in these patients. The purpose of this study is to characterize visual pathway abnormalities in the congenital Zika syndrome using MRI and CT.

Methods:
Preliminary neuroimaging information was obtained from a referred sample of 106 infants with clinical and epidemiologic data consistent with congenital Zika syndrome. All infants were from the Pernambuco state of Brazil. Subjects were excluded if images were of inadequate quality for interpretation. Head CT images adequate for interpretation were available for 55, and brain MRI images adequate for interpretation were available for 21. 4 infants had both CT and MRI images. We systematically evaluated a total of 76 scans from 72 infants for abnormalities of the visual pathways.

Results:
Scans from 34 males and 38 females were included in the analysis. The mean age of the infants at the time of neuroimaging was 15 weeks post-gestational age (range 0 days to 12 months). Overall, 72 of 76 (95%) scans showed occipital volume loss, while 8 (11%) showed optic atrophy, 1 (1%) showed chiasmal atrophy, and 1 (1%) showed a globe abnormality.

Conclusions:
Our results suggest that cortical visual impairment related to structural abnormalities of the occipital cortex likely is an important cause of visual impairment in children with congenital Zika syndrome. Further study correlating the degree of occipital cortical abnormality to visual outcomes is required.

References: Brito C. Zika virus: A new chapter in the history of medicine. Acta Med Port. 2015;28(6):679-80. de Paula Freitas B, Ventura CV, Maia M, Belfort R, Jr. Zika virus and the eye. Curt Opin Ophthalmol. 2017;28(6)595-9. del Campo M, Feitosa IM, Ribeiro EM, et al. The phenotypic spectrum of congenital Zika syndrome. Am J Med Genet A. 2017;173(4):841-57. Ventura LO, Ventura CV, Dias NC, et al. Visual impairment evaluation in 119 children with congenital Zika syndrome. J AAPOS. 2018;22(3):218-22. Ventura LO, Ventura CV, Lawrence L, et al. Visual impairment in children with congenital Zika syndrome. J AAPOS. 2017;21(4):295-9.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Monday, March 18th from 2:15 - 2:30 pm
A Prospective Outcomes Study of Pediatric Optic Neuritis

Stacy Pineles[1], Michael Repka[2], Grant Liu[3], Elizabeth Lazar[4], Amy Waldman[5], Mark Borchert[6], Sangeeta Khanna[7], Gena Heidary[8], Jennifer Graves[9], Veeral Shah[10], Mark Kupersmith[11], Ray Kraker[4], David Wallace[12]

[1]Stein Eye Institute, UCLA, Los Angeles, California, USA, [2]Wilmer Eye Institute, Baltimore, USA, [3]University of Pennsylvania, Philadelphia, USA, [4]Jaeb Center for Health Research, Tampa, USA, [5]childrens hospital of philadelphia, philadelphia, USA, [6]childrens hospital of los angeles, los angeles, USA, [7]Saint Louis University, saint louis, USA, [8]boston childrens hospital, boston, USA, [9]UCSD, san diego, USA, [10]baylor college of medicine, houston, USA, [11]mt sinai, new york, USA, [12]Indiana University, indianapolis, USA

Introduction:
We are aware of no prospective data on visual outcomes in children with optic neuritis (ON).

Methods:
In a non-randomized observational study, we prospectively enrolled 3-<16 year olds with a clinical diagnosis of acute ON (onset within 2 weeks) and at least one of the following: visual acuity (VA) deficit ≥0.2 logMAR below age-based norms in the affected eye, diminished color vision, abnormal visual field, or optic disc swelling. The outcome was percentage of study eyes within age-normal VA range after 6 months.[1-3]

Results:
Fifty-four eyes of 44 participants age 3-15 years were enrolled; 41% were female. Regarding type of ON and central nervous system associations: 14 participants had unilateral isolated ON, 10 had bilateral isolated ON, 8 had acute disseminated encephalomyelitis, 5 had multiple sclerosis, 5 had neuromyelitis optica spectrum disorder, and 1 had myelin oligodendrocyte glycoprotein-associated demyelination. Twenty-two (51%) had cerebral white matter lesions and 39 (89%) were treated with steroids. Of the 31 affected eyes with 6-month follow-up, 8 (26%) had VA within age-normal range at enrollment (median 0.50 logMAR, range -0.20 to 1.70 logMAR) and 24 (77%) eyes had VA within age-normal range (median 0.00 logMAR, range -0.22 to 0.60 logMAR) after 6 months.

Conclusions:
This is the first prospective study of VA outcomes in pediatric ON. Despite poor VA at presentation (median Snellen equivalent = 20/63), there was marked improvement (median = 20/20) in the majority of eyes six months after onset. Associated neurologic syndromes were relatively common in this cohort.

References: [1] Pan Y, Tarczy-Hornoch K, Cotter SA, Wen G, Borchert MS, Azen SP, et al. Visual acuity norms in pre-school children: the Multi-Ethnic Pediatric Eye Disease Study. Optom Vis Sci. 2009;86:607-12. [2] Drover JR, Felius J, Cheng CS, Morale SE, Wyatt L, Birch EE. Normative pediatric visual acuity using single surrounded HOTV optotypes on the Electronic Visual Acuity Tester following the Amblyopia Treatment Study protocol. Journal of AAPOS : the official publication of the American Association for Pediatric Ophthalmology and Strabismus / American Association for Pediatric Ophthalmology and Strabismus. 2008;12:145-9. [3] Yamada T, Hatt SR, Leske DA, Moke PS, Parrucci NL, Reese JJ, et al. A new computer-based pediatric vision-screening test. J AAPOS. 2015;19:157-62.

Keywords: Pediatric neuro-ophthalmology, Optic neuropathy, Demeylinating disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Monday, March 18th from 2:30 - 2:45 pm
Long-term OCT follow-up in Children with Optic Disc Drusen

Lasse Malmqvist[1], Alexander Thomsen[1], Steffen Hamann[1]

[1]*Department of Ophthalmology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark*

Introduction:
A better understanding of optic disc drusen (ODD) etiology and pathophysiology might be possible by visualizing progression of ODD and potential precurser lesions. The purpose of this study was to examine the progression of ODD and scleral canal diameter in children previously diagnosed with ODD and to assess potential precursor lesions in children with newly developed ODD.

Methods:
Five-year follow-up enhanced depth imaging optical coherence tomography (OCT) scans of the optic nerve head from 724 children aged 16-17 were assessed. Presence of ODD and comparison with previous examination was assessed in all children. Scleral canal diameter was measured in 15 children with ODD and in 115 controls.

Results:
Of the 724 re-examined children, 16 (2.2 %) had ODD in one or both eyes. Children with ODD had a mean scleral canal diameter of 1377 µm (95%CI 1332-1423 µm), whereas it was 1484 µm (95%CI 1455-1512µm) in the 115 controls without ODD (P<0.001). Hyperreflective lines on OCT were found in all children with ODD and in 24 children without ODD (P<0.001). Healthy children with hyperreflective lines had a smaller scleral canal than healthy children without hyperreflective lines (-155 µm, 95%CI -44- -268 µm).

Conclusions:
This study found an increased prevalence of ODD compared with the same cohort four years ago. The prevalence is now comparable with histopathological prevalences of ODD in cohorts including older patients suggesting that ODD develops before adulthood. Similar to the initial examination, OCT revealed a narrow scleral canal in children with ODD compared with healthy children, which further establishes a small scleral canal as a predisposing factor to ODD. The finding of hyperreflective lines at the initial examination in eyes from three out of four children with newly developed ODD and hyperreflective lines in eyes from all children in the re-examination suggests these as precursor lesions.

References: None.

Keywords: Optic neuropathy, Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

Grant Support: Jørgen Bagenkop Nielsens Myopi-Fond Fight for Sight Denmark Synoptik-Fonden.

Monday, March 18th from 2:45 - 3:00 pm
Progressive Neurodegeneration of the Retinal Nerve Fiber Layer in Veterans with Mild Traumatic Brain Injury

Randy Kardon[1], Kelvin Lim[2], Casey Gilmore[2], Johannes Ledolter[3]

[1]Department of Veterans Affairs and University of Iowa, Iowa City, Iowa, USA, [2]Department of Veterans Affairs (Minneapolis VA) and University of Minnesota, Minneapolis, Minnesota, USA, [3]Department of Veterans Affairs (Iowa City VA) and the University of Iowa, Iowa City, Iowa, USA

Introduction:
The purpose of this investigation was to prospectively evaluate the structure and functional changes over time in the visual and central nervous system in veterans with a history of mild traumatic brain injury compared to age-matched control group of veterans. There is concern for progressive neurodegeneration after traumatic brain injury leading to Chronic Traumatic Encephalopathy (CTE), resulting in dementia, depression and suicide. We have prospectively evaluated veterans for structural (OCT) and functional changes (acuity, contrast sensitivity and visual field) over time in the visual system and central nervous system (neurobehavioral tests and structural and functional MRI). Here we report the results of retinal layer evaluation.

Methods:
67 veterans with mild TBI and 69 age-matched control veterans without any other eye disorder were enrolled and are being evaluated every 6 months. Optical Coherence Tomography (OCT) was recorded in addition to tests of visual function, cognition and structural and functional MRI. Outcome measures were evaluated for linear slope.

Results:
49 mild TBI veterans and 54 controls had at least 3 time points recorded to date. The mean RNFL slope in mild TBI showed significantly more loss compared to the normal veteran group (-1.25 microns/year TBI vs -0.1 micron/year normal; ANOVA: $F(1,101)=9.03$, $p=.003$). When adjusted for age and TBI severity as covariates, the difference in slope was still significant (ANCOVA: $F(1,99)=5.18$, $p=.025$). The slope of the average GCL-IPL was not significantly different between the two groups.

Conclusions:
To date, we have found evidence for a significant, progressive loss of RNFL thickness in veterans with mild TBI, indicating that retinal thickness analysis may be useful for predicting neurodegeneration. Continued evaluation of subjects will determine if functional deterioration in the visual and cognitive pathways follow structural loss and whether structural and functional MRI findings at the beginning and end time points also show corresponding changes.

References: None.

Keywords: Optic nerve trauma and treatment, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Stroke Trauma, Neuro-ophth & systyemic disease (eg. MS, MG, thyroid)

Financial Disclosures: Funding from Department of Veterans Affairs RR&D and Department of Defense through the Chronic Effects of Neurotrauma Consortium (CENC).

Grant Support: Funded by the Department of Veterans Affairs RR&D and the DOD through the Chronic Effects of Neurotrauma Consortium (CENC) and the Iowa City VA Center for the Prevention and Treatment of Visual Loss.

North American Neuro-Ophthalmology Society

45th Annual Meeting

March 16 – March 21, 2019
Red Rock Casino, Resort & Spa • Las Vegas, Nevada
Program Schedule

Tuesday, March 19

6:00 am – 6:45 am	**Yoga**	**Veranda DE**
6:30 am – 7:30 am	**Breakfast**	**Charleston Ballroom**
6:30 am – 5:00 pm	**Registration/Help Desk**	**5th floor Registration Desk**
6:30 am – 7:30 am	**JNO Editorial Board Meeting**	**Veranda AB**
7:30 am – 10:00 am	**Scientific Platform Session II**	**Red Rock Ballroom**

Moderators: Michael Vaphiades, DO and Kimberly K. Gokoffski, MD, PhD

7:30 am – 7:45 am	**Adduction-induced Deformations of the Optic Nerve Head Evokes Peripapillary Folds in Papilledema**, *Patrick A. Sibony, MD*
7:45 am – 8:00 am	**Tree Shrew Spontaneous Retinal Venous Pulsation Changes Due to Changes in the Translaminar Pressure Difference**, *Michael Dattilo, MD, PhD*
8:00 am – 8:15 am	**Near Infrared Videography versus Direct Ophthalmoscopy for the Detection of Spontaneous Venous Pulsations**, *Perry J. Thompson, BA*
8:15 am – 8:30 am	**Quantitative Optical Coherence Tomography Angiography (OCTA) and Visual Field Defects in Idiopathic Intracranial Hypertension**, *Melinda Chang, MD*
8:30 am – 8:45 am	**Detection of Visual Loss in IIH with Static Automated Perimetry: Temporal Wedge Defects**, *Michael Wall, MD*
8:45 am – 9:00 am	**Artificial Intelligence for Detection and Classification of Abnormal Optic Discs on Fundus Photographs**, *Dan Milea, MD, PhD*
9:00 am – 9:15 am	**The Untuned Visuo-temporal Cortex in Patients with Visual Snow**, *Ghislaine L. Traber, MD*
9:15 am – 9:30 am	**Object Recognition in Acquired and Developmental Prosopagnosia: Is it Really Just About Faces?** *Jason S. Barton, MD, PhD, FRCPC*
9:30 am – 9:45 am	**eMULES in concussion: A quantitative 'Look' at the Eye Movements**, *Todd E. Hudson, PhD*
9:45 am – 10:00 am	**Positional Testing in Acute Vestibular Syndrome: A Transversal and Longitudinal Study**, *Joao Lemos, MD, PhD*

10:00 am – 10:30 am	**Coffee with Exhibitors** (with support from EMD Serono)	**Charleston Ballroom**
10:30 am – 12:30 pm	**Scientific Platform Session III**	**Red Rock Ballroom**

Moderators: Jeffrey Bennett, MD, PhD and Heather Moss, MD, PhD

10:30 am – 10:45 am	**rAAV2/2-ND4 Treatment of Leber Optic Neuropathy: 72-Week Data from the REVERSE Phase III Clinical Trial**, *Nancy Newman, MD*
10:45 am – 11:00 am	**Efficacy of Chronic Immunotherapy for Myelin Oligodendrocyte Glycoprotein-IgG Disease***, John J. Chen, MD, PhD*
11:00 am – 11:15 am	**Amnion-derived Multipotent Progenitor Cells Attenuate Optic Nerve and Spinal Cord Demyelinating Disease**, *Kenneth S. Shindler, MD, PhD*
11:15 am – 11:30 am	**MEK Inhibitor Treatment Promotes Retinal Ganglion Cell Preservation without Preventing Retrobulbar Demyelination in Neurofibromatosis Mice***, Steven F. Stasheff, MD, PhD*
11:30 am – 11:45 am	**Melanopsin: Targeted Ectopic Expression for Optogenetic Visual Restoration***, Michael J. Gilhooley, MA, MB, BChir, FRCOphth*
11:45 am – 12:00 pm	**The Stressed Optic Nerve at High Altitude and Treatment with Chemical Chaperon***, Yaping (Joyce) Liao, MD, PhD*
12:00 pm – 12:15 pm	**Physiologic Electrical Fields Direct Retina Ganglion Cell Axon Growth**, *Kimberly K. Gokoffski, MD, PhD*
12:15 pm – 12:30 pm	**Visual Impairment in Patients with Giant Cell Arteritis Treated with Tocilizumab in Real-World Clinical Practice***, Timothy J. McCulley, MD*

12:30 pm – 1:00 pm	**Lunch**	**Charleston Ballroom**
1:00 pm – 3:00 pm	**Poster Session II: Scientific Advancements**	**Red Rock Ballroom A-C**
1:00 pm – 2:00 pm	**Odd Numbered Posters**	
2:00 pm – 3:00 pm	**Even Numbered Posters**	
3:00 pm – 4:00 pm	**Abstract Committee Meeting**	**Veranda D**
3:15 pm	**Optional Excursions (advanced registration required)**	
4:15 pm – 5:15 pm	**Consortium of Pediatric Neuro-Ophthalmologists Meeting (CPNO) - All are welcome to attend** *Facilitator: Paul Phillips, MD*	**Veranda AB**

SCIENTIFIC PLATFORM SESSION II

Tuesday, March 19, 2019 - 7:30 am – 10:00 pm
Red Rock Ballroom
Moderators: Michael Vaphiades, DO and Kimberly K. Gokoffski, MD

9:30 am - 9:45 am	Todd E. Hudson, PhD eMULES in Concussion: A Quantitative 'Look' at the Eye Movements	**269**
9:45 am - 10:00 am	Joao Lemos, MD, PhD Positional Testing in Acute Vestibular Syndrome: A Transversal and Longitudinal Study	**270**

Tuesday, March 19th from 7:30 - 7:45 am
Adduction-induced deformations of the optic nerve head evokes peripapillary folds in papilledema

Patrick Sibony[1], Wei Hou[2]

[1]State University of New York at Stony Brook, Stony Brook, New York, USA, [2]Department of Family, Population and Preventive Medicine, SUNY Stony Brook., Stony Brook, New York, USA

Introduction:
Peripapillary wrinkles (PPW,"Paton's folds") is a time-tested sign of optic disc edema. We have observed that PPW are more evident in adduction than primary or abduction. Occasionally PPW not otherwise present in primary, become evident only in adduction. This report examines the frequency, mechanism and clinical utility of this novel clinical sign of papilledema.

Methods:
We examined the OCTs of 32 patients (64 eyes) with papilledema, 10 normals(20eyes) and 12(20 eyes) with optic nerve head drusen. The transverse-axial and en-face images acquired in primary-position and 30°abduction/30°adduction were examined for the presence and distribution of PPW. Using a generalized estimating equations (GEE) model we determined how gaze-induced angular-deformations between abduction/adduction ("seesaw deformations") of the optic nerve head(ONH) are associated with the pattern of PPWs.

Results:
There were four patterns of folds in papilledema: A. 20/64 (31%) no folds; B. 8/64 (13%) folds in primary position without change in abduction/adduction; C. 24/64 (38%) folds in primary/abduction, worse in adduction D. 12/64 (19%) folds present only in adduction. The mean gaze-evoked angular deformation in group D(mean±SD:14.6°±4.8°) was significantly larger than A(8.4°±3.2°, $p<0.0001$), B(7.6°±4.16°, $p<0.004$), or C(12.0°±5.6°, $p=0.003$). C was significantly larger than A($p<0.0001$). A-B and B-C were not significantly different. There were no folds in primary or eccentric gaze among patients with optic disc drusen or normal subjects.

Conclusions:
PPW help distinguish papilledema from pseudo-papilledema. In papilledema, PPW may be exaggerated (38%) or evoked (19%), when the eye is 30°adducted. The exaggeration of folds is a consequence of mechanical strain on the ONH- greatest in adduction especially among patients with large gaze-induced "seesaw" deformations. Examination of the ONH in adduction enhances the appearance of PPW by both OCT and ophthalmoscopy. The exaggeration of PPW (even if only visible in adduction) and or large gaze-induced seesaw deformations are novel distinctive signs particularly helpful in distinguishing low-grade papilledema from pseudo-papilledema.

References: Sibony, P. A., Kupersmith M. J., Feldon, S. E. Wang J. K., Garvin M. and OCT substudy , IIHTT. "Retinal and Choroidal Folds in Papilledema." Invest Ophthalmol Vis Sci 56(10): 5670-5680. (2015) Sibony, P. A., Kupersmith M. J. and OCT substudy , IIHTT. "Paton's Folds" Revisited: Peripapillary Wrinkles, Folds, and Creases in Papilledema." Ophthalmology 123(6): 1397-1399. (2016). Sibony, P. A. "Gaze Evoked Deformations of the Peripapillary Retina in Papilledema and Ischemic Optic Neuropathy." Invest Ophthalmol Vis Sci 57(11): 4979-4987. (2016).

Keywords: Pseudotumor Cerebri, Optic neuropathy, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

Financial Disclosures: Heidelberg Engineering, invited speaker honorarium, International Spectralis Symposium and AAO meeting 2018.

Grant Support: None.

Tuesday, March 19th from 7:45 - 8:00 am

Tree Shrew Spontaneous Retinal Venous Pulsation Changes Due to Changes in the Translaminar Pressure Difference

Michael Dattilo[1], Brian Samuels[2], C. Ross Ethier[3]

[1]Emory Eye Center, Emory University School of Medicine, Atlanta, Georgia, USA, [2]University of Alabama at Birmingham, Birmingham, Alabama, USA, [3]Georgia Institute of Technology, Atlanta, Georgia, USA

Introduction:
Spontaneous retinal venous pulsations (SRVPs) are known to be affected by the translaminar pressure difference (TLPD). SRVPs occur less frequently and have smaller amplitudes in glaucoma patients, are absent in syndromes of elevated intracranial pressure (ICP) and are used clinically to qualitatively assess ICP. Although SRVPs are influenced by the TLPD, the exact relationship between SRVPs, intraocular pressure (IOP), and ICP remains uncertain.

Methods:
SRVP screening: Live en face optical coherence tomography (OCT) video output of the retinal vasculature of anesthetized adult tree shrews was recorded and analyzed to determine SRVP incidence under normal physiologic conditions (+SRVP) and to quantify central retinal vein diameter changes. IOP & ICP manipulation: Under anesthesia, the intracranial cerebrospinal fluid-containing space and the anterior chamber of a +SRVP tree shrew were cannulated. ICP was pressure clamped at 7 mmHg and IOP was incrementally changed from 5 to 30 and back to 5 mmHg. ICP was increased to 30 mmHg and the IOP protocol was repeated. SRVP changes were recorded and analyzed.

Results:
SRVPs were detected in 12/16 tree shrews. In an +SRVP tree shrew, an IOP of 10 mmHg was necessary to generate SRVPs at an ICP of 7 mmHg, while an IOP of 20.5 mmHg was necessary to generate SRVPs at an ICP of 30 mmHg. Increasing ICP also affected SRVP amplitude; SRVP amplitude was smaller at an ICP of 30 mmHg compared to an ICP of 7 mmHg.

Conclusions:
Tree shrew SRVP frequency and characteristics are similar to the reported SRVP frequency and characteristics in humans. Therefore, tree shrews likely are a good animal system to further study SRVPs. Since there does not appear to be a simple, one-to-one correlation between changes in the TLPD and changes in SRVP characteristics, further studies are necessary to understand the complex relationship between SRVPs, IOP, and ICP.

References: Berdahl JP, Fautsch MP, Stinnett SS, Allingham RR. Intracranial pressure in primary open angle glaucoma, normal tension glaucoma, and ocular hypertension: a case-control study. Invest Ophthalmol Vis Sci, 49:5412-8, 2008. Zhang X, Medow JE, Iskandar BJ, et al. Invasive and noninvasive means of measuring intracranial pressure: a review. Physiol Meas 38:R143-R82, 2017. Golzan SM, Graham SL, Leaney J, Avolio A. Dynamic association between intraocular pressure and spontaneous pulsations of retinal veins. Curr Eye Res 36:53-9, 2011. Levine DN, Bebie H. Phase and amplitude of spontaneous retinal vein pulsations: An extended constant inflow and variable outflow model. Microvasc Res 106:67-79, 2016.

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: NIH/NEI T32EY007092-31 (MD) NIH/NEI R21EY02621 (BCS).

Tuesday, March 19th from 8:00 - 8:15 am
Near Infrared Videography versus Direct Ophthalmoscopy for the Detection of Spontaneous Venous Pulsations

Perry Thompson[1], Luai Eldweik[2], Yao Wang[2], Michael Lee[2], Michael Shyne[2], Ahmed Kassem[2], John Chen[3], Collin McClelland[2]

[1]University of Minnesota Medical School, Minneapolis, Minnesota, USA, [2]University of Minnesota, Minneapolis, Minnesota, USA, [3]Mayo Clinic, Rochester, Minnesota, USA

Introduction:
Spontaneous venous pulsations (SVPs), a specific examination finding of non-elevated intracranial pressure, have been observed in about 90% of the general population and about 80% of eyes using direct ophthalmoscopy (DO). We compare the prevalence of SVPs detected with DO to the prevalence of SVPs detected with near infrared videography in a normal population.

Methods:
Normal, undilated subjects were examined at a state fair using DO and Spectralis optical coherence tomography near infrared videography (OCT-IRV). DO and OCT-IRV were performed for 60 seconds to look for the presence or absence of SVPs. Two authors, masked to the DO findings, independently reviewed the near infrared videos for SVPs later, and conflicts in interpretation were adjudicated. 517 eyes (267 subjects) were included in the study.

Results:
OCT-IRV was significantly more sensitive in the detection of SVPs in eyes (88.78%; $X2 = 105.34$; $p < 0.0001$) and subjects (95.13%; $X2 = 46.349$; $p < 0.0001$) than DO (61.12% of eyes, 73.78% of subjects). Of the eyes with SVPs present on OCT, 91.28% (95% CI: 87.95, 94.63) had visible pulsations within the first 15 seconds of video. When using DO, higher SVP detection rates were observed by attending physicians (65.77% of eyes, $p < 0.0001$; 76.88% of subjects, $p = 0.0034$) and the fellow (66.67% of eyes, $p < 0.0001$; 80.77% of subjects, $p = 0.0052$) than the resident (34.18% of eyes; 52.38% of subjects).

Conclusions:
Infrared videography is widely available technology and may improve the detection of SVPs in a clinical setting. These results suggest that physicians in training and clinicians who do not regularly perform direct ophthalmoscopy may find near infrared videography an especially useful method to assess SVPs.

References: Levin, The Clinical Significance of Spontaneous Pulsations of the Retinal Vein, Archives of Neurology, 35, 37-40, 1978. Lorentzen, Incidence of Spontaneous Venous Pulsation in the Retina, Acta Ophthalmologica, 48, 765-770, 1970.

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.

Tuesday, March 19th from 8:15 - 8:30 am
Quantitative Optical Coherence Tomography Angiography (OCTA) and Visual Field Defects in Idiopathic Intracranial Hypertension

Melinda Chang[1]

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Introduction:
Introduction: Idiopathic intracranial hypertension (IIH) is characterized by papilledema and visual field (VF) defects. The role of optical coherence tomography angiography (OCTA) in IIH and the relationship between OCTA and VF defects in IIH have not been previously explored.

Methods:
We prospectively recruited 12 patients with IIH and 12 age-matched controls. All subjects underwent complete neuro-ophthalmic exam including automated VF testing, in addition to optical coherence tomography (OCT) and OCTA of the optic nerve using the Optovue RTVue with Angiovue software. We compared capillary density (CD) by OCTA in the whole image (wiCD), optic disc (odCD) and peripapillary region (ppCD) between patients with IIH and normal controls. In IIH patients, OCTA and OCT measures were correlated to VF mean deviation (MD). Additionally, the accuracy of perfusion deficits on OCTA for identifying the location of VF defects was calculated.

Results:
IIH patients with papilledema had significantly increased optic disc CD compared to controls (54% vs. 52%, p=0.009), while resolved papilledema was associated with decreased odCD and ppCD (both 48%, p=0.04). The wiCD and ppCD on OCTA were strongly correlated with VF MD in IIH subjects (both r=0.76, p=0.0001). The correlations between VF MD and OCT structural measures (ganglion cell complex and retinal nerve fiber layer thickness) were weaker (r=0.63 and 0.36, respectively). The location of peripapillary perfusion deficits on OCTA agreed with VF defect location in 81% of cases.

Conclusions:
IIH was associated with significant optic nerve and peripapillary vascular changes, as demonstrated by OCTA. OCTA measures strongly correlated with visual function by automated VF testing, and were superior to structural OCT measures for predicting degree of VF loss. Quantitative OCTA may be a useful objective measurement in the evaluation of patients with IIH.

References: None.

Keywords: Pseudotumor Cerebri, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Tuesday, March 19th from 8:30 - 8:45 am
Detection of Visual Loss in IIH with Static Automated Perimetry: Temporal Wedge Defects

Michael Wall[1], Ashwin Subramani[2], Luke Chong[3], Ramon Galindo[2], Randy Kardon[2], Matthew Thurtell[2], Jane Bailey[2], Andrew Turpin[4]

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Introduction:
The peripheral visual field outside of the central 30° is rarely tested with static automated perimetry. We performed a cross-sectional clinical study to characterize visual loss across the full visual field in idiopathic intracranial hypertension (IIH) patients with mild central visual loss.

Methods:
We tested the full visual field (64 central and 64 far peripheral test locations: 50° nasal, 80° temporal, 30° superior, 45° inferior) of one eye of 39 IIH patients. We developed the software on the Octopus 900 perimeter running the Open Perimetry Interface with stimulus size V. The subjects met the Dandy criteria for IIH and had at least Frisén grade 1 papilledema with better than -5 dB mean deviation (MD) centrally. Two observers (MW, AS) evaluated the visual field defects, adjudicated any differences and reviewed OCT data.

Results:
We found a greater magnitude of loss with MD peripherally than centrally (central 26°): -3.43 dB ± 4.42 vs -1.37 dB ±1.4, $p < 0.001$). There were about 30% more abnormal test locations identified in the periphery and the mean defect depth increased linearly with eccentricity. The most frequent defect found was a temporal wedge defect in the periphery. While the presence of papilledema limited correlation, 47% of the temporal wedge defects had OCT RNFL deficits of the related superior nasal optic disc. Other common defects were inferonasal loss, superonasal loss, superior and inferior arcuate defects. Four patients (10%) had visual field defects in the periphery with normal central visual field testing.

Conclusions:
We found significantly more visual loss outside 30° of the visual field compared to inside 30° with the depth of the defect increasing linearly with eccentricity. Temporal wedge defects were the most common visual field defect, occurring mostly in the far periphery. Static threshold perimetry of the full visual field appears to be clinically useful in IIH patients.

References: None.

Keywords: Visual fields, Pseudotumor Cerebri, High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: Supported by a VA Merit Review.

Tuesday, March 19th from 8:45 - 9:00 am
Artificial Intelligence for Detection and Classification of Abnormal Optic Discs on Fundus Photographs

Dan Milea[1], Zhubo Jiang[2], Caroline Vasseneix[3], Swetha Komma[4], Barnabe Rondet-Courbis[5], Shweta Singhal[1], Raoul Kannav Khanna[6], Sebastian Kuechlin[7], Daniel Ting[1], Clare Fraser[8], Wolf Lagreze[7], Christophe Chiquet[9], Pedro Fonseca[10], Philippe Gohier[11], Catherine Vignal[6], Miguel Raimundo[10], Marie-Bénédicte Rougier[12], Richard Kho[13], Lars Fuhrman[7], Raymond Najjar[1], Sharon Tow[1], Ambika Selvakumar[4], Jost Jonas[14], Nancy Newman[3], Neil Miller[15], Yong Liu[2], Valerie Biousse[3], Tien Yin Wong[1]

[1]Singapore National Eye Centre, Singapore, Singapore, [2]Institute of High Performance Computing, AStar Singapore, Singapore, Singapore, [3]Emory University School of Medicine, Atlanta, USA, [4]Sankara Nethralya Chennai, Chennai, India, [5]Ophthalmology, Angers University Hospital, Angers, France, [6]Fondation A de Rothschild Paris, Paris, France, [7]Klinik für Augenheilkunde Universitätsklinikum, Freiburg, Germany, [8]Sydney Eye Hospital, Sydney, Australia, [9]Grenoble University Hospital, Grenoble, France, [10]University Hospital of Coimbra, Coimbra, Portugal, [11]Angers University Hospital, Angers, France, [12]Hopital Pellegrin, Bordeaux University Hospital, Bordeaux, France, [13]American Eye Center, Manila, Manila, Philippines, [14]Ophthalmology Heidelberg, Heidelberg, Germany, [15]Johns Hopkins University, Baltimore, USA

Introduction:
The aim of this study was to assess the performance of artificial intelligence, using a deep learning algorithm, for automated detection and classification of abnormal optic nerve heads, based on colour fundus photographs.

Methods:
International study including 12 centres in 8 countries (USA, India, France, Singapore, Germany, Portugal, Philippines, Australia), and using supervised deep convolutional neural networks (CNN) applied to fundus photographs in 1) patients with abnormal discs related to confirmed optic neuropathies (papilledema, anterior ischemic optic neuropathies, papillitis, pallor), and 2) patients with pseudopapilledema (such as drusen, hyperopia, etc), compared with normal controls. Curation of the included images was followed by pre-processing, normalization and bootstrap training with a transfer learning strategy, using a deep CNN, pre-trained on more than a million images. Global average pooling was used to convert feature maps from CNN output into a feature vector resulting in automated optic disc identification and classification.

Results:
A total of 6443 fundus images (including 3563 abnormal discs) were analyzed (5066 images for training and 1377 images for testing) in 2623 participants, including 1776 patients with abnormal discs. In the testing dataset, the algorithm had excellent performance in discriminating abnormal from normal optic discs (receiver operating area under curve (AUC), 0.96, sensitivity 0.87, specificity 0.95). The system could accurately distinguish papilledema (AUC, 0.97), anterior ischemic optic neuropathy (AION) (AUC, 0.95) and optic disc pallor (AUC, 0.95), from controls. The algorithm also could distinguish papilledema from optic disc swelling in AION (AUC, 0.95), and true papilledema from pseudopapilledema (AUC, 0.95). Multiple diagnostic classification could be achieved with good accuracy (0.88), in a sample test on 298 images.

Conclusions:
Deep learning algorithms achieve high performance for automated identification and classification of optic nerve head abnormalities on standard fundus photographs, suggesting that Artificial Intelligence-based fundus photography may enhance neuro-ophthalmologic diagnoses.

References: 1/ Ting DSW, Cheung CY,...Hsu W, Lee ML, Wong TY. Development and Validation of a Deep Learning System for Diabetic Retinopathy and Related Eye Diseases Using Retinal Images From Multiethnic Populations With Diabetes. JAMA, 2017 12;318(22):2211-23. 2/ De Fauw J, Ledsam JR,...Cornebise J, Keane PA, Ronneberger O. Clinically applicable deep learning for diagnosis and referral in retinal disease. Nat Med, 2018;24(9):1342-50. 3/ Hood DC, De Morales CG. Efficacy of a Deep Learning System for Detecting Glaucomatous Optic Neuropathy Based on Color Fundus Photographs. Ophthalmology, 2018;1225(8):1207-8.

Keywords: Optic neuropathy, High intracranial pressure/headache, Pseudotumor Cerebri, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: A*Star SERC strategic funding, Singapore.

Tuesday, March 19th from 9:00 - 9:15 am
The Untuned Visuo-temporal Cortex in Patients with Visual Snow

Ghislaine Traber[1], Njoud Aldusary (shared first author)[2], Marco Piccirelli[2], Jamaan Alghamdi[2], Bujar Saliju[1], Shila Pazahr[2], Reza Mazloum[2], Fahad Alshehri[3], Klara Landau[1], Spyridon Kollias[2], Lars Michels[2]

[1]Dept of Ophthalmology, University Hospital Zurich, University of Zurich, Switzerland, Zurich, Switzerland, [2]Department of Neuroradiology, University Hospital Zurich, Zurich, Switzerland, Zurich, Switzerland, [3]Medical Imaging Dept, Medical College, Qassim University, Buriadah, Saudi Arabia, Buriadah, Saudi Arabia

Introduction:
Visual snow (VS) is a distressing condition with persistent visual phenomena often leading to multiple unnecessary examinations and treatment attempts. VS impairs daily life by interfering with visual perception, particularly with reading. Neuronally, VS patients are thought to have differences in regional metabolism resulting in modulation of neuronal sensitivity and excitability. We hypothesize to see altered functional connectivity in patients with VS in brain regions associated with visual perception.

Methods:
Using functional magnetic resonance imaging (fMRI), spontaneous resting-state signal fluctuations were examined in 10 patients with VS and 10 age- and gender-matched healthy controls (HC). Resting-state functional connectivity (rsFC) was assessed in- and outside visual brain regions. Further, group differences in grey matter (GM), white matter (WM), and size of the lateral geniculate nucleus (LGN) were investigated.

Results:
Patients with VS were found to have significant ($p < 0.05$, corrected) hyperconnectivity of visuo-temporal brain regions compared to HC. Symptom duration positively correlated with hyperconnected brain regions. VS patients had a lower mean LGN volume ($p = 0.01$). In addition, three patients had an increase in left occipital volume with left occipital bending in one of them.

Conclusions:
Our results support the view that VS is associated with abnormal excitability of brain regions involved in visual and motional perception. We conclude that rsFC can be used as a marker of symptom duration. LGN volume differences might reflect the LGN's involvement in higher order visual functions.

References: None.

Keywords: Higher visual functions, Neuroimaging

Financial Disclosures: GLT reports a grant from the University of Zurich, Zurich, Switzerland (filling the gap program).

Grant Support: GLT reports a grant from the University of Zurich, Zurich, Switzerland (filling the gap program).

Tuesday, March 19th from 9:15 - 9:30 am
Object recognition in acquired and developmental prosopagnosia: is it really just about faces?

Jason Barton[1], Andrea Albonico[1], Tirta Susilo[2], Brad Duchaine[3], Sherryse Corrow[4]

[1]University of British Columbia, Vancouver, Canada, [2]Victoria University of Wellington, Wellington, New Zealand, [3]Dartmouth University, Dartmouth, New Hampshire, USA, [4]Bethel University, St Paul, Minnesota, USA

Introduction:
Whether face and object recognition are dissociated in prosopagnosia continues to be debated: a recent review (Geskin and Behrmann, 2018) highlighted deficiencies in prior studies regarding the evidence for such a dissociation. Our goal was to study cohorts with acquired and developmental prosopagnosia with a complementary battery of tests of object recognition that address prior limitations, as well as evaluating for residual effects of object expertise.

Methods:
We studied 15 subjects with acquired and 12 subjects with developmental prosopagnosia on three known tests: four components of the Old/New Test of Object Recognition (cars, horses, guns and glasses), the Cambridge Bicycle Memory Test, and the Expertise-adjusted Test of Car Recognition.

Results:
On the Old/New Tests, almost all subjects with developmental prosopagnosia were normal, but for acquired prosopagnosia, subjects with occipitotemporal lesions often showed impairments while those with anterior temporal lesions did not. Ten subjects showed a putative classical dissociation between the Cambridge Face and Bicycle Memory Tests, eight of whom had normal reaction times. Both developmental and acquired groups showed impairments on the Expertise-adjusted Test of Car Recognition, though their performance still showed residual effects reflecting the degree of car expertise of the subject. Overall, only two subjects with developmental prosopagnosia met highly stringent criteria for normal object recognition across all tests.

Conclusions:
Strong evidence for intact object recognition can be found in a few subjects but the majority show deficits, particularly those with the acquired form. Both acquired and developmental forms show residual but reduced effects of individual expertise in other object processing. This pattern is most consistent with selective face-processing pathways that are anatomically adjacent to regions that participate in high-level recognition of other objects.

References: Geskin, J., & Behrmann, M. Congenital prosopagnosia without object agnosia? A literature review. Cogn Neuropsychol, 35(1-2), 4-54, (2018).

Keywords: Higher Visual Cortical functions, Higher visual functions

Financial Disclosures: The authors had no disclosures.

Grant Support: Canadian Institutes of Health Research operating grant (MOP-102567), Canada Research Chair (950-228984), Marianne Koerner Chair in Brain Diseases (JB); Royal Society of New Zealand Marsden Fund 16-VUW-175 (TS); Economic and Social Research Council (UK) RES-062-23-2426, the Hitchcock Foundation, and the National Science Foundation 1634098 (BD); National Eye Institute F32 EY023479 (SC).

Tuesday, March 19th from 9:30 - 9:45 am
eMULES in concussion: A quantitative 'look' at the eye movements

Todd Hudson[1], John-Ross Rizzo[1], John Martone[1], Laura Balcer[1], Steven Galetta[1], Janet Rucker[1]

[1]New York University School of Medicine, New York, USA

Introduction:
MULES (Mobile Universal Lexicon Evaluation System) is a recently developed test of rapid picture naming, which has shown promise in its sensitivity to detect concussion through a post-injury increase in total picture identification times. Our previous work has demonstrated prolonged inter-saccadic-intervals in concussion patients for rapid automatized naming tasks, such as rapid number naming. Here we will compare saccadic biomarkers in patients with concussion and control participants while completing a digital version of the MULES test (eMULES).

Methods:
61 healthy participants (mean age 25.9 years, range: 18-58) and 31 participants with chronic concussion (more than 3 months) (mean age 37.4 years, range: 15-69) performed the eMULES. Subjects were instructed to identify each picture as quickly as possible and to progress from picture to picture in a left to right and top to bottom quasi-reading strategy. The full test consisted of three screens of pictures, each with 18 pictures arranged in three rows of six. Video-oculographic measures (EyeLink 1000+) were obtained while participants completed the task.

Results:
Participants with concussion demonstrated prolonged total naming times (32.2s vs. 26.6s, $p<0.05$) and inter-saccadic intervals (195ms vs. 163ms, $p<0.05$). In addition, participants with concussion made smaller saccades on average (9.2 vs. 10.4 deg, $p<0.05$), and made a larger proportion of intra-picture saccades (0.59 vs. 0.51, $p<0.05$) [intra-picture saccades both begin and end spatially within the regional bounds of a single picture]. Saccade peak velocities and durations showed no differences between participant groups.

Conclusions:
Objective eye movement recording during eMULES performance identifies ocular motor differences between concussed and control participants, thus providing a neurophysiological basis for prolonged test completion times in concussed individuals, augmenting paper and pencil assessment.

References: Rizzo JR, Hudson TE, Dai W, Birkemeier J, Pasculli RM, et al., Rapid number naming in chronic concussion: eye movements in the King-Devick test. Ann Clin Transl Neurol. 3(10):801-811, 2016.

Keywords: Higher Visual Cortical functions

Financial Disclosures: The authors had no disclosures.

Grant Support: NYS-DOH ECRIP.

Tuesday, March 19th from 9:45 - 10:00 am
Positional Testing In Acute Vestibular Syndrome: A Transversal And Longitudinal Study

Joao Lemos[1], Ana Martins[1], Cristina Duque[1], Sara Pimentel[2], Cesar Nunes[1], Antonio Goncalves[1]

[1]Coimbra University Hospital Centre, Coimbra, Portugal, [2]Coimbra University, Coimbra, Portugal

Introduction:
The use of positional testing as a diagnostic tool is not usually indicated in the assessment of patients with acute vestibular syndrome. We sought to evaluate the clinical utility of positional testing (ie. focusing on positional modulation of spontaneous nystagmus and incidence of central positional paroxysmal nystagmus [CPPN]) in patients with peripheral and central acute vestibular syndrome (pAVS, cAVS, respectively).

Methods:
Consecutive AVS patients underwent video-oculography in upright, supine and head hanging positions at presentation, 3-month and 1-year follow-up.

Results:
15 pAVS and 15 cAVS patients were included. Mean age (SD) was 53.3 (16.6) (11 males) in pAVS group and 56.5 (17.8) (11 males) in cAVS group (p= .49). Acutely, in supine, in patients whose nystagmus was present in both head rotation sides, 12/13 (93%) pAVS and only 4/12 (33%) cAVS patients showed direction-fixed positional nystagmus which was stronger when turning the head to the slow phase side. One patient in each group showed direction-changing ageotropic (i.e., towards the ceiling) nystagmus. The remaining cAVS patients showed either stronger direction-fixed nystagmus when turning the head to the fast phase side, or direction-changing geotropic (i.e., towards the ground) nystagmus. During follow-up, ageotropic and geotropic forms of positional nystagmus became common in both groups. In head hanging, 5 (33%) cAVS patients showed CPPN (3, downbeat; 2, upbeat) and 2 other showed augmentation of saccadic intrusions. Positional downbeat nystagmus and saccadic intrusions were still present after 1 year.

Conclusions:
The presence of acute geotropic nystagmus or stronger nystagmus when turning the head to the fast phase side, and acute or chronic head hanging CPPN, should raise the suspicion for central AVS. Chronic geotropic and ageotropic nystagmus following AVS might be an underrecognized manifestation of vestibular compensation.

References: Büki B, Tarnutzer AA. Vertigo and Dizziness. Oxford University Press; 2013. Kattah JC, Talkad A V., Wang DZ, Hsieh Y-H, Newman-Toker DE. HINTS to Diagnose Stroke in the Acute Vestibular Syndrome. Stroke. 2009;40(11):3504-3510. Choi J-Y, Kim JH, Kim HJ, Glasauer S, Kim J-S. Central paroxysmal positional nystagmus: Characteristics and possible mechanisms. Neurology. 2015;84(22):2238-2246. Palla A, Marti S, Straumann D. Head-shaking nystagmus depends on gravity. J Assoc Res Otolaryngol. 2005;6(1):1-8. Curthoys IS, Halmagyi GM. Vestibular compensation: a review of the oculomotor, neural, and clinical consequences of unilateral vestibular loss. J Vestib Res. 5(2):67-107.

Keywords: Ocular manifestations of vestibular disorders, Nystagmus, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

SCIENTIFIC PLATFORM SESSION III

Tuesday, March 19, 2019 - 10:30 am – 12:30 pm
Red Rock Ballroom
Moderators: Jeffrey Bennett, MD, PhD and Heather Moss, MD, PhD

Tuesday, March 19th from 10:30 - 10:45 am
rAAV2/2-ND4 Treatment of Leber Optic Neuropathy: 72-Week Data from the REVERSE Phase III Clinical Trial

Nancy Newman[1], Mark Moster[2], Alfredo Sadun[3], Thomas Klopstock[4], Catherine Vignal[5], Valerio Carelli[6], Patrick Yu-Wai-Man[7], Jose Sahel[8], Barrett Katz[9]

[1]Emory University School of Medicine, Atlanta, Georgia, USA, [2]Wills Eye Hospital, Sidney Kimmel Medical College of Thomas Jefferson University, Philadelphia, Pennsylvania, USA, [3]Doheny Eye Institute and Department of Ophthalmology, UCLA, Los Angeles, California, USA, [4]Friedrich-Baur-Institute, University Hospital of LMU, Munich, Germany, [5]CHNO Quinze-Vingts and Fondation Ophtalmologique Rothschild, Paris, France, [6]University of Bologna, Bologna, Italy, [7]Moorfields Eye Hospital, UCL Institute of Ophthalmology, University of Cambridge, London and Cambridge, United Kingdom of Great Britain and Northern Ireland, [8]University of Pittsburgh and CNO 15/20 in Paris, France, Pittsburgh, Pennsylvania, USA, [9]GenSight, Paris, France

Introduction:
LHON is a mitochondrially inherited disease that causes bilateral central vision loss. A point mutation in the mitochondrial ND4gene at nucleotide position 11778 accounts for 75% of LHON cases. rAAV2/2-ND4is a gene therapy enabling allotopic expression and delivery of the wildtype ND4 protein to mitochondria within retinal ganglion cells. The clinical efficacy of rAAV2/2-ND4 (GS010) is currently being assessed in several Phase 3 trials of ND4-LHON subjects.

Methods:
REVERSE (NCT02652780) is a randomized, multicenter, double-masked, sham-controlled trial of 37 LHON subjects with the G11778A-ND4mutation. All subjects received a single unilateral intravitreal injection of rAAV2/2-ND4. Multiple visual functions and spectral-domain OCT measurements of germane retinal anatomy were monitored for 72 weeks.

Results:
At Week 72 an improvement of +15 ETDRS letters was seen in rAAV2/2-ND4 treated eyes; sham-treated eyes also showed improvement in acuity (+12 ETDRS letters). Contrast sensitivity improved as well: GS010-treated and sham-treated eyes gained respectively on average +0.21 LogCS and +0.15 LogCS, compared to baseline. The proportion of GS010-treated eyes that achieved a clinically meaningful improvement of 0.3 LogCS or greater (45.9%) was statistically significantly higher than that of sham-treated eyes (24.9%; p=0.0047). A generalized estimating equation model showed drug treated eyes to be significantly more likely to achieve vision of 20/200 or better than sham-treated eyes (p=0.0012).Ganglion cell layer (GCL) volume, papillo-macular bundle thickness and total macular ETDRS thickness were significantly preserved in treated vs. sham eyes, all 3 metrics reaching statistical significance.

Conclusions:
Seventy-two weeks after rAAV2/2-ND4 administration a clinically meaningful improvement in visual functions and sustained preservation of LHON-relevant retinal anatomy were seen in drug-treated eyes suggesting that the biological targets of this gene therapy were successfully engaged. Week 96 readout of results is expected in mid 2019.

References: None.

Keywords: Genetic Disease, Optic neuropathy

Financial Disclosures: Consultant for GenSight Biologics; Research support from GenSight Biologics and Santhera Pharmaceuticals.

Grant Support: Industry funding from GenSight Biologics.

Tuesday, March 19th from 10:45 - 11:00 am
Efficacy of chronic immunotherapy for myelin oligodendrocyte glycoprotein-IgG disease

John Chen[1], Collin McClelland[2], Eric Eggenberger[3], Alfonso Lopez Chiriboga[1], Victoria Pelak[4], Heather Moss[5], Aubrey Gilbert[6], Michael Lee[2], Marie Acierno[7], Muhammad Bhatti[1], Jiraporn Jitprapaikulsan[1], Gregory Van Stavern[8], Divyanshu Dubey[1], Andrew McKeon[1], Jeffrey Bennett[9], Sean Pittock[1], Eoin Flanagan[1], Ore-ofe Adesina[10], Shannon Beres[11], Dean Cestari[12], Gena Heidary[13], Byron Lam[14], Veeral Shah[15], John Fraser[16]

[1]Mayo Clinic, Rochester, Minnesota, USA, [2]University of Minnesota, Minneapolis, Minnesota, USA, [3]Mayo Clinic, Jacksonville, Florida, USA, [4]University of Colorado Denver School of Medicine, Aurora, Colorado, USA, [5]The Stanford University Medical Center, Palo Alto, California, USA, [6]The Permanente Medical Group, Vallejo, California, USA, [7]Mayo Clinic, Scottsdale, Arizona, USA, [8]Washington University in St. Louis School of Medicine, St. Louis, Missouri, USA, [9]University of Colorado School of Medicine, Aurora, Colorado, USA, [10]McGovern Medical School at the University of Texas at Houston, Houston, Texas, USA, [11]Stanford University, Palo Alto, California, USA, [12]Harvard Medical School, Mass Eye & Ear, Boston, Massachusetts, USA, [13]Boston Children's Hospital, Boston, Massachusetts, USA, [14]Bascom Palmer Eye Institute, Miami, Florida, USA, [15]Texas Children's Hospital/Baylor College of Medicine, Houston, Texas, USA, [16]Western University, London, Ontario, Canada

Introduction:
Myelin oligodendrocyte glycoprotein autoantibody (MOG-IgG) is a recently established serum biomarker of demyelinating disease that is associated with recurrent CNS attacks. The optimal treatment to lower the risk of or prevent relapses is unknown. The goal of this study was to determine the efficacy of chronic immunotherapy in preventing relapse of MOG-IgG-positive demyelinating events.

Methods:
A multicenter retrospective chart review was performed to determine the frequency of relapses in patients on various chronic immunotherapy treatments for MOG-IgG demyelinating disease. Inclusion criteria were: 1) History of demyelinating attack; 2) MOG-IgG seropositivity; 3) Chronic steroid sparing immunotherapy for at least 6 months. Patients were reviewed for demyelinating attacks before and during chronic immunotherapy to determine the percentage of patients relapsing on these treatments.

Results:
Sixty-two patients with MOG-IgG-related demyelinating disease were treated with chronic immunotherapy and met inclusion criteria. The median age of onset of neurologic symptoms was 29 years, with a range of 3-61. Sixty percent were female. The median annualized relapse rate (ARR) prior to treatment was 2.35. Eleven of 18 (61%) patients treated with azathioprine, 13 of 17 (76.5%) patients treated with mycophenolate, 21 of 37 (57%) patients treated with rituximab, and 1 of 9 (11%) patients treated with monthly IVIG had at least one relapse. All immunotherapies had a median follow-up period of over 1 year. The median ARR on treatment with these medications was 0.8. All 10 patients treated with a multiple sclerosis (MS) disease modifying agent had a relapse.

Conclusions:
In this cohort of patients with MOG-IgG-positive relapsing disease, chronic immunotherapy was associated with reduced recurrent demyelinating attacks, but many patients still had relapses despite these medications. MS disease modifying agents appeared to be ineffective. Monthly IVIG was associated with the largest reduction in relapses, but longitudinal and randomized studies will be required to confirm its efficacy.

References: None.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Tuesday, March 19th from 11:00 - 11:15 am
Amnion-derived Multipotent Progenitor Cells Attenuate Optic Nerve and Spinal Cord Demyelinating Disease

Kenneth Shindler[1], Reas Khan[1], Kimberly Dine[1], Ahmara Ross[1], Keirnan Willett[1], Rick Banas[2], Larry Brown[2]

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Introduction:
ST266 is the biological secretome of Amnion-derived Multipotent Progenitor (AMP) cells. ST266 proteins accumulate in eyes and optic nerves following intranasal delivery, resulting in selective suppression of optic neuritis in the experimental autoimmune encephalomyelitis (EAE) model of multiple sclerosis, without suppressing spinal cord lesions. We tested the hypothesis that systemic AMP cell administration could suppress both optic neuritis and myelitis in EAE.

Methods:
C57/BL6 EAE mice, induced by immunization with myelin oligodendroglial glycoprotein peptide, were administered 2x106 AMP cells, or were sham-injected, by either intravenous or intraperitoneal injection on day 9 after EAE induction. Additional mice received repeated administrations of 1x106 AMP cells on days 9, 12, and 15. Spinal cord dysfunction was assessed by daily scoring of EAE-induced ascending paralysis, and visual function was assessed by optokinetic responses weekly until sacrifice 6 weeks post-immunization. Retinal ganglion cells (RGCs) were immunolabeled with Brn3a antibodies and counted. Inflammation was assessed by H&E and Iba1 staining, and demyelination by luxol fast blue staining, of spinal cord and optic nerve sections.

Results:
Single high-dose intravenous and intraperitoneal, and repeated low-dose intravenous, administration of AMP cells significantly reduced ascending paralysis in EAE mice ($p<0.001$). Repeated low-dose intravenous and intraperitoneal AMP cell administration significantly attenuated visual dysfunction in EAE mice ($p<0.05$). All four AMP cell treatment cohorts demonstrated increased RGC survival ($p<0.05$) and decreased optic nerve inflammation ($p<0.05$) as compared with sham-treated EAE mice, and AMP cells induced variable levels of improvement in optic nerve demyelination and spinal cord inflammation and demyelination.

Conclusions:
Systemic AMP cell administration inhibits RGC loss and reduces visual dysfunction induced by EAE optic neuritis, similar to previously demonstrated effects of intranasally-delivered ST266. Importantly, AMP cells also promote neuroprotective effects in EAE spinal cords, marked by reduced paralysis. Further investigation of AMP cells as a potential therapy for inflammatory demyelinating disease is warranted.

References: None.

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

Financial Disclosures: Grant funding to support experiments has been received from NIH Grant EY019014; Research to Prevent Blindness; the F. M. Kirby Foundation: and Noveome Biotherapeutics, Inc. I have received consulting fees from Noveome Biotherapeutics, but this was more than 12 months ago.

Grant Support: NIH Grant EY019014; Research to Prevent Blindness; the F. M. Kirby Foundation: and Noveome Biotherapeutics, Inc.

Tuesday, March 19th from 11:15 - 11:30 am

MEK inhibitor treatment promotes retinal ganglion cell preservation without preventing retrobulbar demyelination in neurofibromatosis mice

Steven Stasheff[1], Francisco Nadal-Nicolas[2], Wei Li[2], Miriam Bornhorst[3], Yuan Zhu[3]

[1]Neuroscience & Gilbert NF Inst, Children's National Health Sys; National Eye Institute, Washington, District of Columbia, USA, [2]Retinal Neurophysiology Section, National Eye Institute, Bethesda, Maryland, USA, [3]Gilbert Neurofibromatosis Institute, Children's National Health System, Washington, District of Columbia, USA

Introduction:

To better understand the disparity frequently seen between optic pathway glioma (OPG) characteristics and visual loss among young children with neurofibromatosis type 1 (NF1), we extend our previous findings of anatomic, physiologic, and behavioral abnormalities in an established animal model. We now report differential effects of treatment targeting the MAPK/ERK cellular pathway: 1) preserving retinal ganglion cell (RGC) number, and yet 2) failing to ameliorate demyelination of the retrobulbar optic nerve.

Methods:

In mutant and littermate transgenic mice with neurofibromin (Nf1) knocked out in glial precursor cells (NF1-OPG), we compared visual behavior (optomotor responses, OMR), in vivo anatomy (optical coherence tomography, OCT), in vitro multielectrode recording of spontaneous and light-evoked RGC activity, and histologic analysis of RGCs, optic nerves and chiasms. Separate cohorts were treated with a MEK inhibitor (PD0325901) from postnatal day 21 (P21) through P49 and studied either within 24 hours or 6 weeks later.

Results:

Among untreated NF1-OPG mice, mutants had moderate to severe loss of OMR sensitivity, thinning of the central retina on OCT, and diffuse or regional loss of RGCs (either discrete sectors or focal patches). Even in neighboring regions with normal RGC density, many cells either had no recordable activity or had higher spontaneous discharge rates and weaker or inverted light responses. In many cases the retrobulbar optic nerve was severely demyelinated – even when the remaining nerve and chiasm were less disrupted. MEK inhibitor treated mice had substantially more RGCs, persisting 6 weeks after treatment, yet retrobulbar demyelination appeared unaffected.

Conclusions:

Our results highlight additional abnormalities in RGC structure and function in NF1-OPG mice that may help explain the disparity seen between visual loss and tumor characteristics among NF1 patients. Ongoing experiments aim to more precisely identify the relationship of abnormal RGC activity with the several identified histologic abnormalities, providing additional targets for more effective treatments.

References: None.

Keywords: Pediatric neuro-ophthalmology, Neuro-ophth & systyemic 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.

Tuesday, March 19th from 11:30 - 11:45 am
Melanopsin: targeted ectopic expression for optogenetic visual restoration

Michael Gilhooley[1], Moritz Lindner[1], Steven Hughes[1], Mark Hankins[1]

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Introduction:
Expression of melanopsin renders neural cells sensitive to light, and is emerging as a prime candidate for clinical optogenetic approaches to visual restoration. The retinal neural tissue surviving in the inherited retinal degenerations (IRDs) after visual loss presents a model target for such approaches, however it is unclear if targeting specific neuronal populations within this tissue is advantageous over non-specific delivery. A fair comparison between these two methods is made difficult by the persistence of native photosensitive retinal ganglion cell (pRGC) responses in IRD models. Here we describe a novel model lacking all native retinal light responses to allow a more robust comparison of optogenetic targets. The purpose of our study is to test the hypothesis that retinae devoid of both canonical and pRGC photoreception will remove the "noise" of intrinsic responses and allow comparison of targeted expression of melanopsin in ON-bipolar cells with non-specific delivery.

Methods:
Retina-degenerate mice lacking native melanopsin and expressing Cre recombinase specifically in retinal ON-bipolar cells (L7.Cre,Opn4-/-,Pde6brd1/rd1) were used. At P45, intravitreal injections of adeno-associated virus containing the human melanopsin gene(OPN4) driven by "floxed" Ef1a(N=8,8), "non-floxed" Cba(N=8) promotors or saline(N=8) were administered. Eight weeks later, behavioural visual assays and ex-vivo multiple electrode array recordings of retinal light responses were performed.

Results:
No significant difference was seen in behavioural responses, sensitivity of electrophysiological responses nor onset kinetics between the two treated groups. Expression in bipolar cells specifically however led to significantly shorter half-life($p<0.001$) & duration($p<0.001$) of responses.

Conclusions:
This represents the first report in the literature of restoration of light responses in a retina devoid of all native photoreception. While there was no apparent difference in sensitivity between targeted and non-specific delivery, when melanopsin was specifically expressed in bipolar cells, offset kinetics of responses were faster, presenting them as attractive targets for clinical optogenetic approaches to visual restoration.

References: None.

Keywords: Genetic Disease, Pupils Retina, Optic nerve trauma and treatment

Financial Disclosures: The authors had no disclosures.

Grant Support: MJG is supported by a Clinical Research Training Fellowship from the Wellcome Trust Grant No. 205151/Z/16/Z. ML is supported by a Clinical Research Postdoctoral Fellowship from the German Research Foundation.

Tuesday, March 19th from 11:45 am - 12:00 pm
The Stressed Optic Nerve at High Altitude and Treatment with Chemical Chaperon

Yaping (Joyce) Liao[1], Alexandra Camargo[1], Matthew Dardet[1], Varun Kumar[1], Mohammad Shariati[1], Roopa Dalal[1], Vinicio de Jesus Perez[1], Louise Mesentier-Louro[1]

[1]Stanford University, Stanford, California, USA

Introduction:
High altitude-associated non-arteritic anterior ischemic optic neuropathy (NAION) [1-3] typically occurs in younger patients who have disc-at-risk and few other risk factors [4-9], raising the possibility that hypobaric hypoxia may be the tipping point of vision loss. In this study, we investigated the effects of systemic hypoxia on the retina and optic nerve and assessed the therapeutic potential of pre-treatment with chemical chaperon 4-phenylbutyric acid (4-PBA), which reduces endoplasmic reticulum (ER) stress.

Methods:
We induced hypoxia in 56 adult C57BL/6 mice in a 10% oxygen chamber (normal 20.9%) for 48h and measured optical coherence tomography (OCT) and immunohistochemistry in 4-PBA- and placebo-treated animals. Statistical analysis was performed using two-way ANOVA with Bonferroni test.

Results:
At the retina, 2 days of hypoxia led to a significant increase in ER stress in retinal ganglion cells (RGCs) and optic nerve astrocytes, as indicated by increase in proapoptotic transcription factor C/EBP homologous protein (CHOP). Although there was no loss of RGCs or change in ganglion cell complex on OCT, there was significant thinning of the total retinal thickness. At the optic nerve, there was a significant increase in glial fibrillary acidic protein (GFAP), a sign of astrocyte activation. Quantification of the optic nerve oligodendrocytes revealed a significant decrease in the number of Olig2+ and CC1+ but not PDGFRalpha+ cells, consistent with a decrease in the mature but not immature oligodendrocytes. Pre-treatment with chemical chaperon 4-PBA significantly restored total retinal thickness and rescued the number of mature oligodendrocytes but did not impact astrocytic GFAP expression.

Conclusions:
Significant changes in the optic nerve glia and RGCs occur within 48h in an animal model of high altitude hypoxia, which can potentially serve as the incipient event that triggers NAION in patients with disc-at-risk. Treatment that lowers endoplasmic reticulum stress can potentially prevent high altitude-associated vision loss.

References: 1. Arnold, A.C., J Neuroophthalmol, 2003. 23(2): p. 157-63. 2. Hayreh, S.S., Progress in retinal and eye research, 2009. 28(1): p. 34-62. 3. Biousse, V. and N.J. Newman, N Engl J Med, 2015. 372(25): p. 2428-36. 4. Bandyopadhyay, S., R. Singh, V. Gupta, and A. Gupta, Indian J Ophthalmol, 2002. 50(4): p. 324-5. 5. Kaiserman, I. and J. Frucht-Pery, Am J Ophthalmol, 2002. 133(4): p. 581-3. 6. Choi, S.S., R.J. Zawadzki, M.A. Greiner, J.S. Werner, and J.L. Keltner, J Neuroophthalmol, 2008. 28(2): p. 120-5. 7. De Bats, F., J. Gambrelle, A. Feldman, M. Mauget-Faysse, M. Germain-Pastene, et al., J Fr Ophtalmol, 2010. 33(10): p. 724-7. 8. Tian, X., B. Zhang, Y. Jia, C. Wang, and Q. Li, Eye (Lond), 2018. 32(2): p. 370-374. 9. Distefano, A.G. and B.L. Lam, Aerosp Med Hum Perform, 2018. 89(11): p. 1005-1007.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: Bonderman Gift Grant, National Eye Institute P30-026877 grant, Medical Scholars Grant.

Tuesday, March 19th from 12:00 - 12:15 pm
Physiologic Electrical Fields Direct Retina Ganglion Cell Axon Growth

Kimberly Gokoffski[1], Xingyuan Jia[2], Guohua Xia[3], Min Zhao[4]

[1]USC Roski Eye Institute, Los Angeles, California, USA, [2]Medical Research Center, Beijing Chaoyang Hospital, Capital Medical University, Beijing, China, [3]Department of Psychiatry and Behavioral Sciences, University of California Davis, Sacramento, California, USA, [4]Department of Ophthalmology and Vision Sciences, University of California, Davis, Sacramento, USA

Introduction:
Cell transplantation-based approaches to restore vision in patients blinded by advanced optic neuropathies show immense promise but are limited by 1) low integration efficiency and 2) of the RGCs that integrated, few axons grew out of the eye. What these experiments demonstrate is that the endogenous cues in the host retina and optic nerve are insufficient to direct the growth of newly transplanted RGC axons out of the eye. There is much interest in the potential of electrical fields (EFs) to promote long distance axon growth: axons of hippocampal neurons have grow directionally when exposed to an EF. Drawing from this, we hypothesized that EFs might exert a similar galvanotropic effect on RGC axon growth. If so, can EFs be exploited to direct RGC axon growth out of the eye.

Methods:
Full thickness, early post-natal mouse retina was cultured in electrotaxis chambers and exposed EFs of varying strengths.

Results:
In the absence of an EF, RGC axons demonstrated indiscriminate directional growth from the explant edge, in vitro. Retinal cultures exposed to an EF of 200 mV/mm showed marked asymmetric growth, with 81.2% of axons oriented towards the cathode ($p<0.001$). RGCs also demonstrated the ability to reroute their direction of growth if EF polarity was switched: 78% of axons re-directed to the "new" cathode in EF treated cultures compared to 33% in control ($p<0.001$). Many axons were noted to change their direction of growth within 30 minutes of EF switch.

Conclusions:
RGC axons exhibit cathode-directed growth. Given the acuity with which axons respond to the switch in EF polarity, the effect of EF on RGC axon growth appears to be direct. The significance of this work lies in its potential to advance the field of optic nerve regeneration. Application of electrical currents may be necessary to direct the growth of newly transplanted RGCs.

References: None.

Keywords: Optic neuropathy, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Tuesday, March 19th from 12:15 - 12:30 pm
Visual Impairment in Patients with Giant Cell Arteritis Treated with Tocilizumab in Real-World Clinical Practice

Timothy McCulley[1], Jinglan Pei[2], Paris Sidiropoulos[2], Christine Birchwood[2], Jennie Best[2], John Stone[3], Sebastian Unizony[3]

[1]The Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA, [2]Genentech, Inc., South San Francisco, California, USA, [3]Massachusetts General Hospital Rheumatology Unit, Harvard Medical School, Boston, Massachusetts, USA

Introduction:
The GiACTA trial demonstrated the efficacy of tocilizumab (TCZ) in giant cell arteritis (GCA) [1]. However, the effectiveness of TCZ for prevention of specific GCA-related visual manifestations is currently unknown. The incidence of GCA-related visual manifestations was analyzed in patients treated with TCZ in a real-world setting.

Methods:
Retrospective analysis of GCA patients treated with TCZ at a single center (2010-2018). Disease flares were assessed among patients with and without visual impairment at diagnosis. Flares and new GCA-related visual manifestations including diplopia, transient blurred vision, amaurosis fugax and permanent vision loss due to anterior ischemic optic neuropathy (AION) or central retinal artery occlusion (CRAO) were assessed before and after TCZ initiation.

Results:
Of 60 GCA patients followed for a median (IQR) of 1.7 (0.7-2.9) years, 22 (36.6%) had visual impairment at diagnosis (AION/CRAO, n=8 [13.3%]; blurred vision, n=18 [30.0%]; amaurosis fugax, n=11 [18.3%]; diplopia, n=2 [3.3%]). On follow-up, 15 of 22 (68.2%) patients with and 28 of 38 (73.7%) without visual impairment at diagnosis had ≥1 disease flare. TCZ treatment was associated with significantly reduced incidence of flare and with longer time to flare (HR=0.22; 95%CI 0.10-0.50; P<0.001). Before TCZ initiation, new visual manifestations (AION, n=2; blurred vision, n=12; amaurosis fugax, n=4; diplopia, n=2) developed in 16/102 (15.7%) disease flares occurring in 43 of 60 (71.7%) patients. In contrast, after TCZ initiation, new visual manifestations (AION, n=0; blurred vision, n=3; amaurosis fugax, n=1; diplopia, n=0) developed in only 3/37 (8.1%) disease flares. Disease flares (18 of 60 patients [30%]) were less common following TCZ initiation.

Conclusions:
Similar incidence of disease flare was observed between GCA patients with or without baseline visual manifestations. TCZ treatment was associated with significantly reduced number of flares and decreased incidence of new visual manifestations. No permanent vision loss (e.g., AION) was observed after TCZ initiation.

References: 1. Stone JH, et al. N Engl J Med. 2017;377(4):317-328.

Keywords: Vascular disorders

Financial Disclosures: Consultant for Genentech, Inc.

Grant Support: None.

Poster Session II: Scientific Advancements in Neuro-Ophthalmology

Tuesday, March 19th- 1:00 pm – 3:00 pm

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

Odd Numbered Posters: 1:00 pm – 2:00 pm

Even Numbered Posters: 2:00 pm – 3:00 pm

Poster #	Abstract Title	Presenting Author
Category: Biomechanics		
138	Long-Term Anatomical Effects of Increased Intracranial Pressure on Optic Nerve Sheath Dilation	Zulqar Islam
139	Changes in the Intraorbital Optic Nerve Length Induced by Horizontal Eye Movements	Eun Hee Hong
140	Does The Eye Only Rotate? Three Dimensional Magnetic Resonance Imaging Study	Han Woong Lim
141	Traumatic Optic Neuropathy Biomechanics: High Speed Camera Assessment In An Animal Model	Nickisa Hodgson
Category: Cognition, Mood & Neuro-degenerative Disease		
142	Impaired cognition in glaucomatous optic neuropathy	Emily Boes
143	Incidence of Mood Disorders in Patients with Idiopathic Intracranial Hypertension	Supritha P. Prasad
144	Rapid Picture Naming in Parkinson's Disease Using the Mobile Universal Lexicon Evaluation System (MULES) Test	Jenna Conway
145	Association of age-related macular degeneration with Alzheimer's disease and Parkinson's disease	Donghyun Jee
146	An Assessment of Electroencephalogram (EEG) Eyeblink Artifact as a Clinical Measurement in Parkinsons Patients	Tavish Nanda
147	Visuo-retinal effects of chemotherapy in hematological malignancy	Sachin Kedar
148	Progressive Supranuclear Palsy Saccadic Deficits: Infrared-oculographic Features and Challenges	John Martone
149	The Post-Illumination Pupil Response (PIPR) Is Associated With Cognitive Measures in an Epidemiologic Cohort	Yanjun Chen
150	The Use of Automated Pupillometry in the Treatment of Opioid Addiction	Crandall Peeler
Category: Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)		
151	Inhibition of glutamate carboxypepptidase II protects retinal ganglionic cell death induced by ischemia-reperfusion in rat	Kyong Jin Cho
152	Nationwide Incidence of Terson Syndrome in Treated Subarachnoid Hemorrhage in South Korea : 2011-2015	Eun Hee Hong
153	Fractionated Targeted Proton Beam Therapy For Optic Nerve Sheath Meningioma	Rabih Hage

154	Dyschromatopsia In Anti-aquaporin-4 antibody-positive Optic Neuritis	Jirat Nimworaphan
155	Multivariate analysis and diagnostic value of OCT and OCT angiography measurements of optic atrophy	Angela Oh
156	Hyperbaric Therapy for Central Retinal Artery Occlusions	Deidre M. St. Peter
157	Neuro-ophthalmological and clinical findings in Wolfram syndrome: what is the real mitochondrial role?	Giulia Amore
158	Neurological findings in patients with Leber's Hereditary Optic Neuropathy	Alexandre Hage
159	Retinal vascular geometry and tortuosity changes in patients withLeber hereditary optic neuropathy (LHON)	Neringa Jurkute
160	Microcystic Macular Degeneration In Autosomal Optic Neuropathy	Raoul K. Khanna
161	Long-term experience from an Expanded Access Program with idebenone in pediatric LHON patients	Xavier Llòria
162	Evaluation of visual field metrics in patients with central scotomas from LHON	Uchenna F. Nwako
163	Natural history of Leber's hereditary optic neuropathy (LHON): findings from a large patient cohort	Magda J. Silva
164	Development of a Novel Gene Therapy Using SIRT1 Signaling for Neuro-protection in Optic Neuropathies	Ahmara G. Ross
165	Visual outcomes of non-arteritic anterior ischemic optic neuropathy after systemic corticosteroid or observation	Haeng-Jin Lee
166	Does time equal vision in the acute treatment of NMOSD and other antibody-mediated optic neuritis?	Hadas Stiebel-Kalish
167	GCC Loss After Acute NAION Is More Rapid Than In Acute Optic Neuritis	Jennifer N. Danesh
168	Peripapillary hyperreflective ovoid mass-like structures (PHOMS) in children	Ye Jin Ahn
169	The Visual Morbidity of Optic Nerve Head Drusen in Children: A Longitudinal Review	Ryan A. Gise
170	Incidence of Optic Disc Drusen in Patients with Papilledema	Jack Ma
171	Optic Disc Drusen Associated Anterior Ischemic Optic Neuropathy: Prevalence of Comorbidities and Vascular Risk Factors	Lea L. Rueløkke
172	Prevalence and histopathological signatures of optic disc drusen based on microscopy of 1713 enucleated eyes	Marie Skougaard
173	The Angioarchitecture of the Optic Nerve Head in Patients with Optic Disc Drusen	Julie Vahlgren
Category: Disorders of the Posterior Visual Pathway and Visual Processing		
174	A serial study of retrograde trans-synaptic degeneration following post-geniculate injury	Rebecca Chen
175	Optic nerve cupping in patients with retrograde trans-synaptic degeneration	Samantha Goldburg
Category: IIH		
176	Evaluating Clinical and Demographic Differences Among Patients with Idiopathic Intracranial Hypertension (IIH)	John P. Gorham

177	Top ten research priorities for Idiopathic Intracranial Hypertension (IIH)	Susan P. Mollan
178	Neuro-Ophthalmologic Evaluation of Patients with Spontaneous Cerebrospinal Fluid (CSF) Leaks	Samuel Bidot
179	The Neuro-Ophthalmologist's Role after a CSF Leak	Brooke T. Johnson
180	Filling the Gap: CSF Fistula as a Presentation of Intracranial Hypertension	Aimee J. Szewka
181	Superonasal Transconjunctival Optic Nerve Sheath Decompression(stOND): A Simplified Technique for Safe and Efficient Decompression	Andrew T. Melson
182	Reported vs. actual height and weight among IIH patients	Deborah C. Parish
183	Use of En Face OCT to Monitor Papilledema in IIH	Andrew R. Carey
184	Quantification of Optic Nerve Head Venous Tortuosity in Idiopathic Intracranial Hypertension Using Optos Imaging	Salina Teja
185	Outcome of patients treated for Intractable Raised Intracranial Hypertension following Cerebral Venous Stenting	Norah S. Lincoff
186	Venous sinus stenting: a therapeutic alternative for refractory idiopathic intracranial hypertension	John E. Paddock
Category: Miscellaneous		
187	Correlation of Magnetic Resonance Imaging findings and Ocular examination in patients of Hypoxic Ischemic Encephalopathy	Gunjan Saluja
Category: Neuro-Imaging		
188	Diffusion Tensor Imaging (DTI) in ehtambutol induced Optic neuropathy	Kumudini Sharma
189	Defining Markers of Neuroaxonal Injury and Repair in a Compressive Model of Optic Neuropathy	Fiona Costello
Category: Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases		
190	Neuro-ophthalmological diagnosis in a series of 1107 patients with suspected ischemic stroke treated with thrombolysis	Joan Crespi
191	Functional-structural assessment of the optic pathways in patients with optic neuritis	Mathias Falck Schmidt
192	MicroRNAs and their use as biomarkers in clinically isolated syndrome and multiple sclerosis	Jette Lautrup Frederiksen Battistini
193	Novel paraclinical methods in patients with neuromyelitis optica spectrum disorders (NMOSD)	Jette Lautrup Frederiksen Battistini
194	Unique challenges in managing NMO Spectrum Disorder in the African American and African-Caribbean population	Laura Palazzolo
195	Characteriests of video head impulse test in patients with posterior inferior cerebellar artery stroke	Hyun-June Shin
196	Retinal Vasculopathy with Cerebral Leukoencephalopathy and Systemic Manifestations (RVCL-S): Description of a New Pedigree	Matthew S. Wieder
197	Optic neuritis: our experience	Mariana de Virgiliis
198	Papilledema as a Sign of Shunt Malfunction in Adults	Roshan T. George
199	Azithromycin as a possible neuroprotective drug in mouse model of optic nerve crush	Nitza Goldenberg-Cohen

200	Retinal microvasculature in pituitary adenoma patients: is optical coherence tomography angiography useful?	Arnaud-Louis A. Jeannerot
201	Elamipretide (MTP-131) Topical Ophthalmic Solution for the Treatment of Leber's Hereditary Optic Neuropathy	Rustum Karanjia
202	Prostate cancer and the visual system	Steven A. Newman
203	Temporal Artery Biopsy Length and Laterality	Jessica R. Chang
204	Involvement of the Posterior Intracranial Circulation in Giant Cell Arteritis	Laura Donaldson
205	Giant Cell Arteritis in African Americans: 10-Year Data from Baltimore	Anna M. Gruener
206	Institutional Analysis of Temporal Artery Biopsies based on Clinical Suspicion for Giant Cell Arteritis	Erik R. Johnson
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Poster 138
Long-Term Anatomical Effects of Increased Intracranial Pressure on Optic Nerve Sheath Dilation

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Introduction:
The purpose of this study was to investigate the long-term anatomical effects of mild traumatic brain injury (mTBI) and increased intracranial pressure (ICP) on optic nerve sheath diameter (ONSD) dilation by analyzing optic nerve sheath fibers 30 days after increasing ICP in a swine model. Our lab has previously demonstrated that a patient history of mTBI is associated with ONSD dilation, post Valsalva, that can be visualized on ultrasonography. We investigated the anatomical etiology for ONSD dilation and discovered a statistically significant thinning of fibers connecting the optic nerve and optic nerve sheath immediately after injury. The long-term anatomical effects of these fibers have not been previously studied and may hold important implications about post-traumatic recovery mechanisms.

Methods:
Increased ICP was induced in two swine models by inflating a fluid-filled catheter in the epidural space. ICP was monitored continuously. The pigs were euthanized 30 days post insult. After enucleation, extracted cross-sections of optic nerve sheath with intact nerve were imaged using a scanning electron microscope. The images were segmented and analyzed using DiameterJ to determine percent porosity of fibers. Percent porosity values for the pigs euthanized 30-days post-insult were compared to the values for two pigs immediately euthanized post-insult and three control pigs.

Results:
The experimental group euthanized 30 days post-insult demonstrated a statistically significant ($p = 0.0092$) increase in percent porosity (57.14%) as compared to the control group (43.36%). There was no significant difference ($p = 0.9485$) in porosity of the experimental group euthanized 30 days post-insult as compared to experimental models euthanized immediately post-insult (57.49%).

Conclusions:
This study demonstrates that injury associated with increased ICP results in an immediate and sustained statistically significant increase in fiber porosity after 30 days. This suggests that the support structure neither heals nor degenerates over time, resulting in the dilated ONSD seen on ultrasound.

References: None.

Keywords: High intracranial pressure/headache, Optic nerve trauma and treatment, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Miscellaneous

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Poster 139
Changes in the Intraorbital Optic Nerve Length Induced by Horizontal Eye Movements

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Introduction:
To investigate the effect of eye movement on the intraorbital portion of optic nerve (ON) length using 3-dimensional (3D) magnetic resonance imaging (MRI), and to measure the degree of ON length changes.

Methods:
We enrolled 71 healthy subjects, 20 to 50 years of age, and performed a prospective observational study. All participants underwent high-resolution T2-weighted MRI of the orbit in axial planes during central, and horizontal gazing. Using multilateral 3D reconstruction based on Visual C++, intraorbital ON length was measured at both medial and lateral side of ON according to the horizontal eye movement. The correlation between ON length changes and axial length (AXL) and eye volume (EV) was evaluated.

Results:
Optic nerve length were 24.60 ± 2.62 mm at medial and 25.60 ± 2.46 mm at lateral side of ON in central gaze. In abduction, both medial and lateral side of ON length were increased, and the mean length of increase were 3.81 ± 1.31 mm ($p<0.001$) and 0.54 ± 0.92 ($p<0.001$), respectively. In adduction, both medial and lateral side of ON length were increased, and the mean length of increase were 0.31 ± 0.93 ($p=0.009$) and 3.48 ± 1.52 ($p<0.001$), respectively. The mean length of ON were negatively correlated with AXL and EV (AXL: medial and lateral, $R = -0.304$ and -0.326, $p=0.012$ and 0.007, respectively; EV: medial and lateral, $R = -0.299$ and -0.366, $p=0.013$ and 0.002, respectively). And the changes of medial ON length in abduction was positively correlated with axial length ($R = 0.461$, $p<0.001$).

Conclusions:
We found significant lengthening in the ON in both abduction and adduction. And these changes were significantly associated with AXL, at medial side of ON during abduction. Considering these changes as physical properties, it allows a better understanding of the biomechanical characteristics of the optic nerve head.

References: None.

Keywords: Ocular Motility

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Poster 140
Does The Eye Only Rotate? Three Dimensional Magnetic Resonance Imaging Study

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Introduction:
To investigate the pattern of eye movement during horizontal and vertical gazing using 3-dimensional (3D) magnetic resonance imaging (MRI).

Methods:
We enrolled 56 healthy subjects who were 20 to 50 years old, and performed a prospective observational study. All participants underwent high-resolution T2-weighted MRI of the orbit (Achieva 3.0T; Philips Medical Systems, Best, The Netherlands) in axial planes during central, horizontal, and vertical gazing. Using multilateral 3D reconstruction based on Visual C++, MRI images were processed to analyze eye movements. The angle of eyeball rotation was measured using Photoshop. The distance between the centroid of the eyeball in central gaze and secondary gaze was measured and the direction of centroid movement was evaluated.

Results:
The mean angles of rotation were abduction 47.4°, adduction 46.4°, elevation 31.1°, and depression 31.3°. 3D MRI revealed displacement of eyeball in all secondary gaze positions. The mean distances of centroid movement were 0.68 ± 0.27 (95% confidence interval [CI]: 0.64– 0.72) mm in horizontal gaze and 0.43 ± 0.21 (95% CI: 0.40–0.47) mm in vertical gaze. Eyeballs were displaced in the same direction during horizontal gazing, while the direction was opposite during vertical gazing.

Conclusions:
In this study, displacement of eyeball is consistently observed in normal subjects during secondary gazing. These findings indicate that eye movement is compound of rotation and translation, and it should be considered when evaluating eye movement precisely.

References: None.

Keywords: Ocular Motility

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Poster 141
Traumatic Optic Neuropathy Biomechanics: High Speed Camera Assessment In An Animal Model

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Introduction:
Indirect traumatic optic neuropathy refers to optic nerve injury with blunt head trauma remote to the optic nerve. Although tied with frontal blows or deceleration, the precise mechanism of axonal disruption remains unknown. In this initial phase of our study, high speed video acquisition was utilized in an animal model to evaluate the biomechanics of indirect traumatic optic neuropathy.

Methods:
An goat cadaveric model was devised to assess the biomechanics of frontal impact. Strain gauge sensors were placed within the orbit and brain. A customized pendulum head impactor was fabricated with a swing arm of adjustable height and length to administer impact to the frontal bone. High speed video at 4000 frames per second was used to record the impact with a Photron Fastcam SA5, allowing precise measure of orbital soft tissue motion relative to adjacent orbital bone. Tracker 5.0 video analysis software was used to compare the relative position of the globe to the orbital rim. The focus of the present study will be largely limited to video analysis.

Results:
The position magnitude of the globe motion was greater compared to the position magnitude of the orbital rim immediately after initial impact. Maximum initial delta globe movement was 2.5 mm anteriorly relative to the orbital rim, with multiple subsequent oscillations ranging 1-3 mm. Concurrently noted strain jump at the optic nerve with initial impact indicates independent tissue motion at the optic nerve.

Conclusions:
Globe motion relative to the bony orbit may contribute to the development of traumatic optic neuropathy. The amount and extent of globe movement may lead to optic nerve stretch and axonal injury. This study is limited by the goat animal model and studies involving human cadaveric models will be necessary. This study delineates the benefit of high speed video acquisition in an animal model of traumatic optic neuropathy.

References: None.

Keywords: Optic nerve trauma and treatment

Financial Disclosures: The authors had no disclosures.

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Poster 142
Impaired cognition in glaucomatous optic neuropathy

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Introduction:
We evaluated cognition in a cohort of glaucoma and pre-glaucoma (suspects) using Montreal Cognitive Assessment (MoCA).

Methods:
Paper based MoCA was administered by trained personnel using standardized instructions to 41 subjects- 18 pre-glaucoma (cupping and/or elevated IOP without visual field defects) and 23 glaucoma. All subjects had 20/40 or better BCVA in both eyes and 3 reproducible Humphrey visual field (HVF). A composite binocular visual field index (OU-VFI) was calculated from the HVF of each subject using published algorithm. We modeled (multiple linear regression) effect of glaucoma severity [defined by OU-VFI] on cognition after controlling for age, gender, race, co-morbid neurological condition, psychotropic medication and ocular diagnosis (glaucoma vs. suspect). We compared MoCA total and domain scores for our cohort with published normative data (Nasreddin et. al.).

Results:
Mean (SD) for age was 65.9 (13.1) years, OU- VFI scores 0.87 (0.18), total MoCA score 24.9 (2.75) and visuospatial component score 3.7 (1). Compared to published normative controls our cohort demonstrated significantly lower scores for total MoCA (27.4 vs. 24.90; p=0.00); cube (0.71 vs. 0.46; p=0.00); clock (2.65 vs. 2.34; p= 0.01); memory (3.73 vs. 2.92; p=0.00); sentence repetition (1.83 vs. 1.68; p=0.03); fluency (0.87 vs. 0.70; p=0.01); and abstraction (1.83 vs. 1.56; p=0.00). After controlling for the effects of ocular diagnosis, age, gender, psychotropic medications and cognitive confounders, total MoCA scores were influenced by OU-VFI (β= 9.5 (95%CI 3.6, 15.5; p=0.00). After controlling for effects of ocular diagnosis, age and cognitive confounders, OU-VFI (β= 3.1 (95%CI 0.8, 5.3; p=0.00), gender (β= 0.7 (95%CI 0.01, 1.4; p=0.04), and psychotropic medications (β= 0.7 (95%CI 0.01, 1.4; p=0.04) influenced visuospatial domain scores.

Conclusions:
Our study shows that glaucoma and pre-glaucoma subjects have significant cognitive deficits, which supports a growing literature suggesting that glaucoma may be a neuro-degenerative disorder.

References: 1. Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, Cummings JL, Chertkow H. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc. 2005 Apr;53(4):695-9. PubMed PMID: 15817019. 2. Bulut, M., Yaman, A., Erol, M. K., Kurtuluş, F., Toslak, D., Coban, D. T., & Başar, E. K. (2016). Cognitive performance of primary open-angle glaucoma and normal-tension glaucoma patients. Arquivos brasileiros de oftalmologia, 79(2), 100–4. doi:10.5935/0004-2749.20160030.

Keywords: Higher Visual Cortical functions

Financial Disclosures: The authors had no disclosures.

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Poster 143
Incidence of Mood Disorders in Patients with Idiopathic Intracranial Hypertension

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Introduction:
Idiopathic intracranial hypertension (IIH) is a condition of unknown etiology characterized by elevated intracranial pressure and normal neurologic exam except for sixth nerve palsy. The majority of IIH patients are obese women and suffer from headaches. Additionally, papilledema is commonly present and may lead to significant vision loss. The focus of IIH research has been on preventing vision loss, with little focus on the condition's psychosocial impact. Studies have examined the relationship between anxiety, depression, and quality of life, but have relied on patient questionnaires, which may introduce participation biases. Our aim was to objectively study the incidence of mood disorders in patients with IIH compared with control groups.

Methods:
A retrospective chart review was performed on patients with IIH and age-matched control groups of non-overweight patients without migraine, overweight patients without migraine, non-overweight patients with migraines, and overweight patients with migraines. Binary logistical regression was applied to compare the odds of any mood diagnosis for all potential pairwise patient diagnoses, with a Šidák correction to control Type I error rate.

Results:
A total of 85,043 patients met inclusion criteria. Patients with IIH had a higher incidence of mood disorders than controls groups of normal or overweight patients ($p<.001$). However, patients with IIH and patients with migraine had a comparable incidence of mood disorders ($p=.99$). Lastly, migraine patients that were also overweight had a higher incidence of mood disorders than migraine patients that were not overweight ($p<.001$). However, the incidence of mood disorders in overweight patients with migraine was not statistically different from patients with IIH ($p=.17$).

Conclusions:
To our knowledge, this is the first study to objectively compare the incidence of mood disorders in patients with IIH compared with control groups. Screening of patients with IIH for mood disorders may lead to appropriate mental health referrals and improved quality of life.

References: Ball, Alex K., and Carl E. Clarke. "Idiopathic intracranial hypertension." The Lancet Neurology 5.5 (2006): 433-442. Digre, Kathleen B., et al. "Quality of life in idiopathic intracranial hypertension at diagnosis IIH Treatment Trial results." Neurology 84.24 (2015): 2449-2456. Ferrari, Alize J., et al. "The burden attributable to mental and substance use disorders as risk factors for suicide: findings from the Global Burden of Disease Study 2010." PloS one 9.4 (2014): e91936. Kesler, Anat, et al. "Psychological correlates of idiopathic intracranial hypertension." IMAJ-RAMAT GAN- 7.10 (2005): 627. Kleinschmidt, J. J., K. B. Digre, and R. Hanover. "Idiopathic intracranial hypertension. Relationship to depression, anxiety, and quality of life. Neurology 2000; 54: 319 324." American journal of ophthalmology 129.6 (2000): 831. Kuzman, Martina Rojnic, et al. "Psychiatric symptoms in idiopathic intracranial hypertension." Psychiatry and clinical neurosciences 62.3 (2008): 367-367.

Keywords: High intracranial pressure/headache, Pseudotumor Cerebri

Financial Disclosures: The authors had no disclosures.

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Poster 144
Rapid Picture Naming in Parkinson's Disease Using the Mobile Universal Lexicon Evaluation System (MULES) Test

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Introduction:
The Mobile Universal Lexicon Evaluation System (MULES) is a test of rapid picture naming that captures an extensive visual network involving afferent/efferent visual and cognitive pathways. MULES performance is impaired in concussion and multiple sclerosis in which visual impairment is common. Similarly, visual deficits also occur in Parkinson's Disease (PD). These visual deficits influence overall motor function and are a risk factor for developing visual hallucinations. Since many of the visual factors captured by MULES may be abnormal in PD (e.g., visual acuity, color discrimination, object recognition, visual processing speed, and saccadic eye movements), MULES may serve as a useful screening tool for visual dysfunction in PD. The purpose of this study was to introduce MULES to visual assessment in PD.

Methods:
MULES, which consists of 54 color photographs of various objects (fruits, animals, and random objects), was administered in a PD cohort and a group of similar-aged disease-free controls.

Results:
Among 49 PD patients (median age 70 years old, range 52-82) and 18 disease-free controls (median age 61.5, range 53-90), MULES scores were significantly worse (slower) in PD patients (63.2 seconds, range 37.8-296.3) vs. controls (49.7 seconds, range 38.6-128.6) ($p=0.04$, accounting for age). Slower MULES times were associated with increased PD motor symptom severity as measured by the Unified Parkinson's Disease Rating Scale (UPDRS) ($rs=0.40$, $p=0.01$). Age, gender, primary language, and disease duration did not predict MULES scores in PD patients.

Conclusions:
The MULES captures an extensive visual network, including many aspects of vision, that can be abnormal in PD. This study demonstrates that MULES performance is reduced in PD and may reflect the degree of motor impairment. As such, MULES is a potentially useful performance assessment tool in PD.

References: None.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 145
Association of age-related macular degeneration with Alzheimer's disease and Parkinson's disease

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Introduction:
The association of age-related macular degeneration (AMD) with Alzheimer's disease (AD) and Parkinson's disease (PD) is yet unclear.

Methods:
The study population consisted of 308,340 men and women aged 50 years or older from the Korean National Health Insurance Service – Health Screening Cohort. After excluding participants with AMD during 2002, participants were detected for AMD during 2003-2005. Starting from 1 January 2006, all participants were followed-up for AD and PD until 31 December 2013. Cox proportional hazards regression was used to calculate the multivariate adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs) for AD and PD risk according to AMD.

Results:
The number of participants without and with AMD were 306,127 and 2,213, respectively. Compared to those without AMD, AMD patients had higher risk for AD (aHR 1.48, 95% CI 1.25-1.74) and PD (aHR 1.46, 95% CI 1.14-1.88). The risk-increasing association of AMD with AD (aHR 1.48, 95% CI 1.25-1.77) and PD (aHR 1.61, 95% CI 1.23-2.10) were preserved after excluding participants diagnosed with AD and PD within the first 3 years of follow-up. Finally, AMD was associated with higher risk of AD (aHR 1.96, 95% CI 1.46-2.65 for age <70 years and aHR 1.53, 95% CI 1.26-1.86 for age ≥70 years) and PD (aHR 1.90, 95% CI 1.29-2.80 for age <70 years and aHR 1.47, 95% CI 1.06-2.04 for age ≥70 years) for all subgroups according to age.

Conclusions:
AMD patients had higher risk for AD and PD compared to those without AMD. Patients with AMD must be closely monitored for the possible subsequent development of AD and PD.

References: None.

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

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Grant Support: None.

Poster 146

An Assessment of Electroencephalogram (EEG) Eyeblink Artifact as a Clinical Measurement in Parkinsons Patients

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Introduction:
Parkinsons is a clinical diagnosis, with limited diagnostic capability in the subtle, early stages of disease. As a complex neuro-muscular reflex, the natural eyeblink may provide clues towards the presence of Parkinsons. Though reduced blink rate and blink hyper-excitability are well-known phenomenon in Parkinson's patients, these can be difficult to quantify. The objective of this study was to assess eyeblink artifact on EEG as a potential data source, in order to identify quantitative values that may relate to a disease-state.

Methods:
Retrospective review of inpatient EEGs in 216 patients; 27 with Parkinsons (avg. 78.7yr) and 189 with normal EEGs (avg. 51.8yr). Patients were evaluated on 21-lead XLTEK Natus Neurology System v.8.1.1 with standardized electrode placement, with eyeblink artifact in Fp1-F3, Fp2-F4, Fp1-F7, and Fp2-F8. An average of 3 isolated (non-series) blinks without gaze preference, artifact, or disorganized background activity, were qualitatively selected per patient (628 blinks). Blink morphology was qualitatively characterized as narrow-complex, wide-complex, or wide small-complex.

Results:
Closing-amplitude was statistically significant between Parkinsons (83.33uv) and controls (157.6uv) ($p=<0.001$). There was no significant difference in closing phase (79.7 & 79.6ms). There was a significant prolongation in opening phase ($p=<0.002$), total blink duration ($p=<0.02$), and a reduced opening-amplitude ($p=<0.001$) in Parkinsons. Parkinsons demonstrated a higher prevalence of wide small-complex (19.5% vs. 6.5%). Paired leads (Fp1-F3/Fp2-F4 and Fp1-F7/Fp2-F8) were nearly identical in both cohorts.

Conclusions:
Blink closure is not affected by disease state or morphology. The three blink morphologies were supported as distinct entities by their quantitative measurements. Lead similarity was congruent with lead placement, supporting the accuracy of our measurements. Parkinsons patients showed a higher prevalence of wide-small complex, with several prolonged segments, and significantly reduced amplitudes. Our opening time was similar to previously published values [1-2]. Eye-blink parameters may provide subtle and quantitative evidence of a diseased state.

References: 1. Caffier PP, Erdmann U, Ullsperger P. Experimental evaluation of eye-blink parameters as a drowsiness measure. European journal of applied physiology. 2003 May 1;89(3-4):319-25. 2. Divjak M, Bischof H. Eye Blink Based Fatigue Detection for Prevention of Computer Vision Syndrome. InMVA 2009 May 20 (pp. 350-353).

Keywords: Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Neuro-ophth & systyemic disease (eg. MS, MG, thyroid), Ocular Motility, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 147
Visuo-retinal effects of chemotherapy in hematological malignancy

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Introduction:
We evaluated visuo-retinal correlates for chemotherapy-related cognitive impairment (CRCI) in hematological malignancy (HM).

Methods:
We prospectively studied 9 HM starting chemotherapy (CTX+), 12 HM on supportive care (CTX-) and 14 healthy comparisons (HC). We measured cognition, contrast sensitivity (CS), global retinal nerve fiber layer thickness (RNFLT) and ganglion cell/inner plexiform layer thickness (GCL-IPLT) at baseline (T1), 1-month (1CTX cycle; T2), and 3-months (3CTX cycles; T3). N2pc amplitudes were measured as electrophysiological correlate of spatial attentional control at all visits. Data were analyzed in SAS using PROC FREQ and MIXED procedures.

Results:
We observed CS worsening across visits in CTX+ group [Mean±SD (logMAR values; T1; T2; T3): CTX+ OD: (0.34±0.15; 0.38±0.16; 0.39±0.05); OS: (0.37±0.13; 0.39±0.11; 0.39±0.04)]. We observed a trend for RNFL thickening at T2 followed by thinning at T3 in CTX+ group: 86% CTX+ showed RNFL thickening from T1 to T2 and 80% CTX+ showed RNFL thinning from T2 to T3 (c2=4.9, p=.09). RNFLT (mm; T1; T2; T3) Mean±SD: CTX+ OD: (93.6±17.8; 98.4±14.0; 88.5±10.8); OS: (93.2±15.9; 97.7±14.7; 91.3±6.5). GCLT showed no change across visits or groups. Modeling CS, changes from T1 to T2 showed significant effects of treatment group (F=6.8, p=.01) and T2-T3 RNFLT changes (F=9.4, p=.01). CS decrease for Ctx+ group (t=3.64, p=.003) was greater than Ctx- (t=3.57, p=.004) and HC (t=2.68, p=.02). N2pc amplitude showed a reduction from T1-T2 for CTX+ (0.47+/-.77), which was associated with RNFL thinning (T2-T3) (F=9.45, p=.0083). RNFL changes were not significantly associated with changes in other cognitive parameters.

Conclusions:
Small changes in CS following chemotherapy were predicted by RNFL thickness changes. Initial RNFL thickening and subsequent thinning may reflect axonal swelling followed by degeneration. The association of electrophysiological measures of cognition and visuo-retinal parameters suggests these could serve as biomarkers of CRCI. A small sample size limits generalizability of our study.

References: None.

Keywords: Chemotherapy and radiation injury

Financial Disclosures: The authors had no disclosures.

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Poster 148
Progressive Supranuclear Palsy Saccadic Deficits: Infrared-oculographic Features and Challenges

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Introduction:
Progressive Supranuclear Palsy (PSP) is a neurodegenerative tauopathy characterized by postural instability, axial rigidity, dysphagia, and supranuclear gaze palsy (SGP). The SGP hallmark is vertical saccade slowing with or without gaze-range limitation. However, clinical diagnosis of saccade slowing can be challenging, especially early; exploration for subclinical horizontal saccade features is also useful. We discuss the spectrum of PSP SGP findings, as well as eye tracking challenges.

Methods:
Participants with suspected PSP underwent clinical examination and infrared-oculography (IOG-Eyelink 1000+).

Results:
Of 12 participants (52-80 years, 9 men), 10 had PSP (disease duration 3 +/-2.05 years) and 2 had PSP-parkinsonism (10 years suspected Parkinson Disease, followed by 1-2 year deterioration). Clinical examination across the cohort revealed square wave jerks (continuous in 6) and suspected vertical saccade slowing. Eight had questionable mild horizontal saccade slowing. When in question, IOG detected subclinical slowing and saccade trajectory abnormalities. Two distinct patterns of saccade abnormalities were observed: long, slow, hypometric saccades or small staircase saccades. A portion of participants exhibited one or the other pattern, while others exhibited aspects of both. Saccadic velocity analysis required manual annotation for slow saccade detection, as they were not identified by current automated detection algorithms.

Conclusions:
Familiarity with the range of SGP features enhances interpretation of quantitative eye movement recordings, as does familiarity with the technical challenges. There is a research need for development of calibration methods that minimize patient interaction and for algorithm advances towards automatic slow saccade detection, given the high noise inherent in eye trackers that depend on video data. With increasing options with regard to potential PSP treatments and increased IOG accessibility, accurate understanding of how clinical and quantitative saccadic abnormalities inter-relate may allow for earlier PSP diagnosis.

References: None.

Keywords: Ocular Motility, Miscellaneous

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Grant Support: None.

Poster 149

The Post-Illumination Pupil Response (PIPR) Is Associated With Cognitive Measures in an Epidemiologic Cohort

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Introduction:

Age-related ocular diseases have far-reaching effects on functionality and are associated with declines in quality-of-life measures independent of vision. The present study seeks to evaluate the association between the PIPR and cognition in a subgroup of the Beaver Dam Offspring Study (BOSS) cohort.

Methods:

We conducted a cross-sectional study in a subgroup of participants in the 10-year follow-up examination of the BOSS, an established, large longitudinal epidemiologic, multi-sensory study of aging. The PIPR was recorded using binocular infrared pupillometer (DP2000 Human Laboratory Pupillometer, Neur-Optics, Inc., Irvine, CA). Cognitive function testing consisted of the Mini-Mental State Examination, Trail Making Test A and B, Rey's Auditory Verbal Learning Test, Digit Symbol Substitution Test, and Verbal Fluency Test. Principal component analysis (PCA) score was calculated to represent overall cognitive function. Linear regression models ware used to test the association between the PIPR and cognitive function (PCA) using SAS version 9.4.

Results:

A total of 403 individuals (172 male and 231 female) participated in the study, with age ranging from 33 to 81 years (mean±SD, 60.7±9.3 years). The pupil recordings from 377 participants were included in the final analysis. Age is associated with smaller mean baseline pupil diameter (mm) (linear regression, y= -0.042x+7.85, R2=0.21). There is a statistically significant correlation between the mean PIPR and PCA cognitive score (linear regression, y=1.99x-0.33, R2=0.03) and the correlation remained significant after adjusting for age, sex, education, use of CNS-acting medications (benzodiazepine, antihistamine, and antidepressants) and beta-blockers, depression, cardiovascular disease, and ocular disease (glaucoma, age-related macular degeneration, and cataract surgery).

Conclusions:

The preliminary analyses of this subset of BOSS participants demonstrated a statistically significant association between the PIPR and cognitive function, suggesting a potential future application of the PIPR in cognitive aging research.

References: 1. Broman AT, Munoz B, Rodriguez J, et al. The impact of visual impairment and eye disease on vision-related quality of life in a Mexican-American population: proyecto VER. Invest Ophthalmol Vis Sci 43(11), 3393-8, 2002 2. Gooley JJ, Lu J, Chou TC, Scammell TE, Saper CB. Melanopsin in cells of origin of the retinohypothalamic tract. Nat Neurosci 4(12), 1165, 2001 3. Lucas RJ, Hattar S, Takao M, Berson DM, Foster RG, Yau KW. Diminished pupillary light reflex at high irradiances in melanopsin-knockout mice. Science 299(5604), 245-7, 2003 4. Park JC, Moura AL, Raza AS, Rhee DW, Kardon RH, Hood DC. Toward a clinical protocol for assessing rod, cone, and melanopsin contributions to the human pupil response. Invest Ophthalmol Vis Sci 52(9), 6624-35, 2011 6. Kang JE, Lim MM, Bateman RJ, et al. Amyloid-beta dynamics are regulated by orexin and the sleep-wake cycle. Science 326(5955), 1005-7, 2009 7. Cruickshanks KJ, Tweed TS, Wiley TL, et al. The 5-year incidence and progression of hearing loss: the epidemiology of hearing loss study. Arch Otolaryngol Head Neck Surg 129(10), 1041-6, 2003.

Keywords: Miscellaneous, Pupils Retina

Financial Disclosures: Unrestricted grant from Research to Present Blindness, University of Wisconsin Department of Ophthalmology and Visual Sciences research funding, and F.A. Davis Fund for vision research.

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Poster 150
The Use of Automated Pupillometry in the Treatment of Opioid Addiction

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Introduction:
The goal of opioid agonist therapy in addiction treatment is to control a patient's withdrawal symptoms without causing excess sedation. Tolerance to opioid medication is variable and dosage decisions are based on a combination of a patient's reported symptoms and clinically observed signs of withdrawal, including a rough estimate of pupil size that is prone to interobserver variability. The goal of this study was to determine whether more precise measurements of pupil size and reactivity, obtained using automated infrared pupillometry, might aid in the dosing of opioid agonist therapy.

Methods:
A prospective study of inpatients at an urban academic hospital between the age of 18 and 50 seeking treatment for opioid addition. Patients on opiate agonist therapy (methadone or buprenorphine/naloxone) consented to have pupil size and several reactivity variables measured - once before and at several time points after medication dosage - using a NeuroOptics NPi-200 pupillometer. Withdrawal symptoms and signs were also assessed using the Clinical Opioid Withdrawal Scale (COWS), the current standard for dosing opioid agonist therapy. Additionally, a survey measuring patient satisfaction with withdrawal symptom control was administered following dosing.

Results:
We enrolled 20 patients (70% male, average age 33.2 years) in the study. There was a statistically significant decrease in pupil size (both light and dark) and dilation velocity when comparing pre-dosing measurements to those obtained at 30 and 60 minutes post-dosing. There was no significant change in constriction velocity, percent constriction, or latency time.

Conclusions:
We report a significant change in pupil size and dilation velocity following administration of opioid agonist therapy. With a larger patient cohort, we hope to identify an average change in these parameters corresponding to optimal control of opioid withdrawal symptoms. We hope that this will provide a more objective tool in the initial dosing of opioid replacement therapy and help to prevent relapse.

References: None.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 151

Inhibition of glutamate carboxypepptidase II protects retinal ganglionic cell death induced by ischemia-reperfusion in rat

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Introduction:
Excessive glutamate receptor activation is thought to be involved in retinal ganglion cell (RGC) death after ischemia- reperfusion damage. Glutamate carboxypeptidase II (GCPII) is an enzyme responsible for the hydrolysis of the neurotransmitter NAAG (N-acetyl-aspartyl-glutamate) to N-acetyl-aspartate and glutamate. Thus, in this study, we examined the effect of 2-(phosphonomethyl) pentanedioic acid (2-PMPA), a GCPII inhibitor, on RGC survival after acute high IOP ischemia-reperfusion damage.

Methods:
Mixed retinal cultures prepared from 8-day old rat retina were underwent hypoxia by reducing oxygen concentration (1 %) for 6 hours and followed by reperfusion for 14 hours. Animal model of ischemia- reperfusion was induced by raising the intraocular pressure for 60 min and followed by reperfusion.

Results:
Western blot analysis showed that the level of GCPII protein after ischemia- reperfusion increased 1.9 fold compared to control. Similar result of GCPII protein increase was observed in vivo animal model. Immunostaining with anti-BRN antibody showed that ischemia- reperfusion caused RGC death (31.5 %) compared to the normal control. Treatment of 2-PMPA (11 and 110 ng per eye) through intra-vitreous injection twice at 0 and 48 hour after reperfusion blocked RGC death; 11 ng PMPA blocked cell death significantly resulting in 12.4 % cell death while 110 ng saved most of cells.

Conclusions:
Induction of GCPII expression in retinal cells after ischemia- reperfusion injury is likely associated with RGC death, and GCPII inhibitor may be useful in retinal disorders in which glutamate excitotoxicity is pathogenic.

References: None.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

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Poster 152
Nationwide Incidence of Terson Syndrome in Treated Subarachnoid Hemorrhage in South Korea : 2011-2015

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Introduction:
To investigate the incidence and mortality of Terson syndrome in patients with treated subarachnoidal hemorrhage (SAH) in South Korea using National Health Insurance (NHI) database.

Methods:
For this nationwide population-based retrospective study, we used the national health claims database from 2011 to 2015, age of ≥ 18 years old, to identify patients diagnosed with treated SAH and Terson syndrome. Subjects with newly diagnosed non-traumatic SAH who underwent clipping or coiling, and newly diagnosed retinal or vitreous hemorrhage within 3 months of SAH were included and among them, subjects with newly diagnosed other ocular pathology causing retinal or vitreous hemorrhage were excluded. Nationwide incidence of Terson syndrome by age groups, gender, and treatment types per 100,000 person-years were calculated and the mortality among Terson syndrome and non-Terson syndrome were compared.

Results:
We identified 22,864 treated SAH cases and 196 Terson syndrome cases among them during the study period. The incidence rate of Terson syndrome in treated SAH was 857.2 per 100,000 person-years (95% confidence interval [CI], 737.7-976.7) overall, and 1104.0 (95% CI 880.9-1327.1), and 713.3 (95% CI 576.0-850.6) per 100,000 person-years among male and female, respectively (male-to-female ratio, 1.548). There was no significant difference in incidence rate among treatment groups. The mortality rate of Terson syndrome in patients with treated SAH was 4.08% in total, and 5.38% and 2.91% in male and female, respectively (male-to-female ratio, 1.894). The mortality rate of non-Terson syndrome was 7.30%.

Conclusions:
This was the first nationwide incidence study of Terson syndrome in all age groups using population-based database. The incidence and the mortality rate of Terson syndrome in treated SAH by gender was higher in male. The mortality rate of Terson syndrome in treated SAH was higher in male, and was not higher than in treated SAH without Terson syndrome.

References: None.

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

Financial Disclosures: The authors had no disclosures.

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Poster 153
Fractionated Targeted Proton Beam Therapy For Optic Nerve Sheath Meningioma

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Introduction:
Management of optic nerve sheath meningiomas (ONSM) remains challenging. Proton beam radiation therapy (PBT) is less widespread than photon therapy because of the cost of the procedure but has the advantage of limiting radiation exposure to adjacent structures. We aimed to report the visual outcome of patients with primary ONSM treated with PBT in France.

Methods:
Retrospective review of all patients with primary ONSM who received PBT alone or after surgery [01/2006-12-2016]. Repeat neuro-ophtalmic examinations were collected (at presentation, after surgery and after radiotherapy). Tumors were measured at diagnosis and at each follow-up MRI examination.

Results:
0 patients (50 women; mean age:45.2±11.1y) were included, of which 29 had surgery. At presentation, 87% of the patients had decreased vision (Average visual acuity: 0.6 logMAR; visual field mean deviation:-13.4dB), Fundus examination (n=58) showed swelling (n=27;46.5%), pallor (n=22;37.9%) or cupping (n=2;3.4%) of the optic disc, opto-ciliary shunt (n=8;13.8%), choroidal folds (n=5;8.6%) or was unremarkable (n=7;12.1%). After treatment, visual acuity and mean deviation were stable overall. Patients who had surgery showed better visual outcome (improvement of more than 0.4 logMAR in 6 patients after surgery vs. in 1 patient after PBT, p=0.02). This improvement was found stable after PBT. 8 patients had worsening of visual field. Fundus examination (n=58) showed pallor (n=47;83.9%), swelling (n=3;5.4%) and cupping (n=2;3.4%) of the optic disc, and was normal in 5 (8.9%). 3 patients developed asymptomatic retinal hemorrhages. The tumor significantly shrunk in 8 patients pre/post PBT and remained stable in all the others. Patients with optociliary shunts had significantly worse visual outcome than other patients.

Conclusions:
PBT alone or in association with surgery appears to be a safe and efficient treatment for ONSM by reducing the growth of the tumor and allowing stability of visual function. The presence of an opto-ciliary shunt at presentation was of poor visual prognosis.

References: 1. Dutton JJ. Optic nerve sheath meningiomas. Surv Ophthalmol. 37:167-183, 1992 2. Egan RA, Lessell S. A contribution to the natural history of optic nerve sheath meningiomas. Arch Ophthalmol Chic Ill 1960. 120:1505-1508, 2002 3. Narayan S, Cornblath WT, Sandler HM, Elner V, Hayman JA. Preliminary visual outcomes after three-dimensional conformal radiation therapy for optic nerve sheath meningioma. Int J Radiat Oncol Biol Phys. 56:537-543, 2003 4. Paulsen F, Doerr S, Wilhelm H, Becker G, Bamberg M, Classen J. Fractionated stereotactic radiotherapy in patients with optic nerve sheath meningioma. Int J Radiat Oncol Biol Phys. 82:773-778, 2012 5. Arvold ND, Lessell S, Bussiere M, et al. Visual outcome and tumor control after conformal radiotherapy for patients with optic nerve sheath meningioma. Int J Radiat Oncol Biol Phys. 75(4):1166-1172, 2009.

Keywords: Tumors, Optic neuropathy, Orbit, Skull Base

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Poster 154
Dyschromatopsia In Anti-aquaporin-4 antibody-positive Optic Neuritis

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Introduction:
Long-term visual outcome in typical optic neuritis (ON) is favorable according to optic neuritis treatment trial. At 6 months, visual acuity (VA) is better than 20/20 in most cases. However, dyschromatopsia has remained and shifted over the course of the disease. Patients with neuromyelitis optica spectrum disorder associated optic neuritis (NMO-ON) usually presents more aggressively with poor visual outcome. Axonal degeneration in NMO-ON is prominent and might affect color mechanism in a different way. Our aim of this study is to evaluate color vision in NMO-ON.

Methods:
A retrospective case review of patients with acute NMO-ON admitted to a tertiary care center was performed. Inclusion criteria were an acute presentation of atypical ON (first episode), aquaporin4-IgG seropositivity, and optic nerve enhancement on contrast-enhanced T1-weighted images with fat suppression of the orbits. All patients underwent thorough neuro-ophthalmological examinations. Ishihara color test and Farnsworth D15 color test (D15) were carried out at their initial and follow-up visits. Steroid and azathioprine were given in all cases.

Results:
Thirty eyes of 23 patients were enrolled. There were 1 male and 22 female patients aged 17-80 years (mean 45.04). Eight patients developed bilateral ON. At the initial visit, the mean logMAR VA of all eyes was 1.72 (SD 0.85); 76.67% presented with VA>1; around 83% had abnormal Ishihara and D15 tests. At the follow-up visit, the mean logMAR VA of all eyes was 0.87 (SD 0.99); 40 % had VA>1; 46.67% and 40 % had abnormal Ishihara and D15 tests respectively. All patients with follow-up VA</=0.3 showed normal color vision.

Conclusions:
At the initial visit, both Ishihara and D15 were impaired in a similar proportion. At the follow-up visit, color vision recovered well in patients with good VA.

References: Katz B. The dyschromatopsia of optic neuritis: a descriptive analysis of data from the optic neuritis treatment trial. Transactions of the American Ophthalmological Society. 1995;93:685-708.

Keywords: Demeylinating disease, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 155
Multivariate analysis and diagnostic value of OCT and OCT angiography measurements of optic atrophy

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Introduction:
Optical coherence tomography (OCT) and angiography (OCTA) [1-6] are common tests to consider in the evaluation of patients with vision loss. It is unclear which OCT and OCTA measurements are most useful and whether OCTA adds substantially to OCT. We performed a cross-sectional study to answer these questions.

Methods:
We recruited 134 (230 eyes) controls and patients with visual defects from ischemic, inflammatory, metabolic, and other optic neuropathies; chiasmal compression; and homonymous hemianopia (7 groups). We compared static perimetry mean deviation compared with OCT retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC) thickness and OCTA optic disc and macular superficial plexus measurements (vessel area density, vessel skeletal density, vessel complexity index, vessel perimetry index, vessel diameter, and flow impairment). OCTA analyses were performed with MATLAB scripts and statistical analyses, in R scripts.

Results:
Using a correlation matrix to compare visual field and all OCT and OCTA measurements, mean deviation most highly correlated with optic disc OCTA measurements (ρ=0.66-0.70; flow impairment ρ=-0.62) and RNFL and GCC thickness (ρ=0.59). The correlation coefficients were lower for macular OCTA measurements (ρ=0.38-0.43; flow impairment ρ=-0.40). Principal components analysis showed that the first principal component accounted for 59% of variance and separated controls from optic atrophy. To determine which measurement was the best predictor of visual field loss, we performed univariate logistic regression and found that the best predictors with lowest error rates (combined false positives and negatives) were (best to worst): GCC and RNFL (10-15%), optic disc OCTA measurements (15-25%), and macular OCTA measurements (25-35%).

Conclusions:
Although visual field, OCT, and OCTA measurements were all significantly different between patients with various neuro-ophthalmic causes of vision loss and controls, OCT (RNFL and GCC) was as good as optic disc OCTA in separating those with vision loss from controls, while macular OCTA was not as good as either.

References: 1. Kashani, A.H., et al., Optical coherence tomography angiography: A comprehensive review of current methods and clinical applications. Prog Retin Eye Res, 2017. 60: p. 66-100. 2. Chen, J.J., et al., Optical Coherence Angiographic Demonstration of Retinal Changes From Chronic Optic Neuropathies. Neuroophthalmology, 2017. 41(2): p. 76-83. 3. Akil, H., et al., Optical Coherence Tomography Angiography of the Optic Disc; an Overview. J Ophthalmic Vis Res, 2017. 12(1): p. 98-105. 4. Rougier, M.B., M.N. Delyfer, and J.F. Korobelnik, OCT angiography of acute non-arteritic anterior ischemic optic neuropathy. J Fr Ophtalmol, 2017. 40(2): p. 102-109. 5. Gaier, E.D., et al., Quantitative analysis of optical coherence tomographic angiography (OCT-A) in patients with non-arteritic anterior ischemic optic neuropathy (NAION) corresponds to visual function. PLoS One, 2018. 13(6): p. e0199793. 6. Borrelli, E., et al., Topographic Macular Microvascular Changes and Correlation With Visual Loss in Chronic Leber Hereditary Optic Neuropathy. Am J Ophthalmol, 2018. 192: p. 217-228.

Keywords: Optic neuropathy

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Poster 156
Hyperbaric Therapy for Central Retinal Artery Occlusions

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Introduction:
There is no standard therapy for central retinal artery occlusions (CRAO), but there are many studies indicating hyperbaric oxygen therapy (HBOT) has the potential to improve visual prognosis. Our goal with this study was to analyze data from patients presenting with non-arteritic CRAO to determine whether there was a significant improvement in visual acuity in patients who received HBOT for CRAO versus those who underwent conservative treatment and whether the time to HBOT or number of treatments impact outcomes.

Methods:
Retrospective analysis of patients admitted to our medical center between 2005-2018 clinically diagnosed with CRAO by fundus exam and visual acuity of 20/200 or worse. We compared presenting and follow-up visual acuities in patients who received HBOT with those who did not. Secondary outcomes included time to hyperbaric and number of treatments on visual outcomes in the treatment group.

Results:
A total of 18 patients were in the control group and 21 patient in the hyperbaric oxygen therapy treatment group with similar presenting visual acuities (control group with logmar visual acuity of 2.258, treatment group of 2.205, p-value 0.797). The visual acuity at follow-up was 1.786 logmar in the HBOT group compared with 2.417 logmar in the control group (p-value 0.015) showing statistically significant improvement in visual acuity in those who received HBOT compared with those who had conservative treatment. Regression analysis identified paracentesis as conservative therapy as a potential confounding factor, but excluding these patients from the control group did not significantly change the outcome data. Neither time to hyperbaric therapy, nor the number of treatments were found to have substantial impact on final visual acuity.

Conclusions:
Hyperbaric oxygen therapy may be an effective treatment for non-arteritic central retinal artery occlusion despite time to treatment or number of treatment sessions.

References: None.

Keywords: Vascular disorders, Pupils Retina, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 157
Neuro-ophthalmological and clinical findings in Wolfram syndrome: what is the real mitochondrial role?

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Introduction:
Wolfram syndrome (WS) type 1, characterized by early-onset diabetes mellitus and optic atrophy, is due to mutations in WSF1 gene. A longstanding debate exists on the possible role of mitochondrial dysfunction.

Methods:
We collected genetic, clinical and neuro-ophthalmological data of 13 recessive WS cases. Retinal nerve fiber layer (RNFL) and ganglion cells layer (GCL) thickness, assessed using Optical Coherence Tomography (OCT), were compared with age-matched groups of controls and Dominant Optic Atrophy (DOA) patients. In a subgroup of patients we evaluated lactic acid (LA) after standardized exercise, brain-MRI 1H-spectroscopy (MRS) and muscle 31P-MRS. Three patients underwent muscle biopsy. Mitochondrial respiration and network were evaluated in fibroblast cell lines.

Results:
Median age: 32.9±13.2 years. Visual loss onset: 10±4 years. All but two had diabetes mellitus. Mean visual acuity was 0.20±0.18 with impaired color vision in all. Fundus oculi demonstrated diffuse optic nerve pallor in 10 patients and temporal pallor in 3. Visual fields showed generalized defect in 11 patients, central scotoma in 2. OCT demonstrated diffuse and severe RNFL thinning in both WS and DOA compared to controls ($p<0.001$). RNFL was thinner in all quadrants in WS compared to DOA ($p<0.001$) except for temporal quadrant. GCL thickness was not significantly different. 8/12 patients had abnormal LA after exercise. Brain MRI variably demonstrated cortical/brainstem/cerebellar atrophy and white matter changes. Brain 1H-MRS did not show pathologica accumulation of LA; muscle 31P-MRS was normal. Muscle biopsy showed signs of mitochondrial myopathy in one patient. Fibroblast studies failed to reveal clear respiration defects and mitochondrial network morphology abnormalities.

Conclusions:
The pattern of diffuse optic atrophy in WS differs from classical mitochondrial optic neuropathies in which temporal fibers of the papillomacular bundle are preferentially affected. Except for the increased LA after exercise, our results, including MRS and fibroblast studies, did not clearly support a primary mitochondrial dysfunction in WS.

References: Delprat B, Maurice T, Delettre C. Wolfram syndrome: MAMs' connection? Cell Death Dis, 9(3):364, 2018 Mar 6 Zmyslowska A, Waszczykowska A, Baranska D, et al. Optical coherence tomography and magnetic resonance imaging visual pathway evaluation in Wolfram syndrome. Dev Med Child Neurol, epub Sep 23, 2018 Carelli V, Ross-Cisneros FN, Sadun AA. Mitochondrial dysfunction as a cause of optic neuropathies. Prog Retin Eye Res, 23(1), 53-89, 2004.

Keywords: Genetic Disease, Optic neuropathy, Neuroimaging

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Grant Support: None.

Poster 158
Neurological findings in patients with Leber's Hereditary Optic Neuropathy

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Introduction:
Extra-ocular manifestations in Leber's Hereditary Optic Neuropathy (LHON) are commonly referred to as LHON "Plus" syndrome. Neurologic anomalies, such as dystonia, peripheral neuropathy, myoclonus and myopathy have been reported in LHON and linked to specific mitochondrial mutations. We aimed to describe neurologic findings in a French cohort of patients with LHON mutations.

Methods:
We retrospectively reviewed the files of all patients carrying LHON mutation that were seen in 2 Parisian Neuro-Ophthalmology centers between January 2009 and September 2018. Patients who had neurologic findings were included. The following data were collected: date of diagnosis, neurologic examination, mutation, visual acuity, fundoscopy, OCT, visual field, and brain MRI findings.

Results:
The files of 183 LHON patients were reviewed. Fifteen patients (8.7%), including 10 men, had neurological findings. Seven patients had demyelinating lesions (DML) on brain MRI: 2 patients had Multiple Sclerosis (MS), 1 had spastic paraplegia and 4 patients were asymptomatic. Two patients had dystonia. Each of the remaining 6 patients had one of the following disorders: pseudo-Leigh syndrome, myasthenia, acoustic neurinoma, cerebro-medullar cavernomatosis, peripheral neuropathy, and MERRF syndrome. All patients had optic neuropathy, except for 1 MS patient. The 11778 mutation was identified in 13 patients, 14484 in 1 patient with DML and 8344 in the patient with MERRF. Mean age at onset of vision loss was 35.3 years old. Mean ETDRS score was 26.8.

Conclusions:
We observed a broad spectrum of neurological disorders in our cohort of LHON. The most common findings were demyelination in 7 patients and basal ganglia lesions in 3 patients. It is possible that the anomalies found in one patient were incidental. Myelin-related diseases were more numerous than axonal or neuromuscular junction disorders. Given the prominent prevalence of neurological findings in our cohort, we advocate for performing systematic brain MRI and neurological examination in all patients with LHON.

References: None.

Keywords: Optic neuropathy, Genetic Disease, Neuro-ophth & systyemic disease (eg. MS, MG, thyroid), Demeylinating disease

Financial Disclosures: The authors had no disclosures.

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Poster 159

Retinal vascular geometry and tortuosity changes in patients withLeber hereditary optic neuropathy (LHON)

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Introduction:

LHON is the most common primary mitochondrial DNA disorder. In the subacute stage, fundus examination typically reveals hyperaemic optic discs, telangiectactic microangiopathy, swelling of the retinal nerve fiber layer and tortuosity of the central retinal vessels. The purpose of the study was to describe and quantify retinal vascular geometry (RVG) and tortuosity in different stages of the disease.

Methods:

The study included 24 (34 eyes) LHON patients and 26 (43 eyes) normal controls (Group I). Based on disease duration, LHON patients were categorized into four groups: Group II (carriers); Group III (subacute); Group IV (dynamic) and Group V (chronic). By applying a fully automated retinal vascular analysis algorithm, RVG and tortuosity parameters were quantified and compared between the groups. A total of 1710 bifurcations and 7153 vessels segments were analysed. For comparison, 1148 bifurcations were included. In addition, optical coherence tomography scans of the macular and peripapillary regions were performed in all LHON patients. The findings were correlated with the retinal vessels parameters. Statistical analysis was performed using IBM SPSS Statistics Software (version 25) and Microsoft Excel 2016.

Results:

All RVG parameters, with the exception of branching angle θ1, were significantly different between the study groups. The absolute diameters of the vessels in a vascular bifurcation were significantly wider in all LHON groups compared with normal controls ($p = 0.00025$), with the widest vessels being observed in carriers and dynamic stage. The least percentage of bifurcations with optimal area ratio and the widest bifurcation angles were observed in Group III, followed by Group V. Two out of the three tortuosity parameters analyzed were significantly different between the study groups, with the least tortuous vessels being observed in Group V and the most tortuous vessels in Group I and II.

Conclusions:

RVG and tortuosity changes in LHON are influenced by disease duration and severity.

References: Sadun AA et al. Leber's Hereditary Optic Neuropathy. Curr Treat Options Neurol. 2011;13(1):109-117. Barboni P et al. Natural History of Leber's Hereditary Optic Neuropathy: Longitudinal Analysis of the Retinal Nerve Fiber Layer by Optical Coherence Tomography. Ophthalmology. 2010;117(3):623-627. Carelli V et al. International Consensus Statement on the Clinical and Therapeutic Management of Leber's Hereditary Optic Neuropathy. J Neuroophthalmol. 2017. Habib MS et al. The association between retinal vascular geometry changes and diabetic retinopathy and their role in prediction of progression--an exploratory study. BMC Ophthalmol. 2014;14:89. Al-Diri B et al. An Active Contour Model for Segmenting and Measuring Retinal Vessels. IEEE Trans Med Imaging. 2009;28(9):1488-1497. Al-Diri B et al. Automated analysis of retinal vascular network connectivity. Comput Med Imaging Graph. 2010;34(6):462-470.

Keywords: Genetic Disease, Optic neuropathy, Miscellaneous

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Poster 160
Microcystic Macular Degeneration In Autosomal Optic Neuropathy

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Introduction:
Patients with autosomal optic neuropathy (AON) can develop microcystic macular degeneration (MMD). MMD has been linked to trans-synaptic retrograde degeneration or vitreo-macular traction (VMT). We aimed to investigate the prevalence of MMD and describe their relationships with retinal layers thicknesses and visual function in subjects with AON related to dominant optic atrophy or Wolfram syndrome.

Methods:
We conducted a retrospective cross-sectional study between 2001 and 2018 in subjects with confirmed AON related to OPA1 or WFS1 mutations. Visual acuity, visual field testing and RNFL thickness were collected. OCTs of the macula were reviewed for MMD and segmented for volume analysis of each layer. Structure-function relationships were assessed comparing patients with and without MMD.

Results:
42 patients (34 OPA1, 8 WFS1, 21 women, median age: 40 years, range: 6.5-68) were included. MMD was found in 12/42 (29%) subjects, including 6 WFS1 (75%) and 6 OPA1 (17%). Total retinal volume (TRV) was increased in subjects with MMD, owing to inner nuclear layer (INL, $p<0.001$) and outer plexiform layer (OPL, $p=0.02$) thickening. Subjects with MMD had thinner superior RNFL ($p=0.045$). WFS1 subjects had greater TRV ($p=0.008$), owing to thickened inner plexiform layer ($p=0.001$), INL ($p<0.001$) and OPL ($p<0.001$). Mean central RNFL thickness was significantly decreased in WFS1 patients ($p=0.002$). MMD was significantly associated with WFS1 mutation. On visual field testing, mean deviation was lower in subjects with WFS1 mutation. There was no significant association between vitreo-macular adhesion and the presence of MMD ($p=0.76$). No patients had VMT.

Conclusions:
MMD was more frequent in WFS1 patients. WFS1 mutation was associated with thickened retinal volumes owing to MMD, more severe optic nerve atrophy and worse visual field impairment. MMD could be related to optic atrophy and the mutation involved. Vitreous body may play a less meaningful role in the etiopathogenesis of MMD in AON.

References: None.

Keywords: Genetic Disease, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 161
Long-term experience from an Expanded Access Program with idebenone in pediatric LHON patients

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Introduction:
LHON results in bilateral, severe central vision loss, and is caused by mitochondrial DNA mutations. LHON is typically diagnosed between 15 – 30 years of age, although it can be detected earlier. Idebenone, the only approved treatment for LHON in Europe, has been shown to be efficacious and safe in a large proportion of adult patients, but pediatric data is limited. The Expanded Access Program (EAP, a named patient program under local regulations) provides insights into the potential of idebenone in pediatric LHON.

Methods:
A retrospective medical chart analysis of visual acuity (VA) –expressed as logMAR– and safety data from patients under 12 years of age was performed. Efficacy was determined as a clinically relevant recovery (CRR, an improvement from off-chart to reading 1 line on the ETDRS chart, or an on-chart improvement of 2 lines) or a clinically relevant stabilization (CRS, maintenance of a baseline VA <1.0 logMAR at last visit (LV)).

Results:
5 (3 males, 2 females) of the 111 enrolled patients were below 12 years of age at baseline (BL) with a time since onset of 1.7 months to 5 years. Patients carried one of the following mutations, G3460A (1), T14484C (2), G11778A (1), A14495G (1). The median best VA at BL was 0.94 logMAR (0.16–1.20). After a median treatment duration of 33.6 months (6.8–40), median best VA at LV was 0.08 logMAR (-0.18–1.36). 3 patients achieved a CRR from nadir (and BL) in both eyes, with a magnitude of recovery 2–9 lines at first observation of CRR, which increased to 4 – 12 lines by LV. No new safety signals were observed.

Conclusions:
This study indicates that idebenone was safe and efficacious in pediatric LHON patients. Despite the limited sample size, the efficacy results are consistent with those observed in the adult LHON population of the EAP.

References: None.

Keywords: Optic neuropathy

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Poster 162
Evaluation of visual field metrics in patients with central scotomas from LHON

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Introduction:
Patients with large dense central scotomas may be unable to reliably complete Stimulus size III (Stim III) Humphrey Visual Fields (HVF). These patients, however, do considerably better with Stimulus size V (Stim V) HVF. In Leber's Hereditary Optic Neuropathy (LHON) the reliability of the HVF varies over the course of the disease. The purpose of this study was to determine if Stim III and Stim V mean deviation (MD) calculations are equivalent in patients with central scotomas from LHON.

Methods:
10 patients with LHON were administered Stim III and Stim V HVF tests on the same day during multiple patient visits. Stim III MD values were obtained from the HVF algorithm. Also, separate Stim III and Stim V MD values were obtained from an investigative algorithm (IA). This IA developed by the University of Iowa Visual Field Reading Center was used to derive patients' MD from Stim III and Stim V HVF raw numerical data. The MD values from the HVF and IA were compared using a Pearson's product-moment correlation coefficient.

Results:
Seventy-two (72) observations, 10 patients and 18 eyes were analyzed. Stim III HVF and IA: r^2=0.99, HVF mean MD=-26.1 with standard deviation (STD)=+/-6.72. Mean IA MD=-24.1 with STD=+/-6.30. Mean absolute difference between HVF and IA =1.98 with STD=+/-0.769. IA Stim III MD and Stim V MD: r^2=0.415, Stim V mean MD=-21.2 with STD=+/-5.52. Mean absolute difference between IA Stim III and Stim V MD=1.98 with STD=+/-2.97.

Conclusions:
There was near perfect correlation of Stim III MD between HVF and IA, validating the algorithm. MD values for Stim III and Stim V, however, were not interchangeable. This may reflect the variability that comes from visualizing the smaller stimulus in subjects with a dense central scotoma.

References: Carelli V, d'Adamo P, Valentino ML, et al. Parsing the differences in affected with LHON: genetic versus environmental triggers of disease conversion. Brain. 2016;139:e17. Meyerson C, Van Stavern G, Mcclelland C. Leber hereditary optic neuropathy: current perspectives. Clin Ophthalmol. 2015;9:1165-76. Wall M, Brito CF, Woodward KR, et al. Total deviation probability plots for stimulus size v perimetry: a comparison with size III stimuli. Arch Ophthalmol. 2008;126(4):473-9. Wall M, Doyle CK, Zamba KD, et al. The repeatability of mean defect with size III and size V standard automated perimetry. Invest Ophthalmol Vis Sci. 2013;54(2):1345-51. https://perimetry.ophth.uiowa.edu/ Gardiner SK, Demirel S, Goren D, et al. The Effect of Stimulus Size on the Reliable Stimulus Range of Perimetry. Transl Vis Sci Technol. 2015;4(2):10. O'Brien C, Poinoosawmy D, Wu J, et al. Evaluation of the Humphrey FASTPAC threshold program in glaucoma. Br J Ophthalmol. 1994;78(7):516-9. Schaumberger M, Schäfer B, Lachenmayr BJ. Glaucomatous visual fields. FASTPAC versus full threshold strategy of the Humphrey Field Analyzer. Invest Ophthalmol Vis Sci. 1995;36(7):1390-7.

Keywords: Visual fields, Perimetry, Genetic Disease, Optic neuropathy, Demeylinating disease

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Grant Support: None.

Poster 163
Natural history of Leber's hereditary optic neuropathy (LHON): findings from a large patient cohort

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Introduction:
LHON is a rare mitochondrial disorder resulting in rapid, painless central vision loss in one eye, followed by a similar loss in the second within days to months, leading to severe vision loss. Current knowledge of LHON epidemiology and the nature of spontaneous recovery is based on a small group of studies, in which the definition of visual acuity (VA) outcomes vary. We report natural history data from an international, multicenter LHON medical record survey.

Methods:
Data was collated from available medical records of patients with a genetically confirmed diagnosis of LHON from 11 worldwide centers. No exclusion criteria were applied. Demographic data, mutation status, date of LHON onset in each eye and visual assessment results were compiled for 383 patients. 83 patients provided long term visual acuity data (Outcomes Population).

Results:
95.8% of the study population carried a primary mutation. Male patients were more frequent across primary mutation carriers compared to non-primary carriers (> 70% vs. 58.8%). Age at onset showed a maximum incidence between 15 and 35 years of age across all mutations, but the incidence by age group (< 12 years, 12 to 15 years, 15 to 35 years and > 35 years) showed some differences amongst mutations. At baseline (BL), 66.3% of patients in the Outcomes Population had a VA < 1.0 logMAR, while at Nadir only 4.8% remained in this category, with 63.9% of patients off-chart (> 1.68 logMAR). At last visit, nearly half of all patients were off-chart, a 10-fold increase from BL. 18.1% of patients had a final VA < 1.0 logMAR, 3.7 times fewer than at BL.

Conclusions:
This study provides a new insight into LHON's epidemiology and natural course over time. Overall, the spontaneous evolution during the first 5 years after onset is that of a relevant and profound deterioration of VA.

References: None.

Keywords: Optic neuropathy

Financial Disclosures: Ms Silva is a regular employee of Santhera Pharmaceuticals.

Grant Support: None.

Poster 164
Development of a Novel Gene Therapy Using SIRT1 Signaling for Neuro-protection in Optic Neuropathies

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Introduction:
Pharmacologic activators and genetic overexperession of sirtuin 1 (SIRT1) promote neuroprotective effects in multiple neurodegenerative disease models, including optic neuropathies. AAV2-SIRT1 mediated overexpression in mouse retina partially attenuates experimental optic neuritis despite only a 21% transduction efficiency for retinal ganglion cells (RGCs) using the AAV2-GFP vector for quantification. Viral vectors with increased transduction efficiency are needed.

Methods:
AAV7m8 vectors were designed to contain the putative RGC-specific gamma-synuclein gene (SNCG) promoter and either the cDNA encoding enhanced protein (eGFP) or a codon optimized human SIRT1. Gene expression was optimized in ARPE-19 cells and SIRT1 expression was determined by RT-qPCR. Vectors were delivered by intravitreal injection in 4 week old C57/Bl6 mice and the RGC transduction profile following intravitreal delivery was tested at 4 weeks post injection using immunohistochemistry techniques. The RGCs were identified with Brn3a staining, and were tested for transduction efficiency by co-localization using the 3xFLAG tag on the vectors.

Results:
The AAV7m8 vector expressing human SIRT1 driven by the SNCG promotor demonstrated enhanced expression of SIRT1 similar to its AAV2 predecessor in vitro. However, intravitreal injections using both vector showed a superior AAV transduction profile by the novel AAV7m8 construct. The AAVm8-SIRT1 vector showed >50% transduction efficiency for RGCs compared with only 21% by AAV2-SIRT1, and AAVm8-SIRT1 drives expression almost exclusively in RGCs whereas AAV2-SIRT1 overexpression is enhanced in multiple retinal layers.

Conclusions:
AAV7m8-SIRT1 vector represents a clinically viable, RGC-specific, and efficient vector for delivering SIRT1 in the retina. This represents an encouraging therapy to enhance visual outcomes and RGC preservation in multiple models of optic neuropathy. Additionally, the development of this vector has the potential to be used as a backbone for gene delivery of other novel gene candidates suggested to enhance neuroprotection that can be designed in the future.

References: None.

Keywords: Optic neuropathy, Optic nerve trauma and treatment, Miscellaneous

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Poster 165
Visual outcomes of non-arteritic anterior ischemic optic neuropathy after systemic corticosteroid or observation

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Introduction:
The mechanism of non-arteritic anterior ischemic optic neuropathy (NAION) is not well-known and there have been no proven effective treatments so far. The use of steroids in NAION, one of the investigated methods to improve the visual outcomes, still remains controversial. We evaluated whether the intravenous (IV) methylprednisolone following oral corticosteroids has any beneficial or adverse effect on visual outcomes in NAION.

Methods:
The study examined 24 patients diagnosed as NAION between and July 2018. The diagnosis of NAION was based on the following criteria: (1) sudden visual loss in the absence of other ocular and neurologic diseases that might explain the patient's visual symptoms, (2) optic disc edema, (3) optic disc related visual field defects, and (4) no signs/symptoms suggestive of giant cell arteritis. IV steroid treatment was considered when it was difficult to completely exclude the optic neuritis, or in patients with last eye or progressive severe visual loss. Factors including age, sex, underlying systemic diseases, visual field, and orbit MRI findings and visual acuity (VA) at initial onset, immediately after IV treatment, at month 1, and final visit were compared between two groups: steroid (n=11) and observation (n=13).

Results:
The initial logMAR VA was 0.94 ± 0.80 in the steroid group and 0.51 ± 0.57 in the observation group (p=0.167). In the steroid group, the VA of 4 patients (36%) worsened more than 2 lines immediately after IV treatment. At month 1, the logMAR VA was 1.10 ± 0.98 in the steroid group and 0.44 ± 0.56 in the observation group (p=0.041), and at final visit, 1.25 ± 0.95 in the steroid group and 0.41 ± 1.25 in the observation group (p=0.018).

Conclusions:
Visual outcomes were poorer after steroid treatment compared to those of observation. Systemic corticosteroid should be considered carefully in NAION, since it seems not to be beneficial.

References: None.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

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Poster 166
Does time equal vision in the acute treatment of NMOSD and other antibody-mediated optic neuritis?

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Introduction:
In contrast to MS, in which visual recovery from optic neuritis (ON) is independent of treatment, ON in neuromyelitis optica spectrum disorders (NMOSD) and other forms of antibody-mediated demyelinating disease (AMDD) is steroid dependent. Disability from AMDM-ON accumulates by poor recovery from attacks. Acute ON attacks are treated with high-dose intravenous methylprednisolone (IVMP). We investigated whether the time from symptom onset to IVMP administration affected visual recovery in NMOSD and AMDM-ON.

Methods:
A retrospective study was performed in a consecutive cohort of patients following their first episode of AQP4-IgG and MOG-IgG ON. Best corrected visual acuity (BCVA) in ON eyes at 3 months was correlated with time-to-IVMP (days). In cases of bilateral optic neuritis, only one eye was included for each patient.

Results:
30/37 AMDD patients (28 NMOSD, 9 MOG-IgG- ON) had ON, two of whom refused treatment. Of the 28 patients included in this study, ten presented with ON later than 6 days from symptom onset. The median 3-mo BCVA of patients whose treatment was started later than seven days from symptom onset was 20/100 (IQR20/100-20/200). Patients treated >4 days had an odds ratio (OR) of 8.3 (95%CI 1.47-47.2) of failure to regain 20/20 vision (p=0.01). The OR of patients treated >7 days was 10.0 (95%CI 1.39-71.9) of failure to regain 20/30 vision (p=0.01). ROC analysis revealed that the optimal criterion of delay in IVMP treatment initiation was ≤4 days, with a sensitivity and specificity of 71.4% and 76.9%, respectively.

Conclusions:
The results of this study strengthen prior studies of other forms of ON, showing that even a seven-day delay in IVMP can be detrimental to vision in NMOSD and AMDD-ON. Further study of the effects of timing of IVMP on OCT and visual fields and on subsequent ON attacks in a larger cohort of patients is currently underway.

References: None.

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

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Poster 167
GCC Loss After Acute NAION Is More Rapid Than In Acute Optic Neuritis

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Introduction:
This study compares the rate of ganglion cell complex(GCC) loss as measured by cirrus spectral-domain optical coherence tomography(SD-OCT) in eyes acutely affected by demyelinating versus non arteritic ischemic optic neuropathy(NAION).

Methods:
A total of 10 eyes of 9 patients were included: 6 eyes affected by demyelinating optic neuritis and 4 eyes affected by NAION. All patients had a complete exam including testing with SD-OCT. Recorded variables included age, gender, date, OCT RNFL and GCC In cases where no baseline OCT data was available, measurements from either the fellow eye (if unaffected) or from published normative data were utilized.

Results:
Rate of GCC loss was analyzed between initial presentation(within 2 weeks of symptom onset) to 16 weeks (early follow up) and thereafter to 60 weeks (late follow up). The rate of GCC loss in the acute period in optic neuritis was 3.8 microns/week as compared to 12.5 microns/week in the NAION group (p=0.33).The rate of GCC loss in the chronic period was 0.04 microns/week in the optic neuritis group compared to 0.03 in the NAION group (p=.92).

Conclusions:
The rate of GCC loss in the NAION group was more rapid in the acute period than the optic neuritis group. This stabilizes across both groups in the chronic period. Inclusion of more patients, which would allow for division into different sub groups (i.e. isolated optic neuritis vs MS vs MOG vs NMO optic neuritides) will allow us to further characterize the rate of loss with greater accuracy and greater statistical power and significance. By describing the different rate of GCC loss in different optic neuropathies, we hope this work will help us distinguish between demyelinating and ischemic optic neuropathies in patients who present with an optic neuropathy outside of the window where an MRI would be diagnostically helpful.

References: None.

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

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Poster 168
Peripapillary hyperreflective ovoid mass-like structures (PHOMS) in children

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Introduction:
To analyze structural characteristics and perifoveal/peripapillary vasculature by optical coherence tomography (OCT) in children with peripapillary hyperreflective ovoid mass-like structurres (PHOMS) and compare the results with those of normal subjects.

Methods:
Forty-five patients (eighty-four eyes) under the age of 18 years were evaluated with spectral domain (SD)-OCT and swept course (SS)-OCT. Patients were divided into four groups, according to presence of PHOMS and then the size of the existing PHOMS. Eyes with visible optic disc drusen (ODD) were not included. Foveal avascular zone (FAZ) and vessel densities from macula and optic disc area were assessed and potential associations between vessel density and structural parameters, such as peripapillary retinal nerve fiber layer (pRNFL), and macular ganglion cell and inner plexiform layer (mGCIPL) thickness were analyzed.

Results:
Among forty-five patients (eighty-four eyes), 53.6% had PHOMS, and coexisting buried ODD were found only in eyes with PHOMS. The scleral canal diameter was significantly smaller in PHOMS positive eyes compared to control eyes. Vessel density measurements from the papillary, peripapillary and optic nerve head (ONH) regions in the large PHOMS group were significantly lower compared to the control group (papillary; P=0.014, peripapillary; P=0.001, ONH; P=0.046, respectively). FAZ area and macular vessel densities showed no difference compared to normal eyes in all three PHOMS groups. pRNFL and mGCIPL thickness did not differ among four groups and correlations were also not significant.

Conclusions:
Children with PHOMS have smaller scleral canal and can entail buried ODD. Vessel densities of optic disc area in large PHOMS eyes are significantly lower than in normal eyes.

References: None.

Keywords: Miscellaneous, Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

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Poster 169
The Visual Morbidity of Optic Nerve Head Drusen in Children: A Longitudinal Review

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Introduction:
The ophthalmic complications of optic nerve head drusen (ONHD) in adults have long been documented, but data regarding the degree of visual morbidity from ONHD in children are more limited. We sought to characterize the extent of vision loss and secondary complications associated with ONHD in a large cohort of pediatric patients followed longitudinally.

Methods:
A retrospective chart review of all patients diagnosed with ONHD at a single, tertiary care ophthalmology department from January 1st 2010 until July 1st 2018 was performed. Patients were identified using ICD-9 and ICD 10 CM codes. Inclusion criteria were age ≤18 years of age and formal documentation of ONHD by ultrasonography, fundus autofluorescence, fundus photography (if visible), or computed tomography.

Results:
Of the 465 number of charts reviewed, 213 patients met inclusion criteria (55% female) for a total of 386 eyes with ONHD confirmed by imaging. Mean age at diagnosis was 10.13 ± 4.09 years and mean follow up was 2.76 ±2.91 years. Formal visual fields, either by Goldmann manual perimetry or Humphrey automated perimetry, were available for 208 eyes. Repeatable visual field defects were noted in 24 eyes (11.5%). The most common defect was a nasal step which occurred in 11/24 eyes (45.8%). Of the eyes that developed visual loss, 15 had visual field defects at presentation and the other 9 developed field loss within 1.39±0.55 years from the time of diagnosis. Choroidal neovascular membranes were clinically apparent in 5 eyes and for which treatment was required in 3 eyes. Non-arteritic Ischemic Optic Neuropathy developed in 3 eyes.

Conclusions:
Visual morbidity associated with ONHD in children is common and may develop in a short period of time after initial diagnosis. Further prospective studies are needed to clarify risk factors for visual complications in children.

References: 1.) Duncan JE, Freedman SF, El-Dairi MA, "The Incidence of Neovascular Membranes and Visual Field Defects From Optic Nerve Head Drusen In Children." J AAPOS 2016; 20(1): 44-48. 2.) Noval S, Visa J, Contreras I, "Visual Field Defects Due to Optic Disk Drusen in Children," Graefes Arch Clin Exp Ophthalmol 2013; 251:2445-2450. 3.) Malmqvist L, Li XQ, Eckmann CL et al, "Optic Disc Drusen in Children: The Copenhagen Child Cohort 2000 Eye Study," Journal of Neuro-Ophthalmology 2018; 38(2): 140-146.

Keywords: Optic neuropathy, Visual fields

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Poster 170
Incidence of Optic Disc Drusen in Patients with Papilledema

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Introduction:
Optic disc drusen (ODD) are congenital acellular proteinaceous deposits of the optic nerve head and have a prevalence of 3.7% in adults and 1.0% in the pediatric population. ODD can cause elevation of the optic nerve head, mimicking the appearance of disc edema, and are a common cause of pseudopapilledema, a condition that is not vision threatening. In contrast, papilledema is potentially vision threatening optic disc swelling caused by elevated intracranial pressure. Historically, ODD and papilledema have been viewed as 2 distinct disease processes; however, a higher prevalence of ODD in children with papilledema has been reported. We hypothesize that ODD are non-coincidental sequelae of papilledema. Our aim is to estimate the incidence of ODD in adult and pediatric patients with papilledema.

Methods:
Retrospective case series estimating the incidence of ODD in patients with papilledema using Spectralis ocular coherence tomography (OCT, Heidelberg, Heifelberg, Germany) at presentation and follow-up.

Results:
43 adults (86 eyes; mean age 32 ±9 years) and 11 children (22 eyes; mean age 11 ±6 years) with papilledema were evaluated. A majority (78%) of patients were female. The most common symptoms on presentation were headache (85%, 46/54), decreased vision (74%, 40/54), and pulsatile tinnitus (43%, 23/54). The incidences of ODD on initial visit were 5% (4/86 eyes) in adults and 18% (4/22 eyes) in children. The incidences on follow-up visits were 13% (12/86 eyes) in adults and 18% (4/22 eyes) in children. The severity of papilledema did not correlate with the presence of ODD. There is a fair agreement (kappa=0.26) for detection of ODD between the initial and follow-up visits.

Conclusions:
Patients with papilledema have a higher incidence of ODD compared to the general population, with fair agreement on detection of ODD between initial and follow up visits using the Spectralis OCT.

References: Birnbaum, Johnson, John, Jun, Machan. Increased Prevalence of Optic Disc Drusen After Papilledoedema From Idiopathic Intracranial Hypertension: On the Possible Formation of Optic Disc Dursen, Neuroophthalmology, 40, 171-80, 2016. Chang, Velez, Demer, Bonelli, Quiros, et al. Accuracy of Diagnostic Imaging Modalities for Classifying Pediatric Eyes as Papilledema Versus Pseudopapilledema, Ophthalmology, 124, 1839-48, 2017. Gospe, Bhatti, El-Dairi. Anatomic and visual function outcomes in paediatric idiopathic intracranial hypertension. Br J Ophthalmol, 100, 505-9, 2016. Malmqvist, Bursztyn, Costello, Digre, Fraser, et al. The Optic Disc Drusen Studies Consortium Recommendations for Diagnosis of Optic Disc Drusen Using Optical Coherence Tomography, J Neuroophthalmol, 38, 299-307, 2018.

Keywords: High intracranial pressure/headache, Pseudotumor Cerebri, Neuroimaging

Financial Disclosures: The authors had no disclosures.

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Poster 171

Optic Disc Drusen Associated Anterior Ischemic Optic Neuropathy: Prevalence of Comorbidities and Vascular Risk Factors

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Introduction:
Non-arteritic anterior ischemic optic neuropathy (NA-AION) associated with optic disc drusen (ODD) is termed ODD-AION, where NA-AION with no evidence of ODD is simply termed NA-AION. Patients with ODD-AION have been found to be younger than those with NA-AION but with similar vascular risk factors. The purpose of this study was to examine ODD as an independent risk factor for AION by comparing the prevalence of risk factors and comorbidities in ODD-AION and NA-AION patients.

Methods:
Case-control study of 13 patients with ODD-AION and 14 patients with NA-AION diagnosed in the period 2008 to 2017. All patients underwent an interview designed to evaluate vascular risk factors and comorbidities, and re-examination including Enhanced Depth Imaging Optical Cohererence Tomography to substantiate the diagnosis and to avoid misclassification of patients. Patients were recorded as having ODD-AION when both the clinical diagnosis of NA-AION was obtained and ODD were diagnosed in the same eye.

Results:
No significant difference was found in demographic characteristics between the ODD-AION and the NA-AION group. Significantly less patients in the ODD-AION group were diagnosed with arterial hypertension (P=0.02) and dyslipidaemia (P=0.05) than in the NA-AION group. Significantly more ODD-AION patients than NA-AION patients had none of the vascular risk factors (smoking, arterial hypertension, diabetes mellitus and dyslipidaemia).

Conclusions:
In contrast to previous findings, our study suggests that vascular risk factors are more prevalent in NA-AION than in ODD-AION patients indicating ODD as an independent risk factor for AION and not just a coincidental coexistence.

References: None.

Keywords: Optic neuropathy, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

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Poster 172
Prevalence and histopathological signatures of optic disc drusen based on microscopy of 1713 enucleated eyes

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Introduction:
Optic disc drusen (ODD) are calcified optic nerve head deposits. Objectives of this study were to examine the prevalence of ODD in eyes removed by enucleation during a 36-year period and to describe related histopathologic signatures of ODD and surrounding tissues.

Methods:
The study was a retrospective observational case series study assessing and re-evaluating enucleated eyes in Denmark from 1980-2015 by microscopy. Optic nerve heads with ODD were assessed for presence of elevated discs and edematous axons. Individual ODD were described based on size, number and location (superficial and/or deep) within the optic nerve. The optic nerve head was assessed for presence of localized peripapillary axonal distension (LPAD) equivalent to the peripapillary hyperreflective ovoid mass-like structures (PHOMS) seen on optical coherence tomography (OCT).

Results:
Microscopy of 1713 eyes revealed ODD in 31 eyes equivalent to a prevalence of 1.8%. No statistically significant difference was found when comparing age, gender and diagnosis in patients with ODD versus patients without ODD. ODD were seen as circular shapes of different sizes and varying number. All ODD were found anterior to lamina cribosa. Elevated discs were present in 15 (54%) of the cases. Thickening of the superficial retinal nerve fiber layer was present in eyes with large deeply located ODD. For more superficial ODD of approximately same size, the retinal nerve fiber layer was considered thinner. Edematous axons were present in 3 eyes. LPAD was seen in 5 eyes.

Conclusions:
Prevalence of ODD in this study of histopathologic signatures was found higher compared to the prevalence found in clinical studies indicating the difficulties of clinical ODD detection. In line with recent studies using OCT our results suggest that large, buried ODD cause crowding and herniation of axons in the optic nerve head leading to a thickened superficial nerve fiber layer, pseudopapilledema and LPAD.

References: None.

Keywords: Optic neuropathy, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 173
The Angioarchitecture of the Optic Nerve Head in Patients with Optic Disc Drusen

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Introduction:
Introduction: The pathophysiology behind optic disc drusen (ODD) is perceived to be an abnormal prelaminary axonal metabolism leading to axonal damage and calcium deposition. Inherited dysplasia of the optic disc and its blood supply has been proposed to play a part in ODD pathology and vascular complications. The aim of this study was to analyze the difference in angioarchitecture of the optic disc between a group of ODD individuals and controls.

Methods:
Methods: Case-control study including 30 controls and 50 ODD individuals. Computer-based fundus analysis and a standardized grid dividing the optic disc into 6 zones and marking the percentage distance from the center was used to investigate the angioarchitecture of the disc. This included pointing out the central retinal artery (CRA) emergement, first branching point, number of bi- and trifurcations of the CRA and central retinal vein (CRV), and prevalence of cilioretinal arteries.

Results:
Results: The CRA emergement was significantly closer to the center of the optic disc for the ODD group compared to the controls ($p<0.001$). The point of the first CRA branching was significantly closer to the center ($p=0.009$) and there was a significant higher number of CRA bifurcations ($p=0.03$) for the ODD group compared to the controls. There was no significant difference in number of bifurcations ($p=0.67$) or the first branching point ($p=0.76$) for the CRV. The point of CRA emergement was mainly within the nasal zone for both the ODD group (77%) and controls (42%). 4 cilioretinal arteries were found in the ODD group and 1 in the control group.

Conclusions:
Conclusion: The distinctive angioarchitecture of the optic disc in ODD individuals found in this study points towards a structural dysfunction in the vascular network either caused by ODD or seen as a component of ODD development.

References: None.

Keywords: Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Optic neuropathy, Vascular disorders

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Poster 174
A serial study of retrograde trans-synaptic degeneration following post-geniculate injury

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Introduction:
Retrograde trans-synaptic degeneration (RTSD) of the retinal nerve fiber layer (RNFL) and the retinal ganglion cell layer (GCL) following post-geniculate injury in adult humans has recently been demonstrated using optical coherence tomography (OCT).The time course of RNFL degeneration has been elucidated; however, GCL thinning has been shown to be more sensitive in detecting RTSD. Here, we examine the time course of RTSD using serial OCT.

Methods:
Charts from 2010-2018 of patients with homonymous hemianopsia were retrospectively reviewed. After excluding patients with pregeniculate disease, 71 remained. A normalized asymmetry score (NAS) was calculated for each eye, with a positive NAS indicating GCL thinning ipsilateral to the post-geniculate injury, and 47 were found to have +NAS OU, indicating RTSD. Of these, 19 had serial OCT measurements. NAS values for each eye in this group were compared over time.

Results:
Fifty-one measurements from 19 patients were analyzed using univariable linear regression for each patient, with elapsed time from cortical damage as the explanatory variable and the mean NAS as the outcome variable. Follow up between injury and final OCT ranged 12-200 months. 17/19 of the cases had a positive slope, indicating progressive GCL thinning over time. The results were analyzed for two groups: those with elapsed time from cortical damage <30 months (n=11) and >30 months (n=8). The average slope was 0.1068 in the shorter latency group and 0.0019 in the longer latency group. The mean slope of the first group was significantly different from zero (p=0.03), whereas the mean slope of the latter group was not significantly different than zero (p=0.66).

Conclusions:
A positive relationship between GCL thinning and elapsed time since cortical damage is demonstrated in this study. However, decreasing slope amplitude as time from injury increases shows that RTSD of the GCL stabilizes after the first 2-3 years.

References: 1. Jindahra P, Petrie A, Plant GT. Retrograde trans-synaptic retinal ganglion cell loss identified by optical coherence tomography. Brain. 2009;132(Pt 3):628-634. 2. Mitchell JR, Oliveira C, Tsiouris AJ, Dinkin MJ. Corresponding Ganglion Cell Atrophy in Patients with Postgeniculate Homonymous Visual Field Loss. J Neuroophthalmol. 2015;35(4):353-9. 3. Jindahra P, Petrie A, Plant GT. The time course of retrograde trans-synaptic degeneration following occipital lobe damage in humans. Brain. 2012;135(Pt 2):534-41. 4. Herro AM, Lam BL. Retrograde degeneration of retinal ganglion cells in homonymous hemianopsia. Clin Ophthalmol. 2015;9:1057-1064.

Keywords: Visual fields, Optic neuropathy

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Grant Support: None.

Poster 175
Optic nerve cupping in patients with retrograde trans-synaptic degeneration

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Introduction:
Retrograde trans-synaptic degeneration (RTSD) refers to the atrophy of retinal ganglion cell layer (GCL) and retinal nerve fiber layer (RNFL) following injury to corresponding post-geniculate neurons. RTSD in adults has recently been demonstrated using optical coherence tomography (OCT), but corresponding morphological changes in the optic disc have not yet been demonstrated. Optic disc cupping has been associated with periventricular leukomalacia in children and attributed to RTSD. We investigated the amplitude of RTSD in relation to latency since post-geniculate injury, and assessed cup size in patients with adult-onset RTSD.

Methods:
Charts from 2010-2018 of patients with homonymous defects were reviewed. 149/451 had undergone OCT. After excluding patients with pregeniculate disease, including glaucoma, 71 remained. Latency from time of post-geniculate injury was determined. OCTs were reviewed to obtain cup-to-disc ratios (CDR). A normalized asymmetry score (NAS) was calculated for each eye, with a positive NAS indicating GCL thinning on the side of the retina ipsilateral to the injury. Patients with bilateral positive NAS in the direction of the homonymous defect were considered to exhibit RTSD. OCTs were obtained in 42 controls within the same age range.

Results:
47/71 (66%) subjects demonstrated bilateral GCL thinning versus 10/42 controls ($p<0.0001$). The amplitude of GCL thinning was significantly greater in cases compared to controls (Mean NAS=0.15 vs. 0.03 OD; 0.13 vs. 0.04 OS; $p<0.0001$ OU). The 47 subjects determined to have RTSD had a significantly greater CDR than controls (OD: 0.49 vs. 0.42, $p=0.03$; OS: 0.49 vs 0.40, $p=0.014$). GCL thinning correlated with latency from time of injury ($r=0.42$, $p<0.0001$ OD; $r=0.49$, $p<0.0001$ OS).

Conclusions:
The positive correlation between RTSD and latency following post-geniculate injury reaffirms that RTSD is a slow, progressive process. Increased CDR in cases compared to controls suggests a structural correlate to RTSD that is potentially observable on fundoscopy.

References: 1. Jindahra P, Petrie A, Plant GT. Retrograde trans-synaptic retinal ganglion cell loss identified by optical coherence tomography. Brain. 2009 Mar;132(Pt 3):628-34 2. Mitchell JR, Oliveira C, Tsiouris AJ, Dinkin MJ. Corresponding Ganglion Cell Atrophy in Patients with Postgeniculate Homonymous Visual Field Loss. J Neuroophthalmol. 2015;35(4):353-9. 3. Jacobson L, Hellstrom A, Flodmark O. Large cups in normal-sized optic discs: a variant of optic nerve hypoplasia in children with periventricular leukomalacia. Arch Ophthalmol. 1997;115:1263–1269 4. Longmuir SQ, Brodsky MC. Postnatal optic disc cupping in a non-glaucomatous infant with periventricular leukomalacia: nosologic implications. Br J Ophthalmol 2012; 96: 606–607.

Keywords: Visual fields, Optic neuropathy

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Grant Support: None.

Poster 176
Evaluating Clinical and Demographic Differences Among Patients with Idiopathic Intracranial Hypertension (IIH)

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Introduction:
The clinical presentation of IIH patients varies greatly, and it is impossible to predict the severity of papilledema based on initial symptoms. We aimed to compare the characteristics of patients with mild (Frisén grade 1-2) papilledema with that of patients with severe (Frisén, 4-5) papilledema.

Methods:
Retrospective review of systematically collected demographic and clinical data in 297 consecutive IIH patients with fundus photographs taken before or within 30 days of lumbar puncture, evaluated at one institution over 28 years. Fundus photographs were independently reviewed by 3 neuro-ophthalmologists for Frisén grade, and by another neuro-ophthalmologist if less than 2 reviewers agreed on the Frisén grade for each eye. Patients were classified into mild (Frisén, 1-2) and severe (Frisén, 4-5) papilledema groups, based on fundus appearance in the worst eye. Grade 3 papilledema or atrophy were excluded. Age, sex, BMI, race, and CSF-opening pressure (CSF-OP) were collected. Analysis of continuous variables were made with a t test and categorical variables with a chi square.

Results:
Median patients' age was similar in both groups (31.53 vs 31.02, p=0.71). Black race was similar in both groups (71/152 (47%) versus 48/87 (55%), p=0.36). Male gender was similar in both groups (12/152 (8%) versus 6/87(7%), p=0.77). Average BMI was similar in both groups (38.64 versus 37.24, p=0.31). Mean CSF-OP was lower in the mild papilledema group (33.69cm H2O) compared with the severe papilledema group (41.89cm H2O), (p<0.0001).

Conclusions:
Patients with mild papilledema had significantly lower CSF-OP compared with patients with severe papilledema. This finding is consistent with data from the IIHTT that confirmed the strong relationship between CSF-OP and Frisén grade. However, age, race, sex, and BMI were similar in patients with mild and severe papilledema, reinforcing the need to take CSF-OP and severity of papilledema at presentation into consideration when trying to predict visual outcome of IIH patients.

References: 1. Fischer WS, Wall M, Mcdermott MP, Kupersmith MJ, Feldon SE. Photographic Reading Center of the Idiopathic Intracranial Hypertension Treatment Trial (IIHTT): Methods and Baseline Results. Invest Ophthalmol Vis Sci. 2015; 56(5): 3292-303.

Keywords: Pseudotumor Cerebri, High intracranial pressure/headache

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Poster 177
Top ten research priorities for Idiopathic Intracranial Hypertension (IIH)

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Introduction:
Idiopathic Intracranial Hypertension (IIH) is under-researched. Patient engagement and patient voice are regarded as central to both the research agenda and funding. The aim was to determine the top 10 research priorities for IIH.

Methods:
The James Lind Alliance (JLA) Priority Setting Partnership (PSP) is a validated process for determining the top priorities in any disease area[1]. This IIH JLA PSP was commissioned by IIH UK, a charity. A modified nominal group technique was used to engage participants who had experience of IIH including: people with IIH, carers, family and friends, and healthcare professionals. Two rounds of surveys were used to identify unique research questions unanswered by current evidence. Key partner organisations included the Association of British Neurologists; the British Association for the Study of Headache; the British and Irish Orthoptic Society; Fight for Sight; The Royal College of Ophthalmologists; The Society of British Neurological Surgeons CSF group; Shine; Neurological Alliance and the United Kingdom Neuro-Ophthalmology Special Interest Group. The most popular 26 uncertainties were presented to stakeholders who then agreed the top 10 topics.

Results:
The top 10 research priorities for IIH included aetiology of IIH; the pathological mechanisms of headache in IIH; new treatments in IIH; the difference between acute and gradual visual loss; the best ways to monitor visual function; biomarkers of the disease; hormonal causes of IIH; drug therapies for treatment of headache; weight loss and its role in IIH; and finally, the best intervention to treat IIH and when should surgery be performed.

Conclusions:
This priority setting encouraged people with direct experience of IIH to collectively identify critical gaps in the existing evidence. The overarching research aspiration was to understand the aetiology and management of IIH. This patient centred research determines the top 10 aspirations for future research in this disease.

References: 1. Cowan, K. and S. Oliver, The James Lind Alliance Guidebook. 2016: http://www.jla.nihr.ac.uk/jla-guidebook/.

Keywords: Pseudotumor Cerebri

Financial Disclosures: The authors had no disclosures.

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Poster 178
Neuro-Ophthalmologic Evaluation of Patients with Spontaneous Cerebrospinal Fluid (CSF) Leaks

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Introduction:
The association between spontaneous skull base CSF leaks and idiopathic intracranial hypertension (IIH) has been suggested. We present the demographics and ocular fundus findings of spontaneous CSF leaks patients.

Methods:
Systematic neuro-ophthalmologic prospective evaluation of demographics and fundus findings of spontaneous CSF leak patients referred by Otolaryngology and Neurosurgery at our tertiary-care institution.

Results:
Of 55 CSF leak patients [age:52±12; 93% women; 51% black; BMI:37.7±10.9], 4 had definite pre-existing IIH, 4 had questionable IIH, and 47 had no history of IIH. Presenting symptoms were rhinorrhea (43, 78%), otorrhea (19, 35%). CSF leaks commonly originated from the ethmoid (24, 44%) and temporal bones (19, 35%). Of the 51 CSF leak patients who had surgical leak repair, 24 (including the 4 IIH patients) had fundus examination pre- and post-operatively. Pre-operative fundus examination (median [IQR]: 27 days [16-39] prior to repair) was: normal in 18/24 patients; active papilledema in 2/24; signs suggestive of previous papilledema in 2/24; optic disc pallor in 2/24. None of the 4 patients with known IIH had active papilledema. Median [IQR] post-repair follow-up was 15 months [8-27]. Post-repair fundus was unchanged in 23 patients; 1 patient developed papilledema (no prior history of IIH). RNFL-OCT remained unchanged following repair (OD:+0.3mm; OS:-1.2mm; p>0.05). 20 patients had post-operative fundus examinations only (median [IQR] follow-up: 18 months [10-44]), and 18 (90%) had normal fundus examinations. Assuming those 18 patients had normal fundus examinations preoperatively, papilledema prevalence prior to repair estimates at 2/42 (4.8%,CI95%:[0.6-16.2]) and rate of new-onset papilledema following repair at 1/36 (2.7%,CI95%:[0.1-14.5]).

Conclusions:
Striking demographic overlap exists between IIH patients and those with spontaneous CSF leaks (obese women). Papilledema prior to surgical repair is uncommon, suggesting that CSF leaks may act as “pressure release valves” for elevated ICP. However, the rate of new-onset papilledema following repair is low, although longer follow-up might reveal delayed papilledema.

References: Clark D, Bullock P, Hui T, Firth J. Benign intracranial hypertension: a cause of CSF rhinorrhoea. J Neurol Neurosurg Psychiatry 1994; 57: 847–849. Bidot S, Levy JM, Saindane AM, Oyesiku NM, Newman NJ, Biousse V. Do most patients with spontaneous cerebrospinal fluid leak have idiopathic intracranial hypertension? J Neuroophthalmol. 2018. (In Press)

Keywords: Pseudotumor Cerebri, High intracranial pressure/headache

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Poster 179
The Neuro-Ophthalmologist's Role after a CSF Leak

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Introduction:
Cerebrospinal fluid (CSF) leak has recently been linked with idiopathic intracranial hypertension (IIH). Neuro-ophthalmic manifestations after repairing CSF leak in patients with IIH have not been adequately explored and most of the evidence comes from the otolaryngology and neurosurgery literature. The primary objective of this study was to explore the neuro-ophthalmologic manifestations in patients who underwent surgical CSF leak repair.

Methods:
This was a retrospective review of individuals diagnosed with spontaneous CSF leak. Data regarding patient's age, sex, ethnicity, CSF leak site, duration of CSF leak, symptoms, ophthalmic examination including visual acuity, and CSF opening pressure on lumbar puncture were all collected pre- and post-operatively whenever possible. Due to a large variation in data documented in patients' charts, this information was analyzed qualitatively.

Results:
Thirty-three patients with spontaneous CSF leaks were identified. Average age at symptom onset was 50 years old. Most patients (84.8%) were female, and the average BMI was 39.3. Most patients (56%) were African American. Defects were found most commonly in the ethmoid sinus on radiography. Rhinorrhea was the most common presenting complaint. Most patients were not referred to neuro-ophthalmology for follow-up. Eye exams were not standardized in those who did have neuro-ophthalmology follow-up. Eye exams were within normal limits, with the exception of 2 patients who showed both pre- and post-operative Frisen grade 1 papilledema. Three patients had CSF opening pressures measured pre-operatively, and two different patients had CSF opening pressures measured post-operatively, with post-operative LPs showing higher opening pressures.

Conclusions:
This retrospective review of patient medical records shows a need for further studies to characterize the neuro-ophthalmic changes that may occur in patients after repair of a CSF leak as well as standardization and coordination of care. This is especially true of patients with symptoms concerning for IIH and of patients with multiple recurrences after leak repairs.

References: None.

Keywords: High intracranial pressure/headache, Pseudotumor Cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 180
Filling the Gap: CSF Fistula as a Presentation of Intracranial Hypertension

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Introduction:
Intracranial hypertension as a cause of skull base defects is well-known in the ENT and neurosurgery literature and nearly absent from the neurology literature. CSF fistula and encephaloceles have been associated with obesity, sleep apnea and elevated intracranial pressure but tend to present in their 4th or 5th decade. Idiopathic intracranial hypertension also is associated with obesity, sleep apnea but patients tend to present in the 2nd or 3rd decade.

Methods:
15 patients with CSF leak or symptomatic encephalocele were identified. A retrospective chart review was performed to record opening pressure on spinal puncture and evaluate for findings consistent with chronic intracranial hypertension on MRI.

Results:
The patient population is similar to previously described cohorts of patients, and include women of average age of 53.5 years (range 32-78 years). They all had BMIs in the overweight or obese categories with an average of 39.3 (range 22-44.3). Only one patient had papilledema at presentation. Only 3 of 15 patients had a history of migraine headaches. Opening pressures averaged 27cm H2O (range of 12 to 45cm H2O). All patients had one or more findings consistent with increased intracranial pressure on MRI. 93% of patients had partial or empty sella on MRI, 67% had multiple encephaloceles. Venous sinus abnormalities were frequently seen in our cohort.

Conclusions:
Our cohort of patients is consistent with previously described cohorts of encephalocele patients in the ENT literature. We hypothesize that these patients may have transient elevations in ICP that are difficult to capture in vivo. Continued collaboration with our ENT program as well as comparison with an IIH cohort to evaluate for differences in the population is planned.

References: None.

Keywords: High intracranial pressure/headache, Neuroimaging

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Grant Support: None.

Poster 181

Superonasal Transconjunctival Optic Nerve Sheath Decompression(stOND): A Simplified Technique for Safe and Efficient Decompression

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Introduction:
Severe, permanent vision loss is a feared sequela of untreated or refractory idiopathic intracranial hypertension (IIH). For patients with progressive vision loss despite maximally tolerated medical treatment, optic nerve sheath decompression remains a viable option to protect vision. In this study, we introduce a modified transconjunctival technique and report on our outcome data, representing one of the largest case series for ONSF of any approach.

Methods:
A retrospective chart review of consecutive patients with IIH by modified dandy criteria who underwent superonasal transconjunctival optic nerve sheath decompression (stOND) between January 2013 and February 2017. Primary outcome measures were best corrected visual acuity (BCVA), post-operative diplopia and operative time. Secondary outcome measures were visual field mean deviation and grading of papilledema by the modified Frisen scale.

Results:
122 eyes of 66 patients were identified; 58 females (88%) and 8 males (12%). The mean age was 30 years (range 18-55). Average lumbar puncture opening pressure was 38 cm H2O. Participants mean body mass index (BMI) was 36 (range 20-59) with an average of grade 3 papilledema. There were no operative complications, post-operative diplopia or eyes with worse visual acuity at 1 week after surgery. The average operative time was 50 minutes (range; 25-89 minutes). The mean decrease in papilledema grading was 2.5 grades (P-value < 0.0001). Snellen visual acuity changes did not meet statistical significance. The overall average HVF mean deviation change was +1.91 (P-value 0.0056). Despite successful bilateral decompressions, 4 patients (6.1%) progressed in their visual loss.

Conclusions:
The stOND technique is a safe, efficient and effective surgical treatment for patients with deteriorating visual function due to IIH. This modified technique safely halts progression of vision loss due to refractory IIH while reducing complications, post-operative diplopia and operative time relative to procedures which involve disinsertion of the medial rectus.

References: Lai, Danesh-Meyer, Kaye, Visual outcomes and headache following interventions for idiopathic intracranial hypertension, J Clin Neurosci, 21(10), 1670-8, 2014 Banta, Farris, Pseudotumor cerebri and optic nerve sheath decompression, Ophthalmology, 107, 1907–1912, 2000 Agarwal, Yoo, Optic neve sheath fenestration for vision preservation in idiopathic intracranial hypertension, Neurosurg Focus, 23, E7, 2007 Nithyanandam, Manayath, Battu, Optic nerve sheath decompression for visual loss in intracranial hypertension: report from a tertiary care center in South India, Indian J Ophthalmol, 56(2), 115-20, 2008 Moreau, Lao, Farris. Optic nerve sheath decompression: a surgical technique with minimal operative complications, J Neuroophthalmol, 34(1), 34-8, 2014 Vaidya, Mahmoud, Buzzacco, Katz, Visual outcomes following optic nerve sheath fenestration via the medial transconjunctival approach, Orbit, 35(5), 271-7, 2016.

Keywords: Pseudotumor Cerebri, High intracranial pressure/headache, Orbit

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Poster 182
Reported vs. actual height and weight among IIH patients

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Introduction:
Idiopathic intracranial hypertension (IIH) primarily affects overweight/obese women. In IIH, obesity is associated with poorer visual outcomes [1] and weight gain can precipitate disease and increase risk of recurrence [2]. Conversely, weight loss can decrease ICP and be an effective IIH treatment [2]. Therefore, accurate height and weight monitoring is important to guide IIH management. Our goal was to compare measured to self-reported BMI among IIH patients vs. non-IIH controls to determine whether weight perceptions differ between the groups and evaluate the need to directly measure height and weight of IIH patients.

Methods:
Retrospective chart review of patients seen in Neuro-Ophthalmology between January 1, 2018 and September 10, 2018 with documented self-reported and measured weight and height. We included IIH patients 18 and over. Patients with IIH were compared to non-IIH patients and matched according to age (+/- 5 years), BMI (+/- 5 kg/m2 unless > 40 kg/m2), gender, and race.

Results:
We included 75 IIH patients (median age: 37, IQR: 30-46; median BMI: 36, IQR: 30-41) and 75 matched controls (median age 39, IQR: 31-47; median BMI: 34, IQR: 29-41). In each group, 39 (52%) were of black race and 71 (95%) were women. The median difference between cases' reported and actual BMI was -0.85 (IQR: -1.79 to -0.25; range: -5.2 to 2.7) and for controls was -0.69 (IQR: -1.66 to -0.03; range: -6.6 to 2.2). Comparing differences between cases to their matched controls, the mean difference was -0.16 kg/m2 (95%CI: -0.68-0.36; p=0.53).

Conclusions:
Both IIH cases and matched controls tended to underestimate their actual BMI by a similar amount; thus, there is no evidence that IIH patients have a different perception of their weight than non-IIH controls. However, the tendency to underestimate weight suggests that its actual measurement remains clinically important.

References: [1] Szewka, AJ; Bruce, BB; Newman, NJ; Biousse, V; Idiopathic intracranial hypertension: relation between obesity and visual outcomes. Journal of Neuroophthalmology, 33 (1): 4-8; 2013 [2] Subramaniam, S; Fletcher, W; Obesity and Weight Loss in Idiopathic Intracranial Hypertension: A Narrative Review. Journal of Neuro-Ophthalmology 37: 197-205; 2017 [3] Maukonen, M; Mannisto, S; Tolonen, H; A comparison of measured versus self-reported antropometric for assessing obesity in adults: a literature review. Scandanavian Journal of Public Health, 46: 565-579; 2018 [4] Mora, T and Gil, J; The determinants of misreporting weight and height: The role of social norms. Economics and Human Biology, 9: 78-91; 2011 [5] Danubio, M; Miranda, G; Vinciquerra, M; Rufo, F; Comparison of self-reported and measured height and weight: Implications for obesity research among young adults. Economics and Human Biology, 6:181-190; 2008.

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

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Poster 183
Use of En Face OCT to Monitor Papilledema in IIH

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Introduction:
En face Optical Coherence Tomography (OCT) uses the data acquired during OCT of the peripapillary retinal nerve fiber layer (ppRNFL) thickness scan to generate a coronal composite fundus image rather than a cross sectional image. This study aims to assess the reliability and validity of en face OCT for monitoring papilledema.

Methods:
Five Cirrus ppRNFL OCT scans from both eyes of 2 patients with papilledema due to idiopathic intracranial hypertension acquired longitudinally over a period of 6-8 months were reviewed retrospectively (20 scans total). Diameter of optic disc edema in both horizontal and vertical dimensions was measured using calipers from Cirrus software and compared with ppRNFL thickness. 4 fellowship-trained neuro-ophthalmologists were asked to rank qualitatively en face images in order from least area of optic disc edema to greatest, while masked from all other clinical data. Rankings were compared with ppRNFL thickness as a gold standard.

Results:
Pearson rank coefficient for horizontal, vertical, and average diameter and estimated area of edema compared with ppRNFL thicknesses were 0.86, 0.87, 0.88, and 0.93, respectively. Compared with ranking by OCT average ppRNFL thickness, participants had a mean Pearson rank coefficient of 0.959 (+/-0.003), 0.80 (+/-0.07), 0.072 (+/-0.06), 0.72 (+/-0.06), and 0.77 (+/-0.03) by average RNFL thickness, horizontal diameter, vertical diameter, average diameter, and estimated edema area, respectively. Participants were able to identify correctly an increase in average ppRNFL thickness >10 microns with a mean accuracy of 91% (+/- 7%). The mean difference of the largest average ppRNFL thickness corresponding to a ranking error was 6 (+/- 6) microns.

Conclusions:
Multiple parameters of en face OCT of optic disc edema have excellent correlation with average ppRNFL thickness and can be used reliably to monitor papilledema. Future research will involve automated measurements, larger cross-sectional data from a validated sample, more participants, and comparison with color photos.

References: 1. Colin J. Scott, MD; Randy H. Kardon, MD, PhD; Andrew G. Lee, MD; et alLars Frisén, MD, PhD; Michael Wall, MD. Diagnosis and Grading of Papilledema in Patients With Raised Intracranial Pressure Using Optical Coherence Tomography vs Clinical Expert Assessment Using a Clinical Staging Scale. Arch Ophthalmol. 2010;128(6):705-711. doi:10.1001/archophthalmol.2010.94 2. Sheils CR1, Fischer WS1, Hollar RA1, Blanchard LM1, Feldon SE2; NORDIC Idiopathic Intracranial Hypertension Study Group1. The Relationship Between Optic Disc Volume, Area, And Frisén Score In Patients With Idiopathic Intracranial Hypertension. Am J Ophthalmol. 2018 Aug 3. pii: S0002-9394(18)30425-2. doi: 10.1016/j.ajo.2018.07.032.

Keywords: Pseudotumor Cerebri, High intracranial pressure/headache, Optic neuropathy, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

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Poster 184

Quantification of Optic Nerve Head Venous Tortuosity in Idiopathic Intracranial Hypertension Using Optos Imaging

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Introduction:
Idiopathic intracranial hypertension (IIH) is a challenging disorder with increasing incidence due to the rising burden of obesity. Despite the clinical findings and testing modalities available to diagnose and follow nerve swelling, few findings can sensitively indicate the trajectory of these patients. This, in part, is due to the fact that there can be marked delay between normalization of ICP levels and resolution of RNFL swelling, as detected by clinical exam or optical coherence tomography (OCT). Tortuosity of the retinal veins has been shown to increase in papilledema and subsequently decrease within 1 hour of ICP lowering (1).

Methods:
This study followed a patient with a new diagnosis of IIH to assess venous tortuosity measured on optos imaging at presentation, and monthly for 6 months after optic nerve sheath fenestration. Baseline measurements were compared to measurements at each follow up examination. Trajectory of these measurements were corroborated with other metrics including Frisen grade, RNFL thickness on OCT, and visual field mean deviation in order to assess which measurements were able to show reduction in nerve swelling the earliest.

Results:
The patient was a 32 year old male. His right eye preoperatively showed a venous tortuosity index (VTI) of 0.32 preoperatively which decreased to 0.21 at 1 month post operatively. His left eye showed a VTI of 0.37 preoperatively which decreased to 0.26 at 1 month postoperatively. These findings were statistically significant ($p<0.05$). His Frisen grade, mean deviation, and OCT RNFL did not show a significant improvement in either eye until post operative month 3.

Conclusions:
Optic nerve head venous tortuosity, as measured by Optos fundus photography can reflect changing ICP in response to treatment earlier than clinical examination, RNFL thickness on OCT and visual fields. This may allow us to more accurately guide our treatment of these patients with medical and surgical options.

References: Moss HE, Vangipuram G, Shirazi Z, Shahidi M. Retinal Vessel Diameters Change Within 1 Hour of Intracranial Pressure Lowering. Trans Vis Sci Tech. 2018;7(2):6.

Keywords: Pseudotumor Cerebri, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Visual fields

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Grant Support: None.

Poster 185
Outcome of patients treated for Intractable Raised Intracranial Hypertension following Cerebral Venous Stenting

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Introduction:
Pseudotumor Cerebri, at times, can be extremely difficult to treat. When patients tolerate, or do not tolerate, maximal medical therapy and are left with headeache, tinnitus, chronic papilledema and progressive visual field loss, stenting is now considered as a new treatment option. We will discuss the very positive 5 year outcome from our Interventional Neurovascular University Center.

Methods:
A prospective collection of data was studied by one Neuro-ophthalmologist at our institution over a 5 year period. Informed consent was obtained from all patients studied.

Results:
A favorable outcome was found in over 90% of patients studied. Reduction in Acetalzolamide dose was almost immediate within the post operative period. Reduction in headache pain scale and frequency, whooshing tinnitus and level malaise were reported in most patients within a few weeks post stenting. Quality of life improvement was reported in >90% of patients. Complication rate was low , and mainly consisted of scalp discomfort in the surgical incision area.

Conclusions:
Cerebral Venous Stenting is a good viable new option in patients suffering from Intractable Raised Intracranial Hypertension. This approach is easier on patients with what appears to be a much lower failure rate long term, compared to patients who undergo ventricular-peritoneal or lumbo-peritoneal shunting. This new approach is still in it's infancy, and results will likely vary considerably depending on the different institutions comfort and learning curve regarding the procedure.

References: 1. Dinkin M, Patsalides A, Venous sinus stenting in Idiopathic Intracranial Hypertension: results of a prospective trial, Neuroophthalmol 2017;37:114-121 2. Friedman D, Liu G, Digre K, Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children, Neurology 2013;81:1159-1165 3. Wall M, Kupersmith M, Thurtell E, Moss H, et al- NORDIC study group, The longitudinal idiopathic intracranial hypertension trial: Outcomes from months 6-12, Am J Ophthalmol 2017;176:102-107.

Keywords: Pseudotumor Cerebri, High intracranial pressure/headache, Interventional neuroradiology

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Poster 186
Venous sinus stenting: a therapeutic alternative for refractory idiopathic intracranial hypertension

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Introduction:
Idiopathic intracranial hypertension (IIH) is a disease of elevated intracranial pressure (ICP) characterized by optic disc edema, visual loss and positional headache (1). Treatment strategies to prevent catastrophic visual loss include carbonic anhydrase inhibition and weight loss but selected patients require surgical intervention including cerebrospinal fluid diversion or optic nerve sheath fenestration. Transverse venous sinus stenosis is a potential pathophysiological mechanism leading transverse venous sinus stenting to be proposed as an alternative procedure to reduce ICP and thereby arrest disease progression (2, 3).

Methods:
We performed a retrospective observational study of all patients who underwent transverse venous sinus stenting at our institution between January 2016 and January 2018. Data reviewed included patient demographics, prior therapies, opening pressure, visual parameters (visual acuity, color vision, Frisen Grade, visual field mean deviation, and retinal nerve fiber layer thickness) pre- and post-procedure.

Results:
Ten patients underwent venous sinus stenting during the time period studied with a mean age of 28.9 years (±11.02). Nine subjects were female. Fifty percent of patients had improvement or resolution of headaches. Visual acuity improved in 4 patients, was stable in 2 others and 4 patients did not follow-up at our institution. Three patients had improvement in color vision, whereas two others were stable. Papilledema improved in 6 patients. Mean deviation on automated visual field measurement was only available on one patient pre- and post-stenting but showed an improvement from -18.56dB to -4.95dB in the right eye and -32.64 to -24.44 in the left eye. The procedure was tolerated with no observed complications in our cohort of patients.

Conclusions:
Venous sinus stenting is an alternative treatment for severe IIH with threatened visual loss. Our study is limited by its retrospective nature and incomplete follow-up. There is a need for prospective, randomized studies examining the utility of this treatment approach for IIH.

References: 1. Dandy WE. Intracranial pressure without brain tumor: diagnosis and treatment. Ann Surg, 106(4), 492-513, 1937 2. Ahmed RM, Wilkinson M, Parker GD, et al. Transverse sinus stenting for idiopathic intracranial hypertension: a review of 52 patients and of model predictions. AJNR Am J Neuroradiol, 32(8), 1408-14, 2011 3. Dinkin M, Patsalides A. Venous sinus stenting in idiopathic intracranial hypertension: results of a prospective trial. J Neuroophthalmol, 37(2), 113-121, 2017.

Keywords: Interventional neuroradiology, High intracranial pressure/headache, Pseudotumor Cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 187

Correlation of Magnetic Resonance Imaging findings and Ocular examination in patients of Hypoxic Ischemic Encephalopathy

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Introduction:

Hypoxic-ischemic encephalopathy (HIE) is an important cause of permanent damage to CNS tissues. Neuroimaging evidence of acute brain injury seen on brain MRI with Hypoxia-Ischemia is also considered as a significant feature as per the recent task force on neonatal encephalopathy . A comprehensive approach of analysing the neuroimaging features can help in better understanding of the patterns of visual impairment.The objective of this study is to evaluate the relationship between ocular findings and MRI pattern of lesions in cases of HIE.

Methods:

A prospective observational study in which 25 diagnosed cases of HIE were recruited from neuro-ophthalmology clinic. HIE patients between 6 months to 5 years were included in the study. Hemodynamically unstable cases, patients with acquired encephalopathy and subjects refusing to give consent were excluded. MRI scan and ocular examination was done of all the patients meeting the inclusion criteria.

Results:

Out of 25 patients meeting the inclusion criteria, 19 were males and 6 were females, all patients had a history of NICU stay. 24/25 patients had hyperopia, refractive error ranged from +2DS to+5DS In MRI 2 patients had periventricular leukomalacia, 7 patients had diffuse cerebral atrophy, encephalic cysts were found in 5 patients, MRI was normal in 1 patient. In patients with visual acuity between 1.778 to 1.30 logMAR (1/60 to 3/60) 4 had cerebral atrophy, 3 had encephalic cyst and 8 had periventricular leukomalacia on MRI. History of premature birth was present in 7 of 25 patients of which 3 patients had cerebral atrophy, 1 patient had encephalic cyst and 3 patients had periventricular leukomalacia on MRI with visual acuity range between 1.3 to 1.778 log MAR units (1/60 to 3/60).

Conclusions:

Radiological findings have a positive correlation with ocular findings and visual acuity suggesting that MRI can be a better predictor of visual impairment in patients of HIE.

References: None.

Keywords: Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 188
Diffusion Tensor Imaging (DTI) in ehtambutol induced Optic neuropathy

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Introduction:
Ethambutol is an antitubercular drug which may cause optic neuropathy. Ethambutol optic neuropathy (EON) is dose related and reversible in most of the cases on discontinuation of therapy. Exact mechanism is not clearly known but hypothesis is that ethambutol chelates metals and disrupts oxidativphosphorylation in mitochondria. Routine magnetic resonance imaging (MRI) sequences do not demonstrate any abnormalities in optic or brain. This study is carried out to evaluate DTI of optic nerve in EON cases.

Methods:
Twenty cases of EON are enrolled in the study. Their baseline visual acuity, perimetery, opticalcoherencetomography (OCT) retinal nerve fibre layer (RNFL) thickness, visual evoked potential (VEP) and MRI-DTI of optic nerve are carried out. After one year follow up these tests will be repeated. All cases of EON with cranial tuberclosis were excluded from the study.

Results:
3cases have completed their one year follow up. 2cases have complete recovery of vision, 1case has incomplete improvement. Significant improvement was observed in Perimetery, VEP, RNFL thickness. MRI of optic nerve and brain did not show any abnormality. Comparative analysis of DTI parameters between 3patients (baseline) and 3controls revealed reduction in FA and increase in ADC values in the patient group. Follow-up analysis reveals increase in the FA values in all 3patients while ADC values showed decrease by 4.72% & 2.27 in the 2patients who showed recovery in vision. In the patient who did not show full recovery in vision ADC value increased.

Conclusions:
DTI parameter showed differences in FA and ADC in patients at baseline when compared to controls. On follow-up FA and ADC showed a trend towards normalization except for one patient who had only partial recovery. The preliminary DTI data and VEP findings suggest axonal and demyelinating changes in optic nerve in EON which improve on stopping ethambutol. Completion of study may validate this initial trend.

References: 1. Naismith T.R., XuJ., Cross HA.. Diffusion Tensor Imaging in Acute Optic Neuropathies. Arch Neurol 2012 Jan;69(1):65-71. 2. Wang Y.M., QiH.P, Shi P.D. Diffusion Tensor Imaging of Optic nerve in Sub acute Anterior Ischemic Optic neuropathy at 3T. AJNR. 2011Aug; 32:1188-1194. 3. Aung YW, Marsand Benzinger TLS. Diffusion Tensor MRI as a biomarker in axonal and myelin damage. Imaging Med. 2013 Oct 1:5(5):427-440.

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

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Poster 189
Defining Markers of Neuroaxonal Injury and Repair in a Compressive Model of Optic Neuropathy

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Introduction:
Cortical adaptation may influence visual recovery in patients with pituitary macroadenomas. In this retrospect cohort study, we compared coherence tomography (OCT) measures of retinal nerve fiber layer (RNFL) and ganglion cell –inner-plexiform layer (GCIP) values in patients with complete versus incomplete post-operative visual recovery after surgical decompression for pituitary macroadenomas. Secondly, we compared post-operative patterns of resting-state functional magnetic resonance imaging (rsMRI) between groups to determine whether this imaging modality could distinguish patients with complete versus incomplete visual recovery.

Methods:
Eighteen subjects with visually symptomatic pituitary macroadenomas underwent standard ophthalmic assessment, and spectral-domain OCT testing. Ten patients experienced good visual recovery, whereas six patients had persistent visual deficits in the post-operative phase. A minimum of one year after surgery, subjects underwent T2* BOLD fMRI in the resting state. A two-sample, two tailed, t-test, assessing for differences in connectivity between groups and controlling for age, was performed for the connectivity map of each region of interest. Correction for multiple comparisons was performed using a cluster-based method.

Results:
Patients with poor visual recovery demonstrated thinner mean peripapillary RNFL (68 microns versus 83 microns, $p = 0.003$) and GCIP (55 versus 71, $p < 0.0001$) measures as compared to patients with good visual outcomes after surgery. Post-operative rsfMRI showed no difference in connectivity of V1 or V2 between groups. Visual area 5 demonstrated significantly increased connectivity with a cluster spanning the right frontal operculum and right insula in the “good” visual outcome group.

Conclusions:
The extent of visual recovery in patients undergoing surgery for pituitary macroadenomas is linked to the extent of neuroaxonal injury sustained in the anterior visual pathway, and may be reflected in higher cortical changes affecting the middle temporal visual area.

References: None.

Keywords: Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Optic neuropathy, Neuroimaging, Tumors, Skull Base

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Poster 190

Neuro-ophthalmological diagnosis in a series of 1107 patients with suspected ischemic stroke treated with thrombolysis

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Introduction:
The prevalence of neuro-ophthalmological conditions among patients with suspected acute ischemic stroke who receive treatment with intravenous thrombolysis (IVT) has not been properly described in the literature.

Methods:
Objective To describe the prevalence of neuro-ophthalmological diagnosis and their clinical characteristics among 1107 consecutive patients admitted in 13 centres in Norway with suspected ischemic stroke treated with IVT. Methods A total of 1107 patients with suspected acute ischemic stroke were evaluated. ICD-10 codes with the final diagnosis after thorough work-up were registered. Demographics, NIHSS at admission and at 24 hours of patients who received a neuro-ophthalmological diagnosis were compared to the rest of the sample.

Results:
Of the 1107 patients (441 females, 39.8%), 6 patients (0.5%; 2 females) received neuro-ophthalmological diagnosis. One patient had amaurosis fugax, 2 patients had ophthalmoplegic or retinal migraine (ICD-10 code is the same for both conditions), 2 patients had retinal vascular occlusion and 1 patient had subjective visual disturbances. The mean age of the whole sample was 70.96 years (SD 13.84, minimum 18 – maximum 99) and of these 6 patients 62.83 (SD 15.82, minimum 41 – maximum 79), p=0.26. The mean NIHSS at admission of the sample was 5.72 (SD 5.35) and of these 6 patients 2.33 (SD 1.63), p=0.003. The mean NIHSS at 24 hours of the sample was 3.61 (SD 5.88) and of these 6 patients 0.67 (SD 0.52), p<0.001.

Conclusions:
In this series of patients with suspected acute ischemic stroke who were treated with IVT, neuro-ophthalmological diagnosis are uncommon but should not be missed, since its management might differ. The 6 patients identified in this study had a lower NIHSS at admission and at 24 hours compared to the whole sample.

References: None.

Keywords: Vascular disorders

Financial Disclosures: The authors had no disclosures.

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Poster 191
Functional-structural assessment of the optic pathways in patients with optic neuritis

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Introduction:
The aim of this study is to evaluate whether spectral domain optical coherence tomography (SD-OCT) and multifocal visual evoked potential (mfVEP) are potentially better biomarkers than conventional fuel field visual evoked potential (ffVEP) in diagnosing Optic Neuritis (ON).

Methods:
A total of 33 patients examined between May 2017 and September 2017. A total of 126 eyes (66 eyes of patients with history of ON and 60 eyes of a sex and age matched healthy control (HC) group) were investigated. Inclusion criteria were normal ffVEP results (i.e. no prolongation of p100 latency and no reduced VEP amplitude) shown in patients suspected of having a first episode of ON. Both eyes of the patients and controls were systematically investigated with SD-OCT (Cirrus 4000), Visual Acuity(VA), ffVEP and mfVEP. Statistical analyses were performed (incl. t-test, Spearman's Rank-Order Correlation test using SPSS Statistics, Version 24.0.).

Results:
With regards to OCT data, a significant group difference was found in mean RNFLt between patients and HC ($p=0.027$) (i.e. 84.24 (±17.00) µm vs 92.54 (±8.59)µm). In correlation analysis, an association was detected in patients between the inter-eye asymmetry of mean RNFLt and global (averaged) mfVEP amplitude ($r = 0.565$, $p = 0.002$). In regards to GCL analyses, a significant difference was found between averaged inter-eye difference of GCLt between patients and HC ($p=0.001$).When analysing mfVEP sectors, a significant group difference was found in mean mfVEP amplitude between patients and HC ($p=0.002$) (i.e. signals produced from the 16 paracentral sectors in the upper hemifield).

Conclusions:
Abnormality is potentially measurable (via reduced RNFLt and focal analysis with mfVEP amplitude) in patients suspected of having a first episode of ON, but where ffVEP reports normal results.The mfVEP and SD-OCT may together be of value as supplementary tools in diagnosing patients on suspicion of a first episode of ON where ffVEP reports no abnormality.

References: None.

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

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Poster 192
MicroRNAs and their use as biomarkers in clinically isolated syndrome and multiple sclerosis

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Introduction:
Multiple sclerosis (MS), a chronic demyelinating disease of the central nervous system (CNS), is thought to be caused by an overreactive proinflammatory response and as a lack of anti-inflammatory response. This leads to infiltration of immune cells into the CNS and local destruction of the myelin sheaths, oligodendrocytes and the blood-brain-barrier. MicroRNAs (miRNAs) are short, non-coding RNA molecules which are involved in a number of biological processes including the immune system. So far, no specific MS biomarkers have been identified. We aimed at investigating whether miRNAs can be used as potential MS biomarkers in order to diagnose, predict prognosis and treatment effect of MS and clinically isolated syndrome (CIS).

Methods:
A structural literature search was conducted in the database PubMed by using relevant keywords and MeSH terms which included biomarkers, multiple sclerosis, CIS and microRNA. We excluded studies which solely investigated children, animal models, other demyelinating diseases, in vitro studies and some foreign language studies.

Results:
The most commonly investigated miRNAs included miR-155, miR-223, miR-146, Let-7, miR-181, miR-30, miR-143, miR-15, miR-26 and miR-326. These and other miRNAs were found to be dysregulated in MS or CIS patients compared to controls or in between MS disease courses. Dysregulation of the different miRNAs was identified in different cells and tissues, including whole blood, serum, plasma, blood leukocytes, cerebrospinal fluid and white matter with some miRNAs demonstrating a pattern of up- or downregulation depending on the investigated medium. Furthermore, a change in miRNA expression was also identified in some of the studies investigating different first- and second line treatments against MS and following autologous hematopoietic stem cell transplantation.

Conclusions:
The included studies demonstrated a heterogenous pattern, which makes it difficult to conclude the use of miRNAs as MS biomarkers. Controlled studies with well-defined cohorts are warranted.

References: None.

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

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Poster 193
Novel paraclinical methods in patients with neuromyelitis optica spectrum disorders (NMOSD)

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Introduction:
Neuromyelitis optica spectrum disorders (NMOSD) are seldom inflammatory diseases of the central nervous system (CNS). Anti-Aquaporin 4-antibodies (AQP4) are frequent, but in some patients Anti-Myelin Oligodendrocyte Glycoprotein (MOG), a surface protein of the myelin sheath in CNS, are found. Still others are seronegative to both antibodies. We investigated if these subgroups differ with regards to clinical and novel paraclinical investigations and compared to optic neuritis (ON) in general.

Methods:
Patients with ON were examined for antibodies against AQPA4 and MOG and had full-field and multifocal visual evoked potentials (VEP) and MRI of the brain at 3T examining the blood brain barrier (BBB) performed.

Results:
MOG positive patients with ON were more frequent than AQPA4Abs positive patients in this consecutively referred population-based cohort in a geographically well-defined area. MOG patients tended to distinguish phenotypically from AQP4+ patients by being younger, have a more equal gender distribution, more often being monophasic with less severe attacks and less VEP pathology and BBB leakage.

Conclusions:
MOG patients seems to distinguish themselves phenotypically and paraclinically from AQP4 patients. MOG are found in other demyelating CNS diseases and are thus not specific for NMOSD. Further research is needed to establish the clinical implications.

References: None.

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

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Poster 194

Unique challenges in managing NMO Spectrum Disorder in the African American and African-Caribbean population

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Introduction:
The authors present a case series of sixteen patients (15 female, 1 male; mean age 34) with new diagnosis of Neuromyelitis Optica Spectrum Disorder (NMOSD) as per the 2015 Wingerchuk diagnostic criteria. [1]

Methods:
Cases were identified in the medical record with search keywords “NMO” or “Neuromyelitis Optica”, and charts from 2010 to 2018 were reviewed. Each case was reviewed for presenting symptoms, past ocular and medical history, initial and post-treatment visual function, MRI, laboratory tests, lumbar puncture findings, treatment regimen and response.

Results:
Ethnic backgrounds included African-Caribbean (n=9/16), African American (n=6/16), and Hispanic (n=1/16). Patients most often presented with acute myelitis (n=12/16) and/or optic neuritis (n=11/16), and ten had positive aquaporin-4 immunoglobulin G antibodies. Uniquely, the majority of patients with optic neuritis described painless visual loss (n=8/11). Five patients had previous admissions for optic neuritis, at which time clinical features of NMO were not present. Lack of adequate clinical response to high dose intravenous corticosteroids was observed in 11/16 patients (69%), requiring plasma exchange. Half of the patients (n=8/16) relapsed while on prolonged immunosuppressive therapy with oral corticosteroid, azathioprine, or rituximab. Four patients had comorbid autoimmune conditions, including systemic lupus erythematosus and Sjogren’s disease.

Conclusions:
Overall, our case series aligns with a prior report by Storoni et al. suggesting African-Caribbean and African American individuals are more likely to have advanced disease at initial presentation, atypical clinical manifestations, and may be less responsive to standard treatment. [2,3]

References: Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015;85(2):177-89. Han J, Yang MG, Zhu J, Jin T. Complexity and wide range of neuromyelitis optica spectrum disorders: more than typical manifestations. Neuropsychiatr Dis Treat. 2017;13:2653-2660. Storoni M, Pittock SJ, Weinshenker BG, Plant GT. Optic neuritis in an ethnically diverse population: higher risk of atypical cases in patients of African or African-Caribbean heritage. J Neurol Sci. 2012;312(1-2):21-5.

Keywords: Demeylinating disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 195
Characteriests of video head impulse test in patients with posterior inferior cerebellar artery stroke

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Introduction:
Video head impulse test (vHIT) is a new and brief testing, which able to assess the overt and covert refixation saccades and measure the vestibulo-ocular reflex (VOR) gain of each semicircular canal. To date, the characteristics of video head impulse test (vHIT) in acute cerebellar stroke have not been clearly established. We sought to find out the abnormal patterns of vHIT indices of all six semicircular canals in posterior inferior cerebellar artery (PICA) stroke.

Methods:
We enrolled adult patients with unilateral PICA territroy infarction from March 2018 to May 2018, who visited our emergency clinics due to acute vertigo. Patients with previous stroke or neuro-otologic diseases were excluded. All the patients underwent vHIT examination within 7 days of onset. Overt and covert refixation saccades and VOR gain of all six semicircular canals were analyzed.

Results:
Total eight-teen patient with acute unilateral PICA infarction were recruited. Of them, twelve patients (67%) showed abnormal findings in vHIT. Five patients had symmetrical VOR gain reduction with overt or covert refixation saccades in bilateral horizontal canals (HCs) and posterior canals (PCs). Another four showed refixation saccades in bilateral HCs and PCs without VOR gain reduction. Three patients had normal VOR gain but showed refixation saccades in bilateral HCs (2 patients) or PCs (1 patient).

Conclusions:
Refixation saccades in bilateral HCs and/or PCs with or without symmetrical VOR gain reduction might be the characteristic abnormal patterns suggestive of acute PICA stroke in patients with acute vertigo.

References: None.

Keywords: Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Stroke Trauma

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 196

Retinal Vasculopathy with Cerebral Leukoencephalopathy and Systemic Manifestations (RVCL-S): Description of a New Pedigree

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Introduction:
Retinal vasculopathy with cerebral leukoencephalopathy and systemic manifestations(RVCL-S), a rare autosomal dominant disorder caused by a TREX-1 (3p21) mutation,results in progressive occlusive microangiopathy, leading to visual deterioration,neurologic deficits and variable systemic disorders in middle age. To date, 34 unrelatedfamilies have been described worldwide. RVCL-S is under-recognized and oftenmisdiagnosed as multiple sclerosis. We describe manifestations of the V235Gfs*6,TREX-1 genetic variant in a new pedigree.

Methods:
A retrospective review of medical data of 21 members from 5 generations of the proband's family and data sourced for the extended family, from Washington University RVCL Research Center, was conducted and manifestations of RVCL-S documented.

Results:
The proband, a 54-year-old woman with hypertension, developed slurred speech, headaches, handwriting changes and visual distortions. Retinal evaluation revealed retino-vasculopathy, with peri-foveal telangiectasia, capillary occlusion and neovascularization. Initially normal, subsequent serial brain MRI revealed progressively increasing T2/FLAIR hyperintense, variably enhancing, multifocal periventricular, white matter and cerebellar lesions. Brain biopsy revealed features suggesting neuro-vasculopathy. Based on neurologic manifestations, she was diagnosed elsewhere with multiple sclerosis and commenced on glatiramer, without effect. The coexistence of progressive retino-vasculopathy and leukoencephalopathy led us to suspect RVCL-S, confirmed by positive genetic analysis for TREX-1 mutation. One of three siblings also tested positive, and currently has asymptomatic retino-vasculopathy and migraines. Three of five suspected RVCL-S cases in preceding generations had ophthalmic and neurologic disorders; one had predominantly ophthalmic disorders and one had neurologic and kidney abnormalities. In the extended family, two TREX-1-positive cousins and their father, suspected of having RVCL-S, started with retino-vasculopathy and later developed neuro-vasculopathy.

Conclusions:
In this pedigree, ocular manifestations were common and frequently theinitiating disorder. Ophthalmologists often are first to be consulted thus early recognitionof the particular retino-vasculopathy with associated progressive leukoencephalopathyand/or systemic disorders should prompt genetic analysis for TREX-1 mutation.

References: 1. Grand MG, Kaine J, Fulling K, et al. Cerebroretinal vasculopathy: A new hereditary syndrome. Ophthalmology.1988;95:649-653. 2. Gutmann DH, Fischbeck KH, Sergott RC. Hereditary retinal vasculopathy with cerebral white matter lesions. Am J Med Genet.1989;34:217-220. 3. Jen J, Cohen AH, Yue Q, Stout JT, Vinters HV, Nelson S, Baloh RW. Hereditary endotheliopathy with retinopathy, nephropathy, and stroke (HERNS). Neurology. 1997 Nov;49(5):1322-30. 4. Stam AH, Kothari PH, Shaikh A, et al. Retinal vasculopathy with cerebral leukoencephalopathy and systemic manifestations. Brain. 2016;139:2909-2922. 5. Richards A, van den Maagdenberg AM, Jen JC, et al. C-terminal truncations in human 3'-5' DNA exonuclease TREX1 cause autosomal dominant retinal vasculopathy with cerebral leukodystrophy. Nature genetics. 2007;39(9):1068-1070. 6. Liszewski KM and Atkinson JP. Retinal Vasculopathy with Cerebral Leukodystrophy. Available at: https://rarediseases.org/rare-diseases/retinal-vasculopathy-cerebral-leukodystrophy/. Accessed Oct 17, 2018. (Updated November, 2018).

Keywords: Genetic Disease, Neuro-ophth & systyemic disease (eg. MS, MG, thyroid), Vascular disorders

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Poster 197
Optic neuritis: our experience

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Introduction:
Optic Neuritis (ON) is an acute inflammatory disorder of the optic nerve. The general characteristics of isolated ON include unilateral, subacute, and painful visual loss without systemic or other neurological symptoms.[1] In the literature, acute typical optic neuritis is the most common optic neuropathy with an estimated lifetime prevalence of 0.6/1000 with age-adjusted and sex-adjusted incidence. In its typical form, optic neuritis presents as an inflammatory demyelinating disorder of the optic nerve, which can be associated with multiple sclerosis. (MS). Atypical forms of optic neuritis can occur, either in association with other inflammatory disorders or in isolation.[2]. This review shows our incidence of ON, the demographic distribution and the main causes.

Methods:
Observational, retrospective and descriptive (case series) of medical records of patients with diagnosis of optic neuritis treated at the Neuro-Ophthalmology Section of the Public Eye: Hospital between January 2012 and December 2017. A database was created with the following variables: age of diagnosis, gender, initial symptom, visual acuity, color test, fundoscopic examination, relative afferent pupillary defect (RAPD), systemic pathology, visual field, optic coherence tomography (OCT), brain and orbits magnetic resonance with enhacement, CSF (if it was necessary).

Results:
From 2012 to 2017, we review 6540 medical records: 106 optic neuritis were diagnosed, the most frequent age range from 20 to 39 years old. 65% of the patients were female. The unilateral commitment was observed in 72.6% of the cases. The etiology was idiopathic in 79% of the cases, 12% MS, and 7% NMO, among others.

Conclusions:
The study of patients with optic neuritis has led to development in the understanding of the pathophysiology of CNS inflammatory diseases. The typical form has been the most frequently reported in the literature, as in our experience.

References: 1-Jenkins, TM, y Toosy, AT. Neuritis óptica. Current Opinion in Neurology, 30 (1), 61–66, 2017 .. 2- Volpe NJ. El ensayo de tratamiento de neuritis óptica: una respuesta definitiva e impacto profundo con resultados inesperados. Arco Oftalmol. ; 126 (7): 996–999, 2008. 3- Beck RW, Cleary PA, Anderson MA, y col. El Grupo de Estudio de Neuritis Óptica es un ensayo aleatorizado y controlado de corticoisteroides en el tratamiento de la neuritis óptica aguda. N Engl J Med, 1992.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 198
Papilledema as a Sign of Shunt Malfunction in Adults

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Introduction:
The purpose of this study is to investigate papilledema as a sign of shunt failure in adults.

Methods:
We conducted a retrospective review of shunt failure patients at an academic medical center between November 2006 and December 2017. Patients 18 years or older at the time of shunt placement who had undergone an ophthalmoscopic examination prior to shunt failure were included. Demographics, age at shunt placement, reason for shunt placement, time from placement to failure, symptoms and signs of failure, time from symptom onset to ophthalmologic examination, presence of papilledema, and imaging findings were recorded. Data were summarized by mean (±SD) or frequency (%).

Results:
Of the 338 patients reviewed, 10 had ophthalmoscopic examinations before shunt failure. Eight (80%) were females with a mean age of 35.3 years (±12.6) at initial shunt placement. Indications for shunt placement included pseudotumor cerebri (PTC;3 [30%]), traumatic brain injury (TBI; 2 [20%]), hydrocephalus (2 [20%]), and one (10%) each with subarachnoid hemorrhage (SAH), brain tumor, and chiari malformation. Mean duration of shunt placement from last shunt revision to current failure was 65 months (±112), with an average of 3.2 revisions (±5.5) due to previous shunt failures. The most common symptom of shunt failure was headache (8 [80%]), followed by nausea/vomiting (4 [40%]) and blurry vision (3 [30%]). Mean duration of symptoms before ophthalmoscopic examination was 15 days (±11). Seven of the eight female patients had papilledema (87.5%); all 3 patients with PTC had papilledema. None of the patients with TBI or SAH had papilledema. Three (30%) patients had increased ventricular size on imaging, but none of these had papilledema.

Conclusions:
Papilledema may be a sign of shunt failure in adults. Three of 7 patients with papilledema had PTC syndrome, while all patients without papilledema had suffered TBI/SAH and demonstrated ventriculomegaly.

References: None.

Keywords: High intracranial pressure/headache, Optic neuropathy

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Poster 199
Azithromycin as a possible neuroprotective drug in mouse model of optic nerve crush

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Introduction:
Azithromycin (AZ) is a macrolide antibiotic approved worldwide to treat a variety of community-acquired infections. Recently, it was reported that AZ reduced oxidative stress in lung ischemia and protected mice following ischemic stroke. Optic nerve crush (ONC) is a common model simulating optic neuropathy and is used in this study to evaluate the neuroprotective effect of AZ.

Methods:
Twenty four C57Bl/6 male mice were randomly allocated to the study, all underwent ONC induction, 12 with a single intraperitoneal (IP) injection of AZ, and 12 served as control. Histological analysis of retinal thickness and retinal ganglion cells (RGCs) loss was conducted on 21 days from the ONC induction (n=6 each group) as well as immunohistochemistry staining. Analysis of gene expression in the retinas (6 each group) and optic nerves was performed on day one.

Results:
On 21 days, retinal thickness in the ONC group without AZ treatment was 208 µm (±6) as compared to 214 µm (±6) of the healthy fellow eye. When treated with AZ, retinal thickness was preserved (212 µm (±11)) and RGCs loss was reduced (32% Vs 46% without treatment). Molecular analysis in the AZ treated retinae showed reduced levels of expression of the pro-apoptotic gene Bax (2-folds), increased levels of NFK-beta (2-folds) HO1(60-folds) and SOD1 (6-folds) . in the optic nerves, molecular analysis revealed reduced levels of expression of the pro-apoptotic gene Bax (6-folds) and increased levels of stress related HO1 gene (3-folds).

Conclusions:
Azithromycin has a neuroprotective effect in mice following ONC induction when injected IP immediately after the induction of the injury. Given AZ is a common and safe drug in regular use, administration of this treatment immediately after trauma may facilitate preservation of RGCs.

References: None.

Keywords: Optic nerve trauma and treatment, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

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Poster 200
Retinal microvasculature in pituitary adenoma patients: is optical coherence tomography angiography useful?

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Introduction:
Pituitary adenoma (PA) is one of the most common causes of benign intracranial masses. Optical coherence tomography angiography (OCTA) is an emerging, non-invasive method to study the microvasculature of the macula and the optic nerve head. The aim of this study was to assess the vasculature changes in the peripapillary and macular areas associated with PA using OCTA.

Methods:
30 eyes of 15 healthy subjects, and 33 eyes of 17 PA patients with good quality OCTA images were included. PA patients were divided into PA with optic neuropathy (17 eyes) and PA without optic neuropathy (16 eyes). 4.5x4.5 mm disc and 3x3 mm macular angiograms were studied. Whole-image (wiVD), peripapillary (ppVD), and superficial macular vessel densities (mVD) were obtained. Mann-Whitney test and Pearson coefficient were used.

Results:
ppVD in PA eyes (48.00 ± 5.31%) was significantly decreased compared to healthy eyes (50.52 ± 2.14 %, $p = 0.03$). This difference was significant in PA patients with optic neuropathy (mean reduction of peripapillary VD of 10.28%) whereas there was no significant difference between PA patients without optic neuropathy and healthy subjects. mVD was also significantly reduced in PA eyes ($p < 0.001$). Pearson's correlation coefficient showed a correlation between ppVD and RNFL thickness ($r=0.76$) and between ppVD and automated perimetry mean deviation ($r=0.77$).

Conclusions:
Vessel densities in PA eyes are significantly lower than in healthy eyes. A diminished microvascular network is associated with RNFL thinning and perimetric alterations. Peripapillary and macular capillary rarefaction in PA eyes could be useful tools to assess the effect of PA on visual function.

References: 1. Lake MG, Krook LS, Cruz SV. Pituitary adenomas: an overview. Am Fam Physician. 2013;88(5):319-27. 2. Ezzat S, Asa SL, Couldwell WT, Barr CE, Dodge WE, Vance ML, McCutcheon IE. The prevalence of pituitary adenomas: a systematic review. Cancer. 2004 Aug 1;101(3):613-9. 3. Fernandez A, Karavitaki N, Wass JA. Prevalence of pituitary adenomas: a community-based, cross-sectional study in Banbury (Oxfordshire, UK). Clin Endocrinol (Oxf). 2010 Mar;72(3):377-82. 4. Fernández-Balsells MM, Murad MH, Barwise A, Gallegos-Orozco JF, Paul A, Lane MA, Lampropulos JF, Natividad I, Perestelo-Pérez L, Ponce de León-Lovatón PG, Erwin PJ, Carey J, Montori VM. Natural history of nonfunctioning pituitary adenomas and incidentalomas: a systematic review and metaanalysis. J Clin Endocrinol Metab. 2011;96(4):905-12. 5. Lopes MBS. The 2017 World Health Organization classification of tumors of the pituitary gland: a summary. Acta Neuropathol. 2017 Oct;134(4):521-535.

Keywords: Optic neuropathy, Visual fields, Tumors, Skull Base, Skull Base

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 201
Elamipretide (MTP-131) Topical Ophthalmic Solution for the Treatment of Leber's Hereditary Optic Neuropathy

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Introduction:
Leber's Hereditary Optic Neuropathy is a mitochondrial disease characterized by sudden and profound vision loss in both eyes. Elamipretide is has been demonstrated to colocalize with cardiolipin in the inner membrane of mitochondria, where it is thought to improve mitochondrial bioenergetics. The purpose of this study was to look at the safety, tolerability and potential efficacy of the topical Elamipretide in patients affected with LHON.

Methods:
Twelve patients affected with LHON were included in this study. Patients between ages 18 and 50 with decreased vision, for at least 1 year and no more than 10 years, and a genetically confirmed diagnosis of 11778 LHON were eligible for this trial. Patients who had concomitant medical conditions were excluded from the study. The primary outcome measure was the assessment of adverse events from the administration of topical Elamipretide 1%. Secondary outcome measures looked at changes in patients' visual acuity, color vision, visual field mean deviation and electrophysiological outcomes. Patients were randomized to one of two arms, Elamipretide in both eyes or Elamipretide in one eye and vehicle in the other eye.

Results:
Seventeen patients were screened for this study to find 12 patients who met the inclusion criteria. There were no serious adverse events reported during the first 52 weeks of the study. There were 9 cases of mild to moderate ocular irritation in patients who were using Elamipretide. There was one severe ocular event in a subject who developed choroidal neovascularization secondary to trauma.

Conclusions:
Elamipretide topical solution is safe for ocular administration with no serious adverse events reported and mild to moderate ocular irritation as the main side effect. All 12 patients have continued in an open label extension study where both eyes are being treated with Elamipretide.

References: None.

Keywords: Optic neuropathy, Genetic Disease

Financial Disclosures: Both Authors are investigators for the described clinical trial. Their institution (UCLA) has received funding in order to conduct the trial.

Grant Support: None.

Poster 202
Prostate cancer and the visual system

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Introduction:
Although far less common than lung and GI cancer, prostate cancer is a common affliction of men. After breast and lung cancer, it is the most common cause of metastatic tumor involving the cranium. Not surprisingly, prostate cancer patients not infrequently complain of visual pathway involvement and are seen through the neuro-ophthalmology service.

Methods:
A retrospective review of patients with prostate cancer seen in a university setting.

Results:
A total of 43 patients were coded as prostate carcinoma and seen by the neuro-ophthalmology service. Several of these were fortuitous with other complaints likely unrelated to the prostate cancer. Treatment of prostate cancer, especially when aggressive, puts patients at risk for secondary problems, including infectious etiology, and several were seen with sepsis, usually due to immune suppression related to chemotherapy. Ocular complications of surgical intervention include, not surprisingly, exposure keratopathy and surface problems. Because of the propensity of metastatic disease to the bone, these patients often present with proptosis, dystopia, ophthalmoplegia producing diplopia, optic neuropathy secondary to compression, and even undifferentiated metastatic disease to the globe. Because of the propensity to metastasize to bone, at least in one case, appearance so spoke of meningioma that a craniofacial resection was preformed prior to making the diagnosis.

Conclusions:
Prostate cancer is common. Ophthalmic manifestations are not rare. The advent of endoscopic sinus surgery and fine needle aspiration biopsy increases the chance of making a specific diagnosis. Patients may respond in some cases to surgical intervention, but often require radiation therapy or chemotherapy. Therapy itself may also increase the risk of ophthalmic manifestations.

References: None.

Keywords: Tumors, Orbit/ocular pathology, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 203
Temporal Artery Biopsy Length and Laterality

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Introduction:
Giant cell arteritis (GCA) is the most common vasculitis in adults and is associated with significant morbidity and mortality (Watts 2004). Temporal artery biopsy (TAB) remains the gold standard for diagnosis in the United States, however practices vary in whether or not bilateral simultaneous biopsies are obtained and in the length of artery obtained (Papadakis 2018).

Methods:
Retrospective chart review of all TAB's performed at a single institution from 2007-2017.

Results:
A total of 586 patients underwent TAB to evaluate for GCA. Out of 405 unilateral biopsies, 68 (16.8%) were positive. Of 181 bilateral biopsies, 20 (11.0%) were bilaterally positive and 5 (2.8%) were discordant, meaning only one side was positive. There was no significant difference in the length of positive and negative TAB specimens (mean length 1.39 +/-0.61 cm in each group, t-test p=0.7).

Conclusions:
While the rate of positive results was not higher in the bilateral group compared to the unilateral group, 2.8% of bilateral biopsies were discordant, similar to previously published rates (Boyev 1999, Durling 2014). Overall this suggests that initial bilateral biopsy may increase diagnostic yield, albeit by a small amount. There was no significant association between greater length of biopsy and a positive result in our data.

References: 1. Watts RA, Scott DG. Epidemiology of the vasculitides. Semin Respir Crit Care Med, 25(5):455-64, 2004. 2. Papadakis M, et al. Temporal artery biopsy in the diagnosis of giant cell arteritis: Bigger is not always better. Am J Surgery, 215:647-650, 2018. 3. Boyev LR, Miller NR, Green WR. Efficacy of Unilateral Versus Bilateral Temporal Artery Biopsies for the Diagnosis of Giant Cell Arteritis. Am J Ophthalmol, 128:211–215, 1999. 4. Durling B, et al. Incidence of discordant temporal artery biopsy in the diagnosis of giant cell arteritis. Can J Ophthalmol 49:157–161, 2014.

Keywords: Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Optic neuropathy, Neuro-ophth & systyemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 204
Involvement of the Posterior Intracranial Circulation in Giant Cell Arteritis

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Introduction:
Giant cell arteritis (GCA) is the most common primary vasculitis affecting the elderly population. GCA preferentially involves the extracranial branches of the carotid artery with sparing of intracranial vessels (Wilkinson and Russell, 1972). Occlusive vasculitis or embolization of inflammatory thrombus can result in ischemic stroke, found in approximately 2-4% of GCA patients. One series reported an incidence of 2.8%, mainly in the posterior circulation, and found that vertebrobasilar stroke was often accompanied by arteritic anterior ischemic optic neuropathy (Gonzalez-Gay et al., 2009). This study determined the prevalence of posterior intracranial vasculitis in a large series of patients with GCA undergoing contrast-enhanced MRI focused on intra- and extracranial vessels.

Methods:
This was a retrospective chart review utilizing a prospective database of GCA patients. Between 2015 and 2018, 197 patients were evaluated for probable or confirmed GCA. MR images were reviewed and positive findings verified by a single neuroradiologist.

Results:
Of 197 patients, 167 had a contrast-enhanced MRI of the head and 55 had evidence of vasculitis. Five patients showed probable or definitive involvement of both the anterior and posterior intracranial circulation with isolated posterior intracranial circulation involvement in one additional patient. One of these patients showed evidence of acute posterior circulation ischemia and presented with vertigo but no evidence of ischemic optic neuropathy or ophthalmic artery enhancement. Of the 55 patients, 14 had abnormal enhancement of the ophthalmic arteries including one with arteritic anterior ischemic optic neuropathy and vertebral arteritis and one patient with involvement of the internal carotid and posterior cerebral arteries but no reported vision changes.

Conclusions:
Although uncommon, clinicians should be aware that GCA can involve the intracranial circulation with both the anterior and posterior circulation affected in most of our cases. More aggressive treatment may be required in these patients to avoid neurologic complications or death (Alsolaimani et al., 2016).

References: 1. Gonzalez-Gay MA, Vazquez-Rodriguez TR, Gomez-Acebo I, Pego-Reigosa R, Lopez-Diaz MJ, Vazquez-Triñanes MC, et al. Strokes at time of disease diagnosis in a series of 287 patients with biopsy-proven giant cell arteritis. Medicine (Baltimore). 2009, Jul;88(4):227-35. 2. Wilkinson IM, and Russell RW. Arteries of the head and neck in giant cell arteritis. A pathological study to show the pattern of arterial involvement. Arch Neurol. 1972, Nov;27(5):378-91. 3. Alsolaimani RS, Bhavsar SV, Khalidi NA, Pagnoux C, Mandzia JL, Tay K, Barra LJ. Severe Intracranial Involvement in Giant Cell Arteritis: 5 Cases and Literature Review. J Rheumatol. 2016 Mar;43(3):648-56.

Keywords: Neuroimaging, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 205
Giant Cell Arteritis in African Americans: 10-Year Data from Baltimore

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Introduction:
The incidence of giant cell arteritis (GCA) is well-documented in white populations, but its relevance among other racial and ethnic groups is less well-established. The purpose of this study was to examine the incidence of biopsy-proven GCA (BP-GCA) in a hospital-based population with a significant proportion of African American (black) patients.

Methods:
The medical records of all patients undergoing temporal artery biopsy (TAB) during the 10-year study period from 2007 until 2017 were reviewed, including self-reported race. Cases of BP-GCA were identified using the electronic medical record system. Associations between race, sex and age were explored and compared with all other patients attending the hospital over the same period.

Results:
Among 586 patients who underwent TAB, 167 (28%) were black and 382 (65%) were white. Of these, 15 (9%) black patients and 75 (20%) white patients were found to have BP-GCA. The mean age of black patients with BP-GCA was 68.9 ±11.6. The youngest patient with BP-GCA was a 46-year-old black man. Women were more often affected than men. Estimated incidence rates for BP-GCA were 3.3 per 100,000 blacks and 4.7 per 100,000 whites within the study population. Population-adjusted age- and sex-standardized rates were 3.2 and 4.0 per 100,000 for blacks and whites, respectively.

Conclusions:
In our study the incidence of BP-GCA in black patients was only slightly lower than in white patients. Our data suggest that rates of GCA in the black population are not as low as previously thought.

References: None.

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

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Poster 206
Institutional Analysis of Temporal Artery Biopsies based on Clinical Suspicion for Giant Cell Arteritis

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Introduction:
Diagnosing Giant Cell Arteritis (GCA) is based on clinical symptoms, signs, labs and temporal artery biopsy (TAB) pathology.(1-4) Biopsies are the gold standard for confirming GCA.(1,3) Recently, a revised American College of Rheumatology (rACR) criteria was proposed with a more extensive set of criteria, which included biopsy.(2) A clinical tool without biopsy was created to stratify patients according to GCA risk.(1) The purpose of this study is to analyze our patient population with temporal artery biopsies according to the proposed rACR clinical criteria and to examine how (i)TABs and (ii) the final diagnosis regardless of biopsy correlated to this clinical suspicion.

Methods:
An IRB-approved retrospective chart review was performed to identify patients who underwent TAB (CPT code 37609) from 2012-2018. The rACR clinical score was calculated and a low clinical score was determined to be 2 or less. Demographic and clinical data were collected. Patients were excluded if their age <50 or if there was insufficient data collected in the chart. The sensitivity, specificity, positive predictive value and negative predictive values (NPV) were calculated for subgroups according to the clinical score.

Results:
31 patients (34 biopsies) met inclusion criteria. Of the 34 biopsies analyzed, 4 were positive, of which 3 belonged to patients with higher clinical suspicion. The NPV of biopsies was 77% for patients regardless of clinical score while the NPV of biopsies was 92.9% for patients with low clinical score. 7/30 (23.3%) patients were continued on GCA treatment despite negative biopsy. The sensitivity of biopsies in our institution was 36% while a high clinical score (over 3) alone had a sensitivity of 63.6% for predicting continued GCA treatment.

Conclusions:
The sensitivity of TAB for GCA diagnosis in our institution was 36%, which falls within the reported range of 15-70%.(1,5) The final diagnosis of GCA is often made clinically despite negative biopsy.

References: 1. Sait MR, Lepore M, Kwasnicki R, Allington R et al. “The 2016 revised ACR criteria for diagnosis of giant cell arteritis—Our case series: Can this avoid unnecessary temporal artery biopsies?” International Journal of Surgery Open, 9, 19-23, 2017. 2. Salehi-Abari, Iraj. “2016 ACR Revised Criteria for Early Diagnosis of Giant Cell (Temporal) Arteritis.” Autoimmune Diseases and Therapeutic Approaches Open Access, 3(1), 1-4, 2016. 3. Yuskel V, Guclo O, Tastekin E et al. “Clinical correlation of biopsy results in patients with temporal arteritis.” Rev Assoc Med Bras, 63 (11), 953-956, 2017. 4. Guevara M and CS Kollipara. “Recent Advances in Giant Cell Arteritis.” Current Rheumatology Reports, 20(25),1-9, 2018. 5. Banz Y and JH Stone. "Why do temporal artery biopsies go wrong? Principles and pearls from a clinician and a pathologist." Rheumatology, 57, ii3-ii10, 2018.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 207
A Retrospective Chart Review of Treated Healing/Healed Arteritis Versus Untreated Healing/Healed Arteritis

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Introduction:
Giant cell arteritis (GCA) is characterized by granulomatous inflammation of the large and medium arteries of the head and neck. Histologically, GCA is grouped into three categories: positive for active GCA, negative for active GCA and healing/healed (HH) arterial injury. The factors that contribute to the decision making while initiating corticosteroid in HH arteritis is not well established. We performed a retrospective chart review of patients with HH arteritis and assessed the clinical characteristics associated with indications for treatment.

Methods:
Electronic records were retrospectively collected from 69 patients with HH arteritis including the presence of the following clinical symptomatology: amaurosis fugax, vision loss, diplopia, headache, jaw claudication, scalp tenderness, polymyalgia rheumatica, constitutional symptoms, RAPD, extraocular muscle movement abnormalities, BRAO, CRAO, cotton wool spots, ischemic optic neuropathy, ocular ischemic syndrome and cerebrovascular accident. Laboratory measures collected included hemoglobin, platelet, ESR and CRP.

Results:
The only non-visual GCA symptom that was significantly associated with the initiation of high-dose prednisone therapy was jaw claudication. A previous history of cerebrovascular accidents was also more frequently associated with patients in b1. Serological markers demonstrated higher levels of mean ESR (b1=60±41, b0=39±30, $p<0.05$) and CRP (b1=56±59, b0=35±44, $p=0.07$) but no significant differences in hemoglobin and platelets ($p>0.05$). Overall, 13% of patients experienced relapse of the GCA-like symptoms upon tapering off corticosteroid treatment (4/52 from b1 and 5/17 from b0). Patients were followed longitudinally for two years and none from b0 was declared to be GCA.

Conclusions:
We demonstrate that jaw claudication was the only clinical indicator more frequently associated with the treatment group. Patients in the b1 group exhibited more advanced disease as evidenced by a comparatively more elevated serum ESR and CRP and associated with higher rates of relapse. These findings suggest the need for long-term corticosteroid treatment for patients with clinical high suspicion for HH arteritis.

References: None.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 208
Temporal Artery Imaging in Suspected Giant Cell Arteritis using the SPECTRALIS OCT FLEX Module

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Introduction:
Diagnosing Giant Cell Arteritis (GCA), which causes cranial ischaemic symptoms such as sudden and permanent loss of vision, is challenging. Definitive diagnosis is by using a combination of clinical history and confirmative test such as temporal artery biopsy (TAB), or ultrasound that requires specialist skills. It is recognized that a reliable and non-invasive test is needed. The aim was to assess the feasibility of spectral domain Optical Coherence Tomography (OCT) to visualize the superficial temporal artery (STA) in vivo and ex vivo.

Methods:
The Heidelberg SPECTRALIS OCT FLEX module, with the anterior segment lens, was used to capture images of the STA of 20 patients. All 20 TAB specimens were imaged after removal from the patient. Additionally, 8 STAs were imaged intra-operatively in situ after the cutaneous and subcutaneous tissues had been dissected to reveal the STA. Images were compared to the correspinding histopathological specimens and select cases are presented.

Results:
This preliminary study revealed that the arterial lumen was visualized in all 20 patients. Different arterial wall layers could be differentiated in 75% of cases and in 60% both sides of the lumen were visualized. In all cases, the lumen appears to be surrounded by a hyperreflective layer, followed by a hyporeflective layer and then an outer hyperreflective layer (presumed to represent the intima, media and adventitia respectively). Measurements of intimal thickening are plotted against final histopathological diagnosis.

Conclusions:
The Heidelberg SPECTRALIS FLEX module enables visualize of the STA wall and lumen. In vivo scanning allowed for more detailed STA identification and assessment of its patency. A reliable immediate non-invasive is required to reduce overtreatment of glucocorticoids in suspected GCA. Further validation is required, to determine the diagnostic utility of this novel technique.

References: None.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 209

Clinical evaluation of adverse outcomes in patients diagnosed with healing/healed arteritis on temporal artery biopsy

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Introduction:
Temporal artery biopsy (TAB) is regarded as the gold standard investigation for confirming the clinical diagnosis of giant cell arteritis (GCA). Healing or healed arterial injury (HH) has been shown through serological markers to represent an intermediate between GCA-positive and GCA-negative TAB. The clinical outcomes of HH, however, have yet to be elucidated. The purpose of this study was to compare the rates of GCA-related adverse events in patients with an initial TAB diagnosis of HH to those with GCA-positive and GCA-negative diagnoses.

Methods:
This was an IRB-approved retrospective cohort study of 393 patients who underwent TABs for clinical suspicion of GCA at a single academic centre between 2009 and 2018. Rates of vision loss, stroke, aortitis, and aortic aneurysms (thoracic or abdominal) were compared between patients with histological TAB diagnoses of GCA-positive, HH, and GCA-negative.

Results:
76 GCA-positive, 77 HH, and 240 GCA-negative TABs were identified. Rates of vision loss, including amaurosis fugax and decreased visual acuity, were not significantly different between the groups (p=0.46). Rates of aortic aneurysms in the GCA-negative, HH, and GCA-positive groups were 3%, 8%, and 12%, respectively. Rates of aortic aneurysms between GCA-negative and HH were not significantly different, whereas patients with GCA-positive TABs demonstrated significantly greater rates of aortic aneurysms (p=0.01). There was no association between pathology results and the rates of future stroke (p=0.66). Findings of aortitis (pathological or radiological) were exceedingly rare, with only two diagnoses made in the GCA-positive group and none in the HH and GCA-negative groups.

Conclusions:
TAB diagnosis of HH was not associated with significantly greater rates of visual or systemic adverse events compared to GCA-negative TABs. There was a dose-response trend in the rate of aortic aneurysms between patients diagnosed with GCA-negative, HH, and GCA-positive TABs.

References: None.

Keywords: Vascular disorders, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 210
Giant Cell Arteritis: Diagnostic Considerations in a Veterans Administration Hospital Cohort

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Introduction:
GCA is one of the most important ophthalmic emergencies, requiring prompt empiric treatment and diagnosis. As new immunotherapy becomes available and diagnostic algorithms are refined, GCA is gaining renewed attention.1-3 However, GCA diagnosis specific to veteran populations has not previously been described. We hypothesize that due to the high rates of medical comorbidities and the disparate prevalence of male versus female veterans, there are inherent differences between veteran and non-veteran patients driving the decision for temporal artery biopsy (TAB) in this cohort.

Methods:
Retrospective chart review of all temporal artery biopsies conducted at a single VA health system from 1999 to 2018. De-identified data with VA and IRB approval and was used to calculate mean, standard deviation, and other descriptive statistics, which were then compared to non-VA population studies.1

Results:
167 patients with TABs were retrospectively analyzed, 21 of whom had biopsies positive for GCA. Average age (+/- SD) of patients at referral was 72 (+/- 10) years, erythrocyte sedimentation rate 55 (+/- 36) mm/hr, high-sensitivity c-reactive protein 38 (+/- 64) mg/L (normal < 11mg/L), and platelet count 267 (+/- 94). Symptoms included 74% new-onset headache, 24.1% jaw claudication,and 45.9% vision changes. New-onset headache had the highest sensitivity at 66.7%, but specificity was only 24.8%. Jaw claudication was found to be the most diagnostic, with a sensitivity of 52.4% and specificity of 75.9%, consistent with prior studies of non-VA patients.1,2 Only 9.1% of specimens were from females, but 33.3% of them were positive, versus only 10.7% of male specimens.

Conclusions:
This study demonstrates that referrals for temporal artery biopsy in the veteran population resemble global experience, except that proportionally fewer females are referred and their biopsy yield is relatively high. This is the first study of GCA diagnosis in the veteran population and serves as pilot data for future prospective multicenter studies.

References: 1. Peral-Cagigal B, Perez-Villar A, Redondo-Gonzalez LM, Garcia-Sierra C, Morante-Silva M, Madrigal-Rubiales B, et al. Temporal headache and jaw claudication may be the key for the diagnosis of giant cell arteritis. Med Oral Patol Oral Cir Bucal. 23(3):e290-e4;2018 2. Ing EB, Lahaie Luna G, Toren A, Ing R, Chen JJ, Arora N, et al. Multivariable prediction model for suspected giant cell arteritis: development and validation. Clin Ophthalmol. 11:2031-42;2017 3. Stone JH, Tuckwell K, Dimonaco S, Klearman M, Aringer M, Blockmans D, et al. Trial of Tocilizumab in Giant-Cell Arteritis. N Engl J Med. 377(4):317-28;2017.

Keywords: Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 211
A Comparison of Giant Cell Arteritis Management in Subspecialty and Primary Care Settings.

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Introduction:
Immediate administration of glucocorticoids is essential in the treatment of suspected giant cell arteritis (GCA). The choice of medication dose and route depends on patient-specific factors, but may also reflect physician-specific ones, including subspecialty discipline. We have compared the management of suspected GCA cases in subspecialty versus primary care settings to: (1) identify possibly discrepancies in management and (2) promote a broader understanding of the evidence-based management of GCA.

Methods:
This retrospective cohort study includes 286 consecutive patients with suspected GCA, all of whom were referred for temporal artery biopsy at the Ottawa Eye Institute between 2009-2016. Data from the initial clinical visit were collected, including: physician subspecialty, patient demographics, symptoms, laboratory investigations and therapies received. Logistic regression models were used to assess whether any covariates were associated with the use of glucocorticoid therapy.

Results:
A total of 172 patients (60.4%) were prescribed glucocorticoids for suspected GCA. The majority (92.4%) of these patients were prescribed the medication orally; only 13 (7.5%) were prescribed intravenous medication. Compared to those evaluated in a subspecialty care setting, patients assessed in a primary care setting had 2.29 times the odds of receiving glucocorticoids (95% CI 1.35 – 3.88, $p < 0.01$); this association remained significant after adjustment of all patient-specific characteristics (OR 2.30, 95% CI 1.12 – 4.72, p=0.02). Patients seen in subspecialty settings also received a higher dose (88.3 mg, IQR 0, 60 mg) than those seen primary care settings (50.0 mg, IQR 0, 60 mg) and were more likely to receive medication intravenously (OR 3.05, 95% CI 0.66 – 14.0, p=0.15).

Conclusions:
Our results suggest that physicians with subspecialty expertise prescribe glucocorticoids more judiciously, but do so more often via an intravenous route and at higher doses. These discrepancies indicate a potential area for improvement in achieving quality, evidence-based care for all patients with GCA.

References: None.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 212
Evidence-Based Guidelines for the Diagnosis and Treatment of Neuromyelitis Optica Spectrum Disorder (NMOSD)

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Introduction:
NMOSD diagnosis and management is an evolving process. Evidence-based guidelines built into clinical information systems can optimize patient care. To this end, an NMOSD expert topic group, under the auspices of the Clinical Knowledge and Content Management (CKCM) service at our institution prepared guidelines. The objectives were to study and adopt evidence-based practices for diagnosis and treatment of NMOSD patients in our region with possible dissemination nationally.

Methods:
Using CKCM methodology, a systematic review was undertaken. Key terms included NMO, NMOSD, LETM, atypical optic neuritis, APS and their mimics, as well as diagnosis and treatment. Medline, Pubmed, DynaMed, Cochrane (1980-present at the time), and hand searching were evaluated. Papers were graded for level of evidence and strength of recommendation, with a focus on resource availability in our region. Expert and consumer panels reviewed the resulting guidelines providing feedback towards the final product.

Results:
For "diagnosis", a total of 405 papers were found, 233 were reviewed and 85 selected/ graded. For "treatment", the respective number of papers were 341, 98 and 61. Most were graded as moderate to low quality of evidence. For diagnosis, the strongest recommendations were for: MRI (with gadolinium) of optic nerves/brain/whole spine; immune testing for NMOSD and mimics including anti-AQP4 antibodies; anti-MOG antibodies; CSF studies (to rule out mimics such as lymphoma and atypical infections); CT/PET imaging to rule out malignancy and other inflammatory disorders; and ophthalmological testing in all NMOSD-like presentations. For acute treatment, our strongest recommendation was for high-dose corticosteroids and early plasmapheresis in non-responders. For plasmapheresis non-responders, low-grade evidence supported rituximab induction and if required, cyclophosphamide. The best evidence for maintenance therapy was for rituximab, azathioprine or mycophenolate mofetil with appropriate prednisone coverage period.

Conclusions:
We have developed standardized protocols for diagnosis and treatment of NMOSD that can be applied nationally in the future.

References: None.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 213
Rituximab May Confer Protective Effect on Retinal Nerve Fiber Layer in Multiple Sclerosis

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Introduction:
Painful visual loss due to optic neuritis is a common presentation for an acute flare of multiple sclerosis (MS). Optical coherence tomography (OCT) has emerged as a tool to evaluate thinning of the retinal nerve fiber layer (RNFL) in patients with demyelinating conditions and may be useful in assessing subclinical progression of disease. Disease modifying therapies such as natalizumab have been implicated in stabilizing RNFL loss in MS (Talmage et al. 2017), but no such study has been done with Rituximab, which is a monoclonal Anti-CD20 antibody shown to be effective in treating MS (Alcala et al., 2018).

Methods:
To retrospectively investigate whether Rituximab may influence rates of retinal nerve fiber layer thinning in relapsing-remitting multiple sclerosis, using optical coherence tomography (OCT). We did a retrospective study of patients with history of unilateral optic neuritis due to multiple sclerosis being treated with Rituximab (n=22) or injectable therapy (glatiramer acetate, n=14, or Interferon beta-1a, n=10) and compared RNFL in both the affected eye and unaffected eye at 6-13 month intervals.

Results:
At a mean follow up time of 204 days from initial OCT, RNFL thinning in the affected eye occurred in both groups but was reduced in the Rituximab group (RNFL loss -2.50 +/- 1.2mm/year) compared to injectable therapy group (RNFL loss -4.77+/- 1.9 mm/year), a difference which was statistically significant. There was numerical reduction of RNFL loss in the unaffected eye (RNFL loss -1.59 +/- 2.4mm/year in Rituximab group and -2.02 +/- 1.4mm/year in the injectable therapy group), but this difference was not statistically significant.

Conclusions:
These data suggest that Rituximab may exert a protective effect on the RNFL in patients with a history of optic neuritis due to MS. This also provides further evidence that OCT may serve as a biomarker of disease activity in MS.

References: None.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 214
Recanalized Internal Carotid Artery Dissection in Cryptogenic Horner Syndrome

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Introduction:
Isolated Horner Syndrome (HS) evaluation does not reveal an underlying etiology in 80% of patients. Thus, isolated HS is most often cryptogenic, and this leads to uncertainty regarding a potential missed diagnosis for both the physician and patient. Internal carotid artery dissection (ICAD) is found in in 8% of HS patients and is the most common identifiable HS etiology. ICADs repair spontaneously, resulting in ICA lumen recanalization within 6 months. HS, however, can persist beyond ICA recanalization, and HS patients may not seek care at symptom onset resulting in presentation delay. Thus, cryptogenic HS may be the result of ICAD that has recanalized by the time of presentation. Following ICAD recanalization, subtle irregularities in ICA caliber that are detectable with ICA imaging can persist, and specialized analysis of ICA imaging from cryptogenic HS patients may support this hypothesis.

Methods:
Patients with cryptogenic HS that received ICA imaging were identified via EMR database from the Washington University Neuro-Ophthalmology clinic. Analysis will involve a two-alternative forced choice method in which neuroradiologists blinded to HS laterality review ICA imaging from cryptogenic HS patients. For images from each patient, the radiologist is forced to designate one ICA as "previously dissected" and the other ICA as "normal". The results will be considered significant if congruency between the previously dissected ICA laterality and HS laterality is statistically greater than 50%.

Results:
31 patients with HS were identified. 13 patients met criteria for inclusion. 15 had identifiable etiology, 4 did not receive imaging. ICA images are being read with the forced choice approach, and analysis will determine if congruency between HS laterality and forced choice dissection laterality is statistically significant.

Conclusions:
Our analytical approach comparing cryptogenic HS laterality and ICA irregularities may provide the first quantitative evidence that recanalized ICAD contributes to cryptogenic HS presentations.

References: None.

Keywords: Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 215
Attitudes and Perceptions of Neurology Residents in the United States to Neuro-ophthalmology

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Introduction:
To identify factors associated with choice of fellowship subspecialties among graduating neurology residents and to understand the perceptions of neurology residents regarding a career in neuro-ophthalmology with a specific desire to understand why this subspecialty is not pursued by more neurology residents.

Methods:
An anonymous 35 question survey was sent to 38 out of 143 ACGME accredited neurology residency programs in the United States to current neurology residents and fellows between April and June 2018. Information regarding residency training, career goals, perceptions regarding the field of neuro-ophthalmology and demographic data was obtained.

Results:
126 responses were obtained across 38 neurology programs (about 15% response rate). 84% of residents either were planning to pursue or already in a fellowship. 15% had decided on a fellowship in neuro-ophthalmology. Factors for pursing a specific fellowship included “Area of strong personal interest” (56/58), “Acquisition of special skills” (32/58), “Rotation in subspecialty during residency” (31/58). Exposure during residency would have made a difference in 18/40 respondents when considering a career in neuro-ophthalmology. 85% of respondents stated a rotation in neuro-ophthalmology was available in their residency however only 43% of programs surveyed had a mandatory rotation in neuro-ophthalmology. When asked about perceived difficulty of neurology subspecialties 68% of respondents stated neuro-ophthalmology was difficult, the highest percentage of perceived difficulty compared to other main neurology subspecialties with reasons being lack of confidence in exam skills and lack of exposure to the field.

Conclusions:
Few neurology residents pursue a career in neuro-ophthalmology with the biggest factor being limited exposure. Although the perception of neuro-ophthalmology was that it is a difficult specialty requiring advanced clinical and exam skills, exposure to this field appears to be the main factor. We hope this will alert neurology residency programs of this issue to promote more neurology residents to pursue a career in neuro-ophthalmology.

References: None.

Keywords: Miscellaneous

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Grant Support: None.

Poster 216
Current Attitudes and Perceptions of Ophthalmology Trainees about Neuro-Ophthalmology

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Introduction:
To identify the attitudes and perceptions of current ophthalmology trainees in the United States regarding the sub-specialty of Neuro-Ophthalmology.

Methods:
An anonymous survey was sent through the AUPO listserv to current ophthalmology residents and fellows in the United States between March and October 2018. Information regarding residency training, career goals, perceptions regarding the field of neuro-ophthalmology and demographic data was obtained.

Results:
Surveys were completed by 254 residents (~18% response rate) and 8 fellows. Of all the residents who completed the survey, 164 (64.6%) were definitely or probably planning on pursing a fellowship, while 90 (35.4%) were definitely or probably not planning on pursing a fellowship. 5 of 254 (2.0%) residents were planning fellowship training in neuro-ophthalmology. Other chosen career paths included surgical retina (25.6%), cornea (19.7%), glaucoma (17.7%), oculo-plastics (9.4%), pediatric ophthalmology (9.1%), comprehensive (7.1%), medical retina (4.3%), uveitis (3.1%) and other (2.0%). 139 of 262 (53%) perceived neuro-ophthalmology to be more difficult than other sub-specialties, citing complex diagnoses and lack of confidence in neuro-anatomy as the most common reasons. 224 of 241 (93%) reported that a role model was important in their choice for fellowship. 131 of 262 (50%) perceived that a fellowship in neuro-ophthalmology limited their career and job opportunities. 220 of 256 (85.9%) perceived the annual income of a neuro-ophthalmologist to be lower than their peers. Reported changes that would increase the likelihood of pursuing fellowship training in neuro-ophthalmology include more surgeries/procedures (50.2%), increased compensation (23.1%), and more job opportunities (9.0%). 48 of 262 (18.3%) would not pursue a career in neuro-ophthalmology.

Conclusions:
Very few ophthalmology residents pursue a career in neuro-ophthalmology. This appears unchanged from previous studies(1,2). This survey identified several factors that trainees reported that would need to change before they considered pursing a fellowship in neuro-ophthalmology including more job opportunities, more surgeries/procedures and higher compensation.

References: 1. Gedde SJ, Budenz DL, Haft P, Lee Y, Quigley HA. Factors affecting the decision to pursue glaucoma fellowship training. J Glaucoma. 2007;16(1):81-7. 2. Gedde SJ, Budenz DL, Haft P, Tielsch JM, Lee Y, Quigley HA. Factors influencing career choices among graduating ophthalmology residents. Ophthalmology. 2005;112(7):1247-54.

Keywords: Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 217
Recruiting ophthalmologists into neuro-ophthalmology

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Introduction:
Ophthalmology trained neuro-ophthalmologists are at risk of becoming an endangered species. One of the strengths of our field is the diversity of backgrounds and training giving different perspectives in the evaluation and treatment of complex disease. We need to ensure we continue to train ophthalmologists in neuro-ophthalmology. We investigated the reasons why ophthalmology residents choose not to pursue training in neuro-ophthalmology in addition to exploring the motivations of those that do choose the field.

Methods:
The first survey was sent out via the AUPO residency director listserv to reach all graduating PGY4 ophthalmology residents who chose not to pursue fellowship in neuro-ophthalmology. The second survey will be sent out via the NANOS YONO listserv to contact recent ophthalmology-trained neuro-ophthalmology fellows.

Results:
96 PGY4 residents responded to the initial survey, with 74% planning to pursue fellowship. The most common fellowships were surgical retina (23%), glaucoma (19%) and cornea (16%). The majority of residents decided on their subspecialty in their PGY3 year, but eliminated neuro-ophthalmology in their PGY2 year. The main factors that influenced the decision not to pursue neuro-ophthalmology included lack of surgery (57%), including specifically intraocular surgery (66%) and types of patients seen (65%). Most residents have a dedicated neuro-ophthalmology rotation in the PGY2 and/or PGY3 years. The didactics, clinical exposure and research opportunities were rated as on par or superior to other fields. Residents typically work with multiple ophthalmology trained neuro-ophthalmologists, many of whom perform surgery, however less than half of residents were exposed to surgery during their rotations. We will also present the data collected from the second survey sent to recent ophthalmology-trained neuro-ophthalmology fellows.

Conclusions:
The perceived lack of surgery as part of a neuro-ophthalmologist's career presents a barrier to recruiting ophthalmology residents into the field. We can work to emphasize the opportunities to incorporate surgery into a neuro-ophthalmology practice.

References: None.

Keywords: Miscellaneous

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Poster 218
Development of a Survey to Explore Current Practice Patterns Amongst Neuro-ophthalmologists

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Introduction:
Neuro-ophthalmologists have diverse practices. Some are dual trained and practice in another subspecialty besides neuro-ophthalmology, and/or perform surgical procedures. There are others who actively incorporate resident education and research in addition to clinical practice. A recent conversation on the NANOS Women in Neuro-ophthalmology list serve highlighted the challenges and advantages in building and maintaining such diverse practices and motivated this project. Our purpose is to design a survey that will explore current practice patterns amongst neuro-ophthalmologists. The data gathered from the survey responses will help to understand the current challenges faced by practicing neuro-ophthalmologists and to make recommendations for improving neuro-ophthalmology training so that it remains an attractive and fulfilling career for current and future practitioners.

Methods:
Survey questionnaire developed by the women in neuro-ophthalmology steering committee members and approved by NANOS board. The survey was developed through discussions by the steering committee members via list serve email and conference calls.

Results:
The survey will inquire about the nature of current neuro-ophthalmology practices, number of currently practicing neuro-ophthalmologists who have additional training and practice another specialty, those having a surgical practice and research funding in addition to neuro-ophthalmology. Responders will be queried about current challenges faced as neuro-ophthalmologists and perceived limitations in pursuing neuro-ophthalmology as a career choice.

Conclusions:
Our survey questions will help to identify current practice patterns and challenges faced by practicing neuro-ophthalmologists. The data gathered from survey implementation will guide potential neuro-ophthalmology applicants of the interdisciplinary strengths of this field.

References: None.

Keywords: Miscellaneous

Financial Disclosures: The authors had no disclosures.

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Poster 219
'Virtual' IIH clinic: demonstrating a safe & efficient method of follow-up in an Ophthalmology centre

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Introduction:
Idiopathic Intracranial Hypertension (IIH) is a sight threatening disease that predominantly occurs in women and its incidence is rising. Our Neuro-Ophthalmology service currently manages a large number of complex conditions; thus, we have streamlined patients into specialised clinics, and have introduced a 'Virtual' IIH clinic.

Methods:
Our orthoptists and photographers perform a detailed patient examination comprising of: visual acuity, colour vision, pupil reaction, goldmann visual fields, OCT and fundus photographs. A proforma is additionally completed reviewing headaches and their characteristics, whooshing tinnitus, visual symptoms, weight, and lastly medication/treatment. The completed assessments are 'virtually' reviewed by a Consultant Neurologist on the same day via computer access to the medical records. Management plans are put in place and fed back within 7 working days to the patient, and any other relevant clinicians involved in their care via a clinical letter.

Results:
We conducted a retrospective analysis of patients reviewed in the 'Virtual' IIH clinic between October2016-April2018. 38 patients were seen, saving 62 appointments in the specialist clinic. Mean number of visits:1.6; mean age of cohort:35 (range18-78); mean opening pressure:34cmH20. Only 7 DNA's were noted within this time period- highlighting the value of this service. Lastly, most importantly no patient lost vision. Our analysis demonstrated that through the 'virtual' clinic we were able to manage patients of varying complexity, making decisions regarding treatment initiation/cessation and discharge without compromising patient safety.

Conclusions:
In a time of finite resources, virtual clinics provide an opportunity for high efficiency whilst maintaining excellent levels of patient care. The implementation of this service has enabled us to demonstrate a safe method of monitoring and treating IIH patients, freeing up a large number of clinical appointments in a busy ophthalmology centre. Our 'Virtual' IIH clinic can provide a framework for other units to safely manage IIH patients and potentially other Neuro-Ophthalmology conditions.

References: None.

Keywords: High intracranial pressure/headache, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 220
Diagnostic Error and Neuro-Ophthalmology

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Introduction:
Despite medical advances, studies show alarmingly high rates of diagnostic error (up to 15% in the USA). Because diagnosis of neuro-ophthalmologic conditions requires resource-intensive analytic reasoning, these conditions are particularly vulnerable to misdiagnosis, it is particularly prone to diagnostic errors. This review summarizes recent literature on diagnostic error relevant to neuro-ophthalmology practice.

Methods:
PubMed search (English language) of relevant studies yielded 42 results on 08/01/2018. Studies that focused on the usefulness of a single test or intervention were excluded. Additional studies identified through hand search were included. A total of 13 studies involving more than 270,000 patients were included in this review.

Results:
Recent studies on diagnostic problems directly relevant to neuro-ophthalmology include studies of misdiagnosis of posterior communicating artery aneurysms, idiopathic intracranial hypertension (IIH), optic neuritis, optic nerve sheath meningiomas (ONSM), and other neuro-ophthalmologic conditions that underwent inappropriate neuro-imaging. These studies identified misdiagnosis rates >60-70% prior to neuro-ophthalmology referral. Major causes of diagnostic error in these conditions included cognitive failures such as failure to gather appropriate history, pre-established biases, and failure to generate an appropriately broad differential diagnosis, and pitfalls with ancillary tests, including failure to provide appropriate information to neuroradiology or lack of access to neuroradiology interpretation of images. Prior to evaluation by a neuro-ophthalmologist, many patients had unnecessary tests and treatments, including lumbar puncture in 16-80%, brain MRI in 16-34%, and inappropriate treatment in 11-76%. Accurate diagnosis was delayed in the 10% of patients misdiagnosed with IIH. Misdiagnosis contributed to poor visual outcome in 64% of patients in whom a diagnosis of ONSM was delayed.

Conclusions:
Diagnostic error of neuro-ophthalmologic conditions leads to delay in diagnosis and unnecessary, costly and potentially harmful diagnostic tests and treatments. Better access to neuro-ophthalmologic evaluation has the potential to decrease inappropriate utilization of diagnostic tests and treatments and medical harm, and improve patient outcomes.

References: 1. Singh H, Meyer AN, Thomas EJ. The frequency of diagnostic errors in outpatient care: estimations from three large observational studies involving US adult populations. BMJ Qual Saf. 2014;23(9):727-31. 2. Elmalem VI, Hudgins PA, Bruce BB, Newman NJ, Biousse V. Underdiagnosis of posterior communicating artery aneurysm in non-invasive brain vascular studies. J Neuroophthalmol. 2011; 31(2): 103–9. 3. Fisayo A, Bruce BB, Newman NJ, Biousse V. Overdiagnosis of idiopathic intracranial hypertension. Neurology. 2016;86(4):341-50. 4. Stunkel L, Kung NH, Wilson B, McClelland CM, Van Stavern GP. Incidence and causes of overdiagnosis of optic neuritis. JAMA Ophthalmol. 2018;136(1):76-81. 5. Kahraman-Koytak P, Vasseneix C, Bruce BB, Peragallo NJ, Biousse V. Misdiagnosis of optic nerve sheath meningiomasPoster presented at: NANOS 44th Annual Meeting; 2018 March 3-8; Waikoloa Village, HI. 6. McClelland C, Van Stavern GP, Shepherd JB, Gordon M, Huecker J. Neuroimaging in patients referred to a neuro-ophthalmology service: the rates of appropriateness and concordance in interpretation. Ophthalmology. 2012 Aug;119(8):1701-4.

Keywords: High intracranial pressure/headache, Neuroimaging, Optic neuropathy, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Miscellaneous

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Poster 221
Overdiagnosis of 3rd nerve palsy: Diagnostic errors in referrals to two tertiary centers

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Introduction:
Third (3rd) nerve palsy is characterized by some combination of lid, pupil, and motility dysfunction. Causes include microvascular ischemia, compression, and aneurysms. Accurate diagnosis is essential to avoid potentially life-threatening consequences and unnecessary testing. We assessed the frequency of 3rd nerve palsy misdiagnosis based upon referrals to two high volume tertiary care neuro-ophthalmology services, and characterized the specific diagnostic errors.

Methods:
A retrospective review of patients with 3rd nerve palsy among patients identified by searching for variations of "3rd nerve palsy" in scheduling comments for referrals. Patients were excluded from the review if they lacked adequate referral documentation or had a known history of compressive brain mass or aneurysm. Incorrect referral diagnoses were analyzed using the DEER criteria. We also collected and analyzed patient characteristics including past medical history, age, gender, referring provider specialty, and results of diagnostic imaging.

Results:
108 patients were reviewed with 44 meeting inclusion criteria. Among the cohort referred for 3rd nerve palsy, 22% were found to have alternate diagnoses including myasthenia gravis, thyroid ophthalmopathy, decompensated strabismus, and internuclear ophthalmoplegia. The most common reason identified for misdiagnosis was misinterpretation of exam findings. Exam findings of elevation deficit, depression deficit, and exodeviation were key differences in the presentation of patients who were correctly versus incorrectly diagnosed on referral. Failure in hypothesis generation, inadequate physical exam, and failure to weigh clinical history were also reasons for misdiagnosis.

Conclusions:
Inaccurate and misdiagnosis of 3rd nerve palsy were common in referrals to two tertiary neuro-ophthalmology centers. Careful attention to physical exam was the major factor in correct diagnosis of 3rd nerve palsy.

References: None.

Keywords: Ocular Motility, Adult strabismus with a focus on diplopia, Neuroimaging, Vascular disorders

Financial Disclosures: The authors had no disclosures.

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Poster 222
Diagnosis of neurodegenerative disease-related visual symptoms: a survey of practicing neuro-ophthalmologists

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Introduction:
As the population ages, the increasing prevalence of neurodegenerative diseases will have profound implications for health care system. Recognizing visual symptoms from neurodegenerative diseases can be challenging, especially in the presence of co-existent eye diseases.

Methods:
To determine diagnostic patterns and barriers, we surveyed attendees at the "neurodegenerative diseases in neuro-ophthalmology" symposium during the 2017 North American Neuro-ophthalmology Society annual meeting who used the ConferenceIO web-based audience response system and agreed to anonymous extraction of their responses for this project. The 7-question survey included demographics, patient prevalence, and perceived barriers.

Results:
Fifty-five practicing neuro-ophthalmologists (33 ophthalmology-trained, 22 neurology-trained) participated in the survey. Twenty(36%) had <5 years of experience, and 19(32%) had >15 years of experience. Forty-one(75%) reported seeing patients more than five half-day/week. Thirty(55%) reported that at least 1 of 10 or 1 of 20 new patients referred have a prior diagnosis of a neurodegenerative disease. Twenty-one(40%) of the respondents reported attributing visual complaints to higher order effects in at least 25% of patients with a prior diagnosis of neurodegenerative disease vs 5(9%) without a prior diagnosis. For those diagnosed with neurodegenerative disease by the neuro-ophthalmologist, reasons for referral were: unknown cause of visual symptom(56%), to confirm diagnosis and/or treat visual complaint due to neurodegeneration(29%), and functional disorder(5%). Perceived barriers to diagnosing visual dysfunction due to neurodegenerative disease included difficulty making a referral to neuropsychologists or behavioral neurologists(73%), lack of time for in-depth assessment(62%), lack of tools to assess visual dysfunction due to neurodegenerative disease(40%) and lack of knowledge about presenting signs and symptoms(31%).

Conclusions:
Visual symptoms from neurodegenerative disease in patients with and without prior diagnoses of neuro-degenerative disease are evaluated by neuro-ophthalmologists. Lack of time, resources and knowledge are barriers to diagnosis. A larger study is warranted to guide programs to improve diagnosis of visual consequences of neurodegenerative disease.

References: None.

Keywords: Higher Visual Cortical functions, Higher visual functions, Neuro-ophth & systyemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

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Poster 223
The standard swinging flashlight test: reliable or not

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Introduction:
The objective of the study is to assess the reliability of the standard swinging flashlight test (S-SFT) for detection of a relative afferent pupillary defect (RAPD) in comparison to an alternative technique using a direct ophthalmoscope (O-SFT). RAPD is an essential sign to determine the integrity of optic nerve function and is most commonly evaluated by the S-SFT. However, this test has limitations due to technical factors and interrater variability. Inherent patient characteristics such as miotic pupils and dark irises may also limit detection of a RAPD.

Methods:
In this prospective validation tool study, 15 raters distributed in three subgroups according to their level of clinical experience (neurologists, neurology residents and medical students) were asked to identify and grade RAPDs using both the S-SFT and O-SFT. Sensitivity and specificity scores were also established for both techniques. Kappa scores were calculated to represent interrater agreement.

Results:
Fifteen raters evaluated 23 participants for each RAPD testing method. The examined cohort consisted of patients with RAPD (73.9%) and healthy controls (26.1%). The detection rates did not differ significantly between the S-SFT (70.03%) and O-SFT (66.09%). Among the S-SFT evaluations, detection rates for subgroups of medical students and neurologists were 75.29% and 66.74% respectively without statistically significant difference. Detection rates with the S-SFT increased with higher RAPD grades (1+ 61.57%; 2+ 76.56% and 3+ 90%). The correct grading rate for the S-SFT was only 41.75%. Results showed modest sensitivity and specificity scores for the S-SFT with 73.61% and 60.00% respectively. The S-SFT kappa score showed poor interrater agreement (-0.00275).

Conclusions:
This study demonstrated low detection rate and poor interrater agreement for the S-SFT suggesting the need to explore other reliable and easily available methods to evaluate RAPD. The use of the direct ophthalmoscope as an alternative technique did not show improvement in detection rates of RAPD.

References: None.

Keywords: Optic neuropathy, Optic neuropathy, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 224
The effect of refractive induced blur on Goldmann kinetic perimetry.

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Introduction:
To determine the effect of induced blur on Goldmann kinetic perimetry.

Methods:
We refracted 3 eyes of three healthy observers to the Goldmann bowl distance (30 cm) to visual acuities of 20/20. Subjects were blurred using plus lenses with a maximum of +7.00 D and reduced by 0.50 D steps until two levels of blur were obtained: 1) The maximum induced blur: the highest plus lens in which the I-1e stimulus is still detected and an isopter can be plotted. 2) The lowest amount of plus lens power in which the I-1e stimulus cannot be detected, thus no isopter is able to be plotted. Two outcomes were obtained from these two points: Outcome 1: the I-1e isopter plot; Outcome 2: the visual acuities measured at the two points of induced blur.

Results:
The results for the two outcomes are as follows: For blur level 1: The isopter plotted showed a constricted I-1e isopter at an induced blur level of +5.42 D (+5.25 D - +5.50 D). The visual acuities measured for this point was an average VA of 20/107 (range of 20/60 - 20/200) For blur level 2: The lowest power in which the I-1e isopter was not detected was at an induced blur of average +6.00 D (+5.75 D to +6.25 D) was associated with visual acuities of 20/169 (range of 20/125 -20/250).

Conclusions:
Refractive blur causes constriction of the I1e isopter at a level up to about 20/100, above this the I1e target may not be seen. Therefore, if the I1e isopter is not seen, the patient's VA is likely worse than 20/100. This may be useful in the setting of non-organic visual loss. Data is currently being collected to increase the sample size of this study.

References: Benedetto, M, and Cyrlin, M. The Effect of Blur upon Static Perimetric Thresholds. 1985. Documenta Ophthalmologica Proceedings Series. Volume 42. Sixth International Visual Field Symposium. May 27-31, 1984. Brenton, R., Thompson, H.S., and Maxner, C. (1989). Crtical Flicker Frequency: A New Look at an Old Test. New Methods of Sensory Visual Testing. New York. Chapter 3. Heuer, D., Anderson, D., Feuer, W. and Gressel, M. (1987). The Influence of Refraction Accuracy on Automated Perimetric Threshold Measurements. Ophthalmology, 94(12), pp.1550-1553. MILES, P. (1951). TESTING VISUAL FIELDS BY FLICKER FUSION. Archives of Neurology And Psychiatry, 65(1), p.3 Phu, J., Khuu, S., Zangerl, B. and Kalloniatis, M. (2017). A comparison of Goldmann III, V and spatially equated test stimuli in visual field testing: the importance of complete and partial spatial summation. Ophthalmic and Physiological Optics, 37(2), pp.160-176.

Keywords: Visual fields, Miscellaneous, Non-organic visual disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 225
Examining referral patterns to neuro-ophthalmologists

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Introduction:
Neuro-ophthalmologists specialize in complex, urgent, vision- and life-threatening problems, diagnostic dilemmas, and management of complex work-ups. Access is currently limited by a relatively small number of neuro-ophthalmologists, and patients may be affected by incorrect or delayed diagnosis of these conditions. We analyzed referral patterns to neuro-ophthalmologists, characterized rates of misdiagnoses and delayed diagnoses in patients referred, and identified characteristics of referrals likely to benefit most from neuro-ophthalmologic evaluation.

Methods:
Retrospective chart review of 300 new patients seen over 45 randomly-chosen days between 06/2011-06/2015 in one tertiary care neuro-ophthalmology clinic. Date range was chosen to utilize comprehensive paper charting. Demographics, distance traveled, time between onset and consultation, time between appointment request and consultation, providers seen before referral, unnecessary tests before referral, referral diagnoses, final diagnoses, and impact of the neuro-ophthalmologist on outcome were collected.

Results:
Patients traveled a median 36.5 miles (IQR:20-85). Median time from onset was 210 days (IQR:70-1100). Median time from referral to visit was 34 days (IQR:7-86), with peaks at one week (urgent requests) and 3 months. 82% (247/300) were complex/very complex. 81% (242/300) were appropriate referrals. Median number of previous providers seen was 2 (IQR:2-4; range:0-10). 40% (119/300) were misdiagnosed; 49% (147/300) were at least partially misdiagnosed; 7% (22/300) had unknown diagnoses. Women were more likely to be at least partially misdiagnosed—57% (87/153) versus 35% (39/112) of men. Mismanagement or delay in care was present in 28% (85/300), unnecessary tests in 19% (56/300), unnecessary consultations in 22% (65/300), and imaging misinterpretation in 5% (16/300). In 59% (178/300) neuro-ophthalmologists provided a diagnosis and directed treatment, and in 21% (62/300) neuro-ophthalmologists played a major role in preserving vision/preventing life-threatening complications/avoiding harmful treatment.

Conclusions:
Many referrals to neuro-ophthalmologists were delayed and misdiagnosis prior to referral was common. Neuro-ophthalmologists frequently prevented vision and life-threatening complications, bolstering advocacy efforts in support of our specialty.

References: 1. Kohn, Linda T., Janet Corrigan, and Molla S. Donaldson. To Err Is Human: Building a Safer Health System. Washington, D.C.: National Academy Press, 1999. 2. Makary MA, Daniel M. Medical error-the third leading cause of death in the US. BMJ. 2016;353:i2139. 3. Berner ES, Graber ML. Overconfidence as a cause of diagnostic error in medicine. Am J Med. 2008;121(5 Suppl):S2-23. 4. Newman-Toker DE, Makary MA. Measuring diagnostic errors in primary care: the first step on a path forward. Comment on "Types and origins of diagnostic errors in primary care settings". JAMA Intern Med. 2013;173(6):425-6. 5. Singh H, Meyer AN, Thomas EJ. The frequency of diagnostic errors in outpatient care: estimations from three large observational studies involving US adult populations. BMJ Qual Saf. 2014;23(9):727-31. 6. Zwaan L, Schiff GD, Singh H. Advancing the research agenda for diagnostic error reduction. BMJ Qual Saf. 2013;22 Suppl 2:ii52-ii57. 7. Graber ML. The incidence of diagnostic error in medicine. BMJ Qual Saf. 2013;22 Suppl 2:ii21-ii27. 8. Graber ML, Franklin N, Gordon R. Diagnostic error in internal medicine. Arch Intern Med. 2005;165(13):1493-9.

Keywords: Miscellaneous

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Poster 226
The diagnostic value of MRI for ophthalmologic emergencies

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Introduction:
There is a concern about the overuse of MRI in emergency services. We report the experience of a tertiary ophthalmology centre with neuro-ophthalmology specialization that benefits from a unique organization with an ophthalmology emergency service (OES), a stroke unit and an MRI working 24h a day.

Methods:
We reviewed all charts of patients who underwent an MRI prescribed at OES during 6 months. We analysed the MRI indications, the suspected and final diagnoses and their concordance to assess the MRI relevance and its contribution to the diagnosis.

Results:
422 of the 17690 patients who consulted at OES underwent an MRI. Out of these 422 cases, the reasons for consultation were visual loss (119 cases), transient visual symptoms (101), diplopia (69), visual field abnormalities (43), or another cause (90). Suspected and final diagnoses were concordant in 304 cases (72%). In case of discrepancy (118 cases, 28%), MRI helped to correct the diagnosis either by rejecting the suspected diagnosis (92 cases) or by finding unexpected positive MRI signs in (26 cases). In 36 patients (8%) in total, MRI revealed an unexpected diagnosis which could be life threatening (17 cases) or led to some specific care in the other cases. 39 IRM had questionable indications and only 10 MRI could be considered as useless. 4 MRI were misinterpreted with 1 missed stroke and 4 false positive MRI that did not change the patients' care. The final diagnoses were oculomotor palsies (48 cases), optic neuritis (41), transient ischemic accident (41), migraine with aura (37), stroke (28), central retinal artery occlusion (26) or another diagnosis (201).

Conclusions:
In most cases, the MRI indication is relevant and confirms the suspected diagnosis. MRI at OES allows the diagnosis of life threatening or treatable diseases unsuspected by the ophthalmologic examination in 8% of our patients.

References: None.

Keywords: Neuroimaging, Optic neuropathy, Stroke Trauma, Ocular Motility, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 227

Inter-observer variability of vertical strabismus measurements using alternate prism cover testing and single Maddox rod

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Introduction:
Reliability of vertical strabismus measurements play an essential role in successfully relieving patient diplopia using both surgical and non-surgical techniques. The purpose of this study was to assess inter-examiner variability using the objective alternate prism cover test (APCT) and the subjective single Maddox rod (SMR) at near and distance fixation.

Methods:
Thirty-nine patients with vertical strabismus completed near (1/3m) and distance (6m) measurements using both methods (APCT and SMR). Each participant was examined by a neuro-ophthalmologist and/or orthoptist. The second examiner was blinded to the measurements of the first examiner. Pearson's correlation coefficient (PCC) and intraclass correlation coefficient (ICC) were used to assess reliability. Paired t-tests were used detect differences among measurement variables.

Results:
There was a strong overall positive linear relationship between examiners, APCT and SMR methods, and distances at which these methods were performed (PCC of 0.81, 0.86 and 0.83, respectively). More specifically, SMR testing had better reliability than APCT (ICC of 0.84 versus 0.77). Within each method, distance fixation yielded higher reliability than near fixation (ICC of 0.832 versus 0.812). Paired t-tests confirmed no statistically significant differences between examiners. There were statistically significant differences between methods with SMR having larger angle measurements than APCT (p-value = 0.015, 95% CI: -1.073, -0.119). Specifically, SMR demonstrated statistically significant larger measurements at near (p-value = 0.003, 95% CI: -1.627, -0.347) but not at distance. Further, overall strabismus measurements were higher at distance than near (p-value = 0.024, 95% CI: -1.138, -0.08).

Conclusions:
SMR testing, as compared to APCT, has less inter-observer variability when measuring vertical strabismus. Therefore, in addition to using APCT, clinicians assessing vertical strabismus on serial exams may benefit from performing SMR, particularly when the exams are performed by different providers.

References: None.

Keywords: Adult strabismus with a focus on diplopia, Ocular Motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 228
Feasibility of a non-mydriatic fundus camera in an outpatient neurology clinic

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Introduction:
Although ocular funduscopic examination is an integral part of the neurologic examination, it is rarely performed in outpatient neurology clinics. We evaluated the feasibility and utility of a non-mydriatic fundus camera in this setting.

Methods:
Non-mydriatic fundus photographs were obtained in 208 patients attending a general neurology clinic with chief complaints of headaches or multiple sclerosis as part of a prospective quality improvement project over 5 weeks. Photographs were taken by a neurologist after <30 minutes of training. Time taken to capture images was recorded; ease of fundus photography from the patients' perspective was recorded on a 10-point Likert scale. Quality of the photographs was graded. Fundus photographs were immediately reviewed by two neuro-ophthalmologists and results were communicated to the neurologists who requested them.

Results:
505 fundus photographs were obtained in 206 patients. Photographs were of some clinical value in ≥1 eye in 203/206 (98.5%) patients. Median time to completion of photographs per patient was 2.12 minutes (3% of total clinic time). Median rating for ease, comfort and speed of photography was 9.73/10. 159 (77.1%) patients had normal fundi, 44 (22.35%) patients had abnormal fundus findings, including optic nerve pallor (22;10.7%), swollen/elevated optic nerves (10;5%), glaucoma (6), retinopathy (6). Abnormalities were missed by neurologists in 37/44 patients (84%). 91% (10/11) of neurologists completed the survey. 100% believed that optic disc assessment is part of the neurologic examination. 70% of neurologists rated their confidence for detecting optic nerve pathology with direct ophthalmoscopy as 5-7/10. All neurologists preferred non-mydriatic fundus photographs over direct ophthalmoscopy.

Conclusions:
Using a non-mydriatic fundus camera in an outpatient neurology clinic is feasible, without disrupting patient flow or causing patient discomfort. Findings of optic nerve pallor, swollen/elevated nerves, or normal optic nerves were particularly relevant to these patients seen for headaches or demyelinating disease and helped immediate diagnosis and management.

References: 1. Biousse, Bruce, Newman, Ophthalmoscopy in the 21st Century, Neurology, 90, 167-175, 2018 2. Thulasi, Fraser, Biousse, Newman, Bruce, Non-mydriatic ocular fundus photography among headache patients in an emergency department, Neurology, 80, 432–437, 2013 3. Sachdeva, Newman, Biousse, Bruce, Optic nerve head edema among patients presenting to the emergency department, Neurology, 90, e373-e379, 2018.

Keywords: Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Optic neuropathy, Pseudotumor Cerebri

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Poster 229

Non-mydriatic fundus photograph quality in patients evaluated acutely for transient ischemic attack in three hospitals

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Introduction:
Up to 20% of patients presenting with a transient ischemic attack (TIA) will have a new stroke or cardiovascular event within 90 days. Our study investigates the role of non-mydriatic fundus photography (NMFP) in patients evaluated acutely for a TIA. Here we provide data regarding the quality of fundus photographs obtained in three Emergency Departments (ED).

Methods:
NMFP were obtained from patients evaluated for TIA in three EDs in one large city: one university tertiary care center [#1]; one community hospital [#2]; one county hospital (level 1 trauma center) [#3]. Demographics and photograph quality (1-5;5 optimal) were collected. The eye with the best quality photograph was used for each patient.

Results:
Of the 607 patients approached between 08/2015-09/2018, 346 were enrolled, among whom 335 had NMFP obtained in >1 eye (mean age: 57±14 years; 53% women; 62% black). Patient enrollment by center was: 140 (42%) from #1 (mean age: 58±14;61% women; 44% black), 50 (15%) from #2 (mean age: 51±16 years; 56% women;70% black), 145 (43%) from #3 (mean age: 58±12 years; 44% women; 78% black). Photograph quality was uneven across centers (#1, mean: 4.16±0.94; #2, mean: 4.34±0.8; #3, mean: 3.29±1.05) with the lowest quality at #3 ($p<0.001$). No difference was noted between #1 and #2. Photograph quality was lower among those of black vs. white race (3.64±1.09 vs. 4.17±0.97; $p<0.001$) and with increasing age (-0.2 decrease in quality per 10-year increase of age; $p<0.001$). Gender did not significantly impact quality. Based on multivariate analyses, age, race, and center were independent factors impacting photograph quality, with decreased quality seen with increased age ($p<0.001$), black race ($p=0.005$), and when photographs were obtained at #3 (vs. another center) ($p<0.001$).

Conclusions:
Our study confirms that NMFP of TIA patients is feasible in busy EDs, but variation exists regarding quality based on patient population and center factors.

References: Lamirel C, Bruce BB, Wright DW, Delaney KP, Newman NJ, Biousse V. Quality of nonmydriatic digital fundus photography obtained by nurse practitioners in the emergency department: the FOTO-ED study. Am J Ophthalmol. 2012;119:617–624.

Keywords: Vascular disorders, Miscellaneous, Stroke Trauma

Financial Disclosures: The authors had no disclosures.

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Poster 230
Learning pupillary examination using the Advanced Pupil Simulator among medical students and residents

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Introduction:
We recently designed a virtual reality-based application, the Advanced Pupil Simulator ® (APS), for training students and residents in performing pupillary examination. We report results for trainee self-perceived confidence and competence to perform pupillary examination after proctored training using the APS.

Methods:
145 trainees (126 first-year medical students, 15 neurology and 4 ophthalmology residents) completed pupillary examination training as part of a Clinical Skills Session. All trainees reviewed an online power-point module and practiced pupillary examination in groups of 3 assigned to the APS and expert faculty for 30 minutes. All trainees completed a Likert-type questionnaire (1 = not confident, 5 = very confident) before and after the session to assess confidence in performing pupillary examination. All trainees were objectively assessed for knowledge, comprehension, application and analysis by the faculty using test mode on the APS. Differences in pre-and post-training confidence was tested using Wilcoxon sign rank test. Group differences in objective scores were tested using Fischer's exact test.

Results:
97% (122) students and 52% (10) residents reported improved confidence in performing pupil examination following training on APS. 80% (101) students and 89% (17) residents were able to correctly list and demonstrate all steps in pupillary examination. 77% (97) students and 74% (14) residents correctly identified relative afferent pupillary defect (RAPD) while 88% (111) students and 95% (18) residents correctly identified Horner's syndrome. 97% (123) students and 95% (18) residents correctly used appropriate pharmacological drops to confirm Horner's pupil. Post training, students reported improved confidence in identification of all 5 pupillary abnormalities (p=0.00), while residents reported improved confidence in diagnosing Adie pupil (p=0.00) and using pharmacologic agent to confirm Horner's pupil (p=0.00).

Conclusions:
All trainees showed improved confidence and competence in pupillary examination after using the APS. Virtual-reality based practical training can shorten time to competency for critical medical examination techniques.

References: None.

Keywords: Miscellaneous, Pupils Retina

Financial Disclosures: The Advanced Pupil Simulator was designed by the coauthors (Sachin Kedar and Deepta Ghate) and is a licensed technology through EON Reality Inc.

Grant Support: Proof of Concept Grant through the Nebraska Research Initiative.

Poster 231

Use of Electro-oculography as a Switch for Computer Assisted Communication in patients with Locked-in Syndrome

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Introduction:
Computer assisted communication devices for patients with severe motor deficits require some form of "switch" activated by the patient to indicate their desired response. Typically these Assistive Technology (AT) systems have used electromyographic signals and eye-tracking to measure or record a response. However, in end-stage or severe neurological disease, patient may not have adequate motor nerve responses nor reliable control of visual fixation. Patient observation revealed that horizontal or vertical voluntary saccades are often preserved late in disease processes. We hypothesised that electrooculography (EOG) could be used to record a voluntary response and control AT.

Methods:
A pre-existing electromyographic (EMG) recording device was modified to detect EOG signals by altering sensitivity, bandwidth, and sampling rates. Different electrodes were tested to find the smallest and most comfortable for long term wear on the eyes. Proof of concept testing was done using 10 normal subjects. The system was then tested on 3 patients with severe locked-in syndromes (motor neuron disease and Guillan-Barre syndrome).

Results:
Testing with normal subjects confirmed that EOG signals could reliably be detected with the system design. Modifications were made through the testing process to improve signal to noise ratio, for example shortening electrode leads to reduce electrical noise and interference. The signal detected had characteristics of an EOG and was distinguishable from orbicularis oculi EMG. EOG responses could be detected in the three test patients. All patients were able to generate adequate EOG signals to control a computer communication device, when all other standard forms of computer control failed.

Conclusions:
The concept of using EOG for communication in end-stage locked-in patients shows promising early results. This provides a form of communication in severe neurological disease, including interfacing with existing AT, with potential to significantly improve quality of life for patients, their carers and family.

References: None.

Keywords: Neuro-ophth & systyemic disease (eg. MS, MG, thyroid), Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Higher visual functions, Ocular Motility, Miscellaneous

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Grant Support: None.

Poster 232
MULES on the Sidelines: A Vision-Based Assessment Tool for Sports-Related Concussion

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Introduction:
The Mobile Universal Lexicon Evaluation System (MULES) is a test of rapid picture naming under investigation. Measures of rapid automatic naming (RAN) have been used for over 50 years to capture vision-based aspects of cognition. MULES was designed as a series of 54 grouped color photographs (fruits, random objects, animals) that integrates saccades, color perception and contextual object identification. Recent changes to the MULES test were made to improve ease of use on the sidelines, including re-sizing to a laminated 8.5x11-inch double-sided version. We examined feasibility for testing of the revised MULES in youth, collegiate and professional athletes for pre-season baseline testing and for sideline post-injury assessment.

Methods:
Our study teams administered the MULES to youth, collegiate and professional athletes during pre-season baseline testing. Sideline post-injury time scores were compared to pre-season baseline scores among athletes with concussion to determine degrees and directions of change.

Results:
Among 681 athletes (age 17±4 years, range 6-37, 38% female), average test times at baseline were 41.2±11.2 seconds. The most common sports were ice hockey (23%), soccer (17%) and football (11%). Age was a predictor of MULES test times, with longer times noted for younger participants ($P<0.001$, linear regression). Consistent with other timed performance measures, significant learning effects were noted for the MULES during baseline testing with trial 1 test times (49.1±13.0 seconds) exceeding those for trial 2 (41.3±11.2 seconds, $P<0.0001$, paired t-test). Among 15 athletes with concussion during the sports seasons (age 18±3 years) all showed prolongation (worsening) of MULES scores from their best pre-season baseline (median 11.4 seconds, range 0.6-164.2, $P=0.01$, Wilcoxon signed-rank test).

Conclusions:
The MULES test is feasibly administered by non-medical personnel among athletes within organizations ranging from recreational leagues to high schools to college teams. Within this diverse athlete cohort, the MULES shows evidence of capacity to identify athletes with sports-related concussion.

References: 1. Cobbs L, Hasanaj L, Rucker JC, Galetta SL, Balcer LJ, Mobile Universal Lexicon Evaluation System (MULES) test: a new measure of rapid picture naming for concussion, J Neurol Sci372:393-8, 2017. 2. Akhand O, Galetta MS, Cobbs L, Hasanaj L, 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 387:199-204, 2018. 3. Seay M, Akhand O, Galetta MS, Hasanaj L, Balcer LJ, Mobile Universal Lexicon Evaluation System (MULES) in MS: evaluation of a new visual test of rapid picture naming. J Neurol Sci 394:1-5, 2018. 4. Akhand O, Rucker JC, Hasanaj L, Galetta SL, Balcer LJ, History and future directions of vision testing in head trauma. J Neuro-Ophthalmol, 2018 [Epub ahead of print].

Keywords: Higher visual functions, Ocular Motility, Neuro-ophth & systyemic disease (eg. MS, MG, thyroid), Stroke Trauma, Miscellaneous

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Poster 233
OCT Diagnosis of Ocular Torsion

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Introduction:
Measurement of ocular torsion in patients with strabismus assists in the differential diagnosis and management. Conventionally, the double Maddox rod test (DMRT) and dilated fundus photography are used to measure ocular torsion (1,2). DMRT depends upon reliable patient response, while dilated fundus photography requires additional time for dilation and analysis. Heidelberg optical coherence tomography (OCT) infrared images provide an assessment of torsion as a disc foveal angle (DFA) and can be easily obtained without dilation. However, this has not been clinically validated. A previous case report describes a method for estimating torsion using OCT images but provides no comparisons to measurements found on DMRT or fundus photography (3). The aim of this study is to describe the correlation between DMRT, fundus photography, and OCT methods of measuring torsion.

Methods:
In an IRB approved prospective study, patients with torsion are being enrolled and compared to normal young healthy controls without strabismus. The subjective measurements were obtained with DMRT and objective with undilated OCT and dilated fundus photographs. Lastly, we compared the OCT measurements to the two other methods.

Results:
Our preliminary results in two patients showed good concordance in The subjective measurements of torsion between the two objective methods. Both patients had an acquired hypertropia due to brain stem infarction consistent with skew deviation. Both OCT images and fundus photos demonstrated conjugate ocular torsion. The first patient had consistent subjective measurements on DMRT, while the second patients reported less torsion on DMRT. None of the 5 controls enrolled showed significant torsion by any method.

Conclusions:
OCT images have the potential of being an accurate tool for measuring the fundus ocular torsion. Given the ease of performing OCT, this could be a complementary tool to DMRT providing objective evidence of torsion without dilation.

References: 1. Kushner BJ, Ocular torsional movements in humans with normal and abnormal ocular motility: Part II--Subjective observations, J Pediatr Ophthalmol Strabismus, Jan-Feb;23(1):4-11, 1986. 2. Jethani J, Dave P, A technique for standardizing disk foveal angle measurement, J AAPOS, Feb;19(1):77-8. doi: 10.1016/j.jaapos.2014.08.015, 2015. 3. Sophocles Sophocleous, Use of optical coherence topography for objective assessment of fundus torsion, BMJ Case Reports, doi:10.1136/bcr-2016-216867, 2017.

Keywords: Ocular Motility, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 234
A simple and inexpensive techniques of documenting and video-recording ocular motility and nystagmus

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Introduction:
Frenzel goggles are a diagnostic tool used for the evaluation of nystagmus. These goggles include a high-powered (+20 diopters) lens in front of each eye and side-illumination system. The high-power lenses serve 2 functions; interfering with fixation (which may suppress nystagmus) via fogging the eyes, and providing the examiner with adequate magnification of the eye to better visualize nystagmus. It is a common practice to utilize Frenzel goggles along with a video camera to document nystagmus for diagnosis, documentation and monitoring of nystagmus especially after interventions such as medications and/or extraocular muscle surgery. Although Frenzel goggles are helpful while examining nystagmus, they have the limitations of bulkiness, high-cost and limited availability.

Methods:
The author presents a simple, low cost, easily reproducible method of examining and video recording nystagmus utilizing Goggle Cardboard goggles. Google Cardboard is a virtual reality platform developed by Google for use with a head mount for a smartphone. Users can either build their own viewer from simple, low-cost components using specifications published by Google, or purchase a pre-manufactured one typically for less than $10. These Cardboard goggles utilize 22.5 Diopter lenses as a near add to allow viewing the smartphone screen. The commonly available goggles can be easily modified via attaching a couple of keychain LED flashlights to provide diffuse illumination of each eye behind each lens. Additionally, a smart phone can be attached to the goggles to perform video recording.

Results:
The proposed technique was used to examine and video-record different patterns of nystagmus.

Conclusions:
This modified device is compact, light weight, widely available and extremely affordable. Additionally, the goggles have the built-in ability to attach a smart phone with the camera facing the eyes to provide stable video recording by eliminating the examiners hand tremors and patient head movement as a source of motion artifacts.

References: 1- Serra, A., & Leigh, R. J. (2002). Diagnostic value of nystagmus: spontaneous and induced ocular oscillations. Journal of Neurology, Neurosurgery & Psychiatry, 73(6), 615-618. 2- Strupp, M., Fischer, C., Hanß, L., & Bayer, O. (2014). The takeaway Frenzel goggles A Fresnel-based device. Neurology, 83(14), 1241-1245. 3- Goggle Cardboard. https://www.google.com/get/cardboard/.

Keywords: Nystagmus, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

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Grant Support: None.

Poster 235
Reflex Upper and Lower Eyelid Movement in Response to Light Stimuli

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Introduction:
In response to a light stimulus, a reflex orbicularis contraction of the upper and lower eyelid occurs in proportion to light intensity. Our purpose was to determine if the photic blink reflex can be used as an objective, clinical measure. To initiate our understanding of this underutilized reflex, we compared the photic eyelid reflex to the pupil light reflex in the same eyes across subjects. We hypothesized that the percent change in fissure narrowing will correlate with the percent change in pupil contraction for the same light stimulus. We also hypothesized that oculosympathetic deficits to Mueller's muscle and the iris dilator muscle would result in deficits in reflex widening of the palpebral fissure correlating to reflex dilation of the pupil.

Methods:
Binocular computerized videography was used to simultaneously record right and left, upper and lower eyelid position, limbus border and pupil size in response to 4 second, 1000 lux white light pulses, repeated 4 times. Video frames were analyzed using a custom, graphic user interface software program to track the movement of the upper and lower eyelid positions. 12 patients with Horner syndrome and 10 age-matched normal subjects were studied. Reflex dilation was enhanced by median nerve stimulation after cessation of the light stimulus.

Results:
The percent narrowing of the palpebral fissure in response to light significantly correlated with the percent pupil contraction. After termination of a light stimulus, the reflex widening of the palpebral fissure was reduced in eyes with sympathetic denervation.

Conclusions:
The reflex contraction of the orbicularis oculi in response to light and the reflex widening of the palpebral fissure due to Mueller muscle sympathetic activation have the potential for clinical use to assess both afferent and efferent defects.

References: None.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 236
Validation of a Portable Pupillometer and Effect of Dark Adaptation

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Introduction:
Quantitative pupillometry may offer advantages over the qualitative clinical pupil exam. However, commercial devices that provide this metric are cumbersome, expensive, and require operator expertise, or are not customizable. Our goal is to configure and validate the use of a portable device to perform quantitative pupillometry.

Methods:
Light stimulation and pupil recording protocols were implemented using the retEVAL device (LKC Technologies Inc) using the Lua programming language following those used by Park et al including manipulation of duration (1,5,10s) and intensity (5,10,50,100,316 cd/m2) of blue light stimuli. Additionally, the effect of dark adaptation times (1,3,10min) on response to a 1-second bright blue flash (316.2 cd/m2) was evaluated. Maximum pupil constriction(MPC) was measured for all stimuli and post-illumination pupil response (PIPR) was measured for 1s stimuli. Full protocols were completed in 1 eye of 2 healthy subjects.

Results:
Increased stimulus duration did not impact MPC. Increased stimulus intensity was associated with increased MPC with a ceiling effect. PIPR was more pronounced for brighter stimulus These results are similar to those reported by Park et al. 1 min dark adaptation was associated with smaller MPC and PIPR. The 3-minute dark adaptation was similar to 10-minute.

Conclusions:
The portable pupilometer is practical for use in the clinical setting. It measured both maximum and post illumination pupillary responses to a bright blue stimulus to be increased for higher intensity stimuli, consistent with previous results. Reducing dark adaptation compromised measurement amplitudes. Additional studies are needed to establish the normal range of responses and clinical role in diagnosis and monitoring using this device.

References: Park JC, Moura AL, Raza AS, Rhee DW, Kardon RH, Hood DC. Toward a clinical protocol for assessing rod, cone, and melanopsin contributions to the human pupil response. Invest Ophthalmol Vis Sci. 2011 Aug 22;52(9):6624-35. doi: 10.1167/iovs.11-7586. PubMed PMID: 21743008; PubMed Central PMCID: PMC3175993.

Keywords: Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Neuroimaging

Financial Disclosures: The authors had no disclosures.

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Poster 237
Segmental Light Reflex Movements of the Pupil During Contraction and Dilation

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Introduction:
Segmental palsies of the pupil sphincter can be observed with the slit lamp exam in post-ganglionic parasympathetic lesions such as Adie pupil. Segmental palsies of the dilator muscle have not been studied, but irregular, out of round pupils can sometimes be observed during dilation in oculosympathetic lesions. Asynchronous movement of the pupil during contraction and dilation may be an important diagnostic feature parasympathetic and sympathetic lesions. Our purpose was to quantify asynchronous iris movements in normal and abnormal pupils. We hypothesized that autonomic nerve deficits cause asynchronous reflex contractions and dilation and maybe useful in diagnosis and localization.

Methods:
Binocular computerized pupillometry was used to simultaneously record right and left pupil movements in response to 4 second, 1000 lux white light pulses, repeated 4 times. Video recordings were analyzed using a custom, graphic user interface software program to track the movement of the pupil border at each clock hour location relative to the limbal border. 12 patients with Horner syndrome and 10 age-matched normal subjects were studied. Reflex dilation was enhanced by median nerve stimulation after cessation of the light stimulus.

Results:
Asymmetric segmental contractions and dilation were quantified relative to the limbus in normal eyes and in eyes with oculosympathetic deficits.

Conclusions:
Segmental contraction and dilation movements of the iris can be quantified with videography and are present in normal and denervated irides.

References: None.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 238
Comparison of Clinical Features between NMOSD and MS Involving the Brainstem and Cerebellum

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Introduction:
We aimed to define the clinical features and involved structures that aid in differentiation of neuromyelitis optica spectrum disorder (NMOSD) from multiple sclerosis (MS) involving the brainstem and cerebellum.

Methods:
We analyzed the clinical and ocular motor findings, and lesion distribution on brain MRIs in 42 patients with MS (17 men, mean age±SD = 37±12) and 26 with NMOSD (3 men, mean age±SD = 43±15) that were recruited from two university hospitals in South Korea (whole study population). An additional subgroup analysis was also conducted in 41 patients presenting acute brainstem or vestibular syndrome (brainstem syndrome population).

Results:
Logistic regression analysis showed that bilaterality of the lesions [odds ratio (OR) = 9.30 (95% CI = 1.65 – 52.46), p=0.012] and horizontal gaze-evoked nystagmus [hGEN, OR = 10.39 (95% CI = 1.1 – 98.40), p=0.041] were more frequently associated with NMOSD than with MS in the whole study population. In brainstem syndrome population, only hGEN [OR = 44.15 (95% CI = 1.94 –1003.14), p=0.017] was more frequent in NMOSD than in MS. The lesions specific for NMOSD were overlapped in the medial vestibular nucleus (MVN) and nucleus prepositus hypoglossi (NPH) at the pontomedullary junction.

Conclusions:
The presence of hGEN and bilateral lesions involving the MVN and NPH favor the diagnosis of NMOSD rather than MS.

References: None.

Keywords: Nystagmus

Financial Disclosures: The authors had no disclosures.

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Poster 239
Tuning of Binocular Fusion by Ocular Proprioception: A Model

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Introduction:
Proper binocular alignment requires intact visual, motor, and proprioceptive signals. It is hypothesized that the eye position signal in the brain is ocular proprioception. Animal models have revealed that it is an important factor in the development and maintenance of interocular alignment. For example, elimination of this signal by lesioning the ophthalmic division of the trigeminal nerve (V1) leads to the development of strabismus. Experiments that inactivated cortical ocular proprioception caused a reduction in convergence during fixation. The empirically determined horopter known as Panum's area of fusion can help us understand this scientific observation. For any given binocular fixation point, Panum's area in 3D space is defined as the area where all objects appear in stereovision. Objects existing outside of this area appear as double images which the cortical visual disparity system uses for generating new targets to make vergence eye movements. If Panum's area is enlarged, then more objects will be in apparent stereovision and the oculomotor system will no longer be able to execute vergence eye movements to these objects. We present a model where Panum's area is modulated by an eye position signal and that this model's output is compared with monkey vergence data where the eye position signal is inactivated.

Methods:
We provide various vergence stimuli to a MATLAB/Simulink model of convergence. We calibrated our stimuli to have an equivalent dynamic output compared with our empirical data in a monkey. We simulated a lesion to an eye position signal that ended up varying Panum's area.

Results:
Convergence distances were reduced by a lesion in the eye position signal. Our simulations were similar to the under convergences seen in our experimental data.

Conclusions:
Panum's area of fusion is a function that requires an intact eye position signal. Without this signal, Panum's area increases and vergence signal gain is reduced.

References: Enoki, Zhang, Singh, Lomber, Sun. Online Control of Interocular Angles is Mediated by Ocular Proprioception. Society for Neuroscience. (Abstract) 2018. Sun and Goldberg. Corollary Discharge and Oculomotor Proprioception: Cortical Mechanisms for Spatially Accurate Vision. Annual Review of Vision Science. 2016. Das. Strabismus and the Oculomotor System: Insights from Macaque Models. Annual Review of Vision Science. 2016. Hung. Dynamic Model of the Vergence Eye Movement System: Simulations Using MATLAB/Simulink. Comput Methods Programs Biomed. 1998.

Keywords: Adult strabismus with a focus on diplopia, Higher Visual Cortical functions, Higher visual functions, Ocular Motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 240
Eye Movement Fatigibility in Myasthenia Gravis Observed by Video-oculography

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Introduction:
Myasthenia gravis is an autoimmune disease characterized by diplopia, ptosis, myasthenia, and ophthalmoplegia. It features fatigibility that fluctuating symptoms and worsen due to muscle movement. Ancillary tests such as antibody assays, edrophonium test can be used. However, 46% of patients are not adequately diagnosed in early stage, and diagnostic gold standard is not defined until now. We therefore analyzed eye movements in myasthenia gravis using video-oculography.

Methods:
We performed a total of 31 MG patients and 15 control patients. All patients complained of ocular symptoms such as ptosis and diplopia. Patients who were positive for one or more of the ancillary test were selected. Video-oculography was performed on the patients and the range of 20 degree was measured for 6 minutes to measure rapid eye movement, and 20 degree range for 6 minutes to measure slow eye movement.

Results:
Saccadic eye movement, 21 patients showed glissade movement, 21 patients showed quiver movement, and 12 patients showed intrasaccadic fatigue. The gain of smooth pursuit, 16 patients presented fatigibility in the left eye, mean value of pre-post difference was 0.089, in right eye was 18, and the mean value of pre-post difference was 0.066. In control group, there were 6 Glissade movements and 4 Quiver movements. Smooth pursuit gain was decreased in 8 patients; mean gain difference was 0.008 in the left eye, -0.04 in the right eye.

Conclusions:
Eye movements are caused by using different rates of twitch fiber and tonic fiber. If tonic fibers are mainly involved, smooth pursuit movement can be impaired. In the rapid eye movement, glissade movement, and drifting quiver movement will also be observed. Therefore, quantitive analysis of the slow eye movement as well as rapid eye movement in patient with MG who showed the fatigibility, can be helpful in early diagnosis and understanding pathology of pure ocular MG.

References: None.

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

Financial Disclosures: The authors had no disclosures.

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Poster 241
Epidemiology and Features of Ocular Myasthenia

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Introduction:
In up to 85% of patients, the initial presenting symptom of myasthenia gravis (MG) is related to the eyes, which is termed ocular MG.1 A population-based incidence of ocular MG has yet to be reported. The purpose of this study was to establish this incidence, as well as identify determinants of transformation to generalized MG, using a population-based record-linkage system.

Methods:
The medical records of all adults (≥ 18 years) diagnosed with MG (N = 65) from January 1, 1970, through December 31, 2017 using a record-linkage system were retrospectively reviewed for symptoms at onset, results of diagnostic testing, and conversion from ocular to generalized MG.

Results:
The annual incidence of MG was 2.20/100,000, with a mean age at diagnosis of 59 years (SD=17) and 62% male. Thirty-three (51%) patients presented with ocular MG, providing an annual incidence of 1.13/100,000. Seventeen (52%) patients presenting with ocular MG converted to generalized MG at a median time of 25 months, with 71% of those generalizing within two years. Acetylcholine receptor antibody (AchR Ab) seropositivity increased the risk of generalizing, where 67% (16/24) of seropositive patients converted to generalized MG compared to 11% (1/9) of those that were seronegative (HR=7.36, p=0.05). Single fiber electromyography (SFEMG) positivity was also associated with increased risk of conversion with 69% (9/13) of those with a positive SFEMG converting to generalized MG at 5 years compared to 18% (2/11) of patients that had a negative SFEMG (HR, 4.35, p=0.03).

Conclusions:
In our population-based study, approximately 50% of patients with MG presented with isolated ocular involvement, with approximately 50% of these patients converting to generalized MG at some point in the course of their disease. Positive SFEMG and AchR Ab seropositivity at the time of diagnosis increased the risk of conversion to generalized MG.

References: None.

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

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Poster 242
The Study of Extraocular Muscle in Ocular Myasthenia Gravis

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Introduction:
Myasthenia gravis (MG) is a neuromuscular junction disorder that frequently affects the extraocular muscles. Atrophic extraocular muscles have been reported in a few cases with ocular MG. It has been observed particularly in chronic cases with treatment difficulties. A few pathological studies demonstrated small muscle fibers, denervation, and fibrosis. Our aim of this study is to evaluate the size of extraocular muscles in patients with MG.

Methods:
A retrospective chart review of patients with MG evaluated between 2009 and 2018 was conducted. There were two groups, namely, MG and normal control groups. Inclusion criteria for MG were clinical characteristics of MG. They had either acetylcholine receptor antibody seropositivity or abnormal neurophysiological tests (jitters with blocking in single fiber electromyography and decremental responses to repetitive nerve stimulation). Inclusion criteria for normal controls were healthy subjects with normal eye movement. Demographic data were recorded in all cases. Thymoma status was evaluated in the MG group using chest computed tomography (CT) scans. Magnetic resonance imaging (MRI) or CT of the brain and orbits were performed in every case. The thickness of four rectus muscles in both eyes was measured using MRI/CT scans. A summation of the muscle thickness was calculated in each case.

Results:
A total of 41 participants were recruited in the study. There were 20 participants in the MG group aged 17-63 years (mean 42). Acetylcholine receptor antibodies were elevated in 10 cases. There were 21 participants in the controls aged 22-80 (mean 57). The mean summation of the muscle thickness was 23.67 mm (SD 4.07) in the MG group and 34.22 mm (SD 3.34) in the controls. Using unpaired T-test, there was a significant difference in mean thickness summation between the two groups ($p < 0.001$).

Conclusions:
Extraocular muscles in MG appeared thinner than those in normal controls. Its atrophic pattern varied among cases.

References: None.

Keywords: Myasthenia, Ocular Motility

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Poster 243
Slow eye movement fatigability in Myasthenia Gravis

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Introduction:
Myasthenia gravis (MG) is caused by abnormal transmission of neuromuscular junction, and is characterized by fatigability with fluctuating symptoms. To evaluate the fatigability of slow eye movements of MG, we analyzed smooth pursuit eye movements as well as saccadic velocities in the newly diagnosed or known MG using video-oculography (VOG).

Methods:
We performed a total of 31 MG patients and 15 control patients. Patients were undertaken routine MG diagnostic evaluations such as repetitive stimulation test, edrophonium test, and acetylcholine receptor antibody titer as well as oculomotor recordings. Smooth pursuit and saccadic eye movements were recorded with the range of 20 degree for 6 minutes each with horizontal and vertical directions.

Results:
Saccadic eye movement recordings revealed frequent glissades (21/31) and quiver movement (21/31), and intrasaccadic fatigability in 12 patients. Smooth pursuit measurement revealed that monocular fatigability in 16 (on the left) and 18 (on the right) patients which were reflected by gain reduction with pre and post difference. In the control group, however, there were 6 glissade movements and 4 quiver movements.

Conclusions:
Eye movements are caused by using different rates of twitch and tonic fiber. If tonic fibers are mainly involved in myasthenia gravis, smooth pursuit movement can be impaired. In the rapid eye movement, glissade movement, which reaches the target after the sliding movement, causes a hypermetric waveform with an abnormally high velocity to move in the center direction can be observed, and the drifting quiver movement will also be a characteristic of MG patients. Therefore, quantitative analysis of the slow eye movement as well as rapid eye movement in patient with MG who is showed fatigability, can be helpful in early diagnosis and understanding pathology of ocular MG. Changes in smooth pursuits eye movements in MG may reflect the peripheral and secondary central mechanisms were involved.

References: None.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 244
OMGRATS: a new rating scale for Ocular Myasthenia Gravis

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Introduction:
We present the first dedicated rating scale for Ocular Myasthenia Gravis (OMG), developed through an international collaboration between neuromuscular and neuro-ophthalmology experts in OMG. A robust and relevant rating scale for OMG is key in clinical trials for this condition. The rating scales recommended for MG research have a predominant focus on generalized disease, and are insufficiently sensitive for OMG. We developed the Ocular Myasthenia Gravis Rating Scale (OMGRATS) to better assess the fluctuations and severity of signs and symptoms caused by OMG.

Methods:
A prospective study of patients with OMG, attending a neuro-ophthalmology clinic from April 2017 to October 2018. The OMGRATS is comprised of two components: physician-examination (OMGRATS-e) and patient questionnaire (OMGRATS-q). We evaluated the external validity and reliability of OMGRATS, using validated MG ratings scales: Myasthenia Gravis Composite (MGC), Myasthenia Gravis Quality of Life (MG-QOL), ocular questions from the Myasthenia Gravis Impairment Index (MGII).

Results:
233 assessments completed for 112 patients (72M 40F, median age 54, range 18-64y). Good external validity of OMGRATS: good correlation of OMGRATS and MGC (0.61); good correlation of OMGRATS-q and MGII (0.84); good correlation of OMGRATS and MG-QOL (0.61). A higher correlation of OMGRATS and MG-QOL (0.61) compared with MGC and MG-QOL (0.42) suggests that the OMGRATS is better for patients with OMG. Good reliability, intraclass correlation coefficient 0.88. Feedback from examiners and patients indicate the OMGRATS is easy to use.

Conclusions:
OMGRATS is an easy-to-use, valid and reliable rating scale for monitoring the severity of Ocular Myasthenia Gravis.

References: Barnett C, Bril V, Kapral M, Kulkarni AV, Davis AM. Myasthenia Gravis Impairment Index: Responsiveness, meaningful change, and relative efficiency. Neurology 2017; 89: 2357–2364. Burns TM, Conaway M, Sanders DB. The MG Composite. Neurology 2010;74(18):1434-1440 Jaretzki A, Barohn RJ, Ernstoff RM, Kaminski HJ, Keesey JC, Penn AS, et al. Myasthenia gravis: recommendations for clinical research standards. Task Force of the Medical Scientific Advisory Board of the Myasthenia Gravis Foundation of America. Neurology 2000; 55: 16–23. Saleem A, Wong SH. Quantifying the severity of Ocular Myasthenia Gravis. Presented at NANOS 2017 Wong SH, Petrie A, Plant GT. Ocular Myasthenia Gravis: Toward a Risk of Generalisation Score and Sample Size Calculation for a Randomized Controlled Trial of Disease Modification. J Neuroophthal 2016; 36(3):252-8 Wong SH. Rating Scale for Ocular Myasthenia Gravis: A Call to Action! J Neuroophthalmol 2017.

Keywords: Myasthenia, Ocular Motility, Miscellaneous

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Poster 245
Skew deviation: a review of 130 patients

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Introduction:
Data regarding clinical settings, clinical features, clinical outcomes, and imaging abnormalities of skew deviation are based on limited studies.

Methods:
We searched the electronic medical records (EMR) at the University of Michigan for "skew deviation"using the Electronic Medical REcord Search Engine (EMERSE).

Results:
There were 130 patients, including 68 men and 62 women, average age 59.1 years (range 18-89. The leading cause was stroke (69). In 113 (87%) cases, skew was accompanied by other signs of brainstem dysfunction. In 79 (60%) cases, vertical misalignment was comitant. Vertical misalignment ranged between 1 and 30 PD, averaging 5 PD. Blurred vision was a more common symptom than diplopia when mialignment was 4 PD or less. Brain imaging showed a pertinent abnormality in 91 (70%). Prism glasses eliminated diplopia in 51 patients (PD averaging 4.9, range 1-18), failed to eliminate diplopia in 38 patients (vertical misalignment averaged 7.4 PD, range 2-30 PD. All but 9 patients in whom prism glasses failed to eliminate diplopia had an incomitant misalignment or a >10 PD comitant misalignment. Skew deviation had resolved by last follow up in 43 (33%) patients, mostly within 7 months.

Conclusions:
Skew deviation was largely caused by brainstem stroke. In nearly 90% of cases, it was accompanied by other neurologic manifestations of brainstem injury. Vertical misalignment was almost evenly split between comitance and incomitance. Most patients reported diplopia, but when vertical misalignment was small, they reported "blurred vision," not diplopia. Prism glasses generally eliminated diplopia except in a minority of patients who had large or very incomitant misalignment. Skew had resolved at last folow-up in 1/3 of the cohort.

References: None.

Keywords: Adult strabismus with a focus on diplopia, Vestibular, Ocular manifestations of vestibular disorders

Financial Disclosures: The authors had no disclosures.

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Poster 246

Peripapillary vascular network assessment by optical coherence tomography angiography in inflammatory optic neuropathy

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Introduction:
The aim of this study was to assess the peripapillary vascular network through optical coherence tomography (OCT) angiography in patients with a history of inflammatory optic neuropathy (ON), and evaluate their correlation to clinical outcome.

Methods:
A total of 21 patients with a history of inflammatory ON (10 with neuromyelitis optica spectrum and 11 with idiopathic ON) and 18 healthy controls underwent spectral OCT and OCT angiography. The vessel density of a peripapillary region was obtained in scans within the annular zone of 1.2 mm to 3.5 mm diameter around the optic disc head. We compared the peripapillary vessel density to clinical outcomes including visual acuity, visual field and retinal nerve fiber layer (RNFL) thickness.

Results:
The peripapillary vessel density in inflammatory ON group was significantly reduced compared with the healthy control (46.9 ± 6.6 vs 59.7 ± 3.5, $p < 0.001$). NMO group had a significantly lower vessel density than idiopathic group (41.4 ± 4.1 vs 51.5 ± 4.2, $p < 0.001$). The peripapillary vessel density correlated well with visual field defect and RNFL thickness, but not visual acuity.

Conclusions:
Our study demonstrated a reduced peripapillary perfusion in inflammatory ON, and this reduction was closely related to RNFL thickness. Thus, OCT angiography may be useful as a surrogate marker of visual outcomes in inflammatory ON.

References: None.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 247
Retinal Vessel Density in Subjects with Asymmetric Cup-to-Disc Ratio

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Introduction:
Asymmetric cup-to-disc ratio (CDR) has been known as one of features of possible glaucoma. Optical coherence tomography angiography (OCT-A) enables non-invasively detect retinal microvasculature network. The aim of this study is to investigate retinal superficial layer flow density (FD) in subjects with asymmetric CDR.

Methods:
Subjects with vertical CDR >0.2 without visual field deficit nor glaucomatous optic neuropathy were recruited. All participants underwent comprehensive eye examinations and OCT-A scan at the optic nerve head and macular area.

Results:
Twenty-five subjects with asymmetric CDR and 30 normal subjects paricipated into this study. Eyes with bigger CDR (average 0.65) had larger disc area when compared with normal eyes (average CDR 0.30; 2.52 vs. 2.14 mm2; p = 0.003). Although eyes with larger CDR generally had lower FD than normal eyes, significance was only present at whole image peripapillary FD (50.05 vs. 48.15%; p = 0.007) and at superior quadrant of parafoveal region (51.27 vs. 46.36%; p = 0.013). No difference in FD was found between eyes with smaller CDR and eyes with bigger CDR. Six persons with asymmetric CDR (7 eyes) had retinal nerve fiber layer (RNFL) thinning on optical coherence tomography images. The RNFL deficit was present in eyes with larger CDR in 5 persons. However, there was no difference in FD between eyes with or without RNFL defect.

Conclusions:
Despite subjects had asymmetric CDR, retinal microvasculature around the optic nerve head and at macula were similar in both eyes. Eyes with larger CDR showed reduction of peripapillary and superior quadrant of parafoveal FD in comparison with normal eyes. Structural changes in superficial retina seems to proceed to vascular impairment. However, studies with large sample size are needed further to confirm our findings.

References: None.

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

Financial Disclosures: The authors had no disclosures.

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Poster 248
Age-associated reduction in retinal tissue perfusion in a health population

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Introduction:
Tissue perfusion is the passage of the blood flow through the circulatory system of certain tissue, usually referring to the delivery of blood to a capillary bed in the tissue. This study was to determine age-related alterations in the retinal tissue perfusion (RTP) in healthy subjects.

Methods:
Total 148 healthy subjects (age 18 to 83 years) were enrolled and divided into four groups (G1 < 35 years, G2, 35 ~ 49 years, G3, 50 ~ 64 years, and G4, ≥ 65 years). Macular blood flow velocity and flow was measured using retinal function imager (RFI) and macular tissue volume was imaged using ultrahigh resolution optical coherence tomography (UHR-OCT). The RTP was calculated as the blood flow supplying the macular area (diameter = 2.5 mm) divided by the perfused tissue volume of the inner retina from the inner limiting membrane to the outer plexiform layer.

Results:
The RTP reached a peak in G2 and therefore G2 was used as the reference group for comparisons among groups. Compared to G2, G4 had significantly lower RTP and retinal blood flow ($P < 0.05$). After 35 years old, age was negatively related to the RTP ($r = -0.26$, $P < 0.05$) with a decline rate of -0.47% per year.

Conclusions:
This is the first study to reveal the age-related decline of the RTP, which may represent a characteristic pattern of normal aging in the healthy population. The measure may be a good candidate which can be developed as an imaging marker for age-related changes in the microcirculation and microstructure.

References: None.

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

Financial Disclosures: The authors had no disclosures.

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Poster 249
Optic Nerve Head Morphology: Non Arteritic Ischemic Optic neuropathy versus Primary Open Angle Glaucoma

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Introduction:
Non-arteritic anterior ischemic optic neuropathy (NAION) and primary open angle glaucoma (POAG) have different morphological optic nerve head features, despite the common axonal loss and irreversible damage to the optic nerve. Characterising the optic nerve head morphology help us to understand the pathophysiology and in the clinical differentiation of this two entities.

Methods:
Observational cross-sectional study including 42 eyes of 42 patients (14 chronic unilateral NOIAN eyes and 14 moderate to severe POAG eyes matched for age, sex and global peripapillary retinal nerve fiber layer thickness, and 14 eyes of 14 age and sex matched healthy-controls). Bruch's membrane opening area, bruch's membrane opening - minimal rim width (BMO-MRW) and anterior lamina cribrosa depth were assessed using spectral-domain optical coherence tomography with enhanced depth imaging.

Results:
NOIAN and POAG eyes had similar global peripapillary retinal nerve fiber layer thickness (pRNFL) (P =0.42). Both groups had significantly thinner pRNFL thickness compared to healthy eyes (P<0.001). Bruch's membrane opening area was similar between the three groups (P=0.856). The global bruch's membrane opening - minimal rim width (BMO-MRW) in POAG eyes was thinner (179.9 +/- 79.3 µm) compared to both NOIAN (291 +/- 69.5 µm)(P<0.001) and healthy eyes (319.6 +/- 53.6 µm)(P<0.001). Lamina cribrosa depth was shallower in NAION (339.6 +/- 0.8 µm) compared to POAG (520.5 +/-122.0 µm) (P<0.001) and healthy eyes (441.6+/-90.1 µm) (P=0.028).

Conclusions:
At the same average pRNFL thickness the BMO-MRW and the lamina cribrosa depth differ between NAION and POAG eyes. Glaucomatous eyes have thinner BMO-MRW and deeper LC. These findings might be helpful in objective differentiation of these two diseases.

References: None.

Keywords: Optic neuropathy

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Poster 250
Circumpapillary and macular vessel density correlates with neural loss in eyes with band atrophy

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Introduction:
Purpose: to compare the circumpapillary and macular vessel density (cpVD/mVD) of eyes with temporal visual field (VF) defect and band atrophy (BA) of the optic nerve from chiasmal compression and normal controls using optical coherence tomography angiography (OCTA). To verify the association between VD parameters and circumpapillary retinal nerve fiber layer (cpRNFL) thickness, macular ganglion cell complex (mGCC) thickness, and severity of VF loss.

Methods:
Thirty-three eyes of 26 patients with BA and temporal VF defect caused by optic chiasm compression, and 42 eyes of 22 age-matched normal controls. Retinal vasculature was evaluated as cpVD and mVD using a swept-source OCT device (DRI OCT Triton Plusâ, Topcon, Japan). cpRNFL and mGCC were expressed as average and sector thickness around the optic disc and in macular quadrants and hemifields (nasal and temporal). Automated perimetry was performed with both the 24-2 and the 10-2 Humphrey SITA-standard protocols. In both perimetry protocols, VF defect was expressed as mean deviation and deviation from normal in four quadrants and two hemifields. Generalized estimated equations were used for group comparisons. Pearson's correlation coefficients were used to assess relationships between measurements.

Results:
Compared to controls, BA eyes displayed smaller average and sector cpVD values, especially in the nasal and temporal sector, and smaller mVD values in the nasal macular quadrants and nasal retina. cpVD and mVD were strongly correlated with cpRNFL thickness, mGCC thickness, and quadrantic and hemifield VF sensitivity loss.

Conclusions:
cpVD and mVD are significantly reduced in BA eyes compared to controls. The reduction is strongly correlated with retinal neural loss and severity of VF damage in compressive chiasmal lesions. Our results suggest cpVD and mVD reduction on OCTA may serve as a surrogate for retinal neural loss in compressive optic neuropathy and may be useful in the diagnosis and management of these conditions.

References: None.

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

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Poster 251
Role Of RNFL Thickness And RPE/BM Angle On SD-OCT In Diagnosis And Prognosis Of Papilledema

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Introduction:
To evaluate the role of Retinal Pigment Epithelium/Bruch's Membrane(RPE/BM) angle and Retinal Nerve Fiber Layer(RNFL) thickness at Optic Nerve Head(ONH) in papilledema and to compare it with papillitis using spectral domain optical coherence tomography(SD-OCT).

Methods:
It was an observational study done on 30 eyes with papilledema, 15 eyes with papillitis and 80 control eyes. With SD-OCT, we measured average RNFL thickness and the RPE/BM angle at the temporal and nasal borders of the neural canal opening(NCO) in papilledema, papillitis and controls. The angle was measured as positive with inward(towards vitreous) angulation and negative with outward angulation. Follow-up was done at 1,2,3 and 6 months. Outcome measures are RNFL thickness and RPE/BM angle at the temporal and nasal border of ONH.

Results:
Baseline RNFL thickness was higher in both groups when compared to controls.The RPE/BM angle was positive(+8.11±3.13) in 29eyes(96.6%) with papilledema and negative(-1.04±3.27) in 29eyes(96.6%) with papillitis. At 1 month followup, both RNFL thickness($p=0.01$) and RPE/BM angle($p=0.001$) reduced significantly in eyes with papilledema. In eyes with papillitis, there was significant reduction in RNFL thickness($p=0.02$) but not in RPE-BM angle($p>0.05$). Significant difference persisted in RPE/BM angle between the papilledema and papillitis eyes but not in RNFL thickness. RNFL thickness in papilledema cases normalized at 3 months but RPE/BM normalized at 6 months of follow up. The sensitivity and specificity of RPE/BM to detect papilledema were 90% & 89.5% respectively on the nasal side and 80% & 96.8% respectively on the temporal side.

Conclusions:
Eyes with papilledema had positive RPE/BM angulation(nasal more than temporal) and more RNFL thickness in all quadrants when compared to papillitis and controls. After appropriate treatment of raised ICP, the RNFL thickness decreased earlier than the RPE/BM angle. Hence RPE/BM angle can be used to differentiate papilledema from papillitis and monitor the disease activity in papilledema.

References: Kupersmith MK; OCT Sub-Study Committee for the NORDIC Idiopathic Intracranial Hypertension Study Group. Invest Ophthalmol Vis Sci. Published online Nov. 4, 2014. Part I, doi:10.1167/iovs.14-14960; Part II, doi:10.1167/iovs.14-14961.

Keywords: Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, High intracranial pressure/headache, Optic neuropathy

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Poster 252
First Peak Fractal Analysis of Optical Coherence Tomography Angiography in Eyes with Papilledema

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Introduction:
Papilledema is swelling of the optic nerve secondary to increased intracranial pressure. Optical coherence tomography angiography (OCTA) is a technique that allows for fast and non-invasive imaging of the peripapillary microvasculature. Here, we analyze OCTA images of eyes with papilledema using fractals and evaluate the fractal resolution at which self-similarity breaks down as a model for microvasculature.

Methods:
A retrospective study was performed using 49 eyes with papilledema and 40 control eyes. OCTA images consisted of 4.5x4.5mm peripapillary scans obtained with the RTVue XR Avanti (Optovue Inc., Fremont, CA), standardized and binarized using ImageJ (NIH, Bethesda, MD). Fractal dimension (FD) was determined by means of a box-counting algorithm which used box sizes with increasing exponential factor of two using Fractalyse (ThéMA, Besançon Cedex, France). FD was plotted against linear box dimension, and first maximum (first peak) represents the smallest box size resolution before breakdown of self-similarity.

Results:
There was no significant difference in first peak in the papilledema group compared to the control group (8.0 ± 0.0). There was also no significant difference in first peak in each of the papilledema subgroups from Grade 0 to Grade 4/5.

Conclusions:
The first peak, or first maximum of FD as a function of box size, represents the smallest box size resolution prior to loss of uniformity of the vascular pattern's fractal dimension. We previously reported that the first peak occurs at larger box sizes in diabetic retinopathy and primary open angle glaucoma compared to controls, indicating the loss of the vascular patterns' self-similarity at those resolutions, thus suggesting loss of smaller vasculature. In this study, the first peak box size was not significantly different between eyes with papilledema and control eyes, suggesting no detectable loss of peripapillary microvasculature in papilledema regardless of severity.

References: None.

Keywords: Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Optic neuropathy

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Poster 253
Optical Coherence Tomography Artifacts in Optic Atrophy

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Introduction:
Optical coherence tomography is a relative new imaging technique which becoming in a complementary tool in the study of the retinal and optic nerve diseases. Automated segmentation is requiered to automatically process the data and produces images of the retinal layers and optic nerve. However, some artifacts can cause error diagnosis as we observed in 3 patients with optic atrophy where the nerve fiber layer (RNFL) appears normal in temporal and nasal area.

Methods:
Neuropthalmic examination, photos of the fundus of the eye, VEP and spectral domain OCT (Carl Zeiss Meditec, Dublin, CA) to measure the RNFL and ganglion cells; were doing in three patients with optic atrophy.

Results:
Neuropthalmic examination showed no light perception. VEP's were absent. OCT RNFL were normal in temporal and nasal quadrants. Ganglion cells were affected in all cases.

Conclusions:
Optica coherence tomography allowqualitative and quantitative assessment of the RNFL. However, algorithm segmentation can sometimes fail and produce errors in the derived RNFL thickness as we observed in our cases. Previous studies have shown that RNFL thickness can only drop to approximately 30–40 mm despite long-standing optic neuropathies with no light perception vision because of residual glial cells, retinal blood vessels, gliosis, and nonfunctioning ganglion cell axons that contribute to the RNFL. We would expect changes in a generalized RNFL but not in an specific area as we observed. Nasal and temporal quadrants resulted normal; despite having a good resolution and alignment of the scans. Probably, when some segmentation algorithms were built into commercial systems, some details of their design were not resolved. The ganglion cell-inner plexiform layer (GCL-IPL) complex was no affected and it provides a more sensitive measure of neuronal loss. A limitation of our study is small sample size. Careful review and clinical correlation should be established.

References: Chen JJ, Kardon RH: Avoiding clinical misinterpretation and artefects of óptica ccoherence tomography analysis of the optic nerve, retinal nerve fiber lawyer, and glanglion cell lawyer. J Neuro- Oppthalmol; 36: 417-438. 2016. Vermeer KA, Vermeer KA, van der Schoot J, Lemij HG,de Boer JF.:Automated segmentation by pixel classification of retinal layers in ophthalmic OCT images.Biomed Opt Express;2(6):1743-56. 2011

Keywords: Optic neuropathy, Pupils Retina, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Miscellaneous

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Poster 254
Thyroid Eye Disease Related Epiblepharon: A Comparative Case Study

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Introduction:
Neuro-ophthalmologists are often the central care provider for patients with thyroid eye disease (TED). This study describe the clinical features and management of epiblepharon as a manifestation of TED. In a clinic-based population, we compare the frequency and age in Asian and non-Asian patients, and discuss pathophysiologic implications.

Methods:
This is single center study involving the retrospective review of a medical record database that identified 172 adult patients (age 19 to 83) with TED that were consecutively evaluated by one author between December 2015 and July 2018. Diagnosis was based upon clinical assessment as documented in the medical record. The primary outcome measure was the presence of epiblepharon.

Results:
In a cohort of 172 patients (mean age 52; 138 female), three patients with acquired epiblepharon were identified, all of whom were Asian. The proportion of affected Asian patients (3 out of 17, 17.6%) was significantly higher than that of non-Asian patients (0 out of 155, $p<0.001$). Patients with epiblepharon were also significantly younger than those without epiblepharon, 29.7 + 2.1 vs. 48.7 + 13 years of age ($p=0.026$). All three patients underwent surgical correction with lateral canthoplasty and anterior lamellar pre-tarsal fixation with successful outcomes.

Conclusions:
Lower eyelid epiblepharon may occur in TED. In our clinic-based population, this finding was significantly more frequent in Asian patients and in younger patients. Relieving horizontal tension in conjunction with anterior lamella pretarsal fixation is an effective method of correcting TED-associated epiblepharon.

References: None.

Keywords: Graves (systemic disease), Orbit

Financial Disclosures: The authors had no disclosures.

Grant Support: Supported in part by an unrestricted grant to the Wilmer Ophthalmological Institute from Research to Prevent Blindness Inc, New York.

Poster 255
Pattern Standard Deviation in Thyroid Eye Disease and Compressive Optic Neuropathy (TED-CON)

Tavish Nanda[1], Kyle Godfrey[2], Andrea Tooley[2], Michael Kazim[2]

[1]Harkness Eye Institute Columbia University Medical Center, New York, USA, [2]Harkness Eye Institute, New York, USA

Introduction:
Mean deviation (MD) on visual fields (VF) is a measurement of global depression and is commonly used to trend progression/improvement. Pattern standard deviation (PSD) compares all points to the 7th most sensitive value in order to differentiate localized from widespread loss and to account for media opacity. TED-CON is associated with certain focal VF patterns, with 67% demonstrating inferior defects [1]. The objective of this study was to report PSD improvement in TED-CON and the relationship to MD.

Methods:
Pre-treatment and post-treatment retrospective analysis of 128 orbits with TED-CON treated with radiotherapy (RT)+oral steroids. CON was confirmed by decreased visual acuity with either an afferent pupillary defect, VF defect on Humphreys 24-2, or color plate deficit on Hardy-Rand-Rittler pseudo-isochromatic plates. Statistics were calculated using Pearsons Correlation (alpha of 0.05).

Results:
MD (avg. -4.23) and PSD (avg. 3.35) showed a 16% and 14.7% improvement (avg. 93.6 days follow-up), with a moderate correlation of -0.73 and -0.76 pre- and post-treatment between PSD and MD. The correlation in improvement between PSD vs. MD was weaker, R=-0.66. There was a large, 51.1% difference when comparing the degree to which MD and PSD improved, with 28 orbits showing >70% difference. 24/28 had larger changes in favor of MD. On qualitative examination, 6 of the 28 orbits had persistent PSD <1.50 due to the physiologic blind spot.

Conclusions:
In clinical practice, VFs are assessed qualitatively, and changes in focal deficits are usually appreciated. Most studies on TED-CON, however, report values only in terms of MD. While overall percentage improvement in pre- and post MD and PSD were similar and well-correlated, the large 51.1% difference between measures demonstrates that those with MD improvement may not have an equally robust PSD improvement. This supports the presence of localized VF deficits in TED-CON and the possible importance of trending PSD in CON.

References: Choi CJ, Oropesa S, Callahan AB, Glass LR, Teo L, Cestari DM, Kazim M, Freitag SK. Patterns of visual field changes in thyroid eye disease. Orbit. 2017 Jul 4;36(4):201-7.

Keywords: Optic neuropathy, Diagnostic Tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 256
Trochleaectomy: An Effective Treatment of Trochlear Pain in Monocular Patients

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Introduction:
Two distinct entities may produce trochlear pain. Primary trochlear headache is a primary headache disorder causing periocular pain that is worsened with eye movement or palpation of the ipsilateral trochlea. Trochleitis is an inflammatory condition that may be idiopathic or associated with orbital or systemic inflammatory disorders. Patients with trochleitis may improve with system anti-inflammatory medications and an injection of local anesthetic and corticosteroid is used to treat both conditions. Local injections often afford only transient relief, requiring frequent return visits for treatment. We encountered three patients with chronic trochlear pain who were functionally monocular and desired a durable treatment for their pain.

Methods:
We describe the characteristics, surgical technique and outcomes in three patients functionally monocular undergoing trochleaectomy for trochlear pain syndromes.

Results:
Pathological examination of the surgical specimens revealed normal tissue without inflammation. Pain improved in all patients with no recurrence as of their last follow-up visit.

Conclusions:
While systemic anti-inflammatory medications and local steroid injections are effective for most patients with trochlear pain, trochleaectomy is a promising treatment for the occasional patient with chronic trochlear pain who is functionally monocular.

References: Smith JH, Garrity JA, Boes CJ. Clinical features and long-term prognosis of trochlear headaches. Eur J Neurol 21, 575-585, 2014. Yangüela J, Sánchez-del-Rio M, Bueno A, et al. Primary trochlear headache: A new cephalgia generated and modulated on the trochlear region. Neurology, 62, 1134-1140, 2004.

Keywords: Orbit, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 257
Venous Malformations of the Orbit: A Single Center Retrospective Review

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Introduction:
Orbital venous malformations, including orbital varix and cavernous hemangioma, are uncommon low-flow, low-pressure vascular systems with connections to normal vascular anatomy. Clinical symptoms of varix and cavernous hemangioma may be similar, and include proptosis, enophthalmos, bruising, restriction of extraocular motility, vision loss, and periorbital pain. Imaging is an important diagnostic tool in differentiating orbital venous malformations.

Methods:
Retrospective chart review of patients seen by the University of Virginia Neuro-Ophthalmology service coded as "orbital varix" or "hemangioma." Exclusion criteria included non-orbital tumor location, age <18 years, current pregnancy, and incarceration.

Results:
Of 18 cases identified as orbital varix, 11 (61%) were female and 7 (39%) were male, ranging from 21-81 years of age. Of 31 cases identified as cavernous hemangioma, 21 (68%) were female and 10 (32%) were male, ranging 18-92 years of age. Venous malformations overall were often discovered incidentally (n=21, 43%). Altogether, periocular pain (n=16, 32%), diplopia (n=13, 27%), blurry vision (n=12, 24%), and proptosis (n=12, 24%) were the most common presenting symptoms. Hemangioma compared to varix was more often associated with examination findings of resistance to retropulsion (hemangioma n=17, 55%; varix n=2, 11%) and globe displacement (hemangioma n=17, 55%; varix n=7, 39%). Two cases of cavernous hemangioma and zero cases of orbital varix underwent surgical resection.

Conclusions:
Characterization of orbital vascular malformations is not always straightforward, and it is important to differentiate varix from other vascular lesions as diagnosis influences management strategy. Time-resolved Magnetic Resonance Angiography may differentiate orbital varix from hemangioma: varices demonstrate homogenous, dense opacification in venous phase, whereas cavernous hemangiomas demonstrate patchy early enhancement, subsequently filling in more solidly over time. Surgical intervention is often not required, but may be considered for cosmesis, pain, progressive lesion expansion, or in unusual cases of threat to vision.

References: None.

Keywords: Orbit, Neuroimaging, Vascular disorders, Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 258
Superior Ophthalmic Vein Thrombosis: A Clinical Study

Michael Vaphiades[1], Houman Sotoudeh[2], Omid Shafaat[3], Noha Aboueldahab[2]

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Introduction:
Superior ophthalmic vein thrombosis (SOVT) is an extremely rare condition. Few studies have been published regarding the clinical aspects of this condition. We have studied the symptoms, underlying etiologies, treatment, parthogenesis and complications of SOVT and tried to classify this entity based on the etiology, treatment, and prognosis.

Methods:
We reviewed the patients data from a tertiary academic referral center. Each patient with SOVT was then reviewed for symptoms associated with SOVT, underlying etiology, treatment protocol, treatment response, complications, possible pathogens, and final outcome.

Results:
Twenty-four cases of SOVT were included in this study. Overall, 13 cases were diagnosed as right-sided SOVT, 8 of which had simultaneous right-sided cavernous sinus thrombosis (CST). Eighteen cases were diagnosed to have left-sided SOVT, 11 of which had simultaneous left-sided CST.

Conclusions:
SOVT can be secondary to different mechanisms: A) Incidental SOVT (good prognosis, usually self-limited and treated by anticoagulation). B) Post-traumatic and post-surgical SOVT (usually good prognosis which is treated by anticoagulation). C) Septic SOVT (secondary to paranasal sinusitis, orbital cellulitis or a history of paranasal sinus surgery with aggressive behavior, has different organisms in comparison to the usual cause of acute sinusitis, and has a high risk of complication which requires specific antibiotics, anticoagulation and surgery). D) Aseptic SOVT (secondary to inflammatory-autoimmune diseases, coagulopathy, CCF and direct tumor invasion, usually requiring treatment for the underlying condition in association with anticoagulation). The CT and MR imaging studies are vital to the correct diagnosis and management of patients with SOVT. Evidence of sinusitis or a history of functional sinus surgery is critical to the diagnosis of septic SOVT. The antibiotic therapy of the septic SOVT must cover the Staphylococcus (including the Methicillin-Resistant Staphylococcus aureus), Pseudomonas, Streptococcus, and mucormycosis families.

References: None.

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

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.

Poster 259

Influence of optic nerve appearance on final visual outcome in pediatric idiopathic intracranial hypertension (IIH)

Jonathan Micieli[1], Beau Bruce[2], Caroline Vasseneix[2], Richard Blanch[3], Damian Berezovsky[4], Nancy Newman[2], Valerie Biousse[2], Jason Peragallo[2]

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Introduction:

Stratification of IIH patients allows for aggressive treatment to prevent vision loss in high-risk patients. Pediatric IIH (PIIH) patients with higher Frisén grade at presentation are at greater risk for permanent vision loss.[1] In adults with IIH, Frisén grade, but not optic disc hemorrhages (ODH) or cotton wool spots (CWS), was an independent risk factor for worse visual outcomes. We investigated these variables in PIIH patients.

Methods:

50/160 consecutive PIIH patients (100 eyes) ≤16 years were included, and were seen within 30 days of lumbar puncture/medical treatment, with fundus photographs at presentation. Patients' characteristics, visual acuity (VA) and visual field grade (VFG)[2] were recorded. Fundus photographs graded by 3 independent reviewers used a standardized protocol for ODH/CWS,[3] and papilledema grade.[4] Multivariable linear and logistic mixed models evaluated the association between Frisén grade, ODH, CWS and visual outcomes controlling for confounding variables.

Results:

41/100 (41.0%) eyes had ≥1 ODH, 27/100 (27.0%) eyes had ≥1 CWS, 20/100 (20.0%) had ≥1 ODH and CWS. Controlling for Frisén grade,[3] BMI, race, and gender, the presence of ODH/CWS was not associated with worse VA and VFG at initial presentation or final follow-up. Severe ODH at presentation were associated with a worse VA and VFG at initial presentation, but not final follow-up ($p<0.03$). Severe CWS at presentation were associated with worse VFG at final follow-up ($p=0.007$). When controlling for age, BMI, gender, and race, Frisén grade correlated with worse VFG at presentation ($p=0.01$) and worse final VA when controlling for initial VA ($p=0.02$).

Conclusions:

As in adults with IIH, when controlling for the severity of papilledema, ODH and CWS did not provide any additional prognostic value in PIIH patients. Frisén grade was the only independent variable associated with worse visual outcomes at final follow-up.

References: 1. Gospe SM, Bhatti MT, El-Dairi MA. Anatomic and visual function outcomes in paediatric idiopathic intracranial hypertension. Br J Ophthalmol 2016;100:505-9. 2. Bruce BB, Preechawat P, Newman NJ, Lynn MJ, Biousse V. Racial differences in idiopathic intracranial hypertension. Neurology 2008;70:861-7. 3. Wall M, Thurtell MJ, NORDIC IIH Study Group. Optic disc haemorrhages at baseline as a risk factor for poor outcome in the Idiopathic Intracranial Hypertension Treatment Trial. Br J Ophthalmol 2017;101:1256-60. 4. Scott CJ, Kardon RH, Lee AG, Frisen L, Wall M. Diagnosis and grading of papilledema in patients with raised intracranial pressure using optical coherence tomography vs clinical expert assessment using a clinical staging scale. Arch Ophthalmol 2010;128:705-11.

Keywords: Pediatric neuro-ophthalmology, Pseudotumor Cerebri

Financial Disclosures: The authors had no disclosures.

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Poster 260

Idiopathic Intracranial Hypertension in the Pediatric Population: Description of Patients without Optic Disc Edema

Kayla Unsell[1], Andrew Sumnicht[1], Timothy Winter[1]

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Introduction:
Idiopathic intracranial hypertension (IIH) in the pediatric population is defined as elevated opening pressure (>28 cm H20) on lumbar puncture (LP). A recent study has found the incidence of IIH without papilledema (IIHWOP) to be approximately 48% in the pediatric population, which is significantly higher than in adults (incidence of 5%). The aim of this study is to verify the incidence of IIHWOP in the pediatric population.

Methods:
Retrospective chart review from January 2013 to July 2018 was performed. 641 patients with IIH, disc edema, and/or disc drusen were identified. Patients with an opening pressure <28 cm H20, abnormal CSF analysis, venous sinus thromboses, space occupying lesion, or those older than 18 years were excluded. Gender and BMI were recorded, as well as presence of findings typical of IIH on review of neuro-imaging. When available, Heidelberg retinal nerve fiber layer (RNFL) analysis was obtained.

Results:
38 patients met inclusion criteria for IIH. Of these, 5 were without papilledema, an incidence of 13.1%. The mean intracranial pressure of IIHWOP was 29.9 compared to 38.45 cm H20 of the IIH patients with papilledema (IIHWP). Of the 5 patients, Heidelberg RNFL was obtained for 1 patient, revealing 101 microns OU. MRIs of IIHWOP patients were compared with those of IIHWP patients, and findings are described as secondary objectives.

Conclusions:
We found that the prevalence of IIHWOP in the pediatric population is higher than in adults, though much less than previously described. The LP opening pressures were also significantly lower in the IIHWOP patients compared to IIHWP patients, suggesting that higher opening pressures are more likely to cause papilledema. Due to the increased incidence of presentation without optic disc edema, evaluation of IIH in the pediatric population with LP must include opening pressure.

References: None.

Keywords: High intracranial pressure/headache, Neuroimaging, Pediatric neuro-ophthalmology, Pseudotumor Cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 261
Endocrine disorders and neuroimaging manifestations in patients with optic nerve hypoplasia

Bo Young Chun[1], Sook Young Kim[2]

[1]Department of Ophthalmology, Kyungpook National University School of Medicine, Daegu, Korea (Republic of), [2]Department of ophthalmology, The Catholic University of Daegu School of Medicine, Daegu, Korea (Republic of)

Introduction:
To evaluate endocrine disorders and neuroimaging manifestations in patients with optic nerve hypoplasia.

Methods:
Patients who were diagnosed with optic nerve hypoplasia from April 2017 to August 2018 was included in this prospective study. Brain MRI and endocrinology evaluations were done and the results were analyzed.

Results:
Nine patients were included in this study, and they all had bilateral optic nerve hypoplasia. Out of 9 patients, 7 patients demonstrated abnormal findings in Brain MRI, and 5 revealed endocrine abnormalities. Among 7 patients with abnormal findings in brain MRI, 4 patients demonstrated absence of posterior pituitary bright spot, 2 patients; hypoplasia of pituitary gland, 2 patients; corpus callosum hypoplasia, and 1 patient; absence of septum pellucidum. Among 5 patients with endocrine abnormalities, 2 patients showed a decrease in the level of IGF-1, 1 patient; increases in levels of TSH and ACTH, 1 patient; increases in levels of prolactin and ACTH, and 1 patient; a decrease in the level of IGF-1 and an increase in the level if TSH. . Two patients with normal brain MRI revealed normal endocrine results, however, among 4 patients with normal endocrine results, 2 patients revealed absence of posterior pituitary bright spot in brain MRI.

Conclusions:
This study demonstrated high incidence of abnormal findings in brain MRI (78%) and endocrine abnormalities (56%) in patients with bilateral optic nerve hypoplasia Considering these results, exams on endocrinology should be regularly checked in patients with bilateral optic nerve hypoplasia who showed abnormal findings in brain MRI.

References: None.

Keywords: Pediatric neuro-ophthalmology, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 262
Impact of time delay to ophthalmology examination on visual outcomes of pediatric brain tumor patients

Caroline Vasseneix[1], Valerie Biousse[1], Nancy Newman[1], Beau Bruce[1], Jason Peragallo[1]

[1]Emory Eye Center, Emory University School of Medicine, Atlanta, Georgia, USA

Introduction:
Children with primary pediatric brain tumors (PBT) may present with, or develop, abnormal visual function, including visual acuity (VA) loss, visual field defects (VFD), and oculomotor abnormalities(1). Visual deficits may go unrecognized until later in life(2). PBT patients may not undergo ophthalmologic examinations for many reasons including limited access, lack of awareness of PBT effects on vision, difficult pediatric examinations, or concentration on treating the PBT without consideration to secondary effects(3). This study evaluated the impact of delayed ophthalmologic examination following initial PBT diagnosis on diagnosing visual deficits and visual outcomes.

Methods:
84 patients <18yo with PBT underwent complete neuro-ophthalmologic examination. Demographics, date, and details of first and last ophthalmic visit were collected. Tumor diagnosis date, type, location, and treatment modalities were collected. Frequency and timing of detection of visual deficits in relation to the date of the diagnosis of the PBT were evaluated.

Results:
The mean time delay (TD) between PBT diagnosis and first ophthalmic visit was 23 months (range=0.6-34). A shorter TD was associated with VA less than 20/40 in either eye at first visit (p=0.023) and VFD in either eye at final visit (p=0.017). Previously unrecognized VFD were first detected during the neuro-ophthalmology visit in 21/84 (25%) patients at a mean TD of 31 months (3.4-61). Older children were more likely to have a shorter TD to first examination (p=0.001). There was no association between TD and presence of strabismus or nystagmus at first or last visit, tumor type, or treatment modality.

Conclusions:
The mean TD between initial PBT diagnosis and first ophthalmic visit was relatively long (23 months). Patients with VA loss related to PBT underwent earlier ophthalmic examinations, presumably due to complaints of vision loss. However, VFD were diagnosed relatively late after the PBT diagnosis. Younger children may be at risk for a longer TD before ophthalmic examination.

References: 1. Wilne S, Collier J, Kennedy C, Koller K, Grundy R et al. Presentation of childhood CNS tumours: a systematic review. Lancet Oncol, 8, 685–695, 2007. 2. Harbert MJ, Yeh-Nayre LA, O'Halloran HS, Levy ML, Crawford JR. Unrecognized visual field deficits in children with primary central nervous system brain tumors. J Neurooncol,107, 545-549, 2012. 3. Jariyakosol S, Peragallo JH. The Effects of Primary Brain Tumors on Vision and Quality of Life in Pediatric Patients. Semin Neurol, 35, 587-598, 2015.

Keywords: Pediatric neuro-ophthalmology, Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: NIH/NEI core grant P30-EY006360 Knights Templar of Georgia grant.

Poster 263
Clinical Characteristics of Spasmus Nutans and Their Association with Optic Pathway Gliomas/Sellar Masses

Neena Cherayil[1], Grant Liu[2], Robert Avery[2]

[1]Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, USA, [2]Children's Hospital of Philadelphia, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, USA

Introduction:
Spasmus nutans (SN) is a rare childhood neuro-ophthalmologic syndrome that presents in the first year of life and is characterized by shimmering asymmetric nystagmus, torticollis and head-bobbing. SN is typically benign and resolves spontaneously but has also been associated with optic pathway gliomas and sellar masses (OPG/SM). We determined which SN clinical features on history and exam were associated with SN due to OPG/SM versus benign SN.

Methods:
We performed a retrospective review of patients evaluated by our pediatric neuro-ophthalmology service between 1997 and 2017. Patients evaluated for or diagnosed with SN were included. Patients who did not undergo MRI or with incomplete clinical data were excluded. The presence or absence of torticollis and head nodding along with nystagmus characteristics were recorded. Patient demographics, medical history, ophthalmologic exam, and imaging findings were also recorded. Chi-square and logistic regression modelling were used to investigate whether clinical data could independently or in combination predict if a patient had OPG/SM on MRI.

Results:
Sixty-four patients diagnosed with SN met inclusion criteria; thirteen other patients were excluded due to incomplete data. All patients studied had asymmetric shimmering nystagmus on exam. Of the 64 cases of SN, MRI revealed OPG/SM in 4 patients (6.3%) and cerebellar abnormalities in another 9 patients (14.1%). None of the patients with OPG/SM manifested head bobbing, but 33/60 (55%) patients with benign SN had head bobbing. Optic nerve pallor was observed in 3/4 (75%) patients with OPG/SM and 6/60 (10%) patients with benign SN ($p = .01$).

Conclusions:
OPG/SM is a relatively uncommon finding among patients presenting with features of SN. The presence of head bobbing, especially without optic nerve pallor, suggests OPG/SM is unlikely and deferring MRI can be considered in such instances.

References: None.

Keywords: Nystagmus, Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Poster 264
Pediatric Anisocoria- how worried should you be?

Margarita Papadopoulou[1], Ken Kawamoto[2], Dionysios Alexandrou[3], Naz Raoof[1]

[1]Moorfields Eye Hospital, London, United Kingdom of Great Britain and Northern Ireland, [2]University College of London Medical School, London, United Kingdom of Great Britain and Northern Ireland, [3]Moorfields Eye Hospital at City Road, London, United Kingdom of Great Britain and Northern Ireland

Introduction:
Anisocoria is a common referral to the pediatric Ophthalmologist. We reviewed the clinical course of patients seen with anisocoria in the pediatric department of our eye hospital.

Methods:
A retrospective case notes review was conducted for pediatric patients referred with anisocoria, from November 2009 to December 2016.

Results:
179 patients (94 males, 85 females), mean age 6.4 years (range 3 weeks - 16 years) were included. In 9 cases anisocoria was not confirmed. Patients were most commonly referred by their Family Practitioner (n = 65) or their optometrist (n = 55). 55 patients presented to the emergency department, while the others were seen direct in clinic. In 84 cases there was documented parental concern in the notes; in the remaining cases the parents had not noticed a problem. Physiological anisocoria was the commonest diagnosis, affecting 147 patients (82%). The other diagnoses were Horner syndrome (n = 13), 3rd nerve palsy secondary to trigeminal schwannoma (n =1), Adie pupil (n = 1), traumatic mydriasis (n = 4), synechiae (n = 2) and post-laser (1). 12 of the children with Horner syndrome also had ptosis at presentation; 6 of these children had a history of birth trauma. Iopidine testing was performed in 43 children and was positive in 9, with no adverse effects described. The positive predictive value for isolated anisocoria (where anisocoria is the sole presenting complaint without associated symptoms or signs) in predicting physiological anisocoria was 100%.

Conclusions:
Our findings highlight the importance of a careful history and thorough examination in children with anisocoria. The most common diagnosis in children referred with anisocoria was physiological anisocoria; isolated anisocoria was not associated with any more serious pathology in any child in this series.

References: None.

Keywords: Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Wednesday, March 20

6:30 am – 7:30 am	**Breakfast**	**Charleston Ballroom**
6:30 am – 7:30 am	**Breakfast with the Novices**	**Charleston 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	**CME Committee Meeting**	**Veranda D**
6:30 am – 5:30 pm	**Registration/Help Desk**	**5th floor Registration Desk**
7:30 am – 9:30 am	**Retinal Microvascular Changes and Neurologic Disorders** *Moderators: Beau Bruce, MD, PhD and Oana Dumitrascu, MD, Msc* *Invited Speaker: Tien Yin Wong, MD, MBBS, MMED (Ophth), MPH, PhD, FRCSE, FRANZCO, FAMS*	**Red Rock Ballroom**

Retinal microvascular changes are increasingly recognized as diagnostic and prognostic indicators in neurologic diseases. In this session, a comprehensive overview of the epidemiology of retinal microvascular changes in relation to acute and chronic neurologic diseases will be reviewed and established and developing methodologies of evaluating those changes will be discussed. Latest advances and current challenges behind their implementation in routine clinical practice will be addressed.

Upon completion of this session, participants should be able to: 1) describe the diagnostic and prognostic significance of retinal microvascular changes in acute and chronic neurologic diseases, 2) discuss state-of-the-art concepts in hypertensive retinopathy and 3) describe current and emerging technologies for evaluating the retinal microvasculature.

7:30 am – 7:45 am	**Retinal Vascular Changes in Acute Neurological Disorders**, *Beau Bruce, MD, PhD*
7:45 am – 8:25 am	**Current Concepts in Retinal Vascular Imaging**, *Tien Yin Wong, MD, MBBS, MMED (Ophth), MPH, PhD, FRCSE, FRANZCO, FAMS*
8:25 am – 8:40 am	**Retinal Vascular Abnormalities in Cerebrovascular and Neurodegenerative Disorders**, *Oana Dumitrascu, MD, MSc*
8:40 am – 9:00 am	**Artificial Intelligence in Retinal Imaging**, *Tien Yin Wong, MD, MBBS, MMED (Ophth), MPH, PhD, FRCSE, FRANZCO, FAMS*
9:00 am – 9:30 am	**Q&A**

9:30 am – 10:00 am	**Coffee with Exhibitors**	**Charleston Ballroom**
10:00 am – 11:25 am	**Dizziness, Vertigo: Just Tell Me What to Do!** *Moderators: Dan Gold, DO and David Newman-Toker, MD, PhD*	**Red Rock Ballroom**

This session will provide a practical approach to the diagnosis and treatment of patients with vestibular disorders. The session will be separated into two parts – dizziness & vertigo in the emergency department and dizziness & vertigo in the clinic. The most common vestibular disorders in each setting will be discussed, with a particular focus on how the history should be approach in addition to the role of the bedside ocular-motor and vestibular examination.

Upon completion of this session, participants should be able to: 1) describe the HINTS exam and its correct application 2) interpret results of the HINTS exam correctly, including central and peripheral patterns 3) apply the diagnostic Dix-Hallpike and supine roll positional maneuvers 4) interpret positionally-triggered nystagmus to localize the affected canal 5) describe the Triage-TiTrATE-Test method and 6) apply the Triage-TiTrATE-Test method to correctly diagnose the etiology of dizziness or vertigo.

10:00 am – 10:30 am	**Dizziness & Vertigo in the ED - When to Worry, When to Image, When to Admit**, *David Newman-Toker, MD, PhD*
10:30 am – 11:15 am	**Dizziness & Vertigo in the Clinic - When to Test, When to Treat, When to Refer**, *Dan Gold, DO*
11:15 am – 11:25 am	**Q&A**

11:25 am – 12:00 pm **Jacobson Lecture: Leber Hereditary Optic Neuropathy: from Bedside to Bench to Bedside** **Red Rock Ballroom**
Speaker: Nancy J. Newman, MD

This lecture will trace the story of our growing understanding of Leber hereditary optic neuropathy (LHON) from clinical recognition, to the first demonstration of a point mutation in the mitochondrial DNA associated with a human disease, to ground-breaking attempts at gene therapy.

Upon completion of this session, participants should be able to: 1) recognize the various clinical phenotypes associated with Leber hereditary optic neuropathy (LHON) 2) apply the appropriate testing to make the diagnosis of LHON and 3) identify the potential treatment options for LHON.

12:00 pm – 12:30 pm **Announcements/JNO/NOVEL Updates** **Red Rock Ballroom**

12:00 pm – 12:05 pm	**Announcements**, *Valerie Biousse, MD*
12:05 pm – 12:15 pm	**JNO Update**, *Laura Balcer, MD*
12:15 pm – 12:25 pm	**NOVEL Update**, *Kathleen Digre, MD*

12:30 pm – 2:00 pm **Lunch Break**

12:30 pm – 2:00 pm **Research Committee Luncheon** **Veranda AB**

2:00 pm – 3:45 pm **EOM/Vestibular Testing Skills Transfer (advanced registration required- sold out)** **Red Rock Ballroom**
Moderators: Dan Gold, DO and David Newman-Toker, MD, PhD
Facilitators: Shannon Beres, MD, Anthony Brune, DO, Marc Dinkin, MD, Eric Eggenberger, DO, Christopher Glisson, DO, MS, Joao Lemos, MD, PhD, Jorge Kattah, MD, Luis Mejico, MD, Mark Morrow, MD, Mark Moster, MD, Kannan Narayana, MD, MBBS, Sashank Prasad, MD, John Pula, MD, Veeral Shah, MD, PhD, Caroline Tilikete, MD, PhD and Konrad P. Weber, MD

This session will provide a practical ocular-motor/vestibular hands-on experience. With the help of NANOS members with expertise in the field, there will be 8 stations: VOR testing, Positional Testing of Posterior Semicircular Canals, Positional Testing of Horizontal Semicircular Canals, Provocative Testing (nystagmus elicitation), Gaze Testing (ocular alignment, saccades, smooth ocular pursuit, and smooth eye-head tracking), Nystagmus Interpretation, Peds Eye Movement, and Cases.

Upon completion of this session, participants should be able to: 1) perform the HINTS exam (head impulse [VOR], nystagmus [naming and interpretation], test of skew [alignment]) 2) perform other ocular motor (saccades, pursuit, eye-head tracking) and provocative testing (head-shaking) to aid in localization 3) apply the diagnostic Dix-Hallpike and supine roll positional maneuvers with proper technique and 4) select the most appropriate therapeutic maneuver and apply this treatment.

2:00 pm – 3:45 pm **Headache Medicine Update - What a Neuro-Ophthalmologist Needs to Know** **Pavilion Ballroom**

There is a large overlap between neuro-ophthalmology and headache medicine. Advances in the understanding of migraine pathophysiology have evolved from bench to bedside with novel medications and devices for patient care. This session will review relevant migraine pathophysiology, focusing on calcitonin gene-related peptide (GCRP) and anatomic pathways targeted by neuromodulation devices, discuss the evidence of efficacy of agents targeting GCRP and neuromodulation devices in the treatment of migraine and cluster headache, and update attendees on visual snow, eye pain and photophobia.

Upon completion of this session, participants should be able to: 1) describe the role of calcitonin-gene related peptide (CGRP) in the pathogenesis of migraine and cluster headache 2) recommend new treatments and devices to patients as appropriate 3) list ophthalmic and neurologic causes of photophobia and 4) explain the role of intrinsically photosensitive retinal ganglion cells in the pathophysiology of photophobia.

2:00 pm – 2:25 pm	**Who, What, and Where: Insights into Migraine Pathophysiology and New Therapeutic Targets***, Benjamin Frishberg, MD*
2:25 pm – 2:55 pm	**Designer Drugs and Neuromodulation for Migraine and Cluster Headache**, *Deborah Friedman, MD, MPH*
2:55 pm – 3:35 pm	**Clinical Conundrums in Migraine: Eye Pain, Photophobia, and Visual Snow**, *Kathleen Digre, MD*
3:35 pm – 3:45 pm	**Q&A**

3:45 pm – 5:30 pm **Reading an OCT Like We Read an MRI** **Red Rock Ballroom**

OCT is capable of the highest resolution images of the retina and optic nerve clinically available of the eye, yet when clinicians examine its output, they frequently rely upon a few quantitative measures to determine whether the nerve fiber layer or ganglion cell complex is thinning or thickening. Reviewing the automated segmentation, signal strength and centering of the study and how they may compare to prior studies is critical, as is looking at where the retinal vessels enter the disc when trying to understand local nerve fiber layer thickness as the nerve fiber layer follows the retinal vessels embryologically. The examination of the visual field side by side with the OCT of the nerve fiber layer and ganglion cell complex lends authority to conclusions when they reinforce one another. The recognition of papilledema from its OCT appearance and its separation from other causes of disc swelling e.g. drusen,

NAION, optic nerve menigioma and hypotony will be addressed and the importance of the peripapillary RPE Burch's membrane conformation on axial OCTs and the recognition of folds on in face images.

Upon completion of this session, participants should be able to: 1) read an OCT like a radiologist reads an MRI 2) distinguish amongst swollen discs when interpreting an OCT and 3) recognize retinal patterns in an OCT.

3:45 pm – 3:50 pm	**Welcome and Introduction**, *Jeffrey G. Odel, MD*
3:50 pm – 4:30 pm	**Reading an OCT Like We Read an MRI**, *Donald Hood, PhD*
4:30 pm – 5:10 pm	**Transverse Axial / en Face OCT in the Assessment of Optic Disc Edema and Pseudopapilledma***, Patrick A. Sibony, MD*
5:10 pm – 5:25 pm	**Cases***, Jeffrey G. Odel, MD*
5:25 pm – 5:30 pm	Q&A

3:45 pm – 5:30 pm **Worldwide Wonders: Cases Defining the International Language of Neuro-Ophthalmology** **Pavilion Ballroom**

Moderators: Clare Fraser, FRANZCO and Susan Mollan, FRCOphth

In this global community, where travel to and from countries outside America is becoming more frequent, it is increasingly likely that doctors will be seeing patients with diseases that would otherwise not be common in their country or have a different phenotype to those typically seen in one's locality. This session is designed to introduce five conditions where regional differences may make a difference in the recognition or management of the condition.

Each presenter will highlight a challenging case from their practice, update us on the current thoughts of how to diagnose, investigate and manage that condition and highlight regional differences.

Upon completion of this session, participants should be able to: 1) recognize and distinguish five common diseases that affect the central nervous system and eye 2) plan an appropriate series of investigations and evaluate the results and 3) recommend a treatment plan.

3:45 pm – 3:50 pm	**Introduction**
3:50 pm – 4:15 pm	**Optic Neuritis: a Worldwide View**, *Simon Hickman, PhD, FRCP*
4:15 pm – 4:40 pm	**Two Cases from a Tick Country**, *Steffen Hamann, MD, PhD*
4:40 pm – 5:05 pm	**In Vitreous Veritas**, *Pedro Fonseca, MD*
5:05 pm – 5:30 pm	**Non-idiopathic Intracranial Hypertension with Happy Ending**, *Ruth Huna-Baron, MD*

6:30 pm – 12:00 am **NANOS Annual Banquet** **Red Rock and Charleston Ballrooms**

Join colleagues for a fun, casual evening of socializing, dining and dancing at the NANOS Annual Banquet! Dinner will take place in the Red Rock Ballroom, followed by dancing in the Charleston Ballroom. This event is complimentary for registered attendees; guests must purchase tickets for $100 per person. Guest tickets available at the Registration Desk.

RETINAL VASCULAR CHANGES IN ACUTE NEUROLOGICAL DISORDERS

Beau B. Bruce, MD, PhD
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Atlanta, GA

LEARNING OBJECTIVES

1. Name the most common ocular fundus abnormality among headache patients presenting the emergency department.
2. Describe the appropriate management of patients presenting with acute retinal ischemia.
3. Discuss what is known about retinal microvascular findings in the evaluation of suspected transient ischemic attack.

CME QUESTIONS

1. True or False: Optic disc edema was the most common ocular fundus abnormality among patients presenting to an emergency department with headache.

2. True or False: A non-urgent, outpatient work-up is appropriate for the evaluation of a patient who presents with transient monocular visual loss.

3. Which of the following retinal microvascular signs have been associated with a diagnosis of transient ischemic attack vs. non-cerebrovascular acute neurologic disease after controlling for $ABCD^2$ score and the presence of diffusion weighted magnetic resonance imaging abnormalities? (Choose all that apply.)
   A. cotton wool spots
   B. retinal hemorrhages
   C. focal arteriolar narrowing
   D. general arteriolar narrowing

KEYWORDS

1. Stroke
2. Ischemia
3. Headache
4. Retinal microvascular changes

HIGHLIGHTS

There are two acute neurological disorders for which retinal vascular changes are of substantial importance: headache and cerebral ischemia.

Headache

In the emergency department, headache is the fourth most common chief complaint and the most common neurologic complaint.[1] Millions of patients visit an emergency department in the United States for headache each year,[2] and about 3–5% of the general population has visited an emergency department in their lifetime because of a headache.[3] The vast majority of these headaches are primary headaches that only need symptomatic therapy, but 2% of all headaches and 18% of sudden, severe

headaches are suffering from a serious underlying cause of headache such as raised intracranial pressure, subarachnoid hemorrhage, or brain tumor.[2, 4-9]

The Fundus Photography vs. Ophthalmoscopy Trial Outcomes in the Emergency Department (FOTO-ED) study evaluated the ocular fundus findings in 497 patients presenting to the emergency department with headache.[10] Forty-two of these 497 patients (8.5%; 95%CI: 6%–11%) had relevant abnormalities of their ocular fundus: 12 had disc edema, 9 had optic nerve pallor, 6 had grade III/IV hypertensive retinopathy, and 15 had isolated retinal hemorrhages. Of the 34 patients with abnormal ocular fundi who had brain imaging, 14 (41%) had normal imaging studies.

Overall, body mass index ≥35 kg/m^2 (odds ratio [OR]: 2.3, p=0.02), younger age (OR: 0.7 per 10-year increase, p=0.02), and higher mean arterial blood pressure (OR: 1.3 per 10 mmHg increase, p=0.003) were independently predictive of ocular fundus abnormalities. Furthermore, these risk factors were associated with one or more of the specific ocular fundus findings: younger age (OR 3.2 per 10 year age decrease, p=0.002) and BMI ≥35 kg/m^2 (OR 1.3, p=0.045) with optic disc edema; higher mean arterial pressure (OR 1.5 per 10 mmHg increase, p=0.0002) with intraocular hemorrhage or grade III/IV hypertensive retinopathy; and BMI ≥35 kg/m2 (OR 1.5, p 5 0.03) with optic disc pallor. Since secondary headaches generally become more prevalent with increasing age, the association of fundus abnormalities with younger headache patients suggests that ocular fundus examination may help identify a key subset of secondary headaches.

Surprisingly, isolated retinal hemorrhages were the most frequent ocular fundus abnormalities detected in patients with headache (36%). These hemorrhages are most likely attributable to systemic hypertension.[11, 12] When these hemorrhages are combined with the 14% of patients with grade III/IV hypertensive retinopathy, it suggests that about half of the findings in headache patients presenting to the emergency department are attributable high blood pressure. The high proportion of patients with headache associated with systemic hypertension may at first appear contrary to large, well-conducted, population-based studies and the consensus of the International Headache Society that no association exists between mild to moderate hypertension and headache.[5, 13] However, headache is one of the most common presenting symptoms of hypertensive urgencies and other studies have found that more severe hypertension is associated with headache.[14] These findings emphasize that consistent and thorough examination of the ocular fundus can help to detect a treatable underlying cause of headache while also offering an early opportunity for intervention against an important cause of morbidity and mortality.

A brief discussion of migraine and retinal vascular findings provides a remarkable segue to the second topic of cerebral ischemia. Migraine with aura has repeatedly been linked to early mortality from coronary heart disease and stroke,[15-16] and the Atherosclerosis Risk in Communities (ARIC) Study found that middle-aged persons with migraine and other headaches were more likely to have vascular retinopathy signs (e.g., hemorrhages, microaneurysms).[17] As retinopathy signs are more strongly associated with cardiovascular disease than other retinal signs,[18] the retina appears to provide a window into the early vascular pathology, likely occurring systemically, that underlies the increased risk of cardiovascular disease among migraineurs.

Cerebral Ischemia

Acute retinal arterial ischemia, which includes transient monocular vision loss, branch retinal artery occlusion, central retinal artery occlusion, and ophthalmic artery occlusion, is the ocular equivalent of acute cerebral ischemia and is an emergency. Although there are no proven, effective treatments that improve visual outcomes following retinal vascular occlusions, patients with acute retinal ischemia are at high risk of further cardiovascular events and require immediate referral to the nearest certified stroke center for further evaluation of the cause of their current episode and for secondary prevention of future cardiovascular events.[19]

With respect to less dramatic retinal microvascular abnormalities, it is known that they are strongly associated with the long-term risk of stroke, but the value of ocular fundus examination remains less clear in the often difficult differentiation of transient ischemic attack (TIA) from its mimics and the prediction of short-term events following a TIA presentation (e.g., stroke or myocardial infarction within the first few weeks or months after presentation).[20-23] However, ocular fundus abnormalities may represent underlying cerebrovascular injury among patients presenting with neurological symptoms that can assist with differentiation of TIA from its mimics, and acute microvascular fundus abnormalities may have an analogous role to diffusion weighted magnetic resonance imaging (DWI) abnormalities in determining the presence of acute ischemia in the cerebral vasculature.[24]

These hypotheses are supported by the FOTO-ED study, which found that among 257 patients with a presenting complaint of focal neurologic deficits that 81 (32%) had cerebrovascular disease (CVD) and 144 (56%; 95%CI: 50-62%) had retinal microvascular abnormalities. Controlling for the commonly used $ABCD^2$ score and diffusion weighted imaging (DWI) abnormalities, a certain severity of focal arteriolar narrowing increased the odds of clinically diagnosed CVD vs. an alternative cause of the focal neurologic symptom by 5.5 times whereas general narrowing increased the odds by 2.6 times.

When the patients were divided into three groups (stroke, TIA, and non-CVD) based on masked neurologist review and those with stroke were excluded, the presence of retinal microvascular findings significantly improved the discrimination of TIA vs. non-CVD after controlling for the $ABCD^2$ score. If these findings bear out in larger studies, fundus photography could provide valuable assistance in separating TIAs from their mimics in the acute setting. A federally-funded, multi-hospital prospective cohort study designed to further evaluate these findings is in progress and results are expected within the next year.

SUMMARY

Headache and cerebral ischemia are two acute neurologic conditions for which the retinal microvasculature provides valuable information. Surprisingly, it was retinal microvascular changes, likely associated with hypertension, that formed the majority of ocular fundus abnormalities in a group of headache patients presenting to an emergency department. Acute retinal ischemia, i.e., transient monocular visual loss and retinal and ophthalmic vascular occlusions, are stroke equivalents and require immediate evaluation. Although it is known that retinal microvascular abnormalities are strongly associated with the long-term risk of stroke, their utility in the acute evaluation of patients with suspected TIA remains unclear. However, there is evidence that the presence of focal and general retinal arteriolar can assist with differentiating TIA from its mimics and an ongoing study should help further elucidate the potential value of retinal microvascular findings in the evaluation of suspected TIA.

CME ANSWERS

1. False
2. False
3. C, D

REFERENCES

1. Pitts S.R., Niska R.W., Xu J., et al.: National Hospital Ambulatory Medical Care Survey: 2006 emergency department summary, Natl Health Stat Report 1-38, 2008.

2. Lucado J., Paez K., Elixhauser A.: Headaches in U.S. Hospitals and Emergency Departments, 2008: HCUP Statistical Brief #111. Rockville, MD: Agency for Healthcare Research and Quality, 2011.
3. Linet M.S., Stewart W.F., Celentano D.D., et al.: An epidemiologic study of headache among adolescents and young adults, JAMA 261:2211-16, 1989.
4. Goldstein J.N., Camargo C.A., Jr., Pelletier A.J., et al.: Headache in United States emergency departments: demographics, work-up and frequency of pathological diagnoses, Cephalalgia 26:684-90, 2006.
5. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition, Cephalalgia 38:1-211, 2018.
6. Fodden D.I., Peatfield R.C., Milsom P.L.: Beware the patient with a headache in the accident and emergency department, Arch Emerg Med 6:7-12, 1989.
7. Landtblom A.M., Fridriksson S., Boivie J., et al.: Sudden onset headache: a prospective study of features, incidence and causes, Cephalalgia 22:354-60, 2002.
8. Locker T., Mason S., Rigby A.: Headache management--are we doing enough? An observational study of patients presenting with headache to the emergency department, Emerg Med J 21:327-32, 2004.
9. Ramirez-Lassepas M., Espinosa C.E., Cicero J.J., et al.: Predictors of intracranial pathologic findings in patients who seek emergency care because of headache, Arch Neurol 54:1506-9, 2997.
10. Thulasi P., Fraser C.L., Biousse V., et al.: Nonmydriatic ocular fundus photography among headache patients in an emergency department, Neurology 80:432-37, 2013.
11. Bruce B.B., Lamirel C., Wright D.W., et al.: Blood pressure threshold for abnormal ocular fundus findings is lower than expected. Hypertension 59:e8-9, 2012.
12. Henderson A.D., Bruce B.B., Newman N.J., et al.: Hypertension-related eye abnormalities and the risk of stroke. Rev Neurol Dis 8:1-9, 2011.
13. Hagen K., Stovner L.J., Vatten L., et al.: Blood pressure and risk of headache: a prospective study of 22685 adults in Norway, J Neurol Neurosurg Psychiatry 72:463-66, 2002.
14. Gupta V.K.: Systemic hypertension, headache, and ocular hemodynamics: a new hypothesis, MedGenMed 8:63, 2006.
15. Schürks M., Rist P.M., Bigal M.E., et al.: Migraine and cardiovascular disease: systematic review and meta-analysis, BMJ 339:b3914, 2009.
16. Gudmundsson L.S., Scher A.I., Aspelund T., Eliasson J.H., Johannsson M., Thorgeirsson G., Launer L., Gudnason V.: Migraine with aura and risk of cardiovascular and all cause mortality in men and women: prospective cohort study, BMJ 341:c3966, 2010.
17. Rose K.M., Wong T.Y., Carson A.P., et al.: Migraine and retinal microvascular abnormalities: the Atherosclerosis Risk in Communities Study, Neurology 68:1694-700, 2007.
18. Wong T.Y., McIntosh R.: Systemic associations of retinal microvascular signs: a review of recent population-based studies, Ophthalmic Physiol Opt 25:195-204, 2005.
19. Dattilo M., Newman N.J., Biousse V.: Acute retinal arterial ischemia, Ann Eye Sci. Epub ahead of print June 6, 2018.
20. Wong T.Y., Klein R., Nieto F.J., et al.: Retinal microvascular abnormalities and 10-year cardiovascular mortality: a population-based case-control study, Ophthalmology 110:933-40, 2003.
21. Cheung C.Y., Chen C., Wong T.Y.: Ocular fundus photography as a tool to study stroke and dementia, Semin Neurol 35:481-90, 2015.
22. Quinn T.J., Cameron A.C., Dawson J.: $ABCD^2$ scores and prediction of noncerebrovascular diagnoses in an outpatient population: a
case-control study, Stroke 40:749-53, 2009.
23. Nahab F., Leach G., Kingston C., et al.: Impact of an emergency department observation unit transient ischemic attack protocol on length of stay and cost, J Stroke Cerebrovasc Dis 21:673-8, 2012.

24. Easton J.D., Saver J.L., Albers G.W., et al.: Definition and evaluation of transient ischemic attack: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association Stroke Council; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing; and the Interdisciplinary Council on Peripheral Vascular Disease, Stroke 40: 2276-93, 2009.
25. Vuong L.N., Thulasi P., Biousse V., et al.: Ocular fundus photography of patients with focal neurologic deficits in an emergency department, Neurology 85:256-62, 2015.

CURRENT CONCEPTS IN RETINAL VASCULAR IMAGING

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LEARNING OBJECTIVES

1. Interpret basic concepts in hypertensive retinopathy and retinal vascular diseases
2. Define the latest developments and studies of retinal vascular imaging, including retinal vessel caliber quantification using computer software techniques, and new technology such as OCT angiography and artificial intelligence
3. Explain studies correlating retinal vascular imaging with stroke, dementia and other neuro-degenerative and neuro-vascular diseases

CME QUESTIONS

1. How is hypertensive retinopathy classified?
2. What conditions have retinal vascular diseases been associated with?
3. What are the limitations of applying retinal vascular imaging in clinical settings?

KEYWORDS

1. Retinal vascular imaging
2. Hypertensive retinopathy
3. Stroke
4. OCT angiography
5. Artificial intelligence

HIGHLIGHTS

The human circulation is difficult to visualize directly in vivo. The retinal circulation, on the other hand, can be imaged non-invasively with a fundus camera, and the retinal vessels share similar embryological origin, anatomical features and physiological properties with the cerebral circulation. Thus, studying the health of the retinal vessels offers a unique and easily accessible “window” to study early pathways and consequences of major vascular diseases such as stroke and heart disease. Studies over the past decade demonstrate that patients with classic retinal vascular diseases such as hypertensive retinopathy signs have a higher risk of developing a stroke, heart and kidney disease and are more likely to die than persons without these retinal diseases. Advances in computer image analysis have further allowed more precise and objective documentation of subtle changes in the retinal vessels, such as quantitatively measured retinal vascular caliber and tortuosity. New clinic- and population-based studies have demonstrated a strong association between presence of retinal vascular changes with risk of subclinical cerebrovascular diseases, clinical stroke, stroke mortality and other cardiovascular conditions. In some

studies, associations with vascular dementia, cognitive decline and MRI cerebral atrophy have been documented.

New technology using OCT-angiography to measure capillary density may also provide further information regarding cerebral degenerative and vascular diseases. Finally, improved software, such as artificial intelligence (AI) based deep learning algorithms, has further enhanced the possibility of using retinal images as an exciting risk prediction and stratification tool to predict stroke and systemic vascular disease.

SUMMARY

The vasculature in the retina can be viewed directly and non-invasively in vivo, offering a unique perspective of the human microvasculature, and therefore, the ability to understand early changes, processes, pathways and consequences of systemic vascular diseases. In the past 20 years, advances in high-resolution digital retinal photography and automated or semi-automated computer image software have been applied to measure and quantify a variety of retinal microvascular parameter, including retinal arteriolar and venular caliber, tortuosity, branching patterns and fractal dimensions. Clinical and epidemiological studies show that hypertension is strongly associated with many of these retinal microvascular changes. Studying changes of retinal blood vessels may provide new understanding the pathogenesis of cerebral diseases, such as stroke, dementia and other neurodegenerative diseases. Studies have shown that a wide range of retinal vascular characteristics, including quantitatively measured retinal vessel caliber and retinal fractal dimension, and other focal retinal signs, including arterio-venous nicking, retinal hemorrhages, microaneurysms and cotton wool spots, are associated with subclinical MRI cerebral infarcts, and predict incident clinical stroke events and stroke deaths, independent of traditional systemic risk factor such as hypertension and diabetes. Advances in OCT-angiography technology have now made it possible to document and study early capillary changes in the retina. This course will discuss new research findings, and possible clinical implications of using retinal imaging techniques as a means to detect early dementia, stroke and cerebrovascular disease.

CME ANSWERS

1. Hypertensive retinopathy is classified as mild (retinal arteriolar changes only), moderate (arteriolar changes with retinal hemorrhages hard exudates, cotton wool spots) and severe (with optic disc and macular edema).
2. Stroke, dementia, heart diseases, cardiovascular mortality
3. First, need fully automated imaging for ease of use in clinical settings. Second, retinal vascular imaging must show improved performance compared to assessment of traditional risk factors. Third, application of retinal vascular imaging technology requires more real-world testing in different scenarios.

REFERENCES

1. Wong TY, Klein R, Klein BE, et al. Retinal microvascular abnormalities and their relationship with hypertension, cardiovascular disease, and mortality. Surv Ophthalmol 46(1):59-80, 2001.
2. Wong TY, Klein R, Couper DJ, et al. Retinal microvascular abnormalities and incident stroke: the Atherosclerosis Risk in Communities Study. Lancet 358(9288):1134-40, 2001.

3. Wong TY, Klein R, Sharrett AR, et al. Retinal arteriolar narrowing and risk of coronary heart disease in men and women. The Atherosclerosis Risk in Communities Study. JAMA 287(9):1153-9, 2002
4. Wong TY, Klein R, Sharrett AR, et al. Cerebral white matter lesions, retinopathy, and incident clinical stroke. JAMA 288(1):67-74, 2002.
5. Wong TY, Mitchell P. Hypertensive retinopathy. N Engl J Med 351, 2310-2317, 2004
6. Wong TY, Kamineni A, Klein R, et al. Quantitative retinal venular caliber and risk of cardiovascular disease in older persons: the cardiovascular health study. Arch Intern Med 166(21):2388-94, 2006
7. Mitchell P, Wang JJ, Wong TY, et al. Retinal microvascular signs and risk of stroke and stroke mortality. Neurology 65(7):1005-9, 2005.
8. Ikram MK, de Jong FJ, Bos MJ, et al. Retinal vessel diameters and risk of stroke: the Rotterdam Study. Neurology 66(9):1339-43, 2006.
9. McGeechan K, Liew G, Macaskill P, et al. Prediction of incident stroke events based on retinal vessel caliber: a systematic review and individual-participant meta-analysis. AmJ Epidemiol 170(11):1323-32, 2009.
10. Cheung CY, Ikram MK, Sabanayagam C, Wong TY. Retinal microvasculature as a model to study the manifestations of hypertension. Hypertension 60(5):1094-103, 2012.
11. Cheung CY, Tay WT, Ikram MK, et al. Retinal microvascular changes and risk of stroke: the Singapore Malay Eye Study. Stroke 44(9):2402-8, 2013.
12. Cheung N, Liew G, Lindley RI, et al. Retinal fractals and acute lacunar stroke. Ann Neurol 68(1):107-11, 2010.
13. Doubal FN, MacGillivray TJ, Patton N, et al. Fractal analysis of retinal vessels suggests that a distinct vasculopathy causes lacunar stroke. Neurology 74(14):1102-7, 2010.
14. Ong YT, De Silva DA, Cheung CY, et al. Microvascular structure and network in the retina of patients with ischemic stroke. Stroke 44(8):2121-7, 2013.
15. Cheung CY, Ong S, Ikram MK, Ong YT, Chen CP, Venketasubramanian N, Wong TY. Retinal vascular fractal dimension is associated with cognitive dysfunction. J Stroke Cerebrovasc Dis 23, 43-50, 2014.
16. Cheung CY, Ong YT, Ikram MK, Chen C, Wong TY. Retinal microvasculature in Alzheimer's disease. J Alzheimers Dis 42 Suppl 4, S339-352, 2014.
17. Cheung CY, Ong YT, Ikram MK, Ong SY, Li X, Hilal S, Catindig JA, Venketasubramanian N, Yap P, Seow D, Chen CP, Wong TY. Microvascular network alterations in the retina of patients with Alzheimer's disease. Alzheimers Dement 10, 135-142, 2014
18. Ting DS, Tan GS, Agrawal R, Yanagi Y, Sie NM, Wong CW, San Yeo IY, Lee SY, Cheung CM, Wong TY. Optical Coherence Tomographic Angiography in Type 2 Diabetes and Diabetic Retinopathy. JAMA Ophthalmology 135(4):306-312, 2017
19. Ting DSW, Liu Y, Burlina P, Xu X, Bressler NM, Wong TY. AI for medical imaging goes deep. Nature Medicine 24(5):539-540, 2018.

RETINAL VASCULAR ABNORMALITIES IN CEREBROVASCULAR AND NEURODEGENERATIVE DISORDERS

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LEARNING OBJECTIVES

1. Describe the retinal vascular changes associated with ischemic and hemorrhagic strokes
2. Define retinal macro- and microcirculatory abnormalities linked to dementia
3. Summarize the retinal vascular examination tools applied in neurovascular and neurodegenerative conditions

CME QUESTIONS

1. The retinal abnormality found to be associated the most with lacunar infarcts is:
   A. Retinal microaneurysms
   B. Retinal venular dilation
   C. Retinal hemorrhages
   D. Macular thinning

2. In patients with cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy, the following retinal vascular changes are associated with the cerebral small vessel disease:
   A. Decreased vessel tortuosity
   B. Increased arterio-venous ratio
   C. Increased complexity of vessel branching
   D. Increased venous diameter

3. Optical coherence tomography angiography examination of asymptomatic patients with preclinical Alzheimer's disease shows:
   A. Significantly decreased retinal flow rate compared to normal controls
   B. Similar choroidal flow rate compared to normal controls
   C. Larger foveal avascular zone compared to normal controls

KEYWORDS

1. Retinal vasculature
2. Stroke
3. Vascular dementia
4. Alzheimer's disease

HIGHLIGHTS

Dysfunction of blood-retina barrier and blood-brain barrier occur simultaneously and thus play a central role in the development of retinal and cerebral microangiopathy[1]. Retinal imaging is suitable to

directly and non-invasively assess the health of the cerebral vasculature and to detect early vascular changes. Ocular fundus photography is one of the most accessible tools to study cerebrovascular disorders and dementia[2], since retinal vascular abnormalities are linked to small vessel brain disease, global cognitive function[3] and amyloid-β deposition in Alzheimer's disease (AD)[4].

The relationship between stroke and retinal macrovascular changes such as retinal arterial or venous occlusions, and retinal artery embolism is well demonstrated[5-7]. Furthermore, indicators of retinal microvascular injury are independently associated with cerebrovascular ischemic diseases, incident stroke[8], prevalent cerebral infarction[9], MRI-defined subclinical cerebral infarcts[10], lacunar infarcts (LI)[11,12], non-lacunar infarcts[13], white matter hyperintensities (WMHI)[14-16], symptomatic intracranial large artery disease[17] and stroke-related mortality[18,19].

A meta-analysis of population-based studies evaluating the quantitative association between retinal microvascular changes and ischemic stroke subtypes showed that even after adjustment for traditional vascular risk factors, focal arteriolar narrowing (FAN) and arterio-venous nicking (AVN) are associated with WMHI and LI; venular dilation is significantly associated with LI, whereas retinal hemorrhages are associated with WMHIs. No single retinal microvascular abnormality showed a greater association with ischemic brain disease categories than a combination of these in the form of retinopathy[20]. Cerebral microbleeds (CMB) location may be a clue to their etiology, either hypertensive (deep) or amyloid angiopathy (lobar). AGES-Reykjavik study showed that concurrently having ≥2 retinal microvascular signs was associated with a 3-fold increased likelihood for deep CMBs but not exclusively lobar CMBs, whereas pure geographic atrophy was significantly associated with strictly lobar CMBs[21]. Patients with deep hemorrhages were more likely than those with nonlacunar infarcts to have severe FAN and AVN and wider retinal venules. Retinal microvascular signs were similar in patients with deep hemorrhages and LI[22].

Retinopathy, as a biomarker of small vessel disease, is a recognized risk factor not only for cerebrovascular disease but also for global cognitive dysfunction and regional brain volume loss, as shown by the Women's Health Initiative Memory Study and the Women's Health Initiative Sight Exam[3]. Midlife vascular risk factors (smoking, diabetes, prehypertension, hypertension) were associated with increased risk of dementia in the Atherosclerosis Risk in Communities (ARIC) participants[23] and any retinopathy was associated with accelerated rates of 20-year cognitive decline, irrespective of race and the presence of diabetes mellitus[24]. Fractal analysis of the retinal vessels demonstrated that rarefaction of the vessels and decreased retinal vessels branching complexity is associated with cognitive dysfunction[25]. Generalized arteriolar narrowing was found to correlate with disabling dementia[26]. In cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), increased arterio-venous ratio, venous diameter and vessel tortuosity correlate with the brain small vessel disease[27,28]; additionally, reduced retinal vessel branching complexity[29], diminished retinal capillary flow, and diminished optic nerve head blood flow were reported[30,31]. Retinal microaneurysms and dot-and-blot hemorrhages are described in a small case-series of patients with cerebral amyloid angiopathy[32]. AD is marked by vascular dysfunction[33]. Vascular attenuation, increasing standard deviation of vessel widths, reduced complexity of the branching pattern, reduced optimality of the branching geometry, less tortuous venules[34], increase in venular width gradient[35], and decrease in arterial fractal dimension[36] were noted in AD patients.

In addition to fundus photography, other retinal vascular imaging modalities such as high frequency flicker light stimulation[37], ocular coherence tomography angiography[38], scanning laser ophthalmoscopy[39], scanning laser Doppler flowmetry[30], and retinal function imager[40] have been investigated in patients with vascular cognitive impairment.

Retinal function imager uses hemoglobin in red blood cells as the intrinsic motion contrast agent[41] to study blood flow rate and flow velocity in pre-capillary retinal arterioles and post-capillary

venules and is useful to characterize the retinal microcirculation. Decreased retinal perfusion was demonstrated in AD[42], with significantly lower macular flow values in AD compared to controls[40].

An optical coherence tomography angiography study investigating the retinal microvascular network at the macular region showed lower microvascular densities in retinal vascular network, superficial vascular plexus, and deep vascular plexus in the annulus in AD patients[38]. Moreover, significantly lower choroidal thickness, and more enlarged foveal avascular zone was reported in AD compared to controls[43]. Cognitively healthy individuals with preclinical AD showed increased foveal avascular zone and decreased mean inner foveal thickness compared with controls in a single-center, case-control study[44].

Quantitative analysis of the retinal vascular abnormalities and development of standardized objective measures using semiautomated and software applications are currently being explored[45], aiming to enhance their applicability in routine clinical neurology practice.

SUMMARY

The connection between various retinal vascular abnormalities and cerebrovascular and neurodegenerative disorders creates promise for the prediction of stroke and dementia using established tools such as fundus photography, but also novel functional retinal vasculature examination modalities.

Vascular cognitive disorders are heterogeneous entities with intricate correlation to neurodegenerative conditions, such as AD, Parkinson's disease, and multiple sclerosis. As asymptomatic vascular changes in mid-life are associated with cognitive decline later in life, early vascular disease identification remains critical. For this purpose, several retinal vascular imaging modalities are being explored in neurodegenerative conditions associated with vascular cognitive impairment. Optical coherence tomography angiography may serve as a useful tool to depict early vascular changes in preclinical AD and therefore to identify individuals in preclinical stages of disease that are more likely to respond to the therapies that are currently being tested in clinical trials.

CME ANSWERS

1. B
2. B, D
3. A, C

REFERENCES

1. London A, Benhar I, Schwartz M. The retina as a window to the brain-from eye research to CNS disorders. Nat Rev Neurol 2013; 9(1): 44-53.
2. Cheung CY, Chen C, Wong TY. Ocular Fundus Photography as a Tool to Study Stroke and Dementia. Semin Neurol 2015; 35(5): 481-90.
3. Haan M, Espeland MA, Klein BE, et al. Cognitive function and retinal and ischemic brain changes: the Women's Health Initiative. Neurology 2012; 78(13): 942-9.
4. Hart NJ, Koronyo Y, Black KL, Koronyo-Hamaoui M. Ocular indicators of Alzheimer's: exploring disease in the retina. Acta Neuropathol 2016; 132(6): 767-87.
5. Zhou Y, Zhu WG, Wang CY. Relationship between retinal vascular occlusions and incident cerebrovascular diseases: A systematic review and meta-analysis. Medicine 2016; 95(26).
6. Woo SC, Lip GY, Lip PL. Associations of retinal artery occlusion and retinal vein occlusion to mortality, stroke, and myocardial infarction: a systematic review. Eye (Lond) 2016; 30(8): 1031-8.

7. Doubal FN, Hokke PE, Wardlaw JM. Retinal microvascular abnormalities and stroke: a systematic review. J Neurol Neurosurg Psychiatry 2009; 80(2): 158-65.
8. Hanff TC, Sharrett AR, Mosley TH, et al. Retinal microvascular abnormalities predict progression of brain microvascular disease: an atherosclerosis risk in communities magnetic resonance imaging study. Stroke 2014; 45(4): 1012-7.
9. Longstreth W, Jr., Larsen EK, Klein R, et al. Associations between findings on cranial magnetic resonance imaging and retinal photography in the elderly: the Cardiovascular Health Study. Am J Epidemiol 2007; 165(1): 78-84.
10. Cooper LS, Wong TY, Klein R, et al. Retinal microvascular abnormalities and MRI-defined subclinical cerebral infarction: the Atherosclerosis Risk in Communities Study. Stroke 2006; 37(1): 82-6.
11. Cheung CYL, Zheng YF, Hsu W, et al. Retinal Vascular Tortuosity, Blood Pressure, and Cardiovascular Risk Factors. Ophthalmology 2011; 118(5): 812-8.
12. De Silva DA, Woon FP, Manzano JJ, et al. The relationship between aortic stiffness and changes in retinal microvessels among Asian ischemic stroke patients. J Hum Hypertens 2012; 26(12): 716-22.
13. Yatsuya H, Folsom AR, Wong TY, Klein R, Klein BE, Sharrett AR. Retinal microvascular abnormalities and risk of lacunar stroke: Atherosclerosis Risk in Communities Study. Stroke 2010; 41(7): 1349-55.
14. Mutlu U, Cremers LG, de Groot M, et al. Retinal microvasculature and white matter microstructure: The Rotterdam Study. Neurology 2016; 87(10): 1003-10.
15. Qiu C, Cotch MF, Sigurdsson S, et al. Microvascular lesions in the brain and retina: The age, gene/environment susceptibility-Reykjavik study. Ann Neurol 2009; 65(5): 569-76.
16. Hughes AD, Falaschetti E, Witt N, et al. Association of Retinopathy and Retinal Microvascular Abnormalities With Stroke and Cerebrovascular Disease. Stroke 2016.
17. De Silva DA, Manzano JJ, Woon FP, et al. Associations of retinal microvascular signs and intracranial large artery disease. Stroke 2011; 42(3): 812-4.
18. Klein R, Klein BE, Moss SE, Meuer SM. Retinal emboli and cardiovascular disease: the Beaver Dam Eye Study. Trans Am Ophthalmol Soc 2003; 101: 173-80; discussion 80-2.
19. Wang JJ, Liew G, Klein R, et al. Retinal vessel diameter and cardiovascular mortality: pooled data analysis from two older populations. Eur Heart J 2007; 28(16): 1984-92.
20. Dumitrascu OM, Demaerschalk BM, Valencia Sanchez C, et al. Retinal Microvascular Abnormalities as Surrogate Markers of Cerebrovascular Ischemic Disease: A Meta-Analysis. J Stroke Cerebrovasc Dis 2018; 27(7): 1960-8.
21. Qiu C, Ding J, Sigurdsson S, et al. Differential associations between retinal signs and CMBs by location: The AGES-Reykjavik Study. Neurology 2018; 90(2): e142-e8.
22. Baker ML, Hand PJ, Liew G, et al. Retinal microvascular signs may provide clues to the underlying vasculopathy in patients with deep intracerebral hemorrhage. Stroke 2010; 41(4): 618-23.
23. Gottesman RF, Albert MS, Alonso A, et al. Associations Between Midlife Vascular Risk Factors and 25-Year Incident Dementia in the Atherosclerosis Risk in Communities (ARIC) Cohort. JAMA Neurol 2017; 74(10): 1246-54.
24. Deal JA, Sharrett AR, Rawlings AM, et al. Retinal signs and 20-year cognitive decline in the Atherosclerosis Risk in Communities Study. Neurology 2018; 90(13): e1158-e66.
25. Cheung CY, Ong S, Ikram MK, et al. Retinal vascular fractal dimension is associated with cognitive dysfunction. J Stroke Cerebrovasc Dis 2014; 23(1): 43-50.
26. Jinnouchi H, Kitamura A, Yamagishi K, et al. Retinal Vascular Changes and Prospective Risk of Disabling Dementia: the Circulatory Risk in Communities Study (CIRCS). J Atheroscler Thromb 2017; 24(7): 687-95.
27. Cavallari M, Stamile C, Umeton R, Calimeri F, Orzi F. Novel Method for Automated Analysis of Retinal Images: Results in Subjects with Hypertensive Retinopathy and CADASIL. Biomed Res Int 2015; 2015: 752957.

28. Cumurciuc RM, P.//Paques, M.//Krisovic, V.//Gaudric, A.//Bousser, M. G.//Chabriat, H. Retinal abnormalities in CADASIL: a retrospective study of 18 patients. Journal of neurology, neurosurgery, and psychiatry 2004; 75(7): 1058-60.
29. Cavallari M, Falco T, Frontali M, Romano S, Bagnato F, Orzi F. Fractal analysis reveals reduced complexity of retinal vessels in CADASIL. PLoS One 2011; 6(4): e19150.
30. Harju MT, S.//Summanen, P.//Viitanen, M.//Poyhonen, M.//Nikoskelainen, E.//Kalimo, H.//Kivela, T. Scanning laser Doppler flowmetry shows reduced retinal capillary blood flow in CADASIL. Stroke 2004; 35(11): 2449-52.
31. Rufa AD, M. T.//Frezzotti, P.//De Stefano, N.//Caporossi, A.//Federico, A. Hemodynamic evaluation of the optic nerve head in cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy. Archives of neurology 2004; 61(8): 1230-3.
32. Lee A, Rudkin A, Agzarian M, Patel S, Lake S, Chen C. Retinal vascular abnormalities in patients with cerebral amyloid angiopathy. Cerebrovasc Dis 2009; 28(6): 618-22.
33. Golzan SM, Goozee K, Georgevsky D, et al. Retinal vascular and structural changes are associated with amyloid burden in the elderly: ophthalmic biomarkers of preclinical Alzheimer's disease. Alzheimers Res Ther 2017; 9(1): 13.
34. Frost S, Kanagasingam Y, Sohrabi H, et al. Retinal vascular biomarkers for early detection and monitoring of Alzheimer's disease. Transl Psychiatry 2013; 3: e233.
35. Csincsik LM, T. J.//Flynn, E.//Pellegrini, E.//Papanastasiou, G.//Barzegar-Befroei, N.//Csutak, A.//Bird, A. C.//Ritchie, C. W.//Peto, T.//Lengyel, I. Peripheral Retinal Imaging Biomarkers for Alzheimer's Disease: A Pilot Study. Ophthalmic Research 2018; 59(4): 182-92.
36. Frost S, Bhuiyan A, Offerman D, et al. Modulation of Retinal Arteriolar Central Reflection by APOE Genotype. Curr Alzheimer Res 2017; 14(9): 916-23.
37. Bettermann KS, J. E.//Shivkumar, V.//Lott, M. E. J. Retinal vasoreactivity as a marker for chronic ischemic white matter disease? Journal of the Neurological Sciences 2012; 322(1-2): 206-10.
38. Jiang H, Wei Y, Shi Y, et al. Altered Macular Microvasculature in Mild Cognitive Impairment and Alzheimer Disease. J Neuroophthalmol 2017.
39. Alten F, Motte J, Ewering C, et al. Multimodal retinal vessel analysis in CADASIL patients. PLoS One 2014; 9(11): e112311.
40. Jiang H, Liu Y, Wei Y, et al. Impaired retinal microcirculation in patients with Alzheimer's disease. PLoS One 2018; 13(2): e0192154.
41. Burgansky-Eliash Z, Lowenstein A, Neuderfer M, et al. The correlation between retinal blood flow velocity measured by the retinal function imager and various physiological parameters. Ophthalmic Surg Lasers Imaging Retina 2013; 44(1): 51-8.
42. Gameiro GR, Jiang H, Liu Y, et al. Retinal tissue hypoperfusion in patients with clinical Alzheimer's disease. Eye Vis (Lond) 2018; 5: 21.
43. Bulut M, Kurtulus F, Gozkaya O, et al. Evaluation of optical coherence tomography angiographic findings in Alzheimer's type dementia. Br J Ophthalmol 2017.
44. O'Bryhim BE, Apte RS, Kung N, Coble D, Van Stavern GP. Association of Preclinical Alzheimer Disease With Optical Coherence Tomographic Angiography Findings. JAMA Ophthalmol 2018.
45. McGrory S, Taylor AM, Pellegrini E, et al. Towards Standardization of Quantitative Retinal Vascular Parameters: Comparison of SIVA and VAMPIRE Measurements in the Lothian Birth Cohort 1936. Transl Vis Sci Technol 2018; 7(2): 12.

ARTIFICIAL INTELLIGENCE IN RETINAL IMAGING

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LEARNING OBJECTIVES

1. To learn basic concepts in artificial intelligence, machine learning and deep learning
2. To appreciate the latest developments and studies of artificial intelligence technology in retinal diseases such as diabetic retinopathy, age-related macular degeneration, glaucoma and optic nerve diseases and in predicting systemic disease such as stroke and cardiovascular risk factors
3. To understand current limitations and challenges in applying artificial intelligence technology in clinical care

CME QUESTIONS

1. What is the difference between traditional algorithm and AI-based deep learning algorithm?
2. How is the performance of AI-based deep learning algorithms in diagnosis of diabetic retinopathy compared to ophthalmologists?
3. What are the 3 major limitations of AI-based technology that it needs to overcome to enable clinical translation?

KEYWORDS

1. Artificial intelligence
2. Machine learning
3. Deep learning
4. Diabetic retinopathy
5. Cardiovascular risk factors

HIGHLIGHTS

Deep learning (DL) techniques are the latest iterations of artificial intelligence (AI) technology and has sparked significant interest in clinical medicine over the past few years. DL techniques may be used to detect diseases from medical images, including diabetic retinopathy and retinal diseases from retinal photographs, or from OCT. In other fields, DL techniques can diagnose lung conditions from chest X-rays, skin cancers from skin photographs and predict cardiovascular risk factors (e.g., blood pressure, smoking and body mass index) from retinal photographs.

DL technology has substantial potential for diagnosis of major retinal diseases such as diabetic retinopathy (DR), age-related macular degeneration, glaucoma and optic neuropathies. In particular, the most advanced application is in DR screening. Previous technology for automated DR screening using traditional “pattern recognition” techniques to detect specific DR lesions (e.g., microaneurysms) have been promising but have not broken the “translational gap” from research to clinical adoption. DL uses

much larger datasets and uses a “black box” approach to mine, extract and learn patterns and/or features to determine a disease state or condition. Recently, researchers from Google using DL technology have reported high sensitivity and specificity (>90%) in detecting referable DR from retinal photographs. However, for translational impact, DL technology should be trained and validated in “real-world” screening programs where fundus images have varying qualities (e.g. cataract, poor pupil dilation, poor contrast/focus), and with patient samples of different ethnicity (i.e. different fundi pigmentation) and systemic glucose control (poor and good control). Furthermore, in any screening programs for DR, the detection of incidental but common vision-threatening conditions such as glaucoma and age-related macular degeneration should be incorporated, as missing such cases may not be acceptable to clinicians. These issues and challenges need to be addressed before AI-based deep learning technology can be applicable in large scale screening programs for DR, diagnosis of retinal disease and applied in other clinical scenarios.

SUMMARY

Artificial intelligence (AI) technology is a major revolution in medicine and has potential impact on healthcare across the spectrum of screening, diagnosis, prediction and prognosis. The most developed system for AI-based technology is its ability to transform screening for diabetic retinopathy (DR) from retinal photographs. Previous technology for automated DR screening using traditional “pattern recognition” techniques to detect specific DR lesions (e.g., microaneurysms) has not broken the “translational gap” from research to clinical adoption. New AI technology uses larger datasets and deep learning techniques to mine, extract and learn patterns and/or features. Recently, several groups using deep learning technology have reported high sensitivity and specificity (>90%) in detecting DR from retinal photographs. For translational impact, such technology should be validated in “real-world” screening programs where retinal images have varying qualities (e.g. cataract, poor contrast/focus), and patient samples are of different ethnicity. Furthermore, in screening programs for DR, the detection of incidental but common vision-threatening conditions such as glaucoma and age-related macular degeneration should be incorporated, as missing such cases may not be acceptable to clinicians. AI has substantial promise for large scale screening programs for DR.

CME ANSWERS

1. Traditional algorithm uses “pattern recognition and segmentation” to identify specific features and requires human level training and is thus considered “supervised training”. Machine learning, and in particular deep learning, uses deep neural networks that are “unsupervised”, with the algorithms learning features themselves to separate labels/outcomes.

2. AI-based deep learning technology shows comparable and better performance versus human assessment.

3. Limitations are as follows. First, AI-based deep learning technology requires large, robust, clearly labelled training datasets (to avoid garbage in, garbage out). These are not easy to obtain. Second, AI-based technology uses a “black box” concept and this is a concern for patient and physician to readily accept their diagnosis. Third, application of AI-technology requires real-world testing in different stations and scenarios and not only in laboratories.

REFERENCES

1. Esteva A, Kuprel B, Novoa RA, et al. Dermatologist-level classification of skin cancer with deep neural networks. *Nature*. 542:115–118, 2017.
2. Ehteshami Bejnordi B, Veta M, et al. Diagnostic Assessment of Deep Learning Algorithms for Detection of Lymph Node Metastases in Women With Breast Cancer. *JAMA.* 318(22):2199-2210, 2017.
3. Gulshan V, Peng L, Coram M, Stumpe MC, Wu D, Narayanaswamy A, et al. Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs. *JAMA.* 316(22):2402-2410, 2017.
4. Ting DSW, Cheung CYL, Lim G, et al. Development and Validation of a Deep Learning System for Diabetic Retinopathy and Related Eye Diseases Using Retinal Images From Multiethnic Populations With Diabetes. *JAMA.* 318(22):2211-2223, 2017.
5. Ting DSW, Liu Y, Burlina P, Xu X, et al. AI for medical imaging goes deep. *Nature Medicine.* 24:539–40, 2018.
6. Abràmoff MD, Lou Y, Erginay A, et al. Improved Automated Detection of Diabetic Retinopathy on a Publicly Available Dataset Through Integration of Deep Learning. *IOVS.* 57(13):5200-5206, 2016.
7. Gargeya R, Leng T. Automated Identification of Diabetic Retinopathy Using Deep Learning. Ophthalmology. 124(7):962-969, 2017.
8. Hood DC, De Moraes CG. Efficacy of a Deep Learning System for Detecting Glaucomatous Optic Neuropathy Based on Color Fundus Photographs. *Ophthalmology.* 125(8):1199-1206, 2018.
9. Burlina PM, Joshi N, Pekala M, et al. Automated Grading of Age-Related Macular Degeneration From Color Fundus Images Using Deep Convolutional Neural Networks. *JAMA Ophthalmol*. 135(11):1170-1176, 2017.
10. Grassmann F, Mengelkamp J, Brandl C, et al. A Deep Learning Algorithm for Prediction of Age-Related Eye Disease Study Severity Scale for Age-Related Macular Degeneration from Color Fundus Photography. *Ophthalmology.* 125(9):1410-1420, 2018.
11. Ting DSW, Pasquale LR, Peng L, et al. Artificial intelligence and deep learning in ophthalmology. *Br J Ophthalmol.* pii: bjophthalmol-2018-313173, 2018. [Epub ahead of print]
12. Wong TY, Bressler NM. Artificial Intelligence With Deep Learning Technology Looks Into Diabetic Retinopathy Screening. *JAMA.* 316(22):2366-2367, 2016.
13. Li Z, Keel S, Liu C, et al. An Automated Grading System for Detection of Vision-Threatening Referable Diabetic Retinopathy on the Basis of Color Fundus Photographs. *Diabetes Care.* pii: dc180147, 2018 [Epub ahead of print]
14. De Fauw J, Ledsam JR, Romera-Paredes B, et al. Clinically applicable deep learning for diagnosis and referral in retinal disease. *Nature Medicine.* 24:1342–1350, 2018.

DIZZINESS, VERTIGO: JUST TELL ME WHAT TO DO!

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LEARNING OBJECTIVES

1. Describe the HINTS exam and its correct application.
2. Interpret results of the HINTS exam correctly, including central and peripheral patterns.
3. Interpret positionally-triggered nystagmus to localize the affected canal.
4. Describe the Triage-TiTrATE-Test method.
5. Apply the Triage-TiTrATE-Test method to correctly diagnose the etiology of dizziness or vertigo.

CME QUESTIONS

1. Which of the following statements are true with regard to a patient presenting with new dizziness or vertigo to the emergency department?

A. Whether or not symptoms worsen with head movements will distinguish the acute vestibular syndrome (AVS - prolonged vertigo, unsteadiness, nausea/vomiting, spontaneous nystagmus lasting for >24 hours) from benign paroxysmal positional vertigo (BPPV)
B. Nystagmus in vestibular neuritis follows an inhibitory pattern, while the nystagmus elicited by the Dix-Hallpike test in posterior canal BPPV follows an excitatory pattern
C. The 'HINTS' exam is superior to MR with diffusion weighted imaging in the first 24-48 hours in a patient presenting with 30-second long bouts of vertigo triggered by rolling over in bed and going from seated to lying in bed
D. Video-oculography (VOG) and video head impulse testing (vHIT) are necessary to make the diagnosis of vestibular neuritis

2. A patient presents to the ED with acute prolonged vertigo. On examination, there is right-beating nystagmus in right gaze, left-beating nystagmus in left gaze, a negative test of skew (i.e., no vertical refixation with alternate cover testing), and an abnormal head impulse test to the right (i.e., when the head is moved quickly to the right, the eyes move with the head to the right initially, and then a corrective [overt] saccade is seen which bring the eyes back to the examiner's nose). Which of the following localizations or etiologies are possible (may be more than one)?

A. Acute right 8th cranial neuropathy
B. Right-sided intracanalicular vestibular schwannoma
C. Right vestibular nucleus infarction
D. Right anterior inferior cerebellar artery distribution stroke

3. True or False: A 35-year-old woman presents to the clinic with recurrent vertigo. She has a history of migraine in her teenage years and a history of motion sickness on long car rides. Attacks typically last 30-60 minutes, are accompanied by photophobia (not headaches), and tend to occur around her

menstrual cycle. She has experienced 10 such episodes in her lifetime. For the same period of time, she has experienced intermittent unilateral or bilateral tinnitus, aural fullness, popping and pressure. Audiogram has shown normal hearing without sensorineural hearing loss in the low-mid frequency range. True or False: This patient is more likely to have Menière's disease than vestibular migraine?

KEYWORDS

1. Dizziness
2. Vertigo
3. HINTS
4. BPPV
5. Vestibular

SUMMARY

Modified from "Approach to the Ocular Motor and Vestibular History and Examination", Neuro-Ophthalmology Virtual Education Library: NOVEL. [online] Full version available at: https://collections.lib.utah.edu/ark:/87278/s64x9bq1 [Accessed October 23, 2018].

HISTORY

- 3T Approach: "TRIAGE — TiTrATE — TEST"[1]
    - **DO NOT TRIAGE BASED ON SYMPTOM QUALITY ALONE** – e.g., dizzy vs vertigo vs giddiness vs lightheaded as patients tend to be inconsistent and the symptom quality can be misleading
- **TRIAGE**
    - Screen for common culprits: medication or drug toxicity, metabolic, cardiac, psychiatric[2]
- **TiTrATE**
    - **Timing:**
        - Onset - acute or gradual
        - Episodic (*seconds* [benign paroxysmal positional vertigo (BPPV), vestibular paroxysmia], *minutes* [migraine, Menière's, Transient Ischemic Attack (TIA)], *hours* [migraine, Menière's, occasionally TIA], *days* [migraine])
        - Constant (acute vestibular syndrome [AVS] due to stroke>demyelinating disease [~20% of AVS] or vestibular neuritis [~80% of AVS])
    - **Triggers:**
        - Positional (*triggered by* movement)
            - BPPV – lying to seated, seated to lying, rolling over in bed, looking up or down, brought on by *head* movement
            - Orthostatic hypotension – arising from lying or seated position (shouldn't come on when going from sitting to lying, which can differentiate from BPPV)
        - Head movement (occurs *during* or time-locked to movement)
            - Bilateral vestibular loss (most common)
            - Unilateral vestibular loss (acute phase prior to compensation)
        - Sound (Tullio phenomenon[3])
            - Superior canal dehiscence syndrome (SCDS)

        - Valsalva (against closed glottis and/or pinched nose)
            - SCDS
            - Cervicomedullary junction lesion (e.g., Chiari)
        - Complex visual stimulation (e.g., grocery store, crowded environments)
            - Vestibular migraine (also may be triggered by sleep deprivation, skipping meals, certain foods, menstrual-related, barometric pressure changes)
            - Persistent positional perceptual dizziness (PPPD)
    - **Targeted Exam:**
        - HINTS[4, 5] (**H**ead **I**mpulse, **N**ystagmus, **T**est of **S**kew) for AVS
            - HINTS 'Plus'[4, 5] (**H**ead **I**mpulse, **N**ystagmus, **T**est of **S**kew, **'Plus'** = bedside assessment of auditory function using finger rub) for AVS
            - Don't forget about associated symptoms common in posterior fossa disease including diplopia, dysarthria, dysphagia, loss of sensation, weakness, room tilt illusion, incoordination, drop attacks, abrupt loss of hearing (remember that the internal auditory artery usually comes off the anterior inferior cerebellar artery)
        - Dix-Hallpike (DH) & supine roll test for positionally-triggered episodes possibly due to BPPV
        - In more chronic balance/vestibular conditions, particular attention to general neurologic exam looking for evidence of parkinsonism; cerebellar disease (e.g., gaze-evoked nystagmus, saccadic smooth pursuit, spontaneous downbeat nystagmus); myelopathy; neuropathy; vestibular exam looking for unilateral or bilateral vestibular loss

- **Test:**
    - Examples
        - Audiogram (ADDITIONAL READING ON AUDIOMETRY) with hearing loss/changes or any aural symptoms (tinnitus, pain, fullness, popping) or when Menière's is suspected
        - Vestibular function testing (ADDITIONAL READING ON VESTIBULAR LAB TESTS) when unilateral or bilateral vestibular loss is suspected and in other special situations
        - MRI DWI with attention to the posterior fossa when stroke is suspected in AVS
        - MRI IAC protocol with gad when acoustic neuroma is suspected
        - MRI with CISS/FIESTA protocol when vestibular paroxysmia is suspected
        - CT temporal bones when SCDS is suspected

Common vestibular disorders[6]

Disorder	Timing	Symptoms	Distinguishing Ocular Motor / Vestibular Findings	Etiology / Treatment
Peripheral Acute Vestibular Syndrome (Vestibular neuritis [VN] / Labyrinthitis)	Acute onset, prolonged	Vertigo/dizziness; disequilibrium; N/V; "*sitting*" oscillopsia at rest (not dependent on head motion, also referred to as "external vertigo") from nystagmus; *aggravated* by head movements; hearing is spared in VN and lost in labyrinthitis (consider labyrinthine ischemia particularly when new hearing loss is present)	'Peripheral' HINTS exam: Contralesional spontaneous mixed horizontal-torsional nystagmus; ipsilesional abnormal head impulse test (HIT); skew deviation absent	Steroids may help expedite recovery[7]; vestibular physical therapy; anti-virals in Ramsay-Hunt; antibiotics in bacterial labyrinthitis
Central Acute Vestibular Syndrome (Stroke> demyelinating disease, encephalitis, Wernicke's, etc)	Acute onset, prolonged	Vertigo/dizziness; disequilibrium; N/V; *sitting* oscillopsia at rest from nystagmus (when present); *aggravated* by head movements; may or may not have additional posterior fossa symptoms and signs	Horizontal, horizontal-torsional (these can be unidirectional) and gaze-evoked nystagmus (GEN) are most common patterns when present; pure torsional or vertical nystagmus may also be seen; skew deviation may be present; ocular lateropulsion (ipsipulsion in lateral medullary syndrome)	Work-up for stroke and secondary stroke prevention
Superior Canal Dehiscence	Episodic seconds to minutes (vertigo / dizziness) and chronic (disequilibrium)	Autophony (hearing internal noises that are not normally perceived – e.g., heartbeat, eye movements); episodic vertigo / dizziness, may have chronic disequilibrium	Valsalva-induced (VIDEO) and/or sound-induced nystagmus and vertigo, in the plane of the stimulated (or inhibited) superior (anterior) semicircular canal; supranormal bone conduction thresholds with an air-bone gap and lowered vestibular evoked myogenic potential thresholds[8]	Usually idiopathic and sometimes incidental; surgery if symptomatic
Vestibular Paroxysmia	Episodic seconds to minutes	Dizziness, vertigo, imbalance commonly associated with ipsilesional aural symptoms often spontaneous and many times each day; can be provoked by exercise or head movements	Hyperventilation-induced nystagmus (usually excitatory or ipsilesional)	Neurovascular compression can be seen on MRI, usually with high resolution FIESTA/CISS imaging (beware of incidental neurovascular contact as well, a common finding in older patients with high resolution imaging); BAERs occasionally helpful; no consistent vestibular lab or exam findings; can try carbamazepine, oxcarbazepine or other anti-seizure medications
Benign Paroxysmal Positional Vertigo (BPPV)	Episodic Triggered, Seconds	Vertigo or dizziness *triggered* by head movements	Posterior canal (PC) BPPV – upbeat-torsional (top poles toward lowermost, affected ear) nystagmus; Horizontal canal (HC) BPPV – geotropic (beats toward	Repositioning maneuvers: PC BPPV – Epley and Semont; HC BPPV – BBQ roll, Gufoni; AC BPPV – deep head hanging

			floor with right or left ear down) or apogeotropic (beats toward ceiling; beware central mimics); Anterior canal (AC) BPPV – downbeat or downbeat-torsional (top poles toward lowermost, affected ear) nystagmus (beware of central mimics)	
Transient Ischemic Attacks	Episodic Spontaneous, minutes>hours	Usually vertigo, but can be any sudden onset symptom (dizzy, lightheaded, disequilibrium, etc); may or may not be associated with other posterior fossa symptoms	Usually normal exam in between events	Work-up for stroke and secondary stroke prevention
Vestibular Migraine	Episodic, seconds, minutes, hours or day	Vertigo, dizziness, imbalance, motion sickness; with or without headache; headache history may be remote	Usually normal inter-ictal exam; during an attack, may have spontaneous nystagmus, although various patterns of positional nystagmus are most common[9]	Abortive and preventative migraine medications/supplements, dietary/lifestyle modifications; vestibular physical therapy in some cases; visual desensitization programs for some[10]
Menière's Disease	Episodic, 20 minutes to 12 hours	Vertigo, aural fullness, hearing loss, and tinnitus	Spontaneous nystagmus during attacks (can vary depending on what phase of the attack the patient is in – i.e., ipsilesional during excitatory or irritative phase or contralesional in inhibitory phase)	Salt restriction, diuretics, steroid intratympanic (IT) injections, gentamicin IT injections in some refractory cases
Bilateral vestibular loss	Chronic	Oscillopsia provoked by head movements ("*walking*" oscillopsia [dependent on head motion]); imbalance (VIDEO)	Bilaterally abnormal HIT (or hypofunction with rotary chair testing, calorics, video HIT); loss of 4 or more lines with dynamic visual acuity; imbalance is maximal in the dark or on uneven surfaces	Commonly related to ototoxicity (gentamicin), can be related to neurodegenerative diseases (multiple system atrophy, spinocerebellar ataxia), autoimmune (mitochondrial), consider CANVAS (cerebellar ataxia, neuropathy, vestibular areflexia syndrome); Treatment includes vestibular PT
Mal de debarquement	Chronic	Rocking or swaying, feeling of being on a boat usually experienced after a cruise, long car ride or flight (note that some cases are spontaneous); symptoms are minimal with passive motion as in a car; significant overlap with migraine	Normal vestibular and neurologic examinations	Unclear etiology but perhaps difficulty unadapting to compensatory changes that occurred while on the cruise; scheduled benzos (clonazepam) and other medications may be tried; readaptation VOR therapy may be beneficial[11]
Persistent Postural Perceptual	Chronic	Following a vestibular, medical or psychiatric event/trigger that causes dizziness/vertigo	Normal vestibular and neurologic examinations aside from abnormalities that might be	Certain SSRI/SNRIs may be helpful (sertraline, citalopram, venlafaxine

Dizziness (PPPD)		or impaired balance, some patients (particularly those prone to anxiety or who had a particularly anxious response to the initial event) develop a maladaptive reaction including stiff/rigid posture which can lead to chronic dizziness (lasting >3 months) with a postural component (worse when upright), visual sensitivity	associated with the inciting event – e.g., if vestibular neuritis, would expect findings consistent with unilateral vestibular loss	[especially when co-existing with vestibular migraine]); cognitive behavioral therapy; physical therapy and rehabilitation[12]

PHYSICAL EXAMINATION

1. **Vestibulo-Ocular Reflex (VOR)**
    - Dynamic Visual Acuity
    - Visually enhanced VOR (vVOR)
    - Head impulse test (HIT)
    - Vibration
    - Head-shaking

2. **Other Audiovestibular Tests and Special Situations**
    - Pressure-induced nystagmus
    - Hyperventilation
    - Dix-Hallpike Maneuver
    - Auditory Testing

3. **'HINTS' testing in the acute vestibular syndrome**

1. Vestibulo-Ocular Reflex (VOR)

The VOR allows for retinal stability during head movements. Ex) a person with a normal VOR can walk down the street and clearly read a sign in front of them since the eyes adjust for head movement with each step and the foveas remain on the target. A person with bilateral vestibular loss will walk down the street and the sign will jump up and down because the head and eyes move together – i.e., the fovea cannot be held on the sign due to impaired VOR, so the image appears to jump up and down (so-called *walking* oscillopsia VIDEO). The following are ways to evaluate VOR function at the bedside.

A. **Dynamic Visual Acuity** (VIDEO): Passive rotation of head (horizontally to evaluate the horizontal SCC and vertically to evaluate the anterior and posterior SCC function) at 2 Hz while viewing a distance (preferred) or near eye chart. A decrease in best-corrected vision of 2 lines or more from baseline is considered abnormal – patients with unilateral vestibular loss may loss 2-3 lines prior to compensation, while patients with bilateral vestibular loss will lose 4 or more lines.

B. **Visually enhanced VOR (vVOR):** Passive rotation through entire horizontal or vertical ocular motor range at 0.5 Hz while fixating on the examiner's nose. This combines smooth pursuit and VOR. If pursuit is impaired and the VOR is hypoactive (e.g., cerebellopathy and bilateral vestibular loss as in cerebellar ataxia, neuropathy, vestibular areflexia syndrome, CANVAS VIDEO), the vVOR will be impaired and will look choppy or saccadic. If either system is functional, this will be smooth.

C. **Head impulse test (HIT** VIDEO): With the patient fixating on the examiner's nose, displace the head 15-20º to one side, then perform a brief, rapid head rotation from lateral to center. In the case of an acute right peripheral vestibulopathy due to vestibular neuritis, a rightward HIT will result in the eyes moving to the right with the head initially, so that a corrective re-fixation saccade will be needed to move the eyes back to the target, or to the left. This is considered an abnormal or positive HIT and generally suggests a peripheral process (although there are exceptions). The opposite reaction will be seen with a lesion on the opposite side.

D. **Vibration** (VIDEO): Vibration of the mastoids and vertex will induce nystagmus with an ipsilesionally-directed slow phase with unilateral vestibular loss, more so acutely than chronically.

E. **Head-shaking (**VIDEO**):** Sustained, rapid, back and forth, horizontal head shaking for ~15 secs may produce a spontaneous nystagmus that slowly dies out. With peripheral lesions, the slow phase is toward the affected ear. With central lesions, the slow phase may be vertical or the nystagmus may change direction from the baseline spontaneous nystagmus. If there's strong head-shaking nystagmus without clear unilateral vestibular loss (VIDEO), consider a central process.

2. Other Audiovestibular Tests and Special Situations

A. **Pressure-induced** (VIDEO)**:** Valsalva against closed glottis, pinched-nose Valsalva, pressure in the external auditory canal causing nystagmus (Hennebert's test) mainly in SCDS (VIDEO), may see Valsalva-induced symptoms with cervicomedullary lesions such as a Chiari I malformation; or **sound-induced nystagmus** (Tullio Phenomenon) mainly in SCDS.

B. **Hyperventilation** (VIDEO): Alkalosis and changes in iCa from 30-60 seconds of hyperventilation may improve conduction through an affected segment of 8th cranial nerve due to vestibular schwannoma (VIDEO) or neurovascular compression, usually causing excitatory nystagmus with a contralesionally-directed slow phase. When a chronic vestibular imbalance has been compensated for by central mechanisms, hyperventilation can cause a transient decompensation and bring out nystagmus with an ipsilesionally-directed slow phase. Hyperventilation can enhance/produce downbeat nystagmus in cerebellar disease.

C. **Dix-Hallpike Maneuver:** Used to test for posterior canal (PC) BPPV**.**

- Example: when *right* posterior canal BPPV is suspected, turn the head 45º to the *right*, and rapidly (~1-2 seconds) move en bloc straight back so that the head is slightly hyperextended (~20 degrees) while hanging over the edge of the examination table with the head still turned 45º to the *right*. This maximally stimulates the right PC SCC. In *right* PC-BPPV, the *right* Dix-Hallpike will provoke upbeat-torsional nystagmus towards the *right* (lowermost) ear, which is due to otoconial debris falling through the canal (causing endolymph movement and cupular deflection in an excitatory direction). The nystagmus **1)** typically begins with a short latency (usually 1-3 seconds[13], but sometimes as long as 30 secs) after change in head position, **2)** peaks within ~5 seconds and lasts less than 1 min, **3)** often reverses direction (downbeat-torsional towards the left ear with right PC-BPPV) when the patient sits up again, and **4)** fatigues with repeated testing. In practice, typically a treatment maneuver will be performed rather than testing items #3 and #4.

D. **Auditory Testing:**

- **Bedside** – Auditory acuity & speech discrimination
  - Hearing loss can be assessed at the bedside via calibrated finger rub (CALFRAST[14]) (note, however, that this can be challenging in high ambient noise environments

such as the emergency department). Speech discrimination can be assessed by whispered speech with distraction (whispering in one ear while rubbing over the opposite ear's pinna to prevent hearing with the fellow ear, so that only one side is being tested at a time). The presence of new, unilateral, moderate to severe hearing loss in the context of an acute vestibular syndrome with an eye movement exam suggesting ipsilesional acute peripheral vestibulopathy should spark consideration of a labyrinthine stroke syndrome.

- **Bedside** – Rinne and Weber **(**VIDEO**)**
  - The Rinne test is an assessment of auditory thresholds to air and bone conduction of sound. The Weber test is a comparison of bone conducted sound of either ear. Conductive hearing loss results in a loss of air conducted greater than bone conducted sound, whereas sensorineural hearing loss results in the loss of both air and bone conducted sound. Peripheral vestibular disease affecting the labyrinth or the 8th cranial nerve can be associated with sensorineural hearing loss. In these cases, the sensitivity to air conduction will remain greater than to bone conduction. Weber will lateralize away from the side of sensorineural hearing loss. As an example, destruction of the right labyrinth (e.g., bacterial labyrinthitis) will cause decreased hearing in the right ear, and air conduction will be greater than bone conduction in the right (affected) and left (unaffected) ears. Weber will lateralize to the left (unaffected) ear. In the case of superior semicircular canal dehiscence (SCDS), there may be increased sensitivity to bony transmission of sound through a (third mobile window) as well as conductive hearing loss, with bone conduction greater than air conduction and Weber lateralizing to the side of the dehiscence.
- **Audiometry** (ADDITIONAL READING ON AUDIOMETRY)

E. **HINTS** (see table below)

CHARACTERISTICS OF POSITIONAL NYSTAGMUS

Site	Peripheral	Central
Direction	• Posterior Canal – mixed upbeat-torsional with (torsional with top poles beating toward the dependent ear VIDEO); reverses on sitting up (VIDEO); treated with Epley or Semont (VIDEO) • Horizontal Canal – either beats toward (geotropic VIDEO) or away from (apogeotropic VIDEO) the ground. Tested with supine roll testing, and when the side is identified to which nystagmus is more intense (right or left ear down), nystagmus will beat toward the affected ear – e.g., more RBN with right ear down, diagnosis is right geotropic HC-BPPV; more RBN with left ear down, diagnosis is right apogeotropic HC-BPPV: treated with BBQ roll (VIDEO) or Gufoni (VIDEO) among others • Anterior Canal – given its parasagittal orientation, nystagmus can be pure downbeat (VIDEO), but more often downbeat-torsional (top poles towards affected ear), and can be brought out with right or left Hallpike, or straight head-hanging – central mimics must be excluded; treated with deep head hanging (VIDEO) among others	Can be pure vertical (down [VIDEO] >up), pure torsional, or can have vertical and torsional components Can be horizontal, more commonly apogeotropic as compared to geotropic Central positional nystagmus is usually associated with other abnormal ocular motor findings
Latency	Typically after a few seconds but may be longer	May or may not have a latency

Duration	<1 minute with canalithiasis, can be longer with cupulolithiasis (otoconia stuck to cupula)	Can be <1 minute or sustained
Fatigability	Yes	Generally does not fatigue, but it may
Symptoms	Yes	Usually less pronounced

3. 'HINTS' testing in the acute vestibular syndrome

	Peripheral Pattern	Central Pattern	Comments
Head Impulse Test (HIT)	Abnormal (VIDEO)	Normal more often than abnormal (VIDEO)	-Can have normal HIT with the rare inferior division vestibular neuritis, which spares the horizontal canal -Can have abnormal HIT with lesions involving the root entry zone of CN8; vestibular nucleus; labyrinthine ischemia among other 'dangerous' etiologies (VIDEO)
Nystagmus (spontaneous)	Mixed horizontal-torsional; unidirectional; follows Alexander's law; suppresses with fixation (VIDEO)	Can be pure horizontal, horizontal-torsional, pure torsional (VIDEO), vertical or torsional-vertical (e.g., medullary, MLF VIDEO); often changes direction with gaze (gaze-evoked VIDEO) but can be unidirectional and follow Alexander's law; may or may not suppress with fixation	-'Central' and 'peripheral' spontaneous or unilateral gaze-evoked nystagmus in the acute vestibular syndrome can be indistinguishable
Test of Skew	Normal (VIDEO)	Normal or Abnormal (VIDEO)	-A skew deviation on a peripheral basis (labyrinth or CN8) is possible, but uncommon, and is generally small (<3-5 prism diopters) and short-lived (disappearing within ~1-3 days) -Presence of a skew should be considered central until proven otherwise -Rarely, a congenital (unrelated) 4th nerve palsy can lead to a false positive 'test of skew'

CME ANSWERS

1. B
2. C, D
3. True

REFERENCES

1. Newman-Toker DE, Edlow JA. TiTrATE: A Novel, Evidence-Based Approach to Diagnosing Acute Dizziness and Vertigo. Neurol Clin 2015;33:577-599, viii.
2. Kerber KA. Acute constant dizziness. Continuum (Minneap Minn) 2012;18:1041-1059.
3. Kaski D, Davies R, Luxon L, Bronstein AM, Rudge P. The Tullio phenomenon: a neurologically neglected presentation. J Neurol 2012;259:4-21.

4. Newman-Toker DE, Kerber KA, Hsieh YH, et al. HINTS outperforms ABCD2 to screen for stroke in acute continuous vertigo and dizziness. Acad Emerg Med 2013;20:986-996.
5. 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.
6. Tusa RJ. Bedside assessment of the dizzy patient. Neurol Clin 2005;23:655-673, v.
7. Strupp M, Zingler VC, Arbusow V, et al. Methylprednisolone, valacyclovir, or the combination for vestibular neuritis. N Engl J Med 2004;351:354-361.
8. Streubel SO, Cremer PD, Carey JP, Weg N, Minor LB. Vestibular-evoked myogenic potentials in the diagnosis of superior canal dehiscence syndrome. Acta Otolaryngol Suppl 2001;545:41-49.
9. Polensek SH, Tusa RJ. Nystagmus during attacks of vestibular migraine: an aid in diagnosis. Audiol Neurootol 2010;15:241-246.
10. Pavlou M. The use of optokinetic stimulation in vestibular rehabilitation. J Neurol Phys Ther 2010;34:105-110.
11. Dai M, Cohen B, Smouha E, Cho C. Readaptation of the vestibulo-ocular reflex relieves the mal de debarquement syndrome. Front Neurol 2014;5:124.
12. Popkirov S, Staab JP, Stone J. Persistent postural-perceptual dizziness (PPPD): a common, characteristic and treatable cause of chronic dizziness. Pract Neurol 2018;18:5-13.
13. Aw ST, Todd MJ, Aw GE, McGarvie LA, Halmagyi GM. Benign positional nystagmus: a study of its three-dimensional spatio-temporal characteristics. Neurology 2005;64:1897-1905.
14. Torres-Russotto D, Landau WM, Harding GW, Bohne BA, Sun K, Sinatra PM. Calibrated finger rub auditory screening test (CALFRAST). Neurology 2009;72:1595-1600.
15. Lempert T, Olesen J, Furman J, et al. Vestibular migraine: diagnostic criteria. J Vestib Res 2012;22:167-172.

Thursday, March 21

6:30 am – 7:30 am	**Breakfast**	**Charleston Ballroom**
6:30 am – 12:00 pm	**Registration/Help Desk**	**5th floor Registration Desk**
7:30 am – 9:30 am	**How Do I Evaluate? Adult versus Kid: Does it Matter?**	**Red Rock Ballroom**
	Moderator: Stacy Pineles, MD, MS and Anthony Arnold, MD	

This session will focus on the management of four neuro-ophthalmic disorders (Horner syndrome, isolated optic neuritis, 3rd cranial nerve palsy, and papilledema) that occur both in pediatric and adult patients. For each topic, an expert for each age group will discuss management, with recommendations based on recent literature and highlight new or controversial data.

Upon completion of this session, participants should be able to: 1) recognize key differences in differential diagnosis 2) utilize correct diagnostic modalities and 3) apply age-appropriate treatments.

7:30 am – 8:00 am	**Horner Syndrome**, *Aki Kawasaki, MD, PhD and Grant Liu, MD*
8:00 am – 8:30 am	**Isolated Optic Neuritis**, *Christopher Glisson, DO, MS and Jason Peragallo, MD*
8:30 am – 9:00 am	**Third Nerve Palsy**, *Karl Golnik, MD, MEd and Paul Phillips, MD*
9:00 am – 9:30 am	**Papilledema,** *Collin McClelland, MD and Robert Avery, DO, MSCE*

9:30 am – 10:00 am	**Coffee break**	**Charleston Ballroom**
10:00 am – 12:00 pm	**Current Concepts in Eye Movement Disorders in Kids: Case-based Potpourri**	**Red Rock Ballroom**
	Moderators: Mark Borchert, MD and Gena Heidary, MD, PhD	

This session will review current concepts in strabismus and gaze abnormalities in pediatric patients. The session will focus on providing a framework for differentiating amongst supranuclear, neuromuscular, genetic, and mechanical causes of strabismus. Specifically, we seek to provide novel insights into pathophysiology of disease, genetic classifications of disease, and the nuances of the clinical presentation which will promote a deeper understanding of eye movement disorders in children. Topics will cover essential infantile esotropia, congenital oculomotor apraxia, Duane syndrome, congenital cranial dysinnervation disorders, Moebius syndrome, and neuromuscular diseases that affect oculomotor function in children.

Upon completion of this session, participants should be able to: 1) differentiate amongst supranuclear, neuromuscular, and mechanical etiologies of pediatric strabismus and 2) apply the appropriate diagnostic testing regarding each and 3) describe novel concepts underlying infantile strabismus.

10:00 am – 10:20 am	**Essential Infantile Esotropia**, *Michael Brodksy, MD*
10:20 am – 10:35 am	**Congenital Ocular Motor Apraxia**, *Jane Edmond, MD*
10:35 am – 10:50 am	**Duane Syndrome**, *Mark Borchert, MD*
10:50 am – 11:10 am	**Congenital Cranial Dysinnervation Disorders,** *Gena Heidary, MD, PhD*
11:10 am – 11:25 am	**Moebius Syndrome**, *Shannon Beres, MD*
11:25 am – 11:45 am	**Neuromuscular Disorders**, *Veeral Shah, MD, PhD*
11:45 am – 12:00 pm	**Panel Discussion and Audience Questions**

HOW DO I EVALUATE HORNER SYNDROME IN AN ADULT?

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LEARNING OBJECTIVES

1. Describe the relevant anatomy of the sympathetic fibers to the head and eye
2. Recognize the signs and symptoms of an oculosympathetic defect
3. Demonstrate when and how to perform pharmacologic testing for diagnosis

CME QUESTIONS

1. True or False: The anisocoria due to Horner syndrome is best observed under bright room lighting.

2. What is the most specific clinical sign of a Horner syndrome?
   A. anisocoria
   B. upper lid ptosis
   C. pupillary dilation lag
   D. conjunctival injection
   E. none of the above

3. What response to topical apraclonidine confirms sympathetic denervation of the eye?
   A. failure of the smaller pupil to dilate
   B. dilation of the smaller pupil
   C. failure of the larger pupil to constrict
   D. constriction of the larger pupil

KEYWORDS

1. Anisocoria
2. Ptosis
3. Oculosympathetic defect

SYLLABUS

I. Clinical Signs

A. Pupil findings: static and dynamic

Anisocoria is the most constant sign of an oculosympathetic defect, present in 98% of patients with Horner syndrome (Maloney et al. 1980). The pupil diameter of a sympathetically denervated eye will be smaller compared to the pupil of the normally-innervated contralateral eye. The actual degree of aniscoria varies. In general, decreased alertness and increased roomlight illumination serve to constrict both pupils, thus minimizing anisocoria in the patient with Horner syndrome. Conversely, the anisocoria of Horner syndrome is best observed under dimlight conditions or following a sudden noise.

In addition to the smaller resting size of the pupil, sympathetic denervation impairs the dilation movement of the pupil. Abrupt light termination or a psychosensory stimulus e.g. loud noise evokes a brisk pupillary dilation. However, a sympathetically denervated pupil dilates slowly and

continuously, mostly from decreasing parasympathetic tone. While pupillary dilation lag is specific to sympathetic denervation of the eye, it is clinically observable in about half of patients with Horner syndrome. Pupillography can provide more objective parameters of dilation dynamics. One popular pupillographic definition of sympathetic failure is delay in the time from peak constriction to 75% of maximal pupil diameter (Smith et al. 1999).

B. Ptosis

The tarsal (Müller) muscles of the upper and lower eyelids are sympathetically innervated. The superior tarsal muscle controls the resting position of the upper lid of the non-closed eye. Its maximum excursion is 3 mm and contributes to but is not the major muscle for lid elevation. Ptosis from ocular sympathetic denervation tends to be mild, on the order of 1 to 2 mm. In one study of 450 patients, only 88% of patients demonstrated clinically-evident upper lid ptosis (Maloney et al. 1980). The inferior tarsal muscle is very small and thin but there is no compensatory voluntary muscle as with the upper eye lid. Paresis of the inferior tarsal muscle leads to a rise in the position of the lower lid, a finding known as lower lid ptosis or inverse ptosis. Lower lid ptosis is subtle, typically less than 1mm, and noted in about 2/3 of patients with Horner syndrome (Nielson 1983). The loss of tonus in the tarsal muscles narrows the palpebral fissure, giving a false impression of enophthalmos.

C. Vasomotor and sudomotor signs

Interruption of the sympathetic pathway leads to anhidrosis and loss of skin flushing, though the extent is dependent on the site of the lesion. Patients with preganglionic Horner syndrome can have hemifacial loss of flushing and sweating which is particularly noticeable during exercise or in babies during strenuous crying, because the pale, dry skin of the denervated side contrasts against the reddish, flushed and sweaty skin of the normally innervated side. This has been called the harlequin sign (Lance et al 1988). In the largest published series of patients with harlequin syndrome (n=39), two thirds had abnormal pupils (Bremner et al.2008). The most common pupil defect was an ipsilateral postganglionic Horner syndrome, suggesting injury at level of the superior cervical ganglion.

D. Other less common symptoms and signs of sympathetic denervation of head and eye

Ocular hypotony and increased accommodation may transiently accompany acute ocular sympathetic denervation. However chronic reduction of intraocular pressure has been reported with longstanding postganglionic Horner syndrome (Wentworth et al.1981).

Iris color is primarily due to the amount and distribution of melanin pigment in the melanocytes of the superficial (anterior) stroma of the iris. The eyes of a newborn are light blue or grayish as melanin production is incomplete and over the first year of life, melanin content increases to reach a genetically-determined adult density. Sympathetic innervation plays a role in the tyrosinase activity and the development of melanin pigment in iris melanocytes. Iris heterochromia in patients with Horner syndrome suggests a congenital origin. But iris melanin content is modifiable: iris heterochromia can appear in adults with longstanding acquired Horner syndrome.

In children, Horner syndrome can also change hair texture. There are a few reports of preganglionic Horner syndrome associated with straight hair on the side of the sympathetic deficit in children aged 3 weeks to 2 years (Ott et al.2018). The mechanism is not established. All human hair fibers exhibit the same basic structure but the three-dimensional arrangement of the fiber determines whether the hair appears straight or curled. Since the follicle of a highly curled hair appears curved, it has been speculated loss of trophic effect of sympathetic stimulation affects the follicle. In contrast to acquired iris heterochromia in rare adults with Horner syndrome, there are no reports of change in hair texture in adults with Horner syndrome. This is a purely pediatric sign.

The parotid gland is innervated by sympathetic and parasympathetic pathways. The non-ocular sympathetic nerves follow the external carotid artery and its branches that extend along the middle meningeal artery carry secretomotor function to the parotid gland. Complete loss of

sympathetic innervation to the parotid gland can lead to a painful condition called “first bite syndrome”. This syndrome typically occurs as a complication of postoperative complication of parapharyngeal space surgery which involves ablation or removal of the superior cervical ganglion. Most patients have an ipsilateral Horner syndrome. Upon the first bite of a meal, there is excruciating pain and cramping in the parotid region which rapidly subsides in a matter of seconds and does not recur with subsequent bites. However, the pain invariably returns with the first bite of the next meal (Kawashima et al.2008). The mechanism is believed to be related to supersensitivity of myoepithelail cells surrounding salivary ducts.

II. Pharmacologic testing for diagnosis of Horner syndrome

A. Cocaine

Pupillary dilation from topical cocaine requires an intact oculosympathetic pathway in which there is continuous release of norepinephrine from presynaptic sympathetic nerve terminals. Cocaine blocks pre-synaptic reuptake of norepinephrine, thus permitting norepinephrine action on postsynaptic receptors to be enhanced. In the event of injury anywhere along the oculosympathetic pathway, cocaine-induced mydriasis is reduced or absent when compared to the fellow normally-innervated eye.

Typically, this is observed as an increase in the baseline anisocoria following cocaine. A more specific criterion for diagnosis of Horner syndrome is finding a post-cocaine anisocoria $\geq$ 0.8mm (Kardon et al.1990).This criterion cannot be used to diagnose bilateral Horner syndrome since the normal eye serves as the control eye (pupil dilates).Caution is advised when performing cocaine test in persons with dark eyes as heavily pigmented irides respond poorly to topical cocaine (melanin tends to bind cocaine and prevents it from reaching sympathetic nerves).

The major advantage of cocaine for diagnosis of Horner syndrome is that it is safe to use in children, even babies, and can be used in acute cases of denervation. Its disadvantages are difficulty in obtaining this schedule II drug, short shelf-life, potential corneal toxicity and limitation to diagnosis of unilateral Horner syndrome. While systemic effects of topical cocaine in adults have not been reported, metabolites of cocaine, particularly benzoylecgonine, may persist for up to 48 hours in urine.

B. Apraclonidine

Apraclonidine is a relatively selective agonist of alpha2-adrenergic receptors which are located in various structures of the eye, notably in the trabecular meshwork, ciliary body epithelium and ciliary muscle. Alpha2 agonists mainly inhibit aqueous production and increase uveoscleral outflow, thus reducing intraocular pressure. Stimulation of the presynaptic alpha-2 adrenergic receptor also inhibits release of norepinephrine from the postganglionic sympathetic neuron, so that apraclonidine has a minimal constricting effect on the pupil. Apraclonidine has a secondary, weaker action as agonist of alpha1-adrenergic receptors which can cause conjunctival vasoconstriction and mild retraction of the upper eyelid (Kirkpatrick et al. 2018). The effect of topical apraclonidine on the normal pupil and eyelid is presumably dose-independent between 0.25% and 1.0%. Systemic side-effects from single use topical apraclonidine have not been reported in adults but may occur in young children.

In 1995, Morales et al noted pupillary dilation in the eye with Horner syndrome (pre and post ganglionic lesions); presumably, this occurs when up-regulation of alpha1-adrenergic receptors in the denervated iris overwhelms the alpha2 effect on pupil size (Morales et al. 2000). The authors proposed that a reversal of anisocoria following topical apraclonidine in both eyes is a diagnostic sign of unilateral Horner syndrome (the Horner pupil becomes the larger pupil post-apraclonidine).

The timing of upregulation of post-synaptic alpha1 receptors in the iris is not established. While a positive apraclonidine test has been reported as early as 36 hours following sympathetic

denervation, a general rule is that apraclonidine is likely to be negative (falsely) in Horner syndrome that is less than one week old.

Which is better: cocaine or apraclonidine? A randomized comparison trial for a pharmacologic test to detect oculosympathetic palsy has not been performed. However, the latest paper examining their pharmacologic effect in both normal and sympathetically denervated eyes gives some guidelines for interpretation of test results (Bremner 2018).

In normal eyes, cocaine typically dilates the pupil and apraclonidine has a mild miotic effect, but the range of their effect on normal pupils is surprisingly large. The average mydriatic effect of cocaine is 2.1mm with maximum of 3.9mm. Some normal pupils constrict slightly (-0.36mm) to cocaine instillation. Apraclonidine generally has a mild miotic effect (mean -0.4mm, maximum -1.3mm). Yet some normal pupils may slightly dilate (up to 0.8mm) in response to topical apraclonidine.

From the normative data, a criterion response that diagnosed a Horner syndrome was established: pupil dilation $\leq$ 0.5mm to cocaine or pupil dilation $\geq$ 0.1mm to apraclonidine. From the criterion response, cocaine testing identified 36 of 95 Horner eyes for a sensitivity of 40%. Why so low? One reason is that the expected "failure to dilate" is not exactly how Horner eyes respond to cocaine (Bremner 2018). This study found that Horner eyes show a mild mydriatic effect to cocaine (mean 0.7mm, max 2.94). Thus, in patients with unilateral Horner syndrome, the criterion of post-cocaine anisocoria $\geq$0.8mm (Kardon et al. 1990) is preferable as test sensitivity is 76%.

For apraclonidine, a pupillary dilation $\geq$ 0.1mm (viewed in dim light 40 minutes after instillation of the drug) was sufficient to detect Horner syndrome in 93% of cases. In other words, it is very rare (5% or less) that a normal pupil dilates at all to apraclonidine. Thus, one advantage of apraclonidine is that it can be used to diagnose patients with bilateral Horner syndrome. If the post-apraclonidine pupil was examined under bright light, the sensitivity for detecting Horner syndrome dropped to 76%. If the criterion of reversal of anisocoria was applied, sensitivity dropped to 75%.

III. Pharmacologic localization

A. Hydroxyamphetamine - is it useful?

Hydroxyamphetamine belongs to a group of indirect-acting adrenergic mydriatics which release endogenous norepinephrine from sympathetic nerve endings. Unlike cocaine, its effect seems to depend largely on the structural integrity of post-ganglionic nerve endings.

Is it useful in clinical evaluation of Horner syndrome? Yes, hydroxyamphetamine is useful for providing localization information about the sympathetic defect, particularly when Horner syndrome is an isolated sign, and helps interpretation of radiologic findings. Failure of the Horner pupil to dilate to hydroxyamphetamine indicates a post-ganglionic site of injury. Is it safe for use in children? The safety profile and effectiveness of hydroxyamphetamine in pediatric patients are not known.

In the practical sense, topical hydroxyamphetamine is not "useful". The drug is no longer a commercial product and requires a compounding pharmacy for fabrication. Paremyd® is a combination ophthalmic solution of 1% hydroxyamphetamine and 0.25%tropicamide and should not be used as a substitute for hydroxyamphetamine (Paredrine®).

Are there alternative pharmacologic agents for localizing a Horner syndrome? Hydroxy-methamphetamine (pholedrine) is a compound related to hydroxyamphetamine and is used to induce systemic hypotension. In ophthalmic solution, 1% pholedrine appears to function like topical hydroxyamphetamine (Bates et al 1995). Dilute phenylephrine theoretically identifies post-ganglionic lesions via a suprasensitivity response (Danesh-Meyer et al.2004) But experience with the dilute pilocarpine test for cholinergic denervation supersensitivity suggests that a pre- vs post-ganglionic distinction cannot be reliably made from the pupil response to a dilute agonist agent. In 31 patients having third nerve palsy (a preganglionic parasympathetic denervation of the sphincter), 35% demonstrated cholinergic supersensitivity (Jacobson 1994). It is not known what percentage of pre-ganglionic sympathetic lesions would dilate in response to dilute phenylephrine.

IV. Causes of Horner syndrome

The 3-neuron sympathetic pathway to the head and eye is well-described. In general, the first-order neuron descends from the hypothalamus to synapse in the nucleus of Budge-Waller in the lower cervical-upper thoracic spinal cord (C8-T2). The second-order neuron ascends the cervical sympathetic chain and stellate ganglion, terminating in the superior cervical ganglion. The third-order oculosympathetic fibers travel with the internal carotid artery and re-enter the intracranial space via the carotid canal. At the orbital apex, they follow the nasociliary nerve to the eye. A few points of the oculosympathetic pathway and their clinical signficance are noted below:

A. Ventral roots

Preganglionic oculosympathetic neurons exit primarily through the first thoracic root (T-1) whereas most of the preganglionic vasomotor and sudomotor fibers dedicated to the face emerge at the level of T-2 and T-3. Horner syndrome has occasionally been described from a T1 disc herniation. The ventral roots are composed of somatic efferent fibers, and roots from C5-T1 converge to form the brachial plexus.

B. Brachial plexus

The preganglionic neurons ascend the medial neck as the cervical sympathetic chain, passing through the stellate ganglion (fusion of the inferior cervical and firt thoracic ganglions) and the middle cervical ganglion, both in close proximity to the roots of the brachial plexus (C5-T1). The brachial plexus traverses the superior sulcus to the armpit, suppling sensory and motor fibers to most of the shoulder, arm and hand. Horner syndrome may accompany brachial plexopathy, for example, compression injury to the brachial plexus, known as “backpack palsy”.

C. Anterior neck

The middle cervical ganglion and sympathetic trunk are located behind the inferior thyroid artery as the artery departs from the thyrocervical trunk. This anatomic relationship is variable but nonetheless makes the sympathetic chain susceptible to injury from thyroid enlargement (goiter) and during thyroidectomy.

The cervical sympathetic chain ends at the superior cervical ganglion at the level of the common carotid bifurcation. At the carotid bifurcation, sudomotor and vasomotor fibers to the medial forehead and the side of the nose travel with ocular sympathetic fibers along the internal carotid artery. Sudomotor and vasomotor fibers to the rest of the face follow the external carotid artery then join branches of the trigeminal nerve.

V. Imaging Horner syndrome

In general, for the adult with an isolated unilateral Horner syndrome that dates back 2 years or more, neuroimaging of the oculosympathetic pathway is optional. For the adult patient with an acquired, non-chronic oculosympathetic defect, a targeted approach to imaging based on anatomic localization of the lesion, either from accompanying symptoms and signs or from pharmacologic (hydroxyamphetamine or similar) testing, is preferred.

For the isolated unilateral Horner syndrome, a pan-scan protocol has been adopted. This may be a CT or MRI protocol which images soft tissues from orbit to T5 and includes angiography of the aortic arch, carotid arteries and intracranial vessels (Davagnanam et al 2013, Beebe et al. 2017). The diagnostic yield of imaging of this subgroup of patients with Horner syndrome is about 20% (Beebe et al 2017) with arterial dissection often the most frequent etiology detected. If imaging is negative, no further testing is needed and management is observational. Rare patients request cosmetic correction of the ptosis. Patients with bilateral Horner syndrome often have other evidence of autonomic dysfunction. The most common cause is diabetes. If the patient is not diabetic, further evaluation for autonomic neuropathy is warranted.

CME ANSWERS

1. False
2. C
3. B

REFERENCES

1. Bates AT, Chamberlain S, Champion M, Foley L, Hughes E, Jani B, Mehta H, Smith SE. Pholedrine: a substitute for hydroxyamphetamine as a diagnostic eyedrop test in Horner's syndrome. J Neurol Neurosurg Psychiatry. 1995;58(2):215-7
2. Beebe JD, Kardon RH, Thurtell MJ. The yield of diagnostic imaging in patients with isolated Horner syndrome. Neurol Clin. 2017;35:145-51
3. Bremner F, Smith S. Pupillographic findings in 39 consecutive cases of harlequin syndrome. J Neuroophthalmol 2008;28:171–7.
4. Bremner F. Apraclonidine is better than cocaine fordetection of Horner syndrome. Frontiers Neurol 2018.
5. Danesh-Meyer HV, Savino P, Sergott R. The correlation of phenylephrine 1% with hydroxyamphetamine 1% in Horner's syndrome. Br J Ophthalmol. 2004 Apr;88(4):592-3.
6. Davagnanam I, Fraser CL, Miszkiel K,Daniel CS, PlantGT. Adult Horner's syndrome: a combined clinical, pharmacological, and imaging algorithm. Eye (2013) 27, 291–298
7. Jacobson DM. A prospective evaluation of cholinergic supersensitivity of the iris sphincter in patients with oculomotor nerve palsies. Am J Ophthalmol. 1994 Sep 15;118(3):377-83.
8. Kardon RH, Denison CE, Brown CK, Thompson HS. Critical evaluation of the cocaine test in the diagnosis of Horner's syndrome. Arch Ophthalmol. 1990;108(3):384-7.
9. Kawashima Y, Sumi T, Sugimoto T, Kishimoto S. First-bite syndrome; a review of 29 patients with parapharyngeal space tumor. Auris Nasus Larynx 2008; 35: 109-113
10. Kirkpatrick C, Shriver EM, Clark TJE, Kardon RH. Upper eyelid response to topical 0.5% apraclonidine. Ophthalmic Plast Reconstr Surg. 2018;34(1):13-19
11. Lance JW, Drummond PD, Gandevia SC, Morris JGL. Harlequin syndrome: the sudden onset of unilateral flushing and sweating. J Neurol Neurosurg Psychiatry 1988;51:635—42.
12. Maloney WF, Younge BR, Moyer NJ. Evaluation of the causes and accuracy of pharmacologic localisation in Horner's syndrome. Am J Ophthalmol 1980; 90:394-402.
13. Morales J, Brown SM, Abdul-Rahim AS, Crosson CE. Ocular effects of apraclonidine in Horner syndrome. Arch Ophthalmol. 2000 Jul;118(7):951-4.
14. Nielson PJ. Upside down ptosis in patients with Horner's syndrome. Acta Ophthalmologica 1983; 61:952-957.
15. Sadaka A, Schockman SL, Golnik KC. Evaluation of Horner Syndrome in the MRI Era.J Neuroophthalmol. 2017 Sep;37(3):268-272.
16. Smith SA, Smith SE. Bilateral Horner's syndrome: detection and occurrence. J Neurol Neurosurg Psychiatry.1999; 66(1):48±51.
17. Wentworth WO. Brubaker RF. Aqueous humour dynamics in a series of patients with third neuron Homer's syndrome. Am J Ophthalmol 1981; 92: 407-15.

HOW DO I EVALUATE HORNER SYNDROME IN A CHILD?

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LEARNING OBJECTIVES

1. Describe the differences and similarities between children and adults with Horner syndrome
2. Recognize when to use cocaine and when to use apraclonidine when evaluating a child with Horner syndrome.
3. Identify various approaches to working up a child with unexplained Horner syndrome.

CME QUESTIONS

1. Carotid dissection is a primary consideration in children with Horner syndrome
2. Apraclonidine drops are safe to use in all children.
3. Neuroblastoma is one important cause of Horner syndrome in a child.

KEYWORDS

1. Horner
2. Cocaine
3. Neuroblastoma

SYLLABUS:

Similarities between children and adults with Horner syndrome.

- Presentation with ptosis, miosis, and anhidrosis
- Neuro-anatomy is the same. Consideration of lesions affecting the first, second, and third-order neurons

Differences between children and adults with Horner syndrome.

- Congenital cases, with birth trauma in the differential diagnosis (Weinstein et al. 1980)
- More presentations with iris heterochromia
- Carotid dissection, lung cancer, and microvascular causes more common in adults.
- Need to avoid apraclonidine testing because of risk of drowsiness and unresponsiveness in young children less than 2 years of age.
- Confirmation with cocaine drop testing preferred in children less than 2 years of age (Martin 2017).
- Neuroblastoma is a consideration, so workup should include urine vanillylmandelic acid (VMA) and homovanillic acid (HVA) testing.
- Despite opinion to the contrary (Smith et al. 2010), we believe that all patients with an obvious or confirmed Horner's syndrome <1 year in duration also should undergo MR imaging of the head, neck, and upper chest to rule out a responsible mass lesion. In our study (Mahoney et al. 2006), of 18 children who had complete imaging and urine studies, and the diagnosis was unknown, responsible mass lesions were found in six (33%).

- Even children with a history of birth trauma or those with Horner's at birth ("congenital") should be evaluated, as these patients may still harbor an underlying neoplasm (Mahoney et al. 2006)
- Caution also should be applied when hydroxyamphetamine is used in children with Horner's syndrome. The normal development of the third-order oculosympathetic neuron and its synaptic connections depends on the integrity of the first and second neuron. In congenital preganglionic lesions, therefore, it is possible that hydroxyamphetamine will completely or partially fail to dilate the involved pupil because of transsynaptic degeneration of postganglionic fibers (Weinstein et al. 1980).
- Carotid dysgenesis is in the differential diagnosis of children with congenital Horner's syndrome (Kadom 2015), so we also recommend MRI-angiography of the neck as part of the workup.
- There have been rare cases of Horner syndrome associated with neuroblastomas arising from the adrenal glands and in the lower thoracic sympathetic chain. In George et al.'s (1998) case, CT of the neck and chest imaging was negative. How distant tumors affect the oculosympathetic pathway is uncertain, but a more generalized disorder of sympathetic neuronal maturation has been proposed. Alternatively, a small cervical metastasis may have been missed without MRI of the neck, as neuroblastoma may be multifocal (John Maris, MD, personal communication). Because of the uncertainty of the relationship with these non-cervical neuroblastomas with the Horner syndrome, currently we are not recommending abdominal imaging as part of the evaluation.
- Children with pharmacologically-confirmed oculosympathetic paresis with no obvious cause and normal imaging and urine testing are given the diagnosis of idiopathic Horner syndrome. One suggested etiology in these cases is regressed neuroblastoma.

Suggested protocol. As in adults, although there are rare exceptions, most causes of Horner syndrome in children of more than one year in duration are benign and imaging is not be mandatory. A work-up in these instances may depend on the level of concern between the parents and physician. The protocol applies to children with Horner syndrome which is acquired or present at birth, with or without a history of birth trauma.

So my suggested protocol for evaluating children with Horner syndrome <1 year in duration is as follows:

1. Palpate the neck, upper chest, axillae, abdomen for masses.
2. Localize the Horner syndrome clinically, confirm with cocaine or apraclonidine (above age 2 years only for the latter). If cocaine cannot be obtained, and the child is less than 2 years of age, then one will have to proceed presumptively.
3. In localizable cases with confirmed Horner syndrome, non-emergent directed imaging.
4. In non-localizable cases with confirmed Horner syndrome, non-emergent evaluation to exclude neuroblastoma and other responsible mass lesions.
   i) Combined chest and neck MRI (conservative approach) and urine VMA and HVA
   ii) Combined head, neck, chest imaging and vascular neck imaging ("nontargeted", "shotgun" approach that I prefer) and urine VMA and HVA.

CME ANSWERS

1. False
2. False
3. True

REFERENCES

1. George NDL, Gonzalez G, Hoyt CS: Does Horner's syndrome in infancy require investigation? Br J Ophthalmol 1998;82:51-54.
2. Jeffery AR, Ellis FJ, Repka MX, et al.: Pediatric Horner syndrome. J AAPOS 1998;2:159-167.
3. Kadom N, Rosman NP, Jubouri S, et al. Neuroimaging experience in pediatric Horner syndrome. Pediatr Radiol 2015;45:1535-1543.
4. Mahoney NR, Liu GT, Menacker SJ, Wilson MC, Hogarty MD, Maris JM. Pediatric Horner's syndrome: etiologies and roles of imaging and urine studies to detect neuroblastoma and other responsible mass lesions. Am J Ophthalmol 2006;142:651-659.
5. Martin GC, Aymard PA, Denier C, et al.: Usefulness of cocaine drops in investigating infant anisocoria. Eur J Paediatr Neurol 2017;21:852-857.
6. Smith SJ, Diehl N, Leavitt JA, et al.: Incidence of pediatric Horner syndrome and the risk of neuroblastoma. Arch Ophthalmol 2010;128:324-329.
7. Weinstein JM, Zweifel TJ, Thompson HS: Congenital Horner's syndrome. Arch Ophthalmol 1980;98:1074-1078.
8. Woodruff G, Buncic JR, Morin JD: Horner's syndrome in children. J Ped Ophthalmol Strab 1988;25:40-44.

ADULT OPTIC NEURITIS

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LEARNING OBJECTIVES

1. Describe the clinical characteristics and outcomes of optic neuritis in adults.
2. Explain the natural history of optic neuritis (and the associated risk of multiple sclerosis), based on data from the Optic Neuritis Treatment Trial (ONTT), the Longitudinal Optic Neuritis Study (LONS) and others.
3. Interpret the outcomes associated with anti-aquaporin-4 and anti-myelin oligodendrocyte glycoprotein antibody positivity in adult optic neuritis.

CME QUESTIONS

1. Which of the following treatment regimens is/are associated with better visual outcomes in adults with optic neuritis?
    A. Immediate treatment with intravenous corticosteroids, 1000 mg daily for 3 days
    B. Immediate treatment with oral steroids, 1250 mg daily for 3 days
    C. Acute treatment with (a) or (b), followed by a 2-week oral prednisone taper
    D. Bilateral optic neuritis at presentation
    E. None of the above

2. Which of the following is associated with a greater risk of multiple sclerosis in adult patients presenting with optic neuritis?
    A. Peripapillary hemorrhage
    B. No-light-perception vision
    C. Periventricular white matter lesions at initial MRI of the brain
    D. Severe optic disc edema
    E. Absence of pain with eye movements

3. The addition of plasma exchange to intravenous methylprednisolone in the acute treatment of NMO-associated acute optic neuritis results in improvement in all of the following <u>except:</u>
    A. Visual field defects
    B. Temporal retinal nerve fiber layer (RNFL) thickness
    C. Color vision
    D. High-contrast letter acuity

KEY WORDS

1. Neuro-ophthalmology
2. Optic Neuritis
3. Myelin oligodendrocyte glycoprotein
4. Neuromyelitis Optica
5. Multiple Sclerosis

HIGHLIGHTS

Acute optic neuritis remains an ideal clinical and experimental opportunity for the application of novel imaging and physiologic modalities, and for the exploration of candidate neuroprotective therapies to improve outcomes related to demyelination, axonal injury and neuronal degeneration. Optic neuritis in the adult differs in clinical course from optic neuritis in the pediatric population; however, there is considerable overlap in treatment strategies and in the potential prognostic utility of emerging biomarkers (such as anti-myelin oligodendrocyte glycoprotein and aquaporin-4 antibodies) that make expertise in both entities of benefit to the clinician.

SUMMARY

Adult optic neuritis is a common presentation to the neuro-ophthalmologist, and the study of this disorder continues to be foundational to our understanding of central nervous system disease. There are several features which distinguish optic neuritis in adults, most notably the tendency for *monocular* vision loss with the *presence of pain* and *absence of visible optic disc edema* (all of which are uncommon in the pediatric population).

Clinical Characteristics

Acute optic neuritis (AON) in adults is characterized by idiopathic, painful, and typically monocular vision loss due to inflammation of the optic nerve.[1] In the United States, the estimated annual incidence of ON is 5 to 6.4 cases per 100,000, with a prevalence of 115 cases per 100,000[2] (although a greater incidence at higher latitudes is recognized,[3] and other characteristics may vary by geography and ethnicity).[4,5] Most patients with so-called “typical” optic neuritis are between the ages of 20 and 45, and two-thirds are women.[6]

In contrast to pediatric optic neuritis,[7] visible swelling of the optic disc is uncommon in adults with fully two-thirds of the optic nerves in affected eyes appearing normal.[6]

Vision at Presentation and Visual Outcomes

The degree of visual acuity loss at presentation is variable, ranging from mild to no-light-perception. Visual field loss is common, but there is no predictable pattern or degree. The most specific clinical features of optic neuritis are dyschromatopsia (typically mixed red-green and blue-yellow[8]), reduced contrast sensitivity, and the presence of an afferent pupillary defect.

From onset, vision loss typically progresses over a period of hours to days but spontaneous improvement thereafter is common,[9] usually within 30 days and corresponding with the resolution of optic nerve inflammation.[10] Although the final visual outcome is not favorably affected, the use of intravenous corticosteroids will hasten the recovery of vision.[11] Maximal visual recovery is achieved within 6 months.[12]

The majority of patients will achieve a satisfactory visual outcome, with or without acute intravenous (IV) steroid treatment.[13,14] However, despite recovery of "normal" vision based on commonly-employed clinical measures, a majority of patients describe subtle deficits in vision following resolution of the acute episode.[15] The resultant reduction in vision-related quality of life may be attributable to a variety of mechanisms including inflammation, demyelination and axonal degeneration in the afferent visual pathways.[16,17] Ongoing efforts to better quantify the pathophysiologic and functional consequences of

optic neuritis using multiple modalities, including low-contrast letter acuity, vision-specific quality-of-life measures, optical coherence tomography (specifically, changes in retinal ganglion cell/inner plexiform layer), and changes in optic nerve diffusion tensor imaging at MRI, are underway.[18]

Neuroimaging

In addition to defining the clinical profile of optic neuritis, the landmark Optic Neuritis Treatment Trial[19] established magnetic resonance imaging (MRI) of the brain as the single most important predictor of multiple sclerosis (MS) for patients presenting with acute idiopathic optic neuritis. Based on the initial data from the ONTT, and from multiple subsequent studies including the Longitudinal Optic Neuritis Study (LONS),[20,21] patients presenting with optic neuritis should be informed that their risk of MS over the ensuing 15 years is 72 percent among those with one or more white matter lesions at MRI, versus 25 percent among those with no lesions. Further, the 2017 revision of the McDonald Criteria permit appropriate lesional findings to constitute "dissemination in time and space," thereby allowing for the diagnosis of clinically-definite MS at the time of initial presentation.[22]

Although optic neuritis is a clinical diagnosis which rarely requires neuroimaging for confirmation, it should be noted that advances in MRI technology (short tau inversion recovery [STIR], fast spin echo [FSE], fluid-attenuated inversion recovery [FLAIR], and diffusion tensor imaging [DTI]) allow for increasingly detailed analysis of the optic nerve, and may provide useful information of diagnostic and prognostic significance.[23,24] Routine imaging of the spine in patients with isolated optic neuritis remains controversial.[25]

Laboratory Workup

Laboratory studies and evaluation of cerebrospinal fluid (CSF) are generally not required for the diagnosis of optic neuritis, and should be considered only in atypical cases. If indicated, however, erythrocyte sedimentation rate (ESR), antinuclear antibodies (ANA), angiotensin converting enzyme (ACE), Bartonella henselae titers, and serologic and CSF investigations for Lyme disease and syphilis may be informative.[26] Testing for serum aquaporin-4 antibodies (neuromyelitis optica or NMO) should be completed for patients with recurrent optic neuritis, especially if MRI does not demonstrate demyelinating lesions.[27] Identification of novel biomarkers, such as serum and plasma neurofilaments NfH and NfL, may eventually provide further pathophysiologic and clinical insights.[28,29]

Neuromyelitis optica (NMO) and MOG-antibody associated demyelinating disease

NMO (Devic disease) and NMO-spectrum disorders are severe neuroinflammatory conditions characterized by optic neuritis that is sometimes bilateral, and by associated visual loss that is often more severe than seen in typical optic neuritis. In addition, NMO-associated optic neuritis is associated with less robust visual recovery, and a greater degree of axonal loss as measured by optical coherence tomography (OCT).[30,31] The disease process in NMO is directed against the aquaporin-4 (AQP4) water channel, which is preferentially expressed in the optic nerves and spinal cord; therefore the immune-mediated demyelination and axonal damage associated with NMO most commonly occur at these sites.

Patients with clinical characteristics suggestive of NMO should be tested for the AQP4 antibody. In addition, patients with sequential optic neuritis in rapid succession,[32] those with recurrent optic neuritis, or patients with normal brain MRI[33] may be especially susceptible to NMO. Similarly, patients with severe or recurrent optic neuritis may be seropositive for antibodies to myelin-oligodendrocyte glycoprotein (MOG), which has also been associated with NMO.[34-37] Consequently, MOG antibody

testing is recommended for patients with recurrent optic neuritis who are negative for aquaporin-4-specific serum autoantibody.

Treatment

Based on data from the ONTT, the mainstay of treatment for AON has been high dose IV methylprednisolone (a total of 1 gram daily for 3 days), sometimes followed by an oral prednisone taper over a period of 11-14 days.[38] Patients treated with IV methylprednisolone were found to have an accelerated rate of visual recovery over the first 15 days, and significantly improved color vision and contrast sensitivity at 6 months. Moreover, patients in the ONTT who received treatment with oral prednisone had a higher risk of recurrent optic neuritis than in the IV or oral placebo groups.[39] There is no difference in eventual visual outcome regardless of IV steroid treatment.[40]

Although IV methylprednisolone is regarded as the current standard of care,[41] discussion and debate regarding novel therapies abound.[42] Plasma exchange (PLEX), either alone or in combination with IV methylprednisolone,[43,44] has shown the potential for benefit in AON and NMO-associated optic neuritis in preliminary studies. A recent trial[45] has demonstrated improvement in post-AON peripapillary retinal nerve fiber layer (RNFL) as measured by OCT and visual-evoked potential (VEP) latencies, and additional investigations are anticipated.[46] A currently-recruiting clinical trial (clinicaltrials.gov; NCT01838174) seeks to compare methylprednisolone and corticotropin use in AON with regard to anti-inflammatory, neuroprotective and restorative effects using OCT and electrophysiology.[47] In general, emerging therapies place an emphasis on supressing inflammation and preventing neuronal damage, which likely contributes to long term (heretofore regarded as "sub-clinical") visual loss following acute optic neuritis.[48]

Multiple sclerosis (MS)

Optic neuritis occurs in 50% of persons with relapsing-remitting MS, and is the initial demyelinating event in 15% to 20% of all MS cases.[49,50]

The 15-year follow-up data from the ONTT determined that the overall risk of developing MS following an episode of AON is 50%. Patients with a normal MRI at presentation had a 25% risk of subsequent MS, while those with one or more lesions at initial MRI had a significantly greater risk (72%) of developing clinically-definite MS within 15 years of the initial optic neuritis event.[51]

Future directions

As in the past, AON provides an ideal model for advancing our ever-expanding understanding of the complex autoimmune basis of inflammatory central nervous system demyelination. Specifically, focus on the functional consequences of optic neuritis on visual quality of life, coupled with burgeoning knowledge being accumulated through the application of retinal imaging and electrophysiology, will assist in further defining the pathophysiology and optimal treatment of demyelination, axonal injury and neuronal degeneration.[47]

CME ANSWERS

1. E
2. C
3. C

REFERENCES

1. Percy AK, Nobrega FT, Kurland LT. Optic neuritis and multiple sclerosis: an epidemiologic study. Archives of Ophthalmology. 1972;87(2):135-139.
2. Rodriguez M, Siva A, Cross SA, O'Brien PC, Kurland LT. Optic neuritis: a population based study in Olmsted County, Minnesota. Neurology. 1995;45:244–250.
3. Shams PN, Plant GT. Optic neuritis: a review. International MS Journal. 2009;16:82–89.
4. Langer-Gould A, Brara S, Beaber BE, et al. The incidence of clinically isolated syndrome in a multi-ethnic cohort. Journal of Neurology. 2014;261:1349-55.
5. Rodriguez M, Siva A, Cross SA, et al. Optic neuritis: a population-based study in Olmsted County, Minnesota. Neurology. 1995;45:244-50.
6. Optic Neuritis Study Group. The clinical profile of optic neuritis: experience of the Optic Neuritis Treatment Trial. Archives of Ophthalmology. 1991;109(12):1673-8.
7. Wiljeto M, Shroff M, Buncic JR, et al. The clinical features, MRI findings, and outcome of optic neuritis in children. Neurology. 2006;67:258-62.
8. Schneck ME, Haegerstrom-Portnoy G. Color vision defect type and spatial vision in the optic neuritis treatment trial. Investigative Ophthalmology and Visual Science. 1997;38:2278–2289.
9. Celesia GG, Kaufman DI, Brigell M et al. Optic neuritis: a prospective study. Neurology. 1990;40:919–923.
10. Beck RW, Cleary PA, Backlund JC. The course of visual recovery after optic neuritis: experience of the Optic Neuritis Treatment Trial. Ophthalmology. 1994;101(11):1771-1778.
11. Sellebjerg F, Nielsen HS, Frederiksen JL, Olesen J. A randomized, controlled trial of oral high-dose methylprednisolone in acute optic neuritis. Neurology. 1999;52(7):1479-1484.
12. Kolappan M, Henderson AP, Jenkins TM, et al. Assessing structure and function of the afferent visual pathway in multiple sclerosis and associated optic neuritis. J Neurol. 2009;256(3):305-319.
13. Visual function 5 years after optic neuritis: experience of the Optic Neuritis Treatment Trial: The Optic Neuritis Study Group. Archives of Ophthalmology. 1997;115(12):1545- 1552.
14. Optic Neuritis Study Group. Multiple sclerosis risk after optic neuritis: final Optic Neuritis Treatment Trial follow-up. Archives of Neurology. 2008;65:727-32.
15. Jasse L, Vukusic S, Durand-Dubief F et al. Persistent visual impairment in multiple sclerosis: prevalence, mechanisms and resulting disability. Multiple Sclerosis Journal. 2013. 19:1618-26.
16. Evangelou N, Konz D, Esiri MM et al. Size-selective neuronal changes in the anterior visual pathways suggest a differential susceptibility to injury in multiple sclerosis. Brain. 2001; 124, Issue 9:1813-20.
17. Deluca GC. The contribution of demyelination to axonal loss in multiple sclerosis. Brain. 2006;129(Pt 6):1507-16.
18. Balcer LJ, Miller DH, Reingold SC, Cohen JA. Vision and vision-related outcome measures in multiple sclerosis. Brain. 2015;138(1):11-27.
19. Beck RW. The Optic Neuritis Treatment Trial. Archives of Ophthalmology. 1988;106(8):1051-1053.
20. Beck RW, Trobe JD, Moke PS et al. Optic Neuritis Study Group. 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. 2003;121(7):944.
21. Optic Neuritis Study Group. Multiple sclerosis risk after optic neuritis: final optic neuritis treatment trial follow-up. Archives of Neurology. 2008;65(6):727.
22. Thompson AJ, Banwell BL, Barkhof F et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurology. 2018;17:162–173.
23. Hickman SJ, Toosy AT, Miszkiel KA et al. Visual recovery following acute optic neuritis: a clinical, electrophysiological and magnetic resonance imaging study. Journal of Neurology. 2004;251(8):996.

24. 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.
25. Meltzer E, Frohman EM, Costello FE, et al. Should spinal MRI be routinely performed in patients with clinically isolated optic neuritis? Journal of Neuro-ophthalmology. 2018: Epub ahead of print; doi: 10.1097/WNO.0000000000000685.
26. Beck RW and Trobe JD. What we have learned from the Optic Neuritis Treatment Trial. Ophthalmology. 1995;102(10):1504.
27. Petzold A, Pittock S, Lennon V, Maggiore C, Weinshenker BG and Plant GT. Neuromyelitis optica-IgG (aquaporin-4) autoantibodies in immune mediated optic neuritis. Journal of Neurology, Neurosurgery and Psychiatry. 2010;81(1):109.
28. Petzold A, Plant GT. The diagnostic and prognostic value of neurofilament heavy chain levels in immune-mediated optic neuropathies. Multiple Sclerosis International. 2012;2012:217802.
29. Modvig S, Degn M, Horowitz H et al. Relationship between cerebrospinal fluid biomarkers for inflammation, demyelination and neurodegeneration in acute optic neuritis. PLoS ONE. 2013;8:e77163.
30. Merle H, Olindo S, Bonnan M et al. Natural history of the visual impairment of relapsing neuromyelitis optica. Ophthalmology. 2007:114:810-815.
31. Naismith RT, Tutlam NT, Xu J et al. Optical coherence tomography differs in neuromyelitis optica compared to multiple sclerosis. Neurology. 2009;72:1077-82.
32. Sellner J, Boggild M, Clanet M et al. EFNS guidelines on diagnosis and management of neuromyelitis optica. European Journal of Neurology. 2010;17(8):1019-32.
33. Pirko I, Blauwet LA, Lesnick TG, Weinshenker BG. The natural history of recurrent optic neuritis. Archives of Neurology. 2004;61(9):1401.
34. Martinez-Hernandez E, Sepulveda M, Rostásy K et al. Antibodies to aquaporin 4, myelin-oligodendrocyte glycoprotein, and the glycine receptor α1 subunit in patients with isolated optic neuritis. JAMA Neurology. 2015;72(2):187.
35. Chalmoukou K, Alexopoulos H, Akrivou S et al. Anti-MOG antibodies are frequently associated with steroid-sensitive recurrent optic neuritis. Neurology, Neuroimmunology and Neuroinflammation. 2015;2(4):e131.
36. Pache F, Zimmermann H, Mikolajczak J et al. MOG-IgG in NMO and related disorders: a multicenter study of 50 patients. Part 4: Afferent visual system damage after optic neuritis in MOG-IgG-seropositive versus AQP4-IgG-seropositive patients. Journal of Neuroinflammation. 2016;13(1):282. Epub 2016 Nov 1.
37. Dos Passos GR, Oliveira LM, da Costa BK MOG-IgG-Associated Optic Neuritis, Encephalitis, and Myelitis: Lessons Learned From Neuromyelitis Optica Spectrum Disorder. Frontiers in Neurology. 2018;9:217. Epub 2018 Apr 4.
38. Perumal JS, Caon C, Hreha S et al. Oral prednisone taper following intravenous steroids fails to improve disability or recovery from relapses in multiple sclerosis. European Journal of Neurology. 2008;15(7):677-680.
39. Beck RW, Cleary PA, Anderson MM Jr et al. The Optic Neuritis Study Group: a randomized, controlled trial of corticosteroids in the treatment of acute optic neuritis. New England Journal of Medicine. 1992;326(9):581-588.
40. Arnold AC. Evolving management of optic neuritis and multiple sclerosis. American Journal of Ophthalmology. 2005;139(6):1101-8.
41. Kaufman DI, Trobe JD, Eggenberger ER and Whitaker JN. Practice parameter-the role of corticosteroids in the management of acute monosymptomatic optic neuritis: report of the Quality Standards Subcommittee of The American Academy of Neurology(1). American Journal of Ophthalmology. 2000;130(4):541.

42. Pula JH, Glisson CC. Should plasma exchange be offered to patients with multiple sclerosis–associated optic neuritis? Journal of Neuro-Ophthalmology. 2015;35(1):86-89.
43. Ruprecht K, Klinker E, Dintelmann T et al. Plasma exchange for severe optic neuritis: treatment of 10 patients. Neurology. 2004;63:1081-3.
44. Deschamps R, Gueguen A, Parquet N et al. Plasma exchange response in 34 patients with severe optic neuritis. Journal of Neurology. 2016;263(5):883-887.
45. Suhs KW, Hein K, Sattler MB et al. A randomized, double-blind, phase 2 study of erythropoietin in optic neuritis. Annals of Neurology. 2012;72:199-210.
46. Diem R, Molnar F, Beisse F et al. Treatment of optic neuritis with erythropoietin (TONE): a randomised, double-blind, placebo-controlled trial—study protocol. BMJ Open.2016;6**:**e010956.
47. Bennett JL, Nickerson M, Costello F et al. Re-evaluating the treatment of acute optic neuritis. Journal of Neurology, Neurosurgery and Psychiatry. 2015;86:7.
48. Khan RS, Dine K, Bauman B et al. Intranasal delivery of a novel amnion cell secretome prevents neuronal damage and preserves function in a mouse multiple sclerosis model. Scientific Reports. 2017;7:41768.
49. Foroozan R, Buono LM, Savino PJ, Sergott RC. Acute demyelinating optic neuritis. Current Opinion in Ophthalmology. 2002;13(6):375-380.
50. Frohman EM, Frohman TC, Zee DS, McColl R, Galetta S. The neuro-ophthalmology of multiple sclerosis. Lancet Neurology. 2005;4(2):111-121.
51. Kaufman DI. The Optic Neuritis Study Group, Multiple sclerosis risk after optic neuritis: final optic neuritis treatment trial follow up. Paper presented at: the American Academy of Ophthalmology; November 12, 2007; New Orleans, LA.

PEDIATRIC OPTIC NEURITIS

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LEARNING OBJECTIVES

1. Describe the clinical characteristics and outcomes of optic neuritis in children.
2. Formulate a diagnostic workup for a pediatric patient with optic neuritis
3. Describe the outcomes associated with anti-aquaporin-4 and anti-myelin oligodendrocyte glycoprotein antibody positivity in pediatric optic neuritis.

CME QUESTIONS

1. What treatment regimen has demonstrated more rapid visual acuity recovery in pediatric optic neuritis patients in a prospective randomized clinical trial?

   A. Rituximab
   B. Methylprednisolone 3-5 days (20-30mg/kg/d)
   C. Intravenous immunoglobulin
   D. B and C
   E. None of the above

2. Which of the following are not associated with a diagnosis of multiple sclerosis in pediatric optic neuritis?

   A. Increasing age
   B. Lesions on brain MRI
   C. Presence of oligoclonal bands
   D. Presence of anti-myelin oligodendrocyte glycoprotein antibodies
   E. Absence of anti-aquaporin 4 antibodies

3. True or False: Visual acuity outcomes in pediatric optic neuritis are better than those for adult optic neuritis in the Optic Neuritis Treatment trial.

KEYWORDS

1. Pediatric neuro-ophthalmology
2. Optic neuritis
3. Neuromyelitis optica
4. Myelin oligodendrocyte glycoprotein
5. Multiple sclerosis

HIGHLIGHTS

Pediatic optic neuritis is associated with more severe initial presentation in terms of vision, but better final outcomes. Children present more often with optic nerve edema, and bilateral involvement, without pain. Treatment is usually initially with intravenous methylprednisolone, but further studies are

needed to define optimal treatment regimens. Anti-myelin oligodendrocyte glycoprotein and aquaporin-4 antibodies have allowed us to categorize patients with higher risk for relapse or neuromyelitis optica spectrum disorder. Further study is necessary.

SUMMARY

Optic neuritis in children is relatively uncommon when compared to the incidence of optic neuritis in adults. The estimated annual incidence of pediatric optic neuritis in a Canadian cohort was 0.2/100,000 when compared to approximately 4.7-5.1/100,000 in adult populations.[1-3]

Clinical Characteristics

In general optic neuritis may present with different clinical characteristics when compared to adults. Obtaining a reliable history in a young child may not be possible. A child with unilateral vision loss may not complain of vision loss until the unaffected eye is occluded for some reason, or until bilateral involvement occurs. In contrast to adults with optic neuritis who usually present with unilateral optic neuritis, a meta-analysis of isolated pediatric optic neuritis found that 72% of children under 10 years of age presented with bilateral involvement, while 70% of children older than 10 years of age had unilateral optic neuritis.[4] Similar rates of bilateral involvement are described in more recent retrospective studies.[5,6] Most cases of optic neuritis in adults are retrobulbar, in contrast to optic neuritis in children which is more often anterior, and presents with disc edema.[7-10] Younger children are more likely to present with optic neve head edema.[8] Unlike adults, children are less likely to complain of pain as a feature of optic neuritis, with complaints of pain at presentation ranging from 43-77%. [7,10,11]

Vision at presentation and Vision outcomes

Initial visual acuities at presentation tend to be worse than in adults, with pediatric optic neuritis patients presenting with visual acuities of 20/200 or worse in 50% of patients, compared to 36% in the Optic Neuritis Treatment Trial.[10,12] However, recovery of vision in children tends to be better than that of adults. Visual outcomes of pediatric optic neuritis in a retrospective study of 59 children demonstrated recovery to 20/40 or better within one year in 89%, with only 3% having visual acuities worse than 20/200 at one year, as compared to 68% of adults recovering to 20/40 or better in the Optic Neuritis Treatment Trial.[10] A retrospective review of 102 children in France had a complete recovery of visual acuity in 72% of patients, with higher rates of recovery recovery for older children.[5] However it should be noted that in this study visual field defects persisted in 34% of patients.[5]

Neuroimaging

Due to the variable nature of the presentation of a child with optic neuritis, the neuroimaging recommended for a child presenting with optic neuritis may different from that of an adult who presents with the clinically "classic" isolated optic neuritis. A child with optic neuritis may present with unilateral or bilateral painless vision loss with disc edema, and therefore other causes of vision loss with disc edema must be evaluated for, including neoplasia. Therefore, an initial evaluation with an MRI of the brain and orbits with and without contrast would usually be performed first. If there is clinical suspicion for neuromyelitis optica, or if further imaging is required to help in making a diagnosis of multiple sclerosis, and MRI spine can be pursued.[13] However, it should be mentioned that routine MRI spine imaging in adults who present with clinically isolated optic neuritis remains controversial, and many of the same arguments can be made for children with clinically isolated optic neuritis.[14]

Laboratory Workup

Once a diagnosis of optic neuritis has been made, laboratory workup for a cause can be pursued. Up to two-thirds of younger children are more likely to have a postinfectious or postvaccination cause for their optic neuritis.[8] A lumbar puncture is recommended to evaluate for underlying infection with basic studies, and to evaluate for oligoclonal bands for suspected multiple sclerosis. Laboratory workup should evaluate for underlying inflammatory causes of optic neuritis with an ACE for sarcoidosis, anti-nuclear antigen for systemic lupus erythematosis, RPR and FTA-Abs for syphilis, Bartonella serology, Lyme serology can be considered in endemic areas.

Neuromyelitis optica (NMO) and and MOG-antibody associated demyelinating disease

Neuromyelitis optica and neuromyelitis optica spectrum disorder (NMO-SD) are more devastating neuroinflammatory diseases that may present initially with optic neuritis. Children with NMO have worse disability and visual disability compared to patients with multiple sclerosis.[15] Antibodies to aquaporin-4 are highly specific for NMO and NMO-SD. Obtaining aquaporin-4 antibodies at initial diagnosis of optic neuritis can help guide treatment to reduce recurrences and poor outcomes. A positive aquaporin-4 antibody test in pediatric NMO is associated with poorer visual outcomes.[16] One study of children with NMO found that 60% presented initially with optic neuritis.[16] Identifying children at risk for worse outcomes can allow them to be treated more aggressively at initial diagnosis, and to undergo immunomodulatory treatment that may prevent relapse and permanent disability.

Anti-myelin oligodendrocyte glycoprotein (MOG) antibodies have been detected in demyelinating disease in children as well. Initially described in association with acute disseminated encephalomyelitis, the clinical spectrum of MOG antibody associated disease has expanded to include isolated optic neuritis, relapsing optic neuritis, multiphasic disseminated encephalomyelitis, neuromyelitis optica spectrum disorder, acute disseminated encephalomyelitis followed by optic neuritis, and clinically isolated syndromes.[17,18] In a cohort of 816 patients suspected of idiopathic inflammatory demyelinating disease in Guangzhou City, China, the presence of MOG antibodies was detected in 50 (6.1%), and was associated with isolated optic neuritis in 12.5% of pediatric patients (n=16) when compared to 41.2% of adults (n=34).[19] In a cohort of 210 children with acute demyelinating syndromes, 65 (31%) were found to have anti-MOG antibodies.[18] Eight children who were MOG antibody positive developed recurrent optic neuritis. [Hennes] Visual acuity outcomes among children with MOG antibody associated optic neuritis are better than those with aquaporin-4 antibody associated optic neuritis.[20,21]

Treatment

Most children will recover vision without treatment, however the possibility that a child is presenting with NMO and isolated optic neuritis is a possibility, and therefore many providers treat isolated optic neuritis to prevent possible permanent injury from NMO. While the Optic Neuritis Treatment Trial (ONTT) defined the treatment regimen used for typical optic neuritis in adults, no such trial for isolated pediatric optic neuritis exists. Therefore, most treatment recommended regimens for children with optic neuritis are extrapolated from the ONTT. The initial treatment for isolated pediatric optic neuritis is intravenous methylprednisolone for 3-5 days (20-30mg/kg/d, 1g maximum).[22] For children who do not respond to steroids, IVIG or plasma exchange can be considered, but there is no consensus on when or how to treat pediatric isolated optic neuritis with these more aggressive measures.

Multiple sclerosis (MS)

In Waldman's meta-analysis of 229 patients in previous studies the overall rate of developing MS following optic neuritis was 29%.[4] The presence of unilateral or bilateral involvement was not independently associated with developing MS after accounting for age.[4] However older children were

more likely to develop MS, with a 32% increase in risk with each year of age.[4] The presence of brain lesions on MRI at presentation of optic neuritis carried a 28-fold risk of being diagnosed with multiple sclerosis.[4] A large retrospective analysis of 357 older children (median 13.6 years, interquartile range 10.8-15.5 years) with optic neuritis confirmed that abnormal MRI at presentation increased the risk of MS (Hazard ratio=5.94) and that age was a risk factor for developing MS (Hazard ratio = 1.08 per year of age).[23] This study also demonstrated that the presence of oligoclonal bands predicted conversion to MS (Hazard ratio = 3.69).[23] The lack of prospective trials with predetermined end-points for follow-up and uniform criteria for the definition of multiple sclerosis are limitations to this data regarding risk of developing MS.

Future directions

The Pediatric Disease Investigator Group (PEDIG) and the Neuro-Ophthalmology Research Disease Investigator Consortium has completed enrolment of children presenting with optic neuritis into a prospective registry.[24] Primary outcome is high-contrast visual acuity at 6-month follow-up. Depending upon outcomes, a prospective pediatric optic neuritis treatment trial may be possible as the next logical study.

CME ANSWERS

1. E
2. D
3. True

REFERENCES

1. Langer-Gould A, Brara S, Beaber BE, et al. The incidence of clinically isolated syndrome in a multi-ethnic cohort. J Neurol 261:1349-55, 2014.
2. Rodriguez M, Siva A, Cross SA, et al. Optic neuritis: a population-based study in Olmsted County, Minnesota. Neurology 45:244-50, 1995.
3. Banwell B, Kennedy J, Sadovnick D, et al. Incidence of acquired demyelination of the CNS in Canadian children. Neurology 72:232-9, 2009.
4. Waldman AT, Stull LB, Galetta SL, et al. Pediatric optic neuritis and risk of multiple sclerosis: Meta-analysis of observational studies. J AAPOS 15:441-6, 2011.
5. Averseng-Peaureaux D, Mizzi M, Colineaux H, et al. Paediatric optic neuritis: factors leading to unfavourable outcome and relapses. Br J Ophthalmol 102:808-13, 2018,
6. Wan MJ, Adebona O, Benson LA, et al. Visual outcomes in pediatric optic neuritis. Am J Ophthalmol 158:503-7, 2014.
7. Wiljeto M, Shroff M, Buncic JR, et al. The clinical features, MRI findings, and outcome of optic neuritis in children. Neurology 67:258-62, 2006.
8. Morales DS, Siatkowski RM, Howard CW, et al. Optic neuritis in children. J Pediatr Ophthalmol Strabismus 37:254-9, 2000.
9. Riikonen R, Donner M, Erkkilä H. Optic neuritis in children and its relationship to multiple sclerosis: A clinical study of 21 children. Dev Med Child Neurol 30:349-59, 1998.
10. Wan MJ, Adebona O, Benson LA, et al. Visual outcomes in pediatric optic neuritis. Am J Ophthalmol 158:503-7, 2014.
11. Alper G, Wang L. Demyelinating optic neuritis in children. J Child Neurol 24:45-48, 2009.
12. Visual function 5 years after optic neuritis: experience of the optic neuritis treatment trial. The optic neuritis study group. Arch Ophthalmol 115:1545–1552, 1997.

13. Chang MY, Pineles SL. Pediatric Optic Neuritis. Semin Pediatr Neurol 24:122-8,2017.
14. Meltzer E, Frohman EM, Costello FE, et al. Should spinal MRI be routinely performed in patients with clinically isolated optic neuritis? J Neuroophthalmol 2018, Epub ahead of print. 2018 Jul 10. doi: 10.1097/WNO.0000000000000685
15. Chitnis T, Ness J, Krupp L, et al. Clinical features of neuromyelitis optica in children: US Network of Pediatric MS Centers report. Neurology 86:245-52, 2016.
16. Absoud M, Lim MJ, Appleton R, et al. Paediatric neuromyelitis optica: clinical, MRI of the brain and prognostic features. J Neurol Neurosurg Psychiatry 86:470-472, 2015.
17. Di Pauli F, Reindl M, Berger T. New clinical implications of anti-myelin oligodendrocyte glycoprotein antibodies in children with CNS demyelinating diseases. Mult Scler Relat Disord 22:35-37, 2018.
18. Hennes EM, Baumann M, Schanda K, et al. Prognostic relevance of MOG antibodies in children with an acquired demyelinating syndrome. Neurology 89:900-8, 2017.
19. Chen L, Chen C, Zhong X, et al. Different features between pediatric-onset and adult-onset patients who are seropositive for MOG-IgG: A multicentre study in South China. J Neuroimmunol 321:83-91, 2018.
20. Zhao G, Chen Q, Huang Y, et al. Clinical characteristics of myelin oligodendrocyte glycoprotein seropositive optic neuritis: a cohort study in Shanghai, China. J Neurol 265:33-40, 2018.
21. Song H, Zhou H, Yang M, et al. Clinical characteristics and prognosis of myelin oligodendrocyte glycoprotein antibody-seropositive paediatric optic neuritis in China. Br J Ophthalmol 2018, Epub ahead of print. 2018 Aug 5, doi:10.1136/bjophthalmol-2018-312399
22. Borchert M, Liu GT, Pineles S, et al. Pediatric optic neuritis: What is new. J Neuroophthalmol 37(Suppl):S14-S22, 2017.
23. Heussinger N, Kontopantelis E, Gburek-Augustat J, et al. Oligoclonal bands predict multiple sclerosis in children with optic neuritis. Ann Neurol 77:1076-82, 2015.
24. Pineles SL, Liu GT, Waldman AT, et al. Pediatric Optic Neuritis Prospective Outcomes Study. J Neuroophthalmol 36:115-7, 2016.

MANAGEMENT OF ACUTE ISOLATED THIRD NERVE PALSY IN ADULTS

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LEARNING OBJECTIVES

1. Describe relevant clinical presentations of 3rd nerve palsy in an adult.
2. Define the management of a patient with acute isolated 3rd nerve palsy.
3. Describe differences in the management of adult versus pediatric 3rd nerve palsy.

CME QUESTIONS

1. The most common etiology of acute isolated 3rd palsy in patients over age 50?
    A. Aneurysm
    B. Tumor
    C. Microvascular
    D. Giant cell arteritis

2. Which of the following factors will determine the etiology of an acute isolated 3rd nerve palsy?
    A. Pain
    B. History of vascular risk factors
    C. Age
    D. None of the above

3. True or False: Computerized tomographic angiography (CTA) is more sensitive than magnetic resonance angiography (MRA) in detecting small (4mm) aneurysms.

KEYWORDS

1. Third nerve palsy
2. Neuroimaging

HIGHLIGHTS

Etiology & Clinical Presentations

Population-based study shows an age- and sex-adjusted annual incidence of acquired third nerve palsy of 4.2/100,000.[1] In patients over 60 years the incidence was 12.5/100000 as compared to 1.7 per 100000 for younger patients. Causes included presumed microvascular (42%), neoplasm (11%), surgical (10%) and aneurysm (6%). However, 5 of 8 aneurysms were cavernous sinus aneurysms and only 3 were posterior communicating artery. Other less common causes included giant cell arteritis, stroke, pituitary apoplexy and "other" (single cases of cavernous sinus fistula and thrombosis, carcinomatosis, migraine, and post-viral). Presumed-microvascular 3rds increased from the 6th through 9th decades of life. This study is important because it is the first to describe incidence and etiology using a population based approach as opposed to large series at tertiary neuro-ophthalmology centers.[2,3] Thus, it may more accurately reflect the population seen by primary care doctors and ophthalmologists.

Clinical presentation may be relevant to the diagnosis and management of acute, isolated third nerve palsy in the adult. "Acute" is defined as less than 1 month symptom duration. "Isolated" is defined as no other neurologic symptoms or signs with the exception of pain. In this setting, relevant clinical factors may include patient's age, presence of pain, symptoms of giant cell arteritis, past medical history, completeness of the palsy and pupil involvement. Microvascular 3rd nerve palsy is increasingly common as age gets over 50 years. The presence of pain is not very helpful as it may occur in both microvascular and aneurysmal 3rd nerve palsy. Patients over 50 years should be questioned about other symptoms of giant cell arteritis. Microvascular 3rd nerve palsy is more common in patients with vascular risk factors such as hypertension, diabetes, and hypercholesterolemia. A history of cancer is always concerning and must be ruled out. Abrupt onset of complete pupil sparing 3rd nerve palsy in a patient over 50 is most likely microvascular. Incomplete 3rd nerve palsy with or without pupil sparing is more worrisome for compressive lesion (aneurysm, tumor).

Management

There seems to be little controversy regarding management of 3rd nerve palsy in adults less than 50 years of age. The controversy is whether all patients older than 50 with acute isolated 3rd nerve palsy should be neuro-imaged. There are only a few prospective studies that help inform as to the appropriate diagnostic evaluation.[4-6]

Chou and associates prospectively evaluated 66 patients age 50 or greater with acute isolated 3rd, 4th and 6th nerve palsies.[4] Twenty-nine had 3rd nerve palsy; the pupil was spared in 20 and 8 of these had complete motility deficit. All 8 patients with complete pupil sparing 3rd nerve palsy were microvascular in nature. However incomplete pupil sparing or pupil involving palsies could be either microvascular or compressive.

Murchison and colleagues prospectively looked at 93 patients 50 years and older with 3rd, 4th, and 6th nerve palsy.[5] Fourteen had 3rd nerve palsy and all were found to be microvascular. There was no comment on pupil sparing and completeness of the palsy. Only 1 patient of the 93 had a causative lesion found on MRI. These authors argued that from a cost perspective neuroimaging should not be obtained in every patient over age 50. Instead it should be obtained if there is a history of cancer, not neurologically isolated, pupil involving or partial in nature, and no resolution after 3 months.

Tamhankar and associates prospectively evaluated 109 patients with acute isolated 3rd, 4th and 6th nerve palsies.[6] Twenty-two had 3rd nerve palsy, 18 were partial and 4 were complete with pupil sparing. One of the complete pupil sparing 3rd nerve palsy patients had pituitary apoplexy. Details of this one patient's medical history were not available from the article.

Neuroimaging for 3rd nerve palsy should include both MRI with contrast and a vascular imaging study. There is some debate about which vascular imaging study (computed tomography angiography (CTA), magnetic resonance angiography (MRA) or intra-arterial digital subtraction angiography (DSA) should be obtained.[7] MRA and CTA are usually considered first as they are less invasive. As opposed to MRA, CTA requires iodine based contrast and there is a radiation dose. On the other hand MRA has been reported to miss aneurysms as large as 7 mm.[8] However a meta-analysis of 12 studies and 960 patients showed MRA to be comparable but slightly less sensitive than CTA in diagnosing small intracranial aneurysms.[9] Interpretation of the neuroimaging studies should be done by a neuro-radiologist as this may be the most important factor in aneurysm detection.[10] These generally good MRA/CTA results and the slight

risk of stroke with DSA has led to the use of DSA only if MRA or CTA are normal and suspicion of aneurysm is high.[7]

SUMMARY

What I Teach.
I think it needs to be kept as simple as possible for physicians who don't see 3rd nerve palsy frequently. Thus, all patients with acute isolated 3rd nerve palsy should be evaluated urgently with MRI and MRA or CTA. If MRA or CTA is normal, but suspicion of aneurysm is high, then obtain DSA. In patients over 50, always ask about symptoms of giant cell arteritis and based on clinical suspicion obtain erythrocyte sedimentation rate, C-reactive protein and complete blood count. If a microvascular etiology is determined, vascular risk factors should be assessed and controlled.

What I Do.
I obtain neuroimaging as described above if the patient is less than 50 years, or if greater than 50 years, if they have a history of cancer, no vascular risk factors, pupil involvement or incomplete motility involvement.
I do not image patients over the age of 50 with vascular risk factors and complete but pupil sparing 3rd nerve palsy. If there is no improvement at 6-week follow-up in this group, I neuroimage (never have had this happen!).

CME ANSWERS

1. C
2. D
3. True

REFERENCES

1. Fang C, Leavitt JA, Hodge DO, Holmes JM, Mohney BG, Chen JJ. Incidence and etiologies of acquired third nerve palsy using a population-based method. JAMA Ophthalmol. 2017;135(1):23-28.
2. Keane JR. Third nerve palsy: analysis of 1400 personally examined inpatients. Can J Neurol Sci. 2010;37(5):662-670.
3. Rush JA, Younge BR. Paralysis of cranial nerves III, IV, and VI: cause and prognosis in 1,000 cases. Arch Ophthalmol. 1981;99(1):76-79.
4. Chou KL, Galetta SL, Liu GT, Volpe NJ, Bennet JL, Asbury AK, Balcer LJ. Acute ocular motor mononeuropathies: prospective study of the roles of neuroimaging and clinical assessment. J Neurol Sci. 2004;219:35-39.
5. Murchison AP, Gilbert ME, Savino PJ. Neuroimaging and acute ocular mononeuropathies. Arch Ophthalmol. 2011;129(3):301-305.
6. Tamhankar MA, Biousse V, Ying GS, Prasad S, Subramanian PS, Lee MS, et al. Isolated third, fourth and sixth cranial nerve palsies from presumed microvascular versus other causes. A prospective study. Ophthalmology 2013;120:2264-2269.
7. Vaphiades MS, Roberson GH. Imaging of Oculomotor (Third) Cranial Nerve Palsy. Neurol Clin. 2017;35(1):101-113.
8. Vaphiades MS, Horton JA. MRA or CTA, that's the question. Surv Ophthalmol. 2005;50:406–10.
9. Sailer AM, Wagemans BA, Nelemans PJ, et al. Diagnosing intracranial aneurysms with MR angiography: systematic review and meta-analysis. Stroke 2014;45:119–26.

10. Elmalem VI, Hudgins PA, Bruce BB, et al. Under diagnosis of posterior communicating artery aneurysm in noninvasive brain vascular studies. J Neuroophthalmol. 2011;31:103–9.

EVALUATION AND MANAGEMENT OF THIRD NERVE PALSY IN CHILDREN

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LEARNING OBJECTIVES

1. List common etiologies of third nerve palsy in children.
2. Describe clinical signs of third nerve palsy in children.
3. Describe the diagnostic evaluation of third nerve palsy in children.
4. Describe treatment of third nerve palsy in children (amblyopia treatment, strabismus surgery and ptosis repair).
5. Identify the differences in the etiology, management, and treatment of third nerve palsy in children compared with adults.

CME QUESTIONS

1. True or False: CN III palsy in children does not occur from an aneurysm.

2. True or False: Congenital CN III palsy does not occur with aberrant regeneration.

3. Children with ophthalmoplegic migraine have involvement of which cranial nerves in decreasing order of frequency.
   A. CN IV > CN VI > CN III
   B. CN VI > CN III > CN IV
   C. CN III> CN VI > CN IV
   D. CN III > CN IV > CN VI

KEY WORDS

1. Oculomotor nerve palsy
2. Third nerve palsy
3. Pediatrics
4. Strabismus surgery

SUMMARY

The evaluation and treatment of children with third nerve palsies are markedly different from that of adults. Ischemic and vascular etiologies (such as aneurysms) are common in adults but are rare in children. Treatment of oculomotor nerve palsies in children entails addressing factors such as amblyopia and fusion. This syllabus will outline the etiologies, clinical signs, diagnostic work-up, and treatment of third nerve palsies in children.

Etiology

The most common etiologies of third nerve palsy in children are congenital, traumatic, and neoplastic[1]. Infectious and inflammatory etiologies are less common. Aneurysms are rare.

Congenital third nerve palsies are most common occurring in 39 – 46 % of cases.[1,2,3] Although some cases are associated with birth trauma, most are idiopathic. Isolated third nerve palsies with aberrant regeneration suggest damage to the peripheral oculomotor nerve. However, central nervous system disease is identified in as many as 70 % of cases.[1,2,4,5] Hamed described congenital midbrain lesions causing third nerve palsy and contralateral hemiparesis (Weber syndrome).[4] Identified etiologies that cause focal brainstem lesions include intrauterine stroke and arteriovenous malformations. Associated central nervous system abnormalities unrelated to third nerve dysfunction have also been described, including optic disc drusen, optic nerve hypoplasia, ventriculomegaly, arachnoid cyst, holoprosencephaly, and craniosynostosis.[1,2,4,5]

Trauma is the second most common cause of third nerve palsies in children occurring in 20 – 40% of cases.[1-3] Traumatic causes include motor vehicles accidents, child abuse, as well as iatrogenic cases that occur after intracranial surgery.[1,3] The trauma is typically severe, associated with skull fractures, intracranial haemorrhage, or both.

Neoplastic etiologies of childhood third nerve palsies account for 10 – 22% of cases.[1-3] Multiple neoplasms have been described including rhabdomyosarcoma, glioblastoma multiforme, brainstem glioma, leptomeningeal sarcoma, lacrimal gland tumor, lymphoma, mesencephalic cyst, cavernous sinus astrocytoma, craniopharyngioma, and schwannoma.[1-3,6-7] Oculomotor nerve schwannomas may be small and difficult to identify on neuroimaging.[8,9] Indeed, many cases of so-called “cryptogenic” third nerve palsies in children may be from schwannomas involving the third nerve that were not identified prior to the advent of modern high resolution magnetic resonance imaging.[6-11]

Inflammatory and infectious etiologies of childhood third nerve palsies have been described, most commonly from bacterial or viral meningitis.[2,3,12] Other inflammatory etiologies include sarcoidosis and Miller-Fisher syndrome.[13,14]

Aneurysms rarely account for third nerve palsies in children. Miller described two cases involving a 16 year-old and a 17 year-old patient. No cases of aneurysm occurred in the series from Mudgil et al[1] and Ng et al.[2] Three children, ages, 6, 7, and 10, that presented with an isolated third nerve palsy from an intracranial aneurysm have been described.[15-17] In all three cases, the aneurysm was identified by CT scan or MRI, prior to angiography. Children with tuberous sclerosis are at increased risk of cerebral aneurysms.[18] Cavernomas, arteriovenous malformations, and embolic infarcts from rheumatic valvular heart disease are rare vascular causes of childhood third nerve palsy.[2]

Rare Etiologies Specific to Children

Congenital third nerve palsy with cyclic spasm usually occurs in the first year of life in a child with congenital partial or complete third nerve palsy.[19] During the spastic phase, the paretic upper lid elevates, the pupil constricts, the eye adducts, and a myopic shift occurs. The spastic phase occurs every 1 ½ to 2 minutes and has a duration that is typically less than a minute, followed by another paretic phase. The etiology is unknown. However, a history of birth trauma or intracranial infection is present in about half of the cases. The cyclic spasms are usually present at presentation. However, children with partial third nerve palsies have been observed to progress to cyclic spasms.

Ophthalmoplegic migraine, a diagnosis of exclusion, most frequently occurs in the first decade of life with no gender predilection.[20-25] This entity is no longer classified as a type of migraine and is considered a neuralgia. A severe ipsilateral headache precedes the attack and may abate hours or days before the onset of cranial nerve dysfunction. The third nerve is most commonly affected, followed by the sixth nerve, and the fourth nerve. A complete third nerve palsy with pupil involvement is most common, although divisional palsies have been described. The duration of the ophthalmoplegia is typically several days and resolves without any permanent extraocular muscle paresis. However, repeated attacks may last longer and cause permanent extraocular muscle weakness, pupillary mydriasis, and oculomotor synkinesis. Magnetic resonance imaging (MRI) studies have shown enlargement and enhancement of the perimesencephalic oculomotor nerve during an attack.[26-28] After the attack, MRI shows reduced enhancement with residual enlargement of the oculomotor nerve although complete resolution with normal magnetic resonance imaging has been described. The etiology of ophthalmoplegic migraine is unknown. Inflammatory and vascular etiologies have been suggested.[20] Systemic steroids may shorten the duration of the paretic phase and reduce residual oculomotor deficits. Migraine prophylaxis with calcium channel blockers and beta blockers have been used to treat patients with recurrent attacks. However, the reported benefits of these treatments are anecdotal and unproven.

Clinical findings

Children present with typical signs of third nerve palsy including ptosis of the upper lid, and limited adduction, elevation, and depression of the involved eye. Aberrant regeneration is common occurring in about 50% of all children.[1,4] The pupil maybe dilated, spared, or miotic. Unlike adults, a miotic pupil of the involved eye occurs in 30 – 60 % of children, most commonly in congenital cases.[2,4] The miotic pupil has been attributed to aberrant regeneration. The observation that some children present with a dilated pupil and develop pupillary miosis concurrent with other signs of aberrant regeneration supports this hypothesis. Children may fixate with the involved eye in 10 – 20% of cases.[2,4,29] Fixation with the involved paretic eye may improve vision by preferentially damping nystagmus in the paretic eye. Visual loss occurs in over 50% of children from ocular/central nervous system structural disease or amblyopia.[1] Amblyopia is the cause of decreased vision in about 30% of children less than 8 years of age.[1] Amblyopia may occur from ptosis, strabismus, anisometropia, or decreased accommodation. The involved eye may develop high myopia and astigmatism, perhaps secondary to ptosis, or excessive hyperopia, possibly from decreased accommodation.[1,4] Rarely, children show signs of fusion, manifested by a head posture to align the eyes. However, because third nerve palsy affects multiple extraocular muscles resulting in large incomitant deviations, most children do not have stereopsis or fusion at presentation. Associated neurological findings are common, even in congenital cases as previously noted.

Diagnostic Evaluation

A detailed evaluation will suggest an etiology in most children with third nerve palsy. Congenital and traumatic etiologies are identified by history. Magnetic resonance imaging of the brain and orbits with gadolinium and MRA is indicated as associated CNS disease is often present, even among congenital cases. A lumbar puncture may be indicated if inflammatory, infectious, or malignant disease is suspected. Unlike adults, aneurysms are rare in children under the age of 10 years, and when present, can often be identified by MRA or CTA. Therefore, angiography is generally not indicated although this is controversial.[15]

Treatment

The initial goal of treatment is to identify and treat amblyopia. Refractive errors are common and must be identified and corrected with glasses. Dynamic retinoscopy is essential to identify decreased accommodation from ciliary muscle paresis.[30] This technique assesses the child's ability to neutralize the

retinoscopic reflex while fixating on a near object. If accommodation is reduced, glasses to correct any hyperopic refractive error and bifocal correction should be prescribed for the involved eye. Refractive error correction of the paretic eye and patching of the fixating eye are often required to treat amblyopia. Unfortunately, treatment is often unsuccessful likely from poor compliance. Congenital cases respond best to amblyopia treatment.[1] Traumatic and neoplastic cases respond poorly, perhaps due to associated medical and neurological issues.

If the third nerve palsy resolves, either from natural history (i.e. ophthalmoplegic migraine) or treatment of the underlying condition (i.e. malignancy), children may regain fusion and stereopsis. Children with permanent third nerve palsy may be treated with strabismus surgery to improve ocular alignment. The goals of strabismus surgery must be addressed with the family and may include improvement of appearance, reduced head posture, decreased frequency of diplopia, fusion, and stereopsis. Unfortunately, fusion and stereopsis are often unobtainable in children with permanent third nerve palsy due to the presence of a large incomitant deviation involving most of the extraocular muscles.[1]

Prior to strabismus surgery, extraocular muscle restriction and function should be assessed by forced ductions and forced generations respectively. If there is residual extraocular muscle function, strabismus can be addressed with standard extraocular muscle surgery such as medial rectus muscle resection and lateral rectus muscle recession. If the medial rectus muscle is completely paralytic and the vertical rectus muscles are relatively intact, nasal transposition of the vertical rectus muscles may improve alignment.[31] If the child has a complete third nerve palsy, strabismus surgery may center the eye improving appearance, and provide a tiny area of fusion. However, most children will not regain significant functional binocularity and will ignore the image from the involved eye. In order to center the eye, the surgical procedure must weaken the lateral rectus muscle and anchor the eye in adduction. The lateral rectus muscle may be weakened by disinsertion and reattachment to the lateral orbital wall.[32,33] Historically, the superior oblique tendon or a fascia latta strip has been attached nasally to anchor the eye in adduction.[34,35] However, these techniques often induced torsional and vertical deviations. In addition, fascia latta cannot be harvested from young children. More recent techniques include tethering the eye in adduction with a non-absorbable suture or an apically based periosteal flap.[36-39] Most recently, the technique used to tether the eye in adduction entails splitting the lateral rectus muscle and nasally transposing each half (the superior half under the superior rectus muscle, the inferior half under the inferior rectus muscle) to the medial rectus muscle insertion.[40-42] Complications have included choroidal effusions and the inability to perform the procedure if previous surgery has been performed on the lateral rectus muscle. The various techniques to tether an eye with a complete third nerve palsy in adduction may successfully reduce the deviation and improve appearance. Unfortunately, undercorrections are common and a functional range of binocularity is not attained with these procedures.

Ptosis in children with third nerve palsy is typically corrected after the eye has been maximally aligned. Patients with moderate levator function can be successfully treated with levator resection. However, patients with minimal or absent levator function may require a frontalis suspension procedure. Children with aberrant regeneration in which the ptotic lid elevates with attempted adduction may have improvement of their ptosis from strabismus surgery on the uninvolved normal eye. A recess-resection procedure that places the uninvolved eye in adduction will create fixation duress that results in attempted adduction of the paretic eye and elevation of the ptotic lid. It is important to recognize that raising the ptotic lid may cause disabling diplopia. In addition, ptosis correction in patients with an absent Bell's phenomenon may be complicated by corneal ulceration.

CME ANSWERS

1. False
2. False
3. C

REFERENCES

1. Mudgil AV, Repka MX. Ophthalmologic outcome after third cranial nerve palsy or paresis in childhood. J AAPOS 3:2-8, 1999
2. Ng YS, Lyons CJ. Oculomotor nerve palsy in childhood. Can J Ophthalmol 40:645-653, 2005.
3. Miller NR. Solitary oculomotor nerve palsy in childhood. Am J Ophthalmol 83:106-111, 1977
4. Hamed LM. Associated neurologic and ophthalmologic findings in congenital oculomotor nerve palsy. Ophthalmology 98:708-714, 1991.
5. Balkan R, Hoyt CS. Associated neurologic abnormalities in congenital third nerve palsies. Am J Ophthalmol 97:315-319, 1984.
6. Yang SS, Li AJ, Liu X, et al. Pediatric isolated oculomotor nerve schwannoma: a new case report and literature review. Pediatric Neurology 48:321-324, 2013.
7. Norman AA, Farris BK, Siatkowski M. Neuroma as a cause of oculomotor palsy in infancy and early childhood. J AAPOS 5:9-12, 2001.
8. Kau HC, Tsai CC, Ortube MC, Demer JL. High-resolution magnetic resonance imaging of the extraocular muscles and nerves demonstrates various etiologies of third nerve palsy. Am J Ophthalmol 143:280-287, 2007
9. Abdul-Rahim AS, Savino PJ, Zimmerman RA et al. Cryptogenic oculomotor nerve palsy. The need for repeated neuroimaging studies. Arch Ophthalmol 107:387-390, 1989.
10. Bisdorff AR, Wildanger G. Oculomotor nerve schwannoma mimicking ophthalmoplegic migraine. Cephalalgia 26:1157-1159, 2006.
11. Mizen TR, Burde RM, Klingele TG. Cryptogenic oculomotor nerve palsies in children. Am J Ophthalmol 100:65-67, 1985.
12. Nazir SA, Murphy SA, Siatkowski RM. Recurrent para-infectious third nerve palsy with cisternal nerve enhancement on MRI. J Neuro-Ophthalmol 24:96-97, 2004.
13. Go T. Partial oculomotor nerve palsy associated with elevated anti-galactocerebroside and anti-GM1 antibodies. J Pediatr 137:425-426, 2000.
14. Sanchez Dalmau BF. Young boy with progressive double vision. Surv Ophthalmol 43:4-52, 1998.
15. Mehkri IA, Awner S, Olitsky SE et al. Double vision in a child. Surv Ophthalmol 44:45-52, 1999.
16. Branley MG, Wright KW, Borchert MS. Third nerve palsy due to cerebral artery aneurysm in a child. Aust N Z J Ophthalmol 20:137-140, 1992.
17. Ebner R. Angiography for IIIrd nerve palsy in children (letter;comment) J Clin Neuroophthalmol 10:154-155, 1990.
18. Shelton JB, Ramakrishnaiah R, Glasier CM, Phillips PH. Cavernous sinus syndrome from an internal carotid artery aneurysm in an infant with tuberous sclerosis. J AAPOS 15:389-391, 2011.
19. Barroso LH, Abreu SG, Finkel E et al. Cyclic oculomotor paresis in Rio. J Clin Neuro-ophthalmol 11:136, 1991.
20. Carlow TJ. Oculomotor ophthalmoplegic migraine: is it really migraine? J Neuro-Ophthalmol 22:215-221, 2002.
21. Peck R. Ophthalmoplegic migraine presenting in infancy: a self-reported case. Cephalalgia 26:1242-1244, 2006.

22. McMillan HJ, Keene DL, Jacob P, Humphreys P. Ophthalmoplegic migraine: inflammatory neuropathy with secondary migraine? Can J Neurol Sci 34:349-355, 2007.
23. Levin M, Ward TN. Ophthalmoplegic migraine. Curr Pain Headache Rep 8:306-309, 2004.
24. Lance JW, Zagami AS. Ophthalmoplegic migraine: a recurrent demyelinating neuropathy? Cephalalgia 21:84-89, 2001
25. Friedman AP, Harter DH, Merritt HH. Ophthalmoplegic migraine. Arch Neurol 7:82-89, 1962.
26. O'Hara MA, Anderson RT, Brown D. Magnetic resonance imaging in ophthalmoplegic migraine of children. J AAPOS 5:307-310, 2001.
27. Bharucha DX, Campbell TB, Valencia I, et al. MRI findings in pediatric ophthalmoplegic migraine: a case report and literature review. Pediatr Neurol 37:59-63, 2007.
28. Stommel EW, Ward TN, Harris RD. MRI findings in a case of ophthalmoplegic migraine. Headache 33:234-237, 1993.
29. Kazarian EL, Flynn JT. Congenital third nerve palsy with amblyopia of the contralateral eye. J Pediatr Ophthalmol Strabismus 15:366-367, 1978.
30. Hunter DG. Dynamic retinoscopy: the missing data. Surv Ophthalmol 46:269-274, 2001.
31. Dawson EL, Boyle NJ, Lee JP. Full-tendon nasal transposition of the vertical rectus muscles-a retrospective review. Strabismus 15:133-136, 2007.
32. Morad Y, Kowal L, Scott AB. Lateral rectus muscle disinsertion and reattachment to the lateral orbital wall. Br J Ophthalmol 89:983-985, 2005.
33. Velez FG, Thacker N, Britt MT et al. Rectus muscle orbital wall fixation: a reversible profound weakening procedure. J AAPOS 8:473-480, 2004.
34. Saunders RA, Rogers GL. Superior oblique transposition for third nerve palsy. Ophthalmology 89:310-316, 1982.
35. Scott AB. Transposition of the superior oblique. Am Orthopt J 27:11-14, 1977.
36. Sharma P, Gogoi M, Kedar S, Bhola R. Periosteal fixation in third-nerve palsy. J AAPOS 10:324-327, 2006.
37. Srivastava KK, Sundaresh K, Vijayalkshmi P. A new surgical technique for ocular fixation in congenital third nerve palsy. J AAPOS 8:371-377, 2004.
38. Goldberg RA, Rosenbaum AL, Tong JT. Use of apically based periosteal flaps as globe tethers in severe paretic strabismus. Arch Ophthalmol 118:431-437, 2000.
39. Ahmed R, Coats DK, Yen MT. Periosteal flap fixation of the globe for surgical treatment of severe restrictive strabismus: a report of eight cases with outcomes. Binocul Vis Strabolog Q *Simms Romano*. 26:230-235, 2011.
40. Shah AS, Prabhu SP, Sadiq MA, Mantagos JS, et al. Adjustable nasal transposition of split lateral rectus muscle for third nerve palsy. JAMA Ophthalmol 132:963-969, 2014.
41. Gokyigit B, Akar S, Satana B, et al. Medial transposition of a split lateral rectus muscle for complete oculomotor nerve palsy. J AAPOS 17:402-410, 2013.
42. Sukhija J, Kaur S, Singh U. Nasal lateral rectus transposition combined with medial rectus surgery for complete oculomotor nerve palsy. J AAPOS 18:395-396, 2014.

PAPILLEDEMA EVALUATION IN AN ADULT

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LEARNING OBJECTIVES

1. Identify when an MRV head is indicated in the evaluation of papilledema
2. Describe the features of presentation, exam, and testing that suggest the diagnosis is NOT primary pseudotumor cerebri
3. List common and uncommon causes of secondary pseudotumor cerebri

CME QUESTIONS

1. In which patient with bilateral papilledema is an MRV head least likely to be helpful diagnostically?
    A. A 20-year-old thin female with a history of idiopathic lower extremity deep vein thrombosis?
    B. A 40-year-old obese female with 5 months of increasing headaches
    C. A 30-year-old obese male with 1 week of severe headaches
    D. A 65-year-old obese female with 1 week of headaches and bilateral abducens palsy.

2. Which of the following CSF findings in an obese 24-year-old female with bilateral optic disc edema raises the greatest concern for a diagnosis other than primary pseudotumor cerebri?
    A. 2 WBCs and 2,000 RBCs on tube 1, 0 WBCs and 300 RBCs on tube 4
    B. Opening pressure of 20 cm H20
    C. Elevated protein of 47 mg/dL (nl= 15-45 mg/dL) in patient with 0 WBC / 2,000 RBCs
    D. 200 WBCs and 1,000 RBCs on tube 4

3. True or False: To convert lumbar puncture opening pressure measured in the prone position to an equivalent lateral decubitus position opening pressure in any given patient, you should subtract 2 cm H20.

KEYWORDS

1. Papilledema
2. Adult
3. Lumbar
4. Puncture
5. Pseudotumor cerebri syndrome

INTRODUCTION

Papilledema is optic disc swelling due to impaired axoplasmic flow of retinal ganglion cells associated with increased intracranial pressure (ICP).[1] The differential diagnosis for papilledema in adults is broad and often differs significantly from children. The majority of papilledema cases in adults are diagnostically simple with most cases hinging on the presence or absence of structural causes of high ICP

on MRI. Unrevealing neuro-imaging is the first step towards a diagnosis of pseudotumor cerebri syndrome (PTC). The astute clinician, however, must always remain cognizant of the criteria for PTC and avoid cutting diagnostic corners. This lecture and syllabus will highlight these criteria and utilize them as a framework to optimize the identification of uncommon primary PTC mimickers.

DIAGNOSTIC CRITERIA

Criteria A-E are required for a "definite diagnosis" of PTC.[2] Criteria A-D are required for a "probable diagnosis" of PTC.

A. Papilledema
B. Normal neurologic examination except for cranial nerve abnormalities
C. Neuro-imaging: Normal MRI brain with and without gadolinium for typical patients. Magnetic Resonance Venography (MRV) is required for atypical patients. Contrast enhanced CT may be substituted if MRI is contraindicated or not available.
D. Normal cerebrospinal fluid (CSF) composition
E. Elevated lumbar puncture opening pressure (>250 mm CSF in adults and >280 mm CSF in children).

PRESENCE OF PAPILLEDEMA

When assessing an abnormal appearing optic nerve head, it is paramount to confirm that the optic nerve is truly swollen. There are a variety of ancillary tests that can be helpful in distinguishing pseudo-papilledema (mostly commonly from optic nerve head drusen) from true optic nerve head swelling including OCT, fluorescein angiography, B-scan ultrasound, fundus auto fluorescence, and CT scan. A complete discussion of these testing modalities is beyond the scope of this talk.

Papilledema is typically bilateral though can be highly asymmetric. In less than 5-10% of cases it may be strictly unilateral.[1,3] Just as papilledema can be unilateral, alternative causes of optic disc edema attributable to ischemia (e.g. non-arteritis anterior ischemic optic neuropathy (NAION)), inflammation (e.g. optic neuritis), malignant infiltration, or infection can cause bilateral optic disc edema. In the setting of mild or moderate papilledema, vision loss is typically mild, limited to peripheral nerve fiber bundle defects, and spares central vision (visual acuity and color vision).[4] Bilateral optic disc swelling with severe vision loss out of proportion to the degree of optic disc swelling should raise suspicion for superimposed non-organic vision loss or for optic disc edema that is not ICP related.

Rarely, bilateral optic disc swelling secondary to incipient NAION, vitreopapillary traction, or papillitis with minimal or no vision loss can mimic papilledema.[5] The absence of other symptoms of ICP elevation such as headaches, pulsatile tinnitus, and horizontal binocular diplopia is a non-specific clue to these alternative diagnoses although patients with papilledema may be also be asymptomatic. Headaches are absent in up to 10% of patients with papilledema.[3]

NORMAL NEUROLOGIC EXAMINATION EXCEPT FOR CRANIAL NERVE ABNORMALITIES

Unilateral or bilateral abducens palsies are common sequelae of increased ICP. Rarely CN 7 nerve palsies and very rarely CN 3 and 4 palsies have been reported in association with ICP elevation from PTC.[6-8] Any cranial nerve palsy other than an abducens palsy in a PTC patient should heighten suspicion for an alternative diagnosis.[9]

By definition, PTC patients have structurally normal brain parenchyma. Thus symptoms of cognitive changes in patients with papilledema are not compatible with PTC and raise concern for alternative diagnoses.[2]

NORMAL NEURO-IMAGING

In patients with papilledema who fit the typical PTC demographic (reproductive age obese females), MRI with and without gadolinium is sufficient to evaluate for structural causes of increased intracranial pressure.[2] Patients who would be considered atypical for PTC (men, children, thin women, or post-menopausal women) should undergo MRV for the detection of dural venous sinus thrombosis (DVST). MRV should also be considered in typical PTC demographic patients with risk factors for DVST such as recent head trauma, active infectious sinusitis / otitis / meningitis, or a personal or family history of hypercoagulable disorders or sequelae.

"Normal" neuro-imaging can depend both on the subtlety of the pathology and the acumen of the provider interpreting the scan. It is important, therefore, for clinicians to re-review all prior relevant neuro-imaging as reinterpretation of previously "normal" scans is common.[10] Inflammatory and malignant meningeal infiltration can lead to a PTC- like clinical picture with subtle findings of meningeal thickening and enhancement early in the disease course. Dural arteriovenous fistulas (DAVFs) can likewise present with a PTC-like clinical picture and demonstrate subtle findings of dilated leptomeningeal or medullary veins.[11] MRA can improve detection of DAVFs.

NORMAL CSF COMPOSITION

Abnormal CSF not explainable by a traumatic LP is incompatible with a diagnosis of PTC and should prompt further work-up for elevated ICP.[2] Traumatic LPs result in an elevated RBC and WBC count but maintain the approximate ratio of RBCs to WBCs seen in the peripheral blood. In the setting of a traumatic LP, the ratio of RBCs to WBCs expected is approximately 750 : 1.[12] Elevated WBCs out of proportion to this ratio raises concern for an infectious, inflammatory, or malignant meningeal process and should prompt more detailed CSF studies.

A traumatic LP may mildly increase CSF protein in proportion to the number of RBCs. One can attribute an elevation of approximately 1 mg / dL (or 0.01 g per L) of protein for each 1,000 RBCs in the CSF.[13] Elevated protein in the presence or absence of pleocytosis can suggest an infectious, inflammatory, or malignant meningeal process and should prompt more detailed CSF studies.

ELEVATED LUMBAR PUNCTURE OPENING PRESSURE (OP)

Opening pressure is a snap-shot surrogate indicator of ICP prone to both falsely high and falsely low values. From a theoretical pathophysiologic perspective, the optimal position for measuring the OP on LP is the lateral decubitus (LD) position with straight legs. Often the result of anxiety or pain, Valsalva maneuvers during LP can falsely elevate the OP by 25 cm H20 over the baseline OP.[14] Due to a shift towards more LPs performed by radiology under fluoroscopic guidance in the prone position, there is a theoretical concern that clinicians will see more falsely elevated OPs. Two prospective studies directly comparing LP OP in prone and LD position found that the prone position was associated with a higher OP on average (1.2 -2.7 cm H20) although in both studies OPs were variable and some patients demonstrated a lower OP in the prone position.[15,16] The lack of consistency in the relationship between OP and positioning make it impossible to utilize a simple corrective formula to convert prone OP to LD OP.

As a result of the intrinsic variability in OP, clinicians should not be over-reliant on opening pressure results when assessing whether a patient has increased ICP. Accordingly, the current diagnostic PTC criteria allow for a diagnosis of "probable PTC" in the absence of an elevated OP. That said, the correct clinical context a normal opening pressure (OP) on lumbar puncture (LP) can also serve as a clue to revisit the possibility that a patient has optic disc edema not related to elevated ICP (see PAPILLEDEMA section above).[2]

CONTRIBUTING MEDICAL CONDITIONS / MEDICATIONS ("SECONDARY" PTC)

Increased intracranial pressure in the absence of a structural etiology on MRI can occur from a variety of medical conditions and medications.[2] These are sometimes referred to as "secondary PTC." It is important to review a papilledema patient's history carefully to identify these potential contributing factors.

Medications highly associated with secondary PTC (not an exhaustive list of all potential associations) include cycline antibiotics, vitamin A derivatives, human growth hormone, lithium, and withdrawal from chronic corticosteroids.

Medical conditions associated with secondary PTC include anemia, renal failure, obstructive sleep apnea, Addison disease, hypoparathyroidism, Down syndrome, and Turner syndrome.

CME ANSWERS

1. B
2. D
3. False

REFERENCES

1. Trobe JD. Papilledema: the vexing issues. *J Neuroophthalmol.* 2011;31(2):175-186.
2. Friedman DI, Liu GT, Digre KB. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children *Neurology.* 2013;81(13):1159-1165.
3. Rigi M, Almarzouqi SJ, Morgan ML, Lee AG. Papilledema: epidemiology, etiology, and clinical management. *Eye Brain.* 2015;7:47-57.
4. Liu GT, Volpe NJ, Galetta S. *Neuro-ophthalmology : diagnosis and management.* 2nd ed. Philadelphia: Saunders Elsevier; 2010.
5. Houle E, Miller NR. Bilateral vitreopapillary traction demonstrated by optical coherence tomography mistaken for papilledema. *Case Rep Ophthalmol Med.* 2012;2012:682659.
6. Bakshi SK, Oak JL, Chawla KP, Kulkarni SD, Apte N. Facial nerve involvement in pseudotumor cerebri. *J Postgrad Med.* 1992;38(3):144-145.
7. Lee AG. Fourth nerve palsy in pseudotumor cerebri. *Strabismus.* 1995;3(2):57-59.
8. Tan H. Bilateral oculomotor palsy secondary to pseudotumor cerebri. *Pediatr Neurol.* 2010;42(2):141-142.
9. Wall M. Idiopathic intracranial hypertension. *Neurol Clin.* 2010;28(3):593-617.
10. McClelland C, Van Stavern GP, Shepherd JB, Gordon M, Huecker J. Neuroimaging in patients referred to a neuro-ophthalmology service: the rates of appropriateness and concordance in interpretation. *Ophthalmology.* 2012;119(8):1701-1704.
11. Kwon BJ, Han MH, Kang HS, Chang KH. MR imaging findings of intracranial dural arteriovenous fistulas: relations with venous drainage patterns. *AJNR Am J Neuroradiol.* 2005;26(10):2500-2507.

12. Greenberg RG, Smith PB, Cotten CM, Moody MA, Clark RH, Benjamin DK, Jr. Traumatic lumbar punctures in neonates: test performance of the cerebrospinal fluid white blood cell count. *Pediatr Infect Dis J.* 2008;27(12):1047-1051.
13. Nigrovic LE, Shah SS, Neuman MI. Correction of cerebrospinal fluid protein for the presence of red blood cells in children with a traumatic lumbar puncture. *J Pediatr.* 2011;159(1):158-159.
14. Neville L, Egan RA. Frequency and amplitude of elevation of cerebrospinal fluid resting pressure by the Valsalva maneuver. *Can J Ophthalmol.* 2005;40(6):775-777.
15. Abel AS, Brace JR, McKinney AM, et al. Effect of patient positioning on cerebrospinal fluid opening pressure. *J Neuroophthalmol.* 2014;34(3):218-222.
16. Schwartz KM, Luetmer PH, Hunt CH, et al. Position-related variability of CSF opening pressure measurements. *AJNR Am J Neuroradiol.* 2013;34(4):904-907.

HOW DO I EVALUATE PAPILLEDEMA IN A CHILD?

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LEARNING OBJECTIVES

1. Identify etiologies of papilledema unique to children (craniosynostosis, IVH/premie; mastoiditis).
2. Explain the influence of age, gender and obesity on the incidence of papilledema/IIH.
3. Describe the appropriate diagnostic imaging methods for children with papilledema.

CME QUESTIONS

1. True or False: In a child with suspected craniosynostosis, a standard MRI or non-contrast CT is sufficient.

2. Children manifesting papilledema without a clear etiology (i.e., IIH, PTCS), their body weight is:
    A. Obese in 100% of cases, regardless of age
    B. Never obese
    C. Obese in most peri-pubescent and pubescent children, but roughly equal proportions of normal weight and obese in pre-pubescent children.

3. Determining if optic nerve head elevation is secondary to drusen or elevated ICP in children is difficult because:
    A. Children never manifest hemorrhages with papilledema
    B. Spontaneous venous pulsations are absent in children
    C. Drusen are more difficult to visualize in young children since they are not always calcified.
    D. No current tests can identify drusen in children

KEYWORDS

1. Pediatric Neuro-Ophthalmology
2. Papilledema
3. Drusen
4. Elevated ICP
5. Headache

OVERVIEW

Many of the same etiologies causing elevated optic nerves secondary to elevated intracranial pressure (ICP), termed papilledema, occur in both children and adults. However, there are also numerous differences in the risk factors, etiologies, exam findings, diagnostic imaging and treatment of children with papilledema compared to adults.

Background and Epidemiology

The incidence of papilledema occurring as part of idiopathic intracranial hypertension/pseudotumor cerebri syndrome (PTCS) is estimated at 0.9/100,000 children,[1] although this number is suspected to have increased given the rise in obesity in some countries. The incidence of papilledema from other etiologies (e.g., brain tumors, craniosynostosis, etc) has not been well established.

Children of all ages and genders can manifest papilledema—the frequency of which depends on the underlying cause of the elevated ICP. Common among pediatric PTCS studies is the greater number of adolescent subjects, although the number of pre-teen and young children (<7 years old) is still remarkable. In a large multicenter study by Sheldon and colleagues, there was an equal incidence of PTCS between males and females before puberty (~11 yo), whereas those who had experienced puberty were overwhelmingly female.[2] Another interesting finding from this large study was the relationship between age and body mass index. While obesity was very common in older males and females, it was relatively uncommon in younger females (<7yo) and males (<8.5 yo) with PTCS.[2]

Risk Factors Unique to Pediatrics

When examining a child, the clinician should always inquire about and consider the association between papilledema and certain acquired and genetic conditions as well as medications. A large number of single patient or small case series have suggested the association between a wide variety of medical conditions and papilledema—their inclusion is beyond the scope of this talk. Both Down Syndrome (Trisomy 21) and sinus venous thrombosis secondary to mastoiditis are two of the more common pediatric conditions associated with the risk of papilledema. Less recognized, but equally important is craniosynostosis. From infancy through early childhood, the 7 independent bones of the skull, all connected by malleable sutures, permit growth and expansion. Craniosynostosis is the premature fusion/closure of ≥ 1 sutures that stops skull growth, thus continued brain growth (i.e., increased volume) will eventually cause elevated ICP and papilledema. Normal head circumference and head shape make some forms of craniosynostosis difficult to recognize and require an evaluation by a craniofacial expert.

Children with a history of brain injury or congenital brain anomalies are at risk for abnormal CSF dynamics. Infants born prematurely that may have experienced an intraventricular hemorrhage (IVH) with or without associated cortical injury is a frequent cause of elevated ICP along with congenital structural abnormalities like spina bifida or aqueductal stenosis. However, in underdeveloped countries, meningitis during infancy is the most common etiology. Brain tumors, both before and after resection, along with prior brain injuries such as stroke also increase the risk of elevated ICP and papilledema.

Over the past two decades, growth hormone treatment has been utilized in many pediatric conditions including congenital short stature, renal failure, Turner syndrome, Noonan syndrome, Prader-Willi syndrome, and acquired growth hormone deficiency from brain tumors or cancer treatment. Minocycline and retin-A are frequently used to treat acne in teenagers. Over the past year, chimeric antigen T cell receptor (CAR-T) therapy has achieved FDA approval for some forms of acute lymphoblastic leukemia. A known side effect of CAR-T includes both cytokine release syndrome (CRS) and CAR-T related encephalopathy syndrome (CRES) that can lead to elevated ICP and papilledema. A recent consensus statement has provided guidelines for treatment of CRS/CRES related papilledema.[3]

Clinical Examination
In general, the neuro-ophthalmic evaluation including dilated eye exam is no different between adults and children. Depending on the age of the child, formal perimetry to document an enlarged blind spot or progressive field loss from papilledema may not be possible due to poor cooperation.

When attempting to differentiate between papilledema and pseudopapilledema with indirect ophthalmoscopy, two important points must be remembered. First, the characteristic appearance of hyper-reflective and "lumpy-bumpy" optic nerve drusen are less common in children. Second, drusen have been reported to simultaneously occur with papilledema in up to 48% of children.[4]

Diagnostic Imaging and Procedures
Optic nerve drusen in children may also have a different appearance when imaged with B-scan ultrasonography (BSUS). Drusen are not typically calcified and or superficial. It is imperative that the BSUS gain is turned down to help identify these less calcified drusen. There is debate about whether peripapillary hyperreflective ovid mass-like structures (PHOMS) represent a form of drusen.[5-7] In our large pediatric neuro-ophthalmology clinic, PHOMS are frequently visualized in children with pseudopapilledema and can occasionally co-exist with papilledema. Fluorescein angiography and autofluorescence have also demonstrated their ability to differentiate between papilledema and pseudopapilledema, but again cooperation and expertise in imaging young children can be a barrier.[8, 9] Oral fluorescein has been suggested to be less invasive alternative for children.[10]

In older obese female patients suspected to have typical PTCS, brain MRI is typically sufficient to rule out a mass lesion or other secondary causes. MRV should be considered in patients with atypical features and or risk factors such as young males or patients with normal BMI. MRV is also important when mastoiditis is on the differential diagnosis. When the etiology of PTCS cannot be identified and craniosynostosis is considered, a head CT with 3D reconstruction is the test of choice. The standard head CT and MRI are less than ideal to determine whether the cranial sutures have prematurely fused—the hallmark of craniosynostosis. Fortunately, head CT with 3D reconstruction can be acquired using a low dose radiation protocol.

The lumbar puncture opening pressure (LP-OP) is an important factor in making the diagnosis of papilledema. In children, the upper limit of normal for the LP-OP has been reported to be 28 cm of water.[11] While patient age and BMI do not influence LP-OP, the depth of sedation does influence the reading. Specifically, those determined to be deeply sedated had higher LP-OP compared to those receiving no sedation.[11] When the child is not sedated, the influence of them struggling or increasing their intra-abdominal pressure should be considered. Beyond these factors, the accuracy of the LP-OP can be influenced by numerous other factors including the operator's experience. For these reasons, clinicians should not rely solely on the LP-OP measure to confirm or refute the diagnosis of papilledema.[12, 13]

Treatment
The treatment algorithm for papilledema is similar between adults and children with a few caveats. Acetazolamide and other diuretics require weight-based dosing. Acetazolamide has a typical starting dose of 15mg/kg/day divided twice daily with a maximum dose of 100mg/kg/day (not to exceed 2 grams in children).[14] Liquid formulations are available for most medications. Children whose papilledema is secondary to craniosynostosis, a cranial vault expansion can lead to resolution of elevated ICP and papilledema.[15, 16] Even though VP shunts have been the primary surgery to decrease ICP, the significant

life-long risk of infection and malfunction should be considered in the decision making.[17] In fact, long term exposure to VP shunt placement in younger children with small ventricles has actually induced craniosynostosis.[18]

SUMMARY

Despite sharing many common elements with adults, there are many unique features that must be considered in the diagnosis and treatment of papilledema in children.

CME ANSWERS

1. False
2. C
3. C

REFERENCES

1. Durcan FJ, Corbett JJ, Wall M. The incidence of pseudotumor cerebri. Population studies in Iowa and Louisiana. Arch Neurol 1988;45:875-877.
2. Sheldon CA, Paley GL, Xiao R, et al. Pediatric Idiopathic Intracranial Hypertension: Age, Gender, and Anthropometric Features at Diagnosis in a Large, Retrospective, Multisite Cohort. Ophthalmology 2016;123:2424-2431.
3. Mahadeo KM, Khazal SJ, Abdel-Azim H, et al. Management guidelines for paediatric patients receiving chimeric antigen receptor T cell therapy. Nat Rev Clin Oncol 2018.
4. Gospe SM, 3rd, Bhatti MT, El-Dairi MA. Anatomic and visual function outcomes in paediatric idiopathic intracranial hypertension. Br J Ophthalmol 2016;100:505-509.
5. Malmqvist L, Sibony PA, Fraser CL, et al. Peripapillary Ovoid Hyperreflectivity in Optic Disc Edema and Pseudopapilledema. Ophthalmology 2018;125:1662-1664.
6. Malmqvist L, Bursztyn L, Costello F, et al. Peripapillary Hyperreflective Ovoid Mass-Like Structures: Is It Optic Disc Drusen or Not?: Response. J Neuroophthalmol 2018.
7. Malmqvist L, Bursztyn L, Costello F, et al. The Optic Disc Drusen Studies Consortium Recommendations for Diagnosis of Optic Disc Drusen Using Optical Coherence Tomography. J Neuroophthalmol 2018;38:299-307.
8. Pineles SL, Arnold AC. Fluorescein angiographic identification of optic disc drusen with and without optic disc edema. J Neuroophthalmol 2012;32:17-22.
9. Chang MY, Velez FG, Demer JL, et al. Accuracy of Diagnostic Imaging Modalities for Classifying Pediatric Eyes as Papilledema Versus Pseudopapilledema. Ophthalmology 2017;124:1839-1848.
10. Ali SMA, Khan I, Khurram D, Kozak I. Ultra-Widefield Angiography With Oral Fluorescein in Pediatric Patients With Retinal Disease. JAMA Ophthalmology 2018;136:593-594.
11. Avery RA, Shah SS, Licht DJ, et al. Reference range for cerebrospinal fluid opening pressure in children. N Engl J Med 2010;363:891-893.
12. Avery RA. Interpretation of lumbar puncture opening pressure measurements in children. J Neuroophthalmol 2014;34:284-287.
13. Avery RA. Reference range of cerebrospinal fluid opening pressure in children: historical overview and current data. Neuropediatrics 2014;45:206-211.
14. Sheldon CA, Paley GL, Beres SJ, McCormack SE, Liu GT. Pediatric Pseudotumor Cerebri Syndrome: Diagnosis, Classification, and Underlying Pathophysiology. Semin Pediatr Neurol 2017;24:110-115.
15. Swanson JW, Aleman TS, Xu W, et al. Evaluation of Optical Coherence Tomography to Detect Elevated Intracranial Pressure in Children. JAMA Ophthalmology 2017;135:320-328.

16. Thompson DN, Malcolm GP, Jones BM, Harkness WJ, Hayward RD. Intracranial pressure in single-suture craniosynostosis. Pediatr Neurosurg 1995;22:235-240.
17. McGirt MJ, Leveque JC, Wellons JC, 3rd, et al. Cerebrospinal fluid shunt survival and etiology of failures: a seven-year institutional experience. Pediatr Neurosurg 2002;36:248-255.
18. Weinzweig J, Bartlett SP, Chen JC, et al. Cranial vault expansion in the management of postshunt craniosynostosis and slit ventricle syndrome. Plast Reconstr Surg 2008;122:1171-1180.

ESSENTIAL INFANTILE ESOTROPIA-POTENTIAL ROLE OF ENHANCED SUBCORTICAL NEUROPLASTICITY

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LEARNING OBJECTIVES

1. Describe the unique pathophysiology of essential infantile esotropia and understand its subcortical ocular motor circuitry.

CME QUESTIONS

1. Essential infantile esotropia involves ocular motor pathways for:
    A. Saccades
    B. Vestibular
    C. Visuovestibular motion detection
    D. Pursuit
    E. C and D

2. The major visual control system for essential infantile esotropia includes:
    A. Accessory optic system
    B. Nucleus of the optic tract
    C. Superior colliculus
    D. Nucleus of Perlia
    E. A and B

3. True or False: Essential infantile esotropia represents a state of active or excessive convergence:

KEY WORDS

1. Essential infantile esotropia
2. Subcortical
3. Optokinetic
4. Accessory optic system

HIGHLIGHTS

Despite its selective involvement of the ocular motor system, essential infantile esotropia is rarely mentioned in neuro-ophthalmology textbooks. This talk contextualizes essential infantile esotropia as a disorder that arises from an abnormal expression of the subcortical visual pathways subserving optokinesis with a secondary remodeling of cortical motion pathways. These subcortical motion pathways are normally shut down after the first few months of infant life, explaining why this disorder creates a scotoma within our neuro-ophthalmologic lexicon.

SUMMARY

Essential infantile esotropia is often attributed to a primary disturbance within the visual cortex based upon the findings of monocular horizontal optokinetic asymmetry an correlative horizontal motion detection asymmetry as measured by visual evoked potentials. However, these physiologic aberrations conform to what would be observed if the visual cortex secondarily reconfigured itself to the preexisting subcortical optokinetic motion template. This lecture examines the alternative perspective that the measured cortical aberrations can be explained by a primary state of prolonged subcortical neuroplasticity, leading to a secondary reconfiguration of the cortical motion pathways.

Evolutionary evidence suggests that essential infantile esotropia is generated by subcortical ocular motor centers that subserve nasalward optokinesis. These phylogenetically older subcortical optokinetic pathways include the nucleus of the optic tract, the accessory optic system, the inferior olive, the cerebellar flocculus, and the vestibular nucleus. In normal humans, the subcortical visual system becomes inactivated after the first few months of infancy. Mutations or other perturbations that prolong subcortical neuroplasticity may create a persistent nasalward optokinetic bias in both eyes to generate infantile esotropia.

ANSWERS TO CME QUESTIONS

1. E
2. E
3. False

REFERENCES

1. Brodsky MC: Essential infantile esotropia: Potential role of enhanced subcortical neuroplasticity. Invest Ophthalmol Vis Sci 2018;59;1964-1968.
2. Brodsky MC: The accessory optic system: The fugitive visual control system in infantile strabismus. Arch Ophthalmol 2012;130:1055-1059.

CONGENITAL OCULAR MOTOR APRAXIA (COMA)

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LEARNING OBJECTIVES

1. Recognize key features of congenital ocular motor apraxia
2. Describe the associated neuroradiologic findings
3. Explain the best management options when presented with a child with COMA

CME QUESTIONS

1. Is head thrusting a universal finding in COMA?
2. What brain abnormalities are associated with COMA?
3. With what condition is the “molar tooth sign” associated?

KEYWORDS

1. Congenital ocular motor apraxia (or congenital oculomotor apraxia)
2. Infantile-onset saccade initiation delay
3. Joubert syndrome
4. Molar tooth sign

HIGHLIGHTS

- COMA is a congenital condition characterized by an impairment of voluntary, saccadic eye movements, typically in the horizontal direction.
- Infants with COMA typically present with poor visual responses, and typically develop compensatory horizontal head thrusting movements after establishment of head control.
- COMA has also been termed oculomotor apraxia (OMA) and infantile-onset saccade initiation delay (ISID).
- Neuroradiological findings may be normal in COMA patients, or may reveal cerebellar anomalies (mainly hypoplastic vermis) and brainstem dysgenesis.
- COMA may be idiopathic, or associated with neurometabolic conditions, ataxia-oculomotor apraxia syndromes and isolated or syndromic structural brain abnormalities. Familial cases have been described.

SUMMARY

Cogan first described this congenital condition which is characterized by an impairment of voluntary, saccadic eye movements in the horizontal direction. Patients with COMA typically present with poor visual responses in early infancy and may appear visually impaired. When head control is established at about 6 months, compensatory horizontal head thrusting movements often develop, seemingly utilizing an exaggerated vestibulo-ocular reflex. The lateral head rotation overshoots the target of regard, with

the eyes lagging behind. When the eyes finally "land" on the visual target the head simultaneously turns back to a normal position with the eyes are in a primary gaze position. Head thrusting is common but not universal. Horizontal slow pursuit movements may be normal or partly impaired in COMA patients, and vertical eye movements are usually preserved.

COMA is the most commonly used term in the medical literature, but some authors prefer "infantile-onset saccade initiation delay" (ISID).

Neuroradiological findings may be normal, with several studies reporting up to 50% of COMA patients with allegedly normal MRI scans. The remaining 50% of COMA patients display neuro-radiologic abnormalities, the most common being cerebellar anomalies (mainly hypoplastic vermis), brainstem dysgenesis and agenesis of the corpus callosum.

COMA is often isolated, but familial cases have been reported. COMA may also be associated with Joubert syndrome, ataxia–telangiectasia, Gaucher's disease and ataxia–oculomotor apraxia syndromes.

Joubert syndrome and related disorders (JSRD) presents as congenital onset nystagmus (torsional and/or see-saw), hypotonia, neonatal respiratory dysregulation. MRI reveals the pathognomonic neuroimaging feature of the "molar tooth sign" which derives from the combination of elongated, thickened and horizontalized superior cerebellar peduncles; hypo/dysplasia of the cerebellar vermis; and an abnormally deep interpeduncular fossa. This group of disorders are ciliopathies and are associated with mutations in more than 30 genes. Depending on the mutation, retinal dystrophy, nephronophthisis, and/or hepatic fibrosis may also develop.

There is no specific treatment for COMA. The compensatory head thrusting tends to improve over time, possibly due to improved saccades or the development of compensatory strategies such as use of smooth pursuit or blinking. A work-up of these children should be obtained and includes, in the minimum, neuro-imaging with MRI for structural abnormalities. Presence of the molar tooth sign is diagnostic of JSRD. Consideration should also be given for neurometabolic disorders. Referral to a geneticist for workup and management is indicated.

CME ANSWERS

1. No, head thrusting is not present before 6 months of age when the child develops head control, and may disappear with time.
2. Cerebellar anomalies (mainly hypoplastic vermis), brainstem dysgenesis and agenesis of the corpus callosum
3. On axial MRI: elongated, thickened superior cerebellar peduncles; hypoplasia of the cerebellar vermis; and an abnormally deep interpeduncular fossa.

REFERENCES

1. Salman M, Ikeda K, et al. Do the Clinical Features in Infantile-Onset Saccade Initation Delay (Congenital Ocular Motor Apraxia) Corelate with Brian Magnetic Resonance Imaging Findings?, N American J Neuro-Ophthalmol Society, 34: 246-250, 2014.
2. Wente S, Schröder S, Buckard J, Büttel H, Deimling von F, Diener W, Häussler M, Hübschle S, Kinder S, Kurlemann G, Kretzschmar C, Lingen M, Maroske W, Mundt D, Sánchez-Albisua I, Seeger J, Toelle

S, Boltshauser E, Brockmann K, et al. Nosological delineation of congenital ocular motor apraxia type Cogan: an observational study, Orphanet J of Rare Diseases, 11:104, 2016.
3. Salman M, Ikeda K, et al. The Syndrome of Infantile-Onset Saccade Initiation Delay, Canadian J of Neurol Sci, 40: 235-240, 2013.
4. Ronsin S, Hannoun S, Thobois S, Petiot P, Vighetto A, Cotton F, Tilikete C, et al. The New MRI marker of ataxia with oculomotor apraxia, European J of Radiology, 110: 187-192, 2019.
5. Gleeson J, Keeler L, Parisi M, Marsh S, Chance P, Glass I, Graham J, Maria B, Barkovich A, Dobyns W, et al. Molar Tooth Sign of the Midbrain-Hindbrain Junction: Occurrence in Multiple Distinct Syndromes, A J of Med Genetics, 125A: 125-134, 2004.
6. Brooks B, Zein W, Thompson A, Mokhtarzadeh M, Doherty D, Parisi M, Glass I, Malicdan M, Vilboux T, Vemulapalli M, Mullikin J, Gahl W, Gunay-Aygun M, et al. Joubert Syndrome: Ophthalmological Findings in Correlation with Genotype and Hepatorenal Disease in 99 Patients Prospectively Evaluated at a Single Center, J A Academy of Ophthalmol, Volume 125, Number 12, Dec 2018.
7. Schweyer K, Busche M, Hammes J, Zwergal A, Buhmann C, Elmeren van T, Höglinger G, et al. Pearls & Oy-sters: Ocular motor apraxia as essential differential diagnosis to supranuclear gaze palsy, J A Academy of Neurology, 90: 482-485, 2018.
8. König J, Kranz B, König S, Schlingmann K, Titieni A, Tönshoff B, Habbig S, Pape L, Häffner K, Hansen M, Büscher A, Bald M, Billing H, Schild R, Walden U, Hampel T, Staude H, Riedl M, Gretz N, Lablans M, Bergmann C, Hildebrandt F, Omran H, Konrad M, et al. Phenotypic Spectrum of Children with Nephronophthisis and Related Ciliopathies, Clin J Am Soc Nephrol, 12: 1974-1983, Dec 2017.

RECONSIDERING CLASSIFICATION OF DUANE'S RETRACTION SYNDROME

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LEARNING OBJECTIVES

1. Describe the historical categorization of Duane's Syndrome and question the nosological and clinical value of such categorization.

CME QUESTIONS

1. Categorization of Duane's Syndrome into 3 types was popularized by:
    A. Thomas Duane
    B. William Hoyt
    C. Warren Harding
    D. Alfred Huber

2. True or False: Duane's Syndrome is always associated with absence of innervation of the lateral rectus by cranial nerve VI.

3. True or False: Individuals with hereditary Duane's Syndrome from the same family have different clinical phenotypes.

KEYWORDS

1. Duane's syndrome
2. Aberrant innervation
3. Incomitant strabismus

HIGHLIGHTS

Clinical manifestations of Duane retraction syndrome should be considered on a spectrum of fibrosis and dysinnervation rather than distinct categories. Treatment should be determined by the clinical findings on a case-by-case basis. Huber's classification system does not promote this approach. The purpose of this talk will be to examine the historical categorization of Duane's Syndrome and question the nosological and clinical value of such categorization.

SUMMARY

Since its first description in the late 19th century, the mechanism for the clinical manifestations of Duane's Retraction Syndrome (limitation of abduction; globe retraction with narrowing of the palpebral fissure on adduction) has been debated with camps generally divided into mechanical and neurogenic theories. Huber theorized that all cases of DRS could be explained by aberrant innervation of the lateral rectus muscle by the oculomotor nerve. To demonstrate this, in 1974 he reported on the electromyographic findings (EMG) from cases of DRS that he divided descriptively into Type I (defective

abduction), Type II (defective adduction) and Type III (both defective abduction and adduction). (Huber 1974) This phenotypic classification system has persisted as the main memorialization of Huber's work. The classification system is now imbedded in the education of ophthalmology and neurology residents without regard for the pathogenic implications or the empirical findings of Huber's work. In this presentation we will review Huber's work, as well as that of numerous preceding and subsequent investigators. We will demonstrate that the classification of DRS provides little, if any, value toward the understanding of the pathophysiology of DRS or its clinical management.

The first clinical description of DRS was by Heuck in 1879, which noted retroplaced medial rectus on patient with absent abduction and globe retraction. (Heuck 1879) Subsequent reports are attributed to Stilling (1887), Sinclair (1895), Turk (1899), and Wolff (1900). In 1905, Alexander Duane compiled 27 cases from the literature, along with 27 of his own cases to provide the most complete description of DRS up until that time. (Duane 1905) Hence, he receives the eponymous association.

Duane's report included plausible explanations for nearly all of the clinical features of the syndrome. He noted that 100% of cases had variable abduction deficits attributed to congenital replacement of the lateral rectus by a fibrous band. He felt any residual abduction could be attributed to co-contraction of the superior oblique and inferior oblique muscles. He also noted some limitation of adduction in 95% of cases, which he attributed to restriction caused by the inelastic lateral rectus, as well as to occasional anomalous insertion of the medial rectus muscle. He similarly hypothesized that globe retraction was due to contraction of the medial rectus against and inelastic lateral rectus. He could provide no explanation for lid fissure changes, but astutely noted that most cases occurred in women and in the left eye.

Subsequently, until the 1960s nearly all reports attributed the abnormal motility and globe retraction to mechanical problems. Numerous more recent reports have also demonstrated cases of restricted eye movements. These have included anomalous medial rectus insertions, fibrous lateral rectus muscles, and fibrous bands between the globe and the orbital wall. (Kruger 1969; Mayou 1934; Nawratzki 1967; Spaeth 1953; vonNoorden 1972)

Huber's report of anomalous innervation of the lateral rectus by the nerve to the medial rectus was the first in the English literature, but others had previously reported this phenomenon. Breinen first demonstrated this with simultaneous EMG recordings from the lateral and medial rectus muscles from a single patient in 1957.(Breinen 1957) In 1959, Sato reported 12 cases of DRS, 10 of which demonstrated increased firing of the lateral rectus on adduction, but two of which had increased firing of the medial rectus on attempted abduction!(Sato 1959)

Huber was also not the first to suggest a classification of DRS phenotypes. In 1949, Malbran described 2 cases of DRS with good abduction, but inability to adduct. (Malbran 1949) He suggested calling this phenotype, Duane's Type II. He also documented a single case with normal horizontal movements, but limited vertical movements that he categorized as Type III.

Huber utilized Malbran's classification of Types I and II, in his first paper on EMG findings in Duane's Syndrome, but dismissed Type III as something other than Duane's Syndrome. (Huber 1964) That paper, written in German, described simultaneous EMG recordings from the lateral and medial recti in four patients with Type I and one with type II. Ten years later, he created an English summary of the previous paper, adding a single case with limited abduction and adduction, that he labeled Duane's Type III. (Huber 1974)

From his six cases with adequate electromyographic studies (EMG), Huber demonstrated that the three types had varying degrees of absence of innervation of the lateral rectus from the abducens nerve and aberrant innervation by the oculomotor nerve. In Type III the abducens nerve was completely replaced by the oculomotor nerve, resulting in no horizontal rectus firing in attempted abduction and complete co-contraction on attempted adduction. Thus, he showed DRS was actually a continuum of relative absence of abducens innervation and aberrance of oculomotor innervation and not three distinct clinical conditions. Nonetheless, Huber's classification of DRS into three types persists as the only memory of this work and has become a principle in medical education about this condition.

Several subsequent large studies have demonstrated that there is not a good correlation between Huber's clinical classification and the EMG findings. (Maruo 1980; Mizukawa 2004) Numerous EMG patterns not described by Huber involving abnormal activity of the oculomotor nerve, as well as the abducens nerve have been found. (Sato 1959; Blodi 1964; Scott & Wong 1972; Mizukawa 2004) Lid fissure narrowing on adduction can be caused by globe retraction from horizontal rectus co-contraction, as well as by abnormal innervation of the levator in some cases. (Scott & Wong 1972; Moore, et al 1988) Families with hereditary, autosomal dominant DRS, have had multiple phenotypes in the same family, including some with involvement of additional cranial nerves and vertical strabismus. (Mizukawa 2004; Chung 2000) These facts, combined with the demonstrated restriction from extraocular muscle fibrosis in numerous cases, suggest that clinical manifestations of DRS should be considered on a spectrum of fibrosis and dysinnervation rather than distinct categories. Treatment should be determined by the clinical findings on a case-by-case basis. Huber's classification system does not promote this approach.

CME ANSWERS

1. D
2. False
3. True

REFERENCES

1. Blodi FC, Van Allen MW, Yarbrough JC. Duane's syndrome; a brain stem lesion. Arch Ophthalmol 72: 172, 1964.
2. Breinen GM. Electromyuography: a tool in ocular and neurologic diagnosis, II. Muscle palsies. Arch Ophthalmol. 57:165, 1957.
3. Chung, M., Stout, JT., Borchert, MS., Clinical diversity of hereditary Duane's retraction syndrome. Ophthalmology. 107:500, 2000.
4. Duane A. Congenital deficiency of abduction associated with impairment of adduction, retraction movement, contraction of the palpebral fissure and oblique movements of the eye. Arch Ophthalmol 34:133-45, 1905.
5. Heuck G. Uber angeborenen verebten Beweglichkeitsdefectder Augen. Klin Monatsbl Augenheilkd 17:253, 1879.
6. Huber A, et al. Zum Problem des Duane Syndromes. Graefes Arch Ophthalmol. 167:169, 1964.
7. Huber A. Electrophysiology of the retraction syndromes. Br J Ophthalmol. 58:293, 1974.
8. Kruger KE. Beitrag zur Ateiologie des Stilling-Turk-Duane syndromes. Acta Ophthalmol. 47:415, 1969
9. Malbran J. Estrabismos y paralysis. Clinica y terapeutica, Burnos Aires, 1949, Editorial Oftalmologia, p. 267.

10. Maruo T, Kubota N, Arimoto H, Kikuchi R. Duane's Syndrome. Rinsho Ganka (Jpn J Clin Ophthalmol) 34: 845-54, 1980.
11. Mayou MS. Presidential address and discussion of squint. Trans Ophthalmol Soc UK 54:3, 1934
12. Mizukawa K, et al. Classification o Duane's retraction syndrome: Two additional electromyogram types. Jpn J Ophthalmol. 48:148, 2004.
13. Moore LD, Feldon SE, Liu SK. Infrared oculography of Duane"s syndrome (type 1). Arch Ophthalmol. 106:943, 1988.
14. Nawratzki I. Atypical retraction syndrome: a case report J Pediatr Ophthalmol 4:32, 1967
15. Sato S. Electromyographic studies on Duane's retraction syndrome. Report I. Qualitative changes of action currents of extraocular muscles in ocular movements. Acta Soc Ophthalmol Jpn 63:2028, 1959.
16. Scott AB, Wong GY. Duane;s syndrome: and electromyographic study. Arch Ophthlamol 87:140, 1972
17. Sinclair WW. Abnormal associated movements of the eyelids. Ophthalmol Rev 14:307, 1895
18. Spaeth EB. Surgical aspects of defection abduction. Arch Ophthalmol 49:49, 1953.
19. Stilling J. Untersuchungen uber die Entstejung der Kurzichtigkeit, Wiebaden, 1887, J.F. Bergmann, p.13.
20. Turk S. Bemerkungen zu einem Falle von Retraction des Auges. Cbl Pract Augenheilk 23:14, 1899.
21. Von Noorden GK. "Special forms of strabismus" in Binocular Vision and Ocular Motility 5th ed. Mosby, St. Louis,1972 p. 430.
22. Wolff J. The occurrence of retraction movements of the eyeball together with congenital defects in the external ocular muscles. Arch Ophthalmol 29:297, 1900.

CONGENITAL CRANIAL DYSINNERVATION DISORDERS

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LEARNING OBJECTIVES

1. Review the current genetic classification of congenital cranial dysinnervation disorders (CCDDs)
2. Explain the phenotypic manifestations and genetic underpinnings of congenital fibrosis of the extraocular muscles (CFEOM) 1, 2, 3
3. Report on surgical management of strabismus in patients with CFEOM

CME QUESTIONS

1. Congenital fibrosis of the extraocular muscles results from dysinnervation involving which cranial nerves?
    A. CN VI
    B. CN III
    C. CN IV
    D. CN III and IV

2. Kallman syndrome is found as part of the phenotypic manifestations of which of the CFEOM subtypes?
    A. CFEOM1
    B. CFEOM2
    C. CFEOM3
    D. Tukel syndrome

3. Which subtype of CFEOM is most likely to be misclassified as Moebius syndrome? And why?
    A. CFEOM1
    B. CFEOM2
    C. CFEOM3
    D. Tukel syndrome

KEYWORDS

1. Congenital Cranial Dysinnervation Disorders
2. Congenital Fibrosis of the Extraocular Muscles
3. Complex Strabismus

HIGHLIGHTS

- Patients with congenital cranial dysinnervation disorders may present as complex strabismus secondary to dysinnervation of the extraocular muscles.
- Identification of the genetic basis of these conditions has informed our understanding of the pathogenesis of disease.

- Patients with congenital fibrosis of the extraocular muscles (CFEOM) will be presented as an example for which genetic stratification may yield keener insight into patient prognosis and clinical outcomes.

SUMMARY

Patients with congenital cranial dysinnervation disorders (CCDD) may present with complex strabismus secondary to dysinnervation of the extraocular muscles. (1-3) Among the CCDDs, congenital fibrosis of the extraocular muscles (CFEOM) is a group of strabismus disorders characterized by blepharoptosis and ophthalmoplegia. Animal models of CFEOM have revealed that the phenotype arises from dysinnervation of oculomotor and/or trochlear nerves (4-6). In humans, this dysinnervation manifests as incomitant strabismus with restriction of both vertical and also horizontal gaze. Historically, patients have been stratified into three phenotypes of CFEOM: 1, 2 and 3; since 2001, the genetic basis of these conditions has been identified. CFEOM1 is dominantly inherited and occurs primarily from mutations in *KIF21A*.(7) CFEOM2 is recessively inherited and occurs from mutations in *PHOX2A*(8). CFEOM3 is dominantly inherited and occurs from mutations in *TUBB3* and rarely in *KIF21A* or *TUBB2B*.(4,9-10) In general, CFEOM is rare and data regarding prevalence of this condition are limited. Based on cases of CFEOM in the Wessex region of the United Kingdom an estimate of 1/230,000 cases has been proposed.(11) Given the limited number of cases of CFEOM, developing general recommendations for strabismus management has been difficult.(12-21)

Nevertheless, we anticipate that knowledge of the underlying genetic mutation may inform surgical recommendations as well as may provide insight into clinical prognosis more broadly given that there are co-morbidities associated with CFEOM based on genetic mutation.(22) This talk will examine the importance of the genetic understanding of CFEOM with respect to surgical management and clinical prognosis.

CME ANSWERS

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REFERENCES

1. Engle EC. The genetic basis of complex strabismus. Pediatr Res 2006;59(3):343-8.
2. Heidary G, Engle EC, Hunter DG. Congenital fibrosis of the extraocular muscles. Semin Ophthalmol 2008;23(1):3-8.
3. Graeber CP, Hunter DG, Engle EC. The genetic basis of incomitant strabismus: consolidation of the current knowledge of the genetic foundations of disease. Semin Ophthalmol 2013;28(5-6):427-37.
4. Tischfield MA, Baris HN, Wu C, et al. Human TUBB3 mutations perturb microtubule dynamics, kinesin interactions, and axon guidance. Cell 2010;140(1):74-87.
5. Cheng L, Desai J, Miranda CJ, et al. Human CFEOM1 mutations attenuate KIF21A autoinhibition and cause oculomotor axon stalling. Neuron 2014;82(2):334-49.
6. Whitman MC, Engle EC. Ocular congenital cranial dysinnervation disorders (CCDDs): insights into axon growth and guidance. Hum Mol Genet 2017;26(R1):R37-R44.
7. Yamada K, Andrews C, Chan WM, et al. Heterozygous mutations of the kinesin KIF21A in congenital fibrosis of the extraocular muscles type 1 (CFEOM1). Nat Genet 2003;35(4):318-21.

8. Nakano M, Yamada K, Fain J, Sener et al. Homozygous mutations in ARIX(PHOX2A) result in congenital fibrosis of the extraocular muscles type 2. Nat Genet 2001;29(3):315-20.
9. Yamada K, Chan WM, Andrews C, et al. Identification of KIF21A mutations as a rare cause of congenital fibrosis of the extraocular muscles type 3 (CFEOM3). Invest Ophth Vis Sci 2004;45(7):2218-23.
10. Cederquist GY, Luchniak A, Tischfield MA, et al. An inherited TUBB2B mutation alters a kinesin-binding site and causes polymicrogyria, CFEOM and axon dysinnervation. Hum Mol Genet 2012;21(26):5484-99.
11. Reck AC, Manners R, Hatchwell E. Phenotypic heterogeneity may occur in congenital fibrosis of the extraocular muscles. Br J Ophthalmol 1998;82(6):676-9.
12. Crawford JS. Congenital fibrosis syndrome. Can J Ophthalmol 1970;5(4):331-6.
13. Apt L, Axelrod RN. Generalized fibrosis of the extraocular muscles. Am J Ophthalmol 1978;85(6):822-9.
14. Letson RD. Surgical Management of the Ocular Congenital Fibrosis Syndrome. Am Orthoptic J 1980;30.
15. Traboulsi EI, Jaafar MS, Kattan H, Parks MM. Congenital fibrosis of the extraocular muscles: Report of 24 cases illustrating the clinical spectrum and surgical management. Am Orthoptic J 1993;43.
16. Ferrer J. Congenital fibrosis of the extraocular muscles. Ophthalmol 1996;103(10):1517-9.
17. Brodsky MC. Surgical Management of the Congenital Fibrosis Syndrome. Am Orthoptic J 1997;47.
18. Yazdani A, Traboulsi EI. Classification and surgical management of patients with familial and sporadic forms of congenital fibrosis of the extraocular muscles. Ophthalmol 2004;111(5):1035-42.
19. Merino P, Gomez de Liano P, Fukumitsu H, Franco G, Ruiz Y. Congenital fibrosis of the extraocular muscles: magnetic resonance imaging findings and surgical treatment. Strabismus 2013;21(3):183-9.
20. Tawfik HA, Rashad MA. Surgical management of hypotropia in congenital fibrosis of extraocular muscles (CFEOM) presented by pseudoptosis. Clin Ophthalmol 2013;7:1-6.
21. Sener EC, Taylan Sekeroglu H, Ural O, Ozturk BT, Sanac AS. Strabismus surgery in congenital fibrosis of the extraocular muscles: a paradigm. Ophthalmic Genet 2014;35(4):208-25.
22. Chew S, Balasubramanian R, Chan WM, et al. A novel syndrome caused by the E410K amino acid substitution in the neuronal beta-tubulin isotype 3. Brain 2013;136(Pt 2):522-35.

MOEBIUS SYNDROME

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LEARNING OBJECTIVES

1. Define the key features of Moebius Syndrome
2. Interpret the brainstem anatomy that causes horizontal and vertical eye movement abnormalities with facial paresis
3. Recognize that there are candidate genes that regulate neuronal migration of cranial nerves and vascularization of the brainstem

CME QUESTIONS

1. What are the two most common cranial nerves and respective nuclei involved in Moebius syndrome?
2. What is the most common eye movement abnormality found in Moebius syndrome?
3. During embryogenesis, what trimester of gestation is the proposed cause of Moebius syndrome?

KEYWORDS

1. Moebius syndrome
2. Bilateral facial palsy
3. Horizontal gaze palsy
4. Sixth nerve palsy
5. Brainstem hypoplasia

HIGHLIGHTS

- Moebius syndrome is a rare non-progressive congenital syndrome with unknown, yet likely multifactorial etiology (teratogenic, genetic, vascular/ischemic)
- Abducens and facial cranial nerve palsies define the clinical syndrome, but other features can be seen including malformations of the extremity, cardiac, other cranial nerves, and trunk.
- Most common eye movement abnormality is bilateral horizontal gaze palsies.
- Strabismus surgery is rarely done to alleviate strabismus in Moebius syndrome and more often the surgical focus is to reanimate the facial diplegia.

SUMMARY

Moebius syndrome is a congenital malformation of the brainstem that is non-progressive typically causing bilateral facial diplegia and horizontal eye movement restriction. The syndrome has variable phenotypes and severity and can be found with other cranial neuropathies such as cranial nerves V, IX, X, and XII.[1,2] The incidence is 1 in 50,000 live births with no gender predilection.[3] The most common eye movement abnormality is a bilateral horizontal gaze palsy although there can be unilateral gaze palsies or sixth nerve palsies, vertical eye movement limitations, and convergence deficits.[4] Similarly, the facial

palsy is usually bilateral, but can be unilateral; and interestingly with more paresis of the upper face than lower face. These nuclear and nerve findings localize to the lower brainstem (sixth and seventh cranial nuclei) primarily with some remote involvement of the ocular motor structure in the midbrain, convergence neurons, and the vertical supranuclear centers.

During embryology, the lower brainstem forms in the fourth and fifth week of development when the cephalic neural crest cells begin to differentiate into cranial nerve nuclei with the sixth and seventh nuclei next to each other during the hindbrain formation.[5] In addition, during the sixth week of development there is critical blood supply changes in which the basilar supply changes to vertebral artery perfusion of the hindbrain as they fuse with simultaneous regression of the primitive otic and hypoglossal arteries.[6] The proposed causative theories of teratogenicity, ischemic injury, and defective candidate genes that regulate neuronal migration of cranial nerves and vascularization of the brainstem are all plausible.

MR imaging of the brain supports the maldevelopment theories with a wide array of different abnormalities including hypoplasia of the lower brainstem, absence of middle cerebellar peduncles, microcalcifications adjacent to the abducens nuclei, and absence of sixth and seventh cranial nerves.[7-9]

The diagnosis is based exclusively on clinical criteria of concomitant complete or partial sixth and seventh nerve palsies, however, with 300 cases reported, more genetic mutations are being discovered. Most cases are thought to be sporadic mutation, however there have been case reports of familial inheritance in 2% of known cases.[3] Candidate gene loci include 1p22, 3q21-q22 (MBS2), 10q21.3-q22.1 (MBS3), and 13q12.2-13 (MBS1).[10]

With limited ocular movement the patients learn compensatory mechanisms with head movements and similar to the other congenital cranial dysinnervation disorders often there is no surgical treatment. Strabismus surgery or eyelid surgery occur on rare occasions. The largest morbidity comes from the 'masked facies' from the facial diplegia and surgical facial reinnervation is an option.

CME ANSWERS

1. Abducens nerve and nuclei; Facial nerve and nuclei
2. Bilateral horizontal gaze palsy
3. First trimester (weeks 4-8 of gestation)

REFERENCES

1. Kulkarni A, Madhavi MR, Nagasudha M, et al. A rare case of Moebius sequence, Indian J Ophthalmol, 60(6):558–560, 2012.
2. Terzis JK, Noah EM (2002) Möbius and Möbius-like patients: etiology, diagnosis, and treatment options, Clin Plast Surg, 29:497–514, 2002.
3. Verzijl H, van der Zwaag B, Cruysberg J, et al. Möbius syndrome redefined: A syndrome of rhombencephalic maldevelopment, Neurology, 61:327–333, 2003.
4. Rucker J, Webb B, Frempong T, et al. Characterization of ocular motor deficits in congenital facial weakness: Moebius and related syndromes, Brain, 137:1068-1079, 2014.
5. Raroque HG, Hershewe GL, Snyder RD. Möbius syndrome and transposition of the great vessels. Neurology 38:1894–1895, 1988.

6. Bavinck JNB, Weaver DD. Subclavian artery supply disruption sequence: hypothesis of a vascular etiology for Poland, Klippel-Feil, and Möbius anomalies, Am J Med Genet, 23:903–918, 1986.
7. Pedraza S, Gamez J, Rovira A, et al. MRI findings in Möbius syndrome: correlation with clinical features, Neurology, 55:1058–60, 2000.
8. Kuhn MJ, Clark HB, Morales A, et al. Group III Mobius syndrome: CT and MR findings. AJNR 11(5):903–904, 1990.
9. Kim N., Kim, J.H., Kim J-S, et al. Möbius syndrome: clinico-radiologic correlation, Graefes Arch Clin Exp Ophthalmol, 256:2219–2223, 2018.
10. Kadakia S, Helman S, Schwedhelm T, et al. Examining the genetics of congenital facial paralysis—a closer look at Moebius syndrome, Oral Maxillofac Surg, 19:109–116, 2015.

PEDIATRIC NEUROMUSCULAR DISORDERS

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LEARNING OBJECTIVES

1. Describe the various pediatric conditions that affect neuromuscular transmission
2. Recognize the diagnosis and clinical management of pediatric, congenital, and neonatal myasthenia gravis,
3. Review botulism with regards to pediatric population

CME QUESTIONS

1. Which of the following is NOT a treatment of pediatric myasthenia gravis?
    a. Pyridostigime
    b. Edrophonium
    c. Oral steroids
    d. Thymectomy
    e. Immunosuppressant therapy

2. Neonatal myasthenia is caused by
    a. Direct infection of an open wound
    b. Genetic mutation affecting neuromuscular transmission
    c. Ingestion of contaminated food
    d. Passive-transfer acetylcholine receptor (AChR) antibodies from mother

3. True or False: Pyridostigime can be used to treat congenital myasthenia gravis?

KEYWORDS

1. Pediatric Myasthenia Gravis
2. Congenital Myasthenia Gravis
3. Botulism

HIGHLIGHTS

Disruption of the neuromuscular transmission, either at the presynaptic or postsynaptic junction, may result in fatigability and muscle weakness that commonly affect ocular motility and lid movement. We will review several of the pediatric disorders that influence neuromuscular transmission.

SUMMARY

Pediatric ocular myasthenia gravis. Myasthenia gravis (MG) is the most common neuromuscular disorder with an incidence of 5 per 100,000, and ocular involvement or symptoms in 75% of those affected (1) MG is an autoimmune disease in which antibodies are made against components of the

neuromuscular junction resulting clinically in ptosis, diplopia, muscle weakness, and, at advanced ages, difficulties with speech, swallowing and breathing.

Pediatric or juvenile MG is similar to adult MG in terms of presentation, pathogenesis and response to therapy. It is distinguished, however, by the ability for the patient to improve with age. Unlike adults, pediatric MG antibody testing is sero-negative a majority (70%) of the time (2). While edrophonium testing is the gold standard in adults, in young children it can be technically quite difficult to perform and the possibility of pharmacologic complications (severe bradycardia, cardiac arrhythmias) make it impractical in the outpatient setting. Alternatively, clinical history, exam findings, ice-pack and sleep test are more amenable in making this diagnosis in young children. Pediatric MG patients respond quite well to cholinesterase inhibitors (pyridostigmine), mild corticosteroids, and in refractory cases steroid-sparing immunosuppressants (3). Adjunctive intervention of a thymectomy, without the presence of a thymoma, has demonstrated improved prolonged remission of the disease (4).

Neonatal myasthenia. Neonatal myasthenia is a transient condition in which a myasthenic mother passively transfers acetylcholine antibodies to her baby resulting in a transient myasthenic syndrome commonly occurring the first 72 hours of life (5). Symptoms include hypotonia, poor suck and swallow reflex, weak cry, facial paralysis, and mild respiratory distress. Fifteen percent of these babies have ocular signs of ptosis, ophthalmoplegia, and weak orbicularis function (6). Clinical symptoms can be managed by pyridostigmine and typically resolve within two to three weeks. Early screening of pregnant myasthenic mothers is recommended to determine the status of their disease (remission vs. subclinical activity) (7).

Congenital myasthenia syndromes. Congenital myasthenia syndrome consists of diverse hereditary conditions that affect neuromuscular transmission. Unlike the other myasthenic syndromes, congenital myasthenia syndrome is NOT mediated by the immune system, but rather by genetic mutations or variants that affect the structural and/or function of the presynaptic, synaptic, or postsynaptic neuro-muscular junction (8,9). It can be distinguished from neonatal myasthenia which is transient and monophasic. Given its genetic nature, congenital myasthenic syndrome can present with a broad spectrum of clinical findings at birth or in the first year of life including hypotonia, proximal muscle fatigue with delayed motor milestones, poor feeding and/or suckle, ptosis and variable degrees of external ophthalmoparesis, and respiratory difficulties. Diagnostically, anti-ACHR antibodies/panel and edrophonium testing are commonly negative, and resultant genetic testing is necessary for definitive diagnosis (8).

Identifying the gene(s) in this condition can help understand the pathogenesis, the expected natural course, and future prognosis as well as possible treatments. Management includes conservative treatment of symptoms and certain conditions can have variable responses to cholinesterase inhibitors (9,10).

Botulism. Botulism toxins are produced by the Clostridium botulinum organism. The botulinum toxin blocks the release of acetylcholine vesicles into the synapse resulting in a presynaptic neural paralysis of skeletal muscle. The toxins can enter the body via ingestion of contaminated food (i.e., spoiled canned food) or direct infection of an open wound (11). Infantile botulism is the direct colonization of the intestine by the Clostridium botulinum organism. It is most commonly seen in infants between 2 weeks to 6 months old. Symptoms include constipation, hypotonia, hyporeflexia, poor feeding, internal and external ophthalmoplegia, and respiratory distress (12). Honey intake in newborn has been linked to infant botulism, and many pediatricians advise not to feed honey to infant younger than 1 year of age

(13). A workup includes stool samples for toxin recovery and an EMG with characteristic patterns (11, 14). Treatments include anti-toxin administration, botulinum immunoglobulin, nasogastric suctioning, enemas, and mechanical ventilation as needed (15).

CME ANSWERS

1. B
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3. True

REFERENCES

1. Avilla CW. Myasthenia Gravis. Am. Orthoptic
2. Della Marina AD, Trippe A, Lutz S, Schara U. Juvenile Myasthenia Gravis: Recommendations for Diagnostic Approaches and Treatment. Neuropediatrics 2014;45:75-83.
3. Kraithat P, Hansapinyo L, Patikulsila. Treatment Outcomes and Predictive Factors in the Pediatric Ocular myasthenia Gravis. International consensus guidance for management of myasthenia gravis
4. Madenci AL, Li GZ, Weil BR, ZurakowksiKang PB Weldon CB. The Role of Thymectomy in the treatment of juvenile myasthenia gravis: a systematic review.
5. O'Carroll PO, bertorini E, Jacob G et al Transient Neonatal myasthenia gravis in baby born to mother with now-onset anti-MuSK mediated myasthenia gravis. Journal of Clinical Neuromuscular Dis. 2009; 11:69-72
6. Gamio S, Garcia-Erro M, Vaccarezza MM, et al . Myasthenia Gravis in Childhood. Bincul Vis StrabismusQ. 2004;19:223-31
7. Norwood F, Dhanjal M , hill M et al. Myastheniain pregnancy: best practice guidelines from the UK multispecialty working group. Journal Neurol Neurosurg Psychiatry. 2013; 85:538-543.
8. Engel AG. Congenital myasthenia syndromes. Neurology Clin. 1994; 12: 401-37
9. Nogajski JH, Kiernan MC, Ouvrier RA et al. Congenital Myasthenic Syndromes. Journal Clini Neuroscience. 200; 16 1-11.
10. Salih MA, Oystreck DH, et al Congenital myasthenia syndrome due to homozygous CHRNE mutation: report of patients from Saudia Arabia. J Neuro-ophthalmology. 2011;31:42-47.
11. Caya JG Clostridium Botulism and the ophthalmologist: A review of botulism, including biological warfare ramifications of botulism toxin. Surv Ophthlamology 2001 46: 25-34
12. Arnon S.S., Midura T.F., Clay S.A., et al: Infant botulism. Epidemiological, clinical, and laboratory aspects.. J. A. M. A. 1977; 237:1946-1951
13. Arnon S.S., Midura T.F., Damus K., et al: Honey and other environmental risk factors for infant botulism. J. Pediatr. 1979; 94:331-336.
14. Hedges TR, III, Jones A, Stark L et al. Botulism Ophthalmoplegia. Clinical and oculographic observation. Arch Ophthalmol. 1983; 101:211-213
15. Arnon S.S., Schechter R., Maslanka S.E., et al: Human botulism immune globulin for the treatment of infant botulism. N. Engl. J. Med. 2006; 354:462-471

KEYWORD INDEX

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