March 15-20, 2025
JW Marriott Starr Pass Resort

Tucson, AZ

North American Neuro-Ophthalmology Society

1975-2025

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51st Annual Meeting

March 15-20, 2025; On Demand April 15 – September 30, 2025
JW Marriott Starr Pass Resort, Tucson, AZ

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EDUCATIONAL OBJECTIVES

After completing this activity, the participant should be better able to:

- Identify recent advances in the diagnosis and treatment of neuro-ophthalmic diseases.
- Identify advances in key areas of cutting-edge research and technology in neuro-ophthalmology.
- Apply skills and techniques from the educational sessions into their daily practice.

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Anat	Galor	MD, MSPH	Speaker	Alcon, Allergan, B&L, Harrow, Dompe, Oyster Point, Novaliq	Consultant
Andrew	Lee	MD	Speaker	Amgen (speaker), Alexion (speaker), consultant: Stoke, Astrazeneca, Catalyst, Bristol Myers Squibb, Viridian.	Speaker and consultant
Benjamin	Frishberg	MD	Speaker	Abbvie	Research

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Neuro-Radiology Symposium: Anatomy and Pathology of the Ophthalmic Segment of the Trigeminal Nerve: Focus on Perineural Tumor Spread (PTS) [1.0 CME]

Moderator: Mays El-Dairi, MD
Speaker: Philip R. Chapman, MD

Upon completion of this session, participants should be able to:

(1) Review normal anatomy of ophthalmic division of trigeminal nerve (V1) and its relationship to adjacent structures in the orbit.

(2) Understand the role of this nerve in perineural tumor spread of cancer around the orbit, especially cutaneous malignancy.

(3) Examine subtle or early cases that can be challenging.

MRI IMAGING OF PERINEURAL TUMOR SPREAD OF OPHTHALMIC DIVISION OF TRIGEMINAL NERVE

Philip R Chapman, MD.
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LEARNING OBJECTIVES

1. Review normal anatomy of ophthalmic division of trigeminal nerve (V1) and its relationship to adjacent structures in the orbit, orbital apex, and cavernous sinus.
2. Discuss the MRI appearance of the normal V1 with conventional MRI and CT.
3. Discuss the role of the ophthalmic division in perineural tumor spread (PNTS) of cancer involving the orbit, especially cutaneous malignancy of the brow and forehead.
4. Introduce a common radiologic pattern of appearance of V1 PNTS on MRI and CT. In the Axial plane, the thickened enhancing pathologic V1 nerve can appear as a curved, hockey stick-shaped structure in the superior orbit.
5. Explore the radiological differential with other pathologies that affect V1 in the orbit.

CME QUESTIONS

1. The difficulties in identifying the normal frontal nerve on MRI include:
   A. It is a motor nerve to superior rectus and gets lost in the muscle.
   B. The normal frontal nerve is very small and essentially sandwiched between the superior rectus muscle and the roof of the orbit
   C. It normally enhances vigorously and therefore difficult to separate from enhancing muscle.
   D. It runs along the same course as the ophthalmic vein and therefore difficult to separate from the vein itself.
   E. It normally contains fatty tissue and difficult to separate from orbital fat.
2. Which of the following statements accurately describes Perineural Tumor Spread (PNTS) in head and neck cancer?
   A. PNTS is diagnosed by the pathologist when the tumor encircles a small nerve at the primary tumor site.
   B. PNTS represents a unique growth pattern where a neoplasm spreads from a primary tumor site to a secondary location along a vector defined by a nerve.
   C. Adenoid Cystic carcinoma is the most frequently encountered tumor in clinical practice that leads to PNTS.
   D. T2 weighted fat-suppressed sequences are optimal for identifying PNTS in imaging of the head and neck.

3. The typical MRI findings of perineural tumor spread along a cranial nerve include:
   A. Segmental atrophy of the nerve with no enhancement
   B. Segmental enlargement and internal enhancement on high resolution T1post-gadolinium sequence with fat saturation.
   C. Notable absence of diffusion restriction of involved nerve, while normal cranial nerves exhibit diffusion restriction on DWI.
   D. T1 hyperintensity due to hemorrhage, which is characteristic of perineural tumor spread.
   E. T2 hypointensity resulting from dense fibrosis along the nerve

KEYWORDS:
1. Perineural tumor spread
2. Ophthalmic division of trigeminal nerve
3. Supraorbital nerve
4. Supratrochlear nerve

CME ANSWERS

1. Answer: [B]. The biggest problem with identifying the frontal nerve or distal V1 nerve is the fact that is relatively small. In the orbit the nerve passes between the superior rectus muscle and the bony roof of the orbit, often with little or no surrounding fat. A, C, D, and E are not correct. It is primarily a sensory nerve that does not enhance normally, does not travel the same course as the superior ophthalmic vein, and does not normally contain fat..
2. Answer: [B]. PNTS represents a unique growth pattern where a neoplasm spreads from a primary tumor site to a secondary location along a vector defined by a nerve. A is not correct. Perineural invasion (PNI) is a description the pathologist would use for identifying tumor cells along or around a distal microscopic nerve in a pathologic specimen. It is related, but does not equate to, PNTS- where macroscopic tumor spreads a distance from the primary site of tumor. C is not correct. Adenoid cystic carcinoma is known for having PNTS, but it is much less common overall than squamous carcinoma in the head and neck, and less common overall for PNTS. D is not correct. While T2 weighted images can show PNTS, the most sensitive and specific findings are typically identified on fat saturated T1 weighted sequences with fat suppression.
3. Answer: [B.] Perineural tumor spread typically shows segmental enlargement and abnormal enhancement. A, C, D and E are not typical features of PNTS.

HIGHLIGHTS

This presentation discusses the use of radiologic imaging in the evaluation of tumor involving the first division, the ophthalmic division, of the trigeminal nerve. The nerve is often referred to as V1. MRI is discussed primarily as the modality of choice, but CT and PET scans are also presented. The normal ophthalmic division is relatively small and difficult to evaluate on routine imaging. Dedicated MRI sequences are necessary to evaluate for potential perineural tumor spread. The most important sequence is the T1 weighted, post contrast fat suppressed sequence, but diagnosis often involves a combination of sequences and planes. For instance, standard T1 weighted sequence without contrast and without fat saturation is often critical in evaluating normal tissue planes. Normal radiologic anatomy is demonstrated, followed by several cases of perineural tumor spread involving V1. Using a case-based approach, a recurring radiologic pattern emerges of the thickened enhancing frontal nerve and its terminal branches in the upper orbit, with medial deviation anteriorly. We refer to this as the ‘Hockey stick” sign. The authors believe this can be a useful sign to expedite the diagnosis of PNTS and provide a framework for directed therapy and follow-up imaging.

SUMMARY

Perineural Tumor Spread in Head and Neck Cancer

Perineural tumor spread (PNTS) in head and neck cancer refers to the extension of malignancy along nerves beyond the primary tumor site, often involving cranial nerves such as the trigeminal (CN V) and facial (CN VII) (1). Unlike perineural invasion (PNI), which is a microscopic histologic finding, PNTS represents macroscopic disease that is often detectable on imaging (2,3). It is commonly associated with mucosal or cutaneous squamous cell carcinoma and salivary gland malignancies, leading to symptoms such as facial pain, numbness, paresthesia, and muscle weakness (4). These symptoms often correlate with radiological findings and guide the extent of surgical resection and adjuvant therapy planning (5). Recognizing PNTS clinically and radiologically is crucial, as it is linked to poor prognosis, increased recurrence risk, and necessitates aggressive treatment, including surgery, radiation, and systemic therapy when needed (6,7).

PNTS and Orbital Involvement

Perineural tumor spread can reach the orbit through various pathways and tumor types, including skin cancer, lacrimal gland tumors, sinonasal malignancies, and nasopharyngeal carcinoma. While virtually any nerve in the head and neck can be affected, the trigeminal nerve (CN V) is most frequently involved, particularly the maxillary division (V2) (8,9). PNTS typically spreads in a retrograde fashion from the primary tumor site toward the brainstem, though anterograde (centripetal) spread can also occur (10). This latter mechanism allows tumors distant from the orbit to extend into the orbital region via the cavernous sinus or Meckel’s cave.

The Ophthalmic Division (V1) of the Trigeminal Nerve

The ophthalmic division (V1) of the trigeminal nerve provides sensory innervation to the forehead, upper eyelids, and portions of the nose. It exits the skull via the superior orbital fissure and divides into three main branches: the frontal, nasociliary, and lacrimal nerves. The frontal nerve further gives rise to the supraorbital and supratrochlear nerves, supplying sensation to the forehead and scalp (11).

Radiological assessment of V1 is challenging due to its small size and specific location, sandwiched in a narrow space between the superior rectus muscle and the bony roof of the orbit (12). The normal V1 segment is typically not visible on routine imaging. However, PNTS involvement of the frontal nerve may occur via retrograde spread from cutaneous malignancies of the brow or forehead, particularly squamous cell carcinoma (13). Involvement of V1 can lead to ptosis, proptosis, ophthalmoplegia, pain and dysesthesia (14, 15). MRI with gadolinium contrast is the preferred imaging modality, as it can reveal nerve thickening and abnormal enhancement indicative of tumor spread. High-resolution imaging, detailed anatomical knowledge, and careful evaluation are essential for detecting early PNTS in V1 and its branches. CT and PET scans can also aid in diagnosis in select cases (16-19).

Radiologic Patterns, Diagnosis and Treatment Considerations

When the frontal nerve and its terminal branches enlarge and enhance due to PNTS, they often assume a distinctive “boomerang” or “hockey stick” shape on axial MRI through the superior orbit (20). The anterior bend of the nerve represents the blade of the hockey stick, a pattern that may serve as an early radiologic sign of PNTS before the tumor reaches the cavernous sinus or Meckel’s cave.

Radiologic evaluation of PNTS in the orbit presents various challenges, both at initial diagnosis and during surveillance (21). Several conditions can mimic PNTS, including other tumors, inflammatory disorders, and atypical infections. Several examples are presented. Recognizing these mimics, while rare, are useful to consider in the differential (22).

Surgical and radiotherapeutic strategies are tailored to the extent of nerve involvement. Postoperative radiotherapy has shown efficacy in controlling PNI, particularly in cases of large nerve involvement where surgical margins may be inadequate (23) Additionally, immunotherapy is being explored as a novel approach to target perineural invasion in cutaneous squamous cell carcinoma (24).

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57th Frank B. Walsh Symposium

Host: Duke University/University of Vermont
Lead Host: Chantal J. Boisvert, OD, MD
Host Committee Members:
Mays El-Dairi, MD, Sidney Gospe III, MD; N. Troy Tagg, MD; Philip Skidd, MD
Expert Panel:
Neuroradiologist: Philip R. Chapman, MD
Neuropathologist: John DeWitt, MD, PhD

These sessions will present complex cases that impact the visual pathways and ocular motor systems. The format is a clinicopathologic conference. Clinical cases will be presented by neuro-ophthalmologists with comments by invited experts in neuro-radiology and neuro-pathology. Neuroimaging, laboratory, and surgical pathology data will illustrate clinical points. Cases will be discussed from clinical, anatomic, radiologic, and pathologic aspects with emphasis on diagnosis, pathophysiology, and management.

Upon completion of these sessions, participants should be able to:
(1) Describe the varied clinical presentations of neuro-ophthalmic disease.
(2) Formulate effective diagnostic testing strategies for complex neuro-ophthalmic cases including the use of new diagnostic tests.
(3) Explain the value and limitations of neuropathology and neuroimaging.
(4) Identify newly described neuro-ophthalmic diseases in clinical practice.

Frank B. Walsh I [2.0 CME]
Moderators: Mays El-Dairi, MD & N. Troy Tagg, MD

7:30 am – 7:45 am	**Welcome/Introduction,** *Heather Moss, MD, PhD, John Chen, MD, PhD, Lindsey De Lott, MD, MS and Chantal J. Boisvert, OD, MD*
7:45 am – 8:05 am	**Blasting Through the Walls,** *Tais Estrela, MD*
8:05 am – 8:25 am	**Follow Your Gut,** *Ruben Jauregui, MD*
8:25 am – 8:45 am	**What Goes Around Comes Around,** *Kathleen Louis-Gray, MD, PhD*
8:45 am – 9:05 am	**An Infiltrator in Our Midst,** *Neena Cherayil, MD*
9:05 am – 9:25 am	**Behind the Swollen Disc,** *Ari August, BA*
9:25 am – 9:30 am	**Wrap Up,** *Mays El-Dairi, MD & N. Troy Tagg, MD*

Frank B. Walsh II [2.0 CME]
Moderators: Chantal J. Boisvert, OD, MD & Philip Skidd, MD

10:15 am - 10: 20 am	**Introduction,** *Chantal J. Boisvert, OD, MD & Philip Skidd, MD*
10:20 am – 10:40 am	**Gut is Going On?,** *Danijel Pericic, MD, MS*

10:40 am – 11:00 am **It's Easy as ABCDCMV,** *Michael Trainer, MD*
11:00 am – 11:20 am **Cutting Through the Pink Tape,** *Murphy Lu, MD, MBA*
11:20 am – 11:40 am **Multiple Sclerosis Treatment Goes Viral,** *Sehrish Momin, MBBS*
11:40 am – 12:00 pm **Under the Surface,** *Betty Situ, MD, MPH*
12:00 pm – 12:15 pm **Wrap-Up,** *Chantal J. Boisvert, OD, MD & Philip Skidd, MD*

Frank B. Walsh III [2.0 CME]

Tucson Ballroom Moderators: Mays Dairi, MD & Sidney Gospe III, MD

3:15 pm – 3:35 pm **No Worming Out of This One,** *Carter Suryadevara, MD, PhD*
3:35 pm – 3:55 pm **A Kid, a Fever, and A Whole Lot of Optic Nerve Drama,** *Nitsan Duvdevan-Strier,MD*
3:55 pm – 4:15 pm **Dancing with "Peggy",** *Arens Taga, MD*
4:15 pm – 4:35 pm **TRUE FANS Will Stand By You, No MATTER What!,** *Hyun Jun Kim, MD*
4:35 pm – 4:55 pm **The Eyes Have It**, *Raghu Mudumbai, MD*
4:55 pm – 5:05pm **Wrap-up,** *Mays Dairi, MD & Sidney Gospe III, MD*
5:05 pm – 5:15 pm **Closing Remarks,** *John Chen, MD, PhD and Lindsey De Lott, MD, MS*

“Blasting Through the Walls”

Tais Estrela [1], Ryan Gise [2]

[1] Mass Eye and Ear/ Boston Childrens Hospital, [2] Boston Childrens Hospital

History & Exam: A 4-year-old boy from the Domenic Republican (DR) presented to a tertiary hospital for a second opinion on a recent diagnosis of Juvenile Idiopathic Arthritis (JIA). He had a one-year history of polyarthritis and anemia requiring blood transfusion and was on daily prednisone and etanercept to control the inflammatory symptoms. In a routine eye exam in DR, it was noted bilateral optic nerve swelling, prompting the ophthalmologist to obtain a head CT which revealed bilateral subdural hematomas. On presentation in the United States, he had normal afferent and efferent visual function. His anterior exam was negative for signs of uveitis (past or present). His motility was otherwise full. A dilated fundus exam revealed Frisen grade 2 papilledema. The physical exam revealed a 3cm firm nodule on R and L anterior skull just behind the hairline, 0.25 cm firm nodule on R temporal skull, and 0.2cm nodule on L posterior skull, all non-tender to palpation. Additional diagnostic testing was recommended.

Financial Disclosures: The authors had no disclosures.

Grant Support: none

“Blasting Through the Walls”

Answer

Final Diagnosis: Metastatic neuroblastoma presenting with bilateral papilledema secondary to venous sinus metastatic invasion and orbital canal narrowing secondary to metastasis to the bone.

Summary of Case: 4-year-old boy with bilateral optic nerve swelling in the setting of a diagnosis JIA under immunosuppressive treatment. The differential diagnosis for optic nerve swelling in a pediatric patient with JIA is broad. Pediatric patients with anterior uveitis can develop papillitis and the resolution of this can lag behind the resolution of uveitis.1 Non-pathologic causes such as anatomic variants or optic nerve head drusen are not uncommon in this age group either.2 Other causes of intracranial hypertension include tumors, venous sinus thrombosis, pseudotumor cerebri syndrome (either primary or secondary) which are vision and in some cases life threatening.3-5 Neuroimaging revealed subdural hematomas. Subsequent MRI of the brain and orbits with contrast and MRV were recommended. Imaging revealed multifocal changes in the calvarium, skull base, and dura, suggesting infiltrative bony involvement. The infiltrative process affected the orbital wall causing narrowing of the optic canals. MRV showed multifocal lesions abutting the falx and anterior superior sagittal sinus with no signs of thrombosis. The optic nerve swelling was secondary to increased intracranial pressure due to compression of the venous sinus and also had a skull base compressive component. The imaging findings were highly suggestive of an infiltrative process with high concern for an oncologic process. MIBG scan revealed diffuse avid osseous disease in the axial and appendicular skeleton, intra-axial and extra-axial calvaria lesions, including the right supraclavicular node, and a conglomerate of left common iliac and left external iliac soft tissue/lymph nodes. IR-guided needle biopsy of the supraclavicular mass revealed poorly differentiated neuroblastoma. Given the longstanding process and initial misdiagnosis, the patient ended up with optic nerve damage in the right eye. With the correct treatment though he survived and has remained cancer free and in otherwise good health.

Struggle/Dilemma of the Clinical Presentation Description: The patient had metastatic disease misdiagnosed as an inflammatory process delaying diagnosis and treatment. Ophthalmologic findings prompted neuroimaging, which ultimately revealed the diagnosis. Neuroblastoma is a known childhood tumor with classic presentation, which includes Horner’s syndrome and opsoclonus. However, in the advanced stage, neuroblastoma can metastasize to the bone causing bone pain mimicking the polyarticular process. A high index of suspicion is needed in order to find the correct diagnosis and treatment.

Keywords: Papilledema, Optic disc edema

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Contact Information: None provided.

“Follow Your Gut”

Ruben Jauregui [1], Akif Guney [1], Steven Galetta [2], Janet Rucker [2]

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History & Exam: A 51-year-old man presented with three weeks of vertical binocular diplopia. History was significant for migraines, with no recent change in headache pattern. Exam revealed a resting right head tilt, reduced right eye supraduction, left hypertropia from a skew deviation, mild non-fatigable end-gaze nystagmus in extreme lateral gaze, non-reproducible transient downbeat nystagmus upon a single supine positioning, slightly saccadic pursuits, impaired vestibulo-ocular reflex suppression, and mildly impaired tandem gait. Infrared oculography showed saccadic pursuits, variable slowing of large horizontal/vertical saccades, square wave jerks, and mild saccadic hypometria. MRI brain/orbits with gadolinium was normal (Figure 1). Serum laboratory work-up including anti-glutamic acid decarboxylase antibodies, celiac panel, and serum paraneoplastic antibody testing (including Hu, Yo, Ri, VGCC, DPPX, Ma/Ta antibodies) was negative.

Financial Disclosures: The authors had no disclosures.

Grant Support: None

"Follow Your Gut"

Answer

Final Diagnosis: RGS8-associated paraneoplastic syndrome

Summary of Case: Lumbar puncture revealed elevated protein (71 mg/dL), normal cell count and glucose. Verbal report from the reference clinical laboratory mentioned "an unclassified antibody pattern may be present in CSF." Given suspicion for paraneoplastic etiology, chest and abdomen/pelvis CT were performed and revealed mesenteric lipodystrophy with lymph node enlargement. Mesenteric biopsy was performed and revealed follicular B-cell lymphoma grade 1,2 (Figure 3, 4). Two additional lumbar punctures had negative cytology and flow cytometry. The patient was treated with 6 cycles of R-CHOP chemotherapy and intrathecal methotrexate for lymphoma. He achieved complete clinical remission. Ocular examination remained stable but diplopia and imbalance persisted. He received intravenous immunoglobulins (IVIG, 35g/day for 5 days, 2g/kg total) with improvement. Symptoms returned one month later, leading to IVIG 1g/kg every 2 weeks for 6 weeks, with subsequent improvement. Five years after presentation, exam and oculography were stable/improved, while MRI brain revealed progressive cerebellar atrophy of unclear etiology (Figure 2). Following discovery of RGS8 antibodies, re-analysis of the patient's initial CSF revealed that the previously reported "unspecified antibody pattern" was specific for RGS8 antibodies, confirmed with tissue indirect-immunofluorescence and an antigen specific line blot. We describe a patient with RGS8-associated paraneoplastic syndrome (PNS) due to a low-grade lymphoma. RGS8 antibody-associated (PNS) is a newly discovered entity that to date is associated with rapidly progressive cerebellar dysfunction and high-grade lymphoma.1, 2 Only five other cases have been reported in the literature, with only three of these clinically described.1, 2 RGS proteins are involved in cell trafficking in B lymphocytes, while RGS8 in particular is densely expressed in Purkinje cell dendrites and bodies, and in the brainstem, including structures involved with eye movement control such as the superior colliculus.3-5 Awareness of RGS8-PNS is important given that neurologic symptoms often precede the cancer diagnosis, as is typical for PNS.

Struggle/Dilemma of the Clinical Presentation Description: Diagnostic uncertainty in a case of mild cerebellar/brainstem ocular motor abnormalities. Despite unrevealing serum paraneoplastic/GAD antibody testing and initial MRI imaging, lumbar puncture was performed and was key to pursuing further workup. Initial CSF findings didn't reveal particular antibody but were suspicious for a PNS, with subsequent work-up leading to a diagnosis of low-grade B-cell lymphoma. Five years later, when RGS8 antibodies had been discovered, re-analysis of the CSF led to establishment of RGS8-related PNS.

Keywords: Paraneoplastic syndromes, Cerebellum, Skew deviation, Efferent visual pathway, Tumor

References: References for Summary of Case 1. Miske R, Scharf M, Stark P, et al. Autoantibodies Against the Purkinje Cell Protein RGS8 in Paraneoplastic Cerebellar Syndrome. Neurol Neuroimmunol Neuroinflamm 2021;8. 2. McKeon A, Lesnick C, Vorasoot N, et al. Utility of Protein Microarrays for Detection of Classified and Novel Antibodies in Autoimmune Neurologic Disease. Neurol Neuroimmunol Neuroinflamm 2023;10. 3. Han JI, Huang NN, Kim DU, Kehrl JH. RGS1 and RGS13 mRNA silencing in a human B lymphoma line enhances responsiveness to chemoattractants and impairs desensitization. J Leukoc Biol 2006;79:1357-68. 4. Itoh M, Odagiri M, Abe H, Saitoh O. RGS8 protein is distributed in dendrites and cell body of cerebellar Purkinje cell. Biochem Biophys Res Commun 2001;287:223-8. 5. Gold SJ, Ni YG, Dohlman HG, Nestler EJ. Regulators of G-protein signaling (RGS) proteins: region-specific expression of nine subtypes in rat brain. J Neurosci 1997;17:8024-37.

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“What Goes Around Comes Around”

Kathleen Louis- Gray [1], Sangeeta Khanna [2], Anamarija Perry [1], Wayne Cornblath [2], Tatiana Deveney [2], Lindsey De Lott [2], Letitia Pirau [1], Jonathan Trobe [1]

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History & Exam: A 14 year-old girl with a BMI of 29 had a 2-month history of headache. Over the past year, she had been treated for pyoderma gangrenosum of the right gluteal region with multiple antibiotics, including doxycycline and prednisone. She was found by the referring ophthalmologist to have bilateral optic disc edema. MRI brain without contrast showed mild cerebellar tonsillar ectopia and a partially empty sella. She was started empirically on acetazolamide 500mg BID. On the initial neuro-ophthalmology clinic visit, visual acuity was 20/20 OU. Ishihara color plates were 10/11 OD and 11/11 OS without APD but there was grade 4 optic disc edema OU. Visual fields showed only enlarged blind spots OU. Lumbar puncture performed elsewhere had an opening pressure of 16 cm H20 (on acetazolamide), WBC 14 (90% lymphocytes), protein 57, and glucose 45. No cytology/flow performed. Brain MRI/MRV with contrast was normal. Repeat lumbar puncture a month later showed an opening pressure of 29 cm H2O with WBC 1 (mature lymphocytes on cytology), protein 49, glucose 50. The flow cytometry report stated “There is a small (30%) CD4/CD8 double-positive T cell population, largely negative for CD7 of uncertain significance. Small populations of double-positive T cells are often seen in reactive conditions, and the absolute number of CSF leukocytes is very low. A reactive etiology is therefore favored, but clinical correlation is advised.” A presumptive diagnosis of viral meningitis with delayed resolution of secondary papilledema was made. She responded well to acetazolamide with papilledema resolution in a few months. She returned 6 months later and reported that she had lost 40 pounds over last few months which was attributed to acetazolamide by her pediatrician. Because she had no headaches or papilledema, acetazolamide was stopped. At 16 months after the initial visit, she developed abdominal pain. A procedure was performed.

Financial Disclosures: The authors had no disclosures.

Grant Support: None

"What Goes Around Comes Around"

Answer

Final Diagnosis: Papilledema secondary to presumed blockage of arachnoid granulations by peripheral T cell lymphoma.

Summary of Case: CT abdomen showed multiple enlarged abdominal and inguinal lymph nodes. Excisional biopsy of a femoral lymph node showed "lymph node with completely effaced architecture by an atypical lymphoid proliferation with a diffuse growth pattern with final diagnosis of Peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS)." Flow cytometry of CSF from a third lumbar puncture that had 7 nucleated cells (normal < 5) showed "Aberrant T-cells, suspicious for T cell neoplasm. Immunophenotypic analysis detects an aberrant T-cell population comprising 68% of the lymphocytes. The main aberrant features are loss of CD7 and CD4+/CD8 double expression. The aberrant T-cells have a monoclonal pattern of TRBC1 expression (TRBC1 negative) suspicious for T cell lymphoma." Bone marrow biopsy confirmed the diagnosis of PTCL-NOS. She was treated with chemotherapy (CHOEP regimen), craniospinal radiation, intrathecal methotrexate and bone marrow transplantation. One year after treatment initiation, she is asymptomatic and shows no signs of recurrence. The neuro-ophthalmologic examination is normal. Peripheral T-cell lymphomas (PTCLs) are a diverse group of uncommon and often aggressive subtypes of non-Hodgkin lymphoma that develop in mature T cells. (Reference 1) PTCLs can affect various parts of the body including the lymph nodes, skin, gastrointestinal tract, liver and spleen. Meningeal and parenchymal brain involvement occurs rarely with risk factors being extranodal (including bone marrow) involvement and stage III-IV disease. (Reference 2)

Struggle/Dilemma of the Clinical Presentation Description: A diagnosis of resolving viral meningitis with lingering papilledema seemed reasonable at first. But that diagnosis was tentative, so a second tap was requested for cytology and flow cytometry, When results could be attributed to an inflammatory condition, CSF became acellular, and clinical features improved, examiners believed that their diagnosis was correct. However, in this rare form of lymphoma, CSF flow cytometry with few cells may not be able to exclude inflammation. (Reference 3)

Keywords: Idiopathic intracranial hypertension (IIH), Lumbar puncture, Complications of cancers

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“An Infiltrator in our Midst”

Neena Cherayil [1], Jared Ahrendsen [1], Barina Aqil [1]

[1] *Northwestern Medicine*

History & Exam: An 80-year-old woman with a history of chronic lymphocytic leukemia (CLL), pre-diabetes, and hyperlipidemia presents with progressive vision loss. Approximately 10 months prior to presentation, she developed painless OS blurring with exam notable for OS BCVA 20/200, left rAPD, and diffuse disc edema. ESR/CRP/CBC were normal. She was diagnosed with non-arteritic ischemic optic neuropathy. Over the next month, OS vision declined to no light perception with persistent disc edema. Brain MRI revealed diffuse left optic nerve enhancement (Figure 1). Repeat MRI ~4 months later for continued disc edema revealed persistent nerve enhancement (Figure 2). Her exam was monitored with eventual pallor of the left optic nerve. Four months later, she began noticing painless OD peripheral blurring with gaze-evoked amaurosis progressive over a week prompting emergency room visit. On presentation, neuro-ophthalmic examination revealed BCVA of 20/30 OD with 11/11 Ishihara color plates and NLP OS with a large left rAPD. Slit lamp examination was notable for mild cataract. Dilated fundus examination revealed diffuse OD disc edema with vessel obscuration and temporal splinter hemorrhage and OS pallor worse temporally with 0.6 cup to disc ratio. MRI revealed enhancement of the bilateral intraconal optic nerves and a 7mm enhancing paramedian right frontal lesion with associated microhemorrhage (Figure 3). In retrospect, this frontal lesion was not present on initial MRI imaging 9 months prior but was present though smaller on imaging 4 months prior. Body imaging revealed diffuse lymphadenopathy and a right upper lung lobe lesion with increased uptake compared to PET scan completed 3 years prior (Figure 4). Extensive work-up was pertinent for positive Quantiferon gold, ANA +1:320 (speckled), negative HIV and RPR, negative sputum AFB x 3, negative paraneoplastic panel, and negative anti-aquaporin-4 antibodies. Biopsy of abdominal lymph node confirmed known CLL without Richter’s transformation. A diagnostic procedure was performed.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“An Infiltrator in our Midst”

Answer

Final Diagnosis: Subacutely progressive sequential infiltrative optic neuropathy secondary to CLL in a patient with newly-diagnosed oligometastatic lung cancer and latent tuberculosis who later developed pupil-involving left 3rd nerve palsy in setting of L PCOM aneurysm.

Summary of Case: Lumbar puncture revealed WBC 11> 8 in tube 4 (96% lymphocytes, 3% monocytes, 1% neutrophils), RBC 692 > 89, protein 52 mg/dL, and glucose 64 mg/dL. CSF MTB PCR was negative. CSF cytology/flow cytometry revealed CLL (Figure 5) but was contaminated by peripheral blood. Right frontal lesion biopsy revealed lung adenocarcinoma with atypical lymphocytic infiltrate consistent with CLL (Figure 6). Patient reported further peripheral constriction OD with worsening acuity 20/50. She was treated with 4 doses of high dose IV methylprednisolone with subjective improvement but persistent visual field constriction. The right optic nerve was irradiated with significant improvement in vision to 20/30 OD. Lung cancer/CLL were treated with osimertinib and acalabrutinib. One year later, she developed new ptosis OS with severe eye pain on Valsalva. Exam was notable for new pupil-involving left 3rd nerve palsy. Imaging revealed a left PCOM aneurysm (Figure 7) that was coiled with improvement. Her vision remains stable on follow-up. CLL is a mature B-cell neoplasm characterized by progressive monoclonal B-cell accumulation. It is identical pathologically to non-Hodgkin small lymphocytic lymphoma (SLL) with the term SLL used when manifestation is primarily nodal. CLL is the most prevalent adult leukemia in the West accounting for up to 35% of all leukemias in the United States (1). CNS involvement of CLL is relatively rare affecting 0.4-0.8% in cohort studies (2)(3) with leptomeningeal involvement tending to confer a poorer prognosis (4). Optic nerve involvement is an even rarer manifestation of CNS CLL. One review found bilateral optic nerve infiltration in 52% of cases (5). Compressive orbital lymphoma was the next main common ophthalmic CLL/SLL manifestation followed by secondary orbital infection. Most patients with asymptomatic CLL are simply observed but radiation or tyrosine kinase inhibition may be recommended for symptomatic or active disease (6).

Struggle/Dilemma of the Clinical Presentation Description: This patient presented with sub-acutely progressive sequential infiltrative optic neuropathies initially mis-diagnosed as NAION in setting of age and vascular risk factors. Work-up was notable for multiple potential etiologies including metastatic lung cancer, tuberculosis, CLL, and paraneoplastic syndromes. CSF cytology was insensitive for definitive diagnosis, but brain biopsy revealed both lung cancer and CLL infiltration. Rapid decline of vision in monocular patient prompted empiric treatment with steroid and radiation for CLL infiltration with improvement.

Keywords: Optic disc edema, 3rd nerve palsy, Tuberculosis, Complications of cancers, Metastatic carcinoma

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“Behind The Swollen Disc”

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History & Exam: A 31-year-old female presented to optometry with headaches, blurred vision OS worse in hot temperatures, and pain with extraocular movements. She had no personal medical history but had a family history of iris melanoma in her mother and glioblastoma multiforme in her maternal grandmother and aunt. Examination showed best corrected visual acuity of 20/20 OU, intraocular pressure of 18 OD and 16 OS, +1 APD OS, inferior and temporal visual field constriction OS, and red desaturation OS. Slit lamp examination was normal. Dilated fundus exam showed severe optic nerve edema with splinter hemorrhages, cotton wool spots, and a cup to disc ratio of 0.01 OS (Figure 1). She was treated with intravenous steroids and a prednisone taper, which temporarily decreased the patient’s pain without visual improvement. Magnetic Resonance Imaging (MRI) of the brain and orbits with and without contrast showed a subtle ovoid enhancing structure posterior to the left globe likely representing an enhancing optic nerve (Figures 2-4). Extensive inflammatory and infectious serologies were normal. One month later, orbital ultrasound revealed an echolucent retrobulbar mass OS (Figures 5-6). Two months after initial presentation, her symptoms worsened. She underwent anterior orbitotomy with biopsy and retrobulbar steroid injection. Pathology showed a spindle cell tumor diagnosed as schwannoma (Figure 7). Persistent worsening of symptoms prompted review of the orbital biopsy by an ophthalmic pathologist which favored choroidal melanoma. Subsequent evaluation by ocular oncology found subtle ocular melanocytosis OS with a 1 mm juxtapapillary nevus with OCT showing compression of choroidal vasculature (Figure 8). Enucleation was performed four months after initial presentation. Pathology confirmed a small focus of primary choroidal malignant melanoma, predominately spindle mixed cell type, and massive extraocular extension (Figures 9-16). She underwent radiation therapy to the left orbit.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“Behind The Swollen Disc”

Answer

Final Diagnosis: The final diagnosis was histopathologically confirmed malignant choroidal melanoma with massive extraocular extension into the retrobulbar orbit and optic nerve sheath, causing optic nerve compression and severe disc edema.

Summary of Case: We present a patient initially treated as an optic neuritis, who was ultimately found to have choroidal melanoma with massive extraocular extension into the retrobulbar orbit and optic nerve sheath, severe optic nerve compression, focal ocular melanocytosis, and severe optic disc edema. The patient’s complicated clinical course resulted in delayed diagnosis of advanced malignancy. Retinoinvasive melanoma is rare and associated with iris or ciliary body melanoma; when secondary to a choroidal melanoma, the lesion is medium to large and apparent on direct fundoscopy [1-4]. Two cases of choroidal melanomas with symptomatic extraocular extension compressing the optic nerve but small, inconspicuous intraocular components have been previously reported [1]. Extrascleral extension of a small choroidal melanoma has been reported in one previously reported case [2]. This patient had both invasion of the optic nerve and its meninges as well as extrascleral extension of a juxtapapillary choroidal melanoma with a 1.5 x 5 mm intraocular component not apparent on initial fundoscopy. Both optic neuritis and the final diagnosis of choroidal melanoma have a higher incidence in middle-aged, female patients [5-6]. Choroidal schwannomas frequently mimic choroidal melanoma as both may present pathologically as S-100 positive spindle cell tumors [7]. However, this patient’s biopsy was positive for Melan-A and HMB45, suggestive of a melanocytic tumor, which ultimately led to appropriate evaluation and management. Genetic testing of the tumor revealed chromosome 3 disomy, partial amplification of 6p and 8q, and GNA11 mutation. Germline BAP-1 and BRCA2 were negative. Six years after presentation the patient developed biopsy-confirmed metastatic melanoma to the frontal lobe treated with resection and adjuvant radiosurgery, and an enhancing medial temporal lobe mass treated with radiosurgery. Eight years following initial presentation, the patient had no other evidence of systemic metastases.

Struggle/Dilemma of the Clinical Presentation Description: The patient’s demographics and presenting symptoms led to an incorrect diagnosis of optic neuritis, with delayed recognition of a retrobulbar lesion on MRI. The patient continued to worsen on steroid treatment, suggesting an alternate etiology. Biopsy of the lesion was initially incorrectly determined to be a benign schwannoma despite positive Melan A and HMB45; only when an ophthalmic pathologist reviewed the case was the correct diagnosis made.

Keywords: Papilledema, Optic disc edema, Optic neuritis, Tumor, Optic nerve

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“Gut Is Going On?”

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History & Exam: A 62-year-old Caucasian female, with uncontrolled diabetes (A1c 10.6%), presented with 2 days of rapidly progressive vision loss OD. Exam with vision OD NLP, OS 20/40; IOP OD 60, OS 11; 2+ APD OD. Slit lamp exam with 2+ microcystic corneal edema OD and a fibrin reaction in the anterior chamber OD. She developed rapid onset of chemosis and proptosis with EOM restriction in the right eye in the ER. B-scan was unremarkable. Following a lateral canthotomy, IOP improved to 30 OD. Serum glucose was 400+ and she was febrile. Blood cultures were normal. Nasal endoscopy showed no necrotic tissue or eschar. CT scan showed clear sinuses, with low suspicion for mucor. Broad spectrum antibiotics and antifungals were started per infectious disease team. MRI brain and orbits with gadolinium showed panophthalmitis OD, diffuse leptomenigitis, and edema along the right optic pathway (Fig 1-3). By day 2, vision worsened to NLP OU. A lumbar puncture (LP) showed opening pressure of 28cm of water, with 11,720 WBC (83% neutrophils), CSF gram stain with many WBCs, no organisms and no growth on culture. A vitreous tap OD showed Clostridium septicum species (Fig 11). Subsequent evisceration – heavy growth of C.septicum (Fig 12-20). On day 15, colonoscopy showed large 6 cm malignant appearing mass in cecum – pathology consistent with adenocarcinoma. On day 24 antibiotics were completed, but had persistent fevers and encephalopathy. Repeat LP with many white cells but no growth on culture. Repeat MRI brain/orbits showed increasing signal along optic tracts (Fig 4-8). Antibiotics were restarted. On day 33 underwent craniotomy, optic chiasm abscess drainage, and right orbitotomy with washout were performed. MRI – improvement in abscess (Fig 9, 10). On day 43, hemicolectomy done to remove cecal mass. Patient discharged in stable condition on six-week antibiotic course.

Financial Disclosures: The authors had no disclosures.

Grant Support: NA

“Gut Is Going On?”

Answer

Final Diagnosis: Endogenous right eye panophthalmitis, bilateral infectious optic neuritis and chiasmal abscess in the setting of trans-colonic dissemination of Clostridium septicum which led to the diagnosis of a previously unknown cecal adenocarcinoma.

Summary of Case: We present a case of bilateral rapid sequential vision loss from trans-colonic dissemination of Clostridium septicum. The patient presented with right eye panophthalmitis with eventual retrograde spread to the optic nerve and chiasm, causing infectious optic neuritis and chiasmal abscess despite evisceration, leading to vision loss in the contralateral eye. This led to a diagnosis of previously unknown cecal adenocarcinoma. Clostridium septicum presenting as a primary endophthalmitis/panophthalmitis has been previously reported but is an exceedingly rare occurrence. 1 This bacterium has been known to be a herald of gastrointestinal tract malignancies since the 1970’s with a reported 71% association with clostridium septicum bacteremia.2 The bacterium, a native of the GI tract, enters the bloodstream through necrotic areas around the malignancy, and can cause devastating and fatal infections with a 79% mortality rate even when treated, due to its production of alpha toxin, an underlying cause of gas gangrene.2 Thus a workup for malignancy must be performed, such as with PET/CT or other imaging modalities, in all patients with positive clostridium septicum cultures from any source.3 A case of bilateral endophthalmitis similar to ours has been reported in the past where the patient expired as a result of her infection 21 days after onset, and autopsy revealed clostridium septicum infection as the cause of her lethal abdominal aorta rupture as well as her corneal perforation.4 For this patient, it is theorized that initially the patient was septic with clostridium septicum, and then had endogenous endophthalmitis spread from her ophthalmic artery leading to retinal & choroidal involvement. The clostridium septicum alpha toxin caused apoptosis and macrophage death, which suppresses inflammation and causes evasion of the innate immunity, leading to extensive choroidal necrosis without significant inflammation as seen on pathology slides (Figure 13-20) and eventual panophthalmitis and posterior extension along the optic nerve.5

Struggle/Dilemma of the Clinical Presentation Description: Persistent negative blood and cerebrospinal fluid cultures despite rapidly progressive right eye panophthalmitis, bilateral vision loss to NLP OU, and optic chiasmal abscess prompting culture of eviscerated contents which revealed a bacteria known to colonize the gastrointestinal tract. Subsequent evaluation revealed a systemic malignancy. Long course antibiotics with persistent encephalopathy necessitated craniotomy and chiasmal abscess drainage to achieve source control with improvement in mental status.

Keywords: Optic chiasm, Vision loss binocular, Infection, Meningo-encephalitis, Complications of cancers

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“It's as Easy as ABCDCMV”

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History & Exam: A 66-year-old man was referred for several months of progressive bilateral blurry and dim vision that did not improve with cataract surgery. He reported no other systemic symptoms. His medical history was notable for multiple myeloma in remission on teclistamab (a bispecific antibody that redirects CD3+ T-cells to BCMA+ myeloma cells) after an autologous bone marrow transplant eight years prior. He received monthly IVIG and took prophylactic acyclovir and trimethoprim-sulfamethoxazole given neutropenia. There was no family history of vision loss. On initial examination, best-corrected acuities were 20/200 OD and 20/100 OS (decreased from 20/60 and 20/40, respectively, one month prior) with a right relative afferent pupillary defect. He saw 0/9 (OD) and 1/9 (OS) Ishihara color plates. Posterior segment examination was notable for 2+ vitreous cell and epiretinal membrane in the right eye with temporal optic nerve head pallor bilaterally (Fig1). Optical coherence tomography demonstrated diffuse bilateral ganglion cell complex loss and mild temporal retinal nerve fiber layer thinning. Humphrey Visual Field 30-2 testing showed mild bilateral cecocentral scotomas with superimposed generalized constriction OD. Neurologic examination was notable for diffuse hyperreflexia. MRI demonstrated T2 hyperintense white matter lesions in the brainstem, cervical cord, and thoracic cord, but no changes of the optic nerves (Figs 2-4). Some lesions showed faint enhancement, but no restricted diffusion. CT of the chest, abdomen, and pelvis showed only myelomatous osseous lesions. PET-CT showed no evidence of hypermetabolic disease. Cerebrospinal fluid analysis demonstrated normal white blood cells (3), protein (56), glucose (54). There were no oligoclonal bands, and IgG index was normal (0.4). AQP4-IgG (serum) and MOG-IgG and Mayo Clinic Paraneoplastic Antibody Panel (serum and CSF) were negative. CSF VZV, HSV, and CMV PCR and unbiased pathogen detection by metagenomic next-generation sequencing (mNGS) were negative.

Financial Disclosures: Michael Trainer: No; Marc Levin: Unrelated financial compensation as: consultant, Jazz Pharmaceuticals; consultant, Vanda Pharmaceuticals; royalties, University of California; Abdelhak Ahmed: received research funding from the German Multiple Sclerosis Society and the Department of Defense and speaker fee from Jansson and Roche.; John Pluvinage: coinventor on a patent application (PCT/US2024/018105, “Compositions and methods related to transcobalamin receptor autoantibodies").; Michael Wilson: No relevant financial relationships. But should disclose he is a coinventor on a patent application (PCT/US2024/018105, “Compositions and methods related to transcobalamin receptor autoantibodies").; Nailyn Rasool: No; Jonathan Horton: No; Rabih Hage: No

Grant Support: None

“It's as Easy as ABCDCMV”

Answer

Final Diagnosis: 1) Bilateral optic neuropathy and dorsal-predominant myelopathy due to CSF transcobalamin receptor CD320 antibodies, leading to autoimmune vitamin B12 central deficiency (ABCD). 2) Unilateral CMV retinitis in an immunosuppressed patient.

Summary of Case: Initially, the patient’s insidious vision loss was thought to be due to evolving bilateral optic neuropathy, with a chronic vitritis of unclear significance in the right eye only. Differential considerations included inflammatory, paraneoplastic, and infectious causes; direct involvement of myeloma; drug toxicity from teclistamab (Ref 1); and a metabolic or hereditary optic neuropathy. An extensive serum workup was unrevealing, including infectious serologies for tuberculosis, HIV, Lyme, syphilis, toxoplasma, and Bartonella. Serum vitamin B12 was normal 916 (pg/mL) and folic acid was borderline low (2.9 ng/mL). His teclistamab was held with a plan for careful surveillance. Six weeks after initial consultation, a diagnostic pars-plana vitrectomy of the right eye yielded negative bacterial, fungal, and AFB cultures, viral PCR (HSV and VZV), cytology, and flow cytometry. No pathogenic genetic alterations were identified on targeted next-generation sequencing. Meanwhile, he developed dysexecutive cognitive symptoms, clonus, and a large-fiber polyneuropathy. He was treated with intravenous corticosteroids and a two-month prednisone taper. A patch of superonasal chorioretinitis and diffuse occlusive vasculopathy blossomed in the right eye (Fig5), with CMV confirmed by anterior chamber tap. He was treated with IV ganciclovir. Two subsequent lumbar punctures did not reveal central nervous system CMV involvement by PCR or mNGS. CSF was sent for research evaluation, including phage display assay, which revealed antibodies to the transcobalamin receptor (CD320), suggestive of the novel disease termed autoimmune vitamin B12 central deficiency (Ref2). He started on intensive intramuscular B12 repletion. Best-corrected vision nadired at 20/400 OD and 20/100 OS two months after B12 repletion. HVF testing demonstrated a dense bitemporal hemianopic pattern of field loss (Fig6) and MRI revealed subtle T2 hyperintensity at the optic chiasm without new cord lesions. The CMV retinitis was now inactive. At the most recent follow-up, nine months after presentation, vision had stabilized at 20/400 OD and 20/70.

Struggle/Dilemma of the Clinical Presentation Description: This immunocompromised patient developed bilateral optic neuropathy and myelopathy. However, repeated CSF analysis and slow time course did not support a demyelinating etiology. Optic neuropathy has not been reported with teclistamab. Evaluation of the vision loss was confounded by CMV retinitis OD, but the progressive bilateral cecocentral scotomas could not be explained by CMV alone given serial negative CSF CMV PCR. Normal serum B12 level masked the diagnosis of immune-mediated central B12 deficiency.

Keywords: Autoimmune diseases, Optic neuropathy, Neurologic disorders, Retinal disorders, Visual field

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“Cutting Through the Pink Tape”

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History & Exam: This 69-year-old female with a history of hyperlipidemia presented with 2 weeks of vision loss. She described a gradual loss of acuity and color vision bilaterally, associated with multicolored photopsias in a halo around objects. She reported difficulty sleeping on her back for 6 months due to bitemporal headaches, which had recently become daily. She also complained of her temperature regulation feeling “off.” Her exam was notable for best corrected visual acuities of 20/100 and 20/400, but no rAPD and was unable to see the control Ishihara plates. Confrontational visual field showed a left superior quadrantanopsia with an additional inferonasal defect OS. Her fundus exam was normal, with no evidence of optic nerve head swelling or pallor. Her efferent exam was normal. HVF revealed generalized depression OD, with a mean deviation of -30.54 dB, and was unable to be completed OS. OCT showed normal thicknesses of the GCCs. Her social history was seemingly unremarkable. She was a lifelong resident of New England with minimal travel abroad, and had never visited Central or South America or Europe or Africa or Asia. She previously worked as a pre-K and elementary school teacher, often with children from families that had immigrated from Central or South America. She had never employed household help and her only pet was an outdoor cat.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“Cutting Through the Pink Tape”

Answer

Final Diagnosis: Optic chiasm and optic radiation compression due to Neurocysticercosis presenting as a solitary, mass-like lesion

Summary of Case: The patient was initially seen in the Neuro-Ophthalmology clinic, and due to the concern for a homonymous field defect and profound vision loss, she was sent to the emergency room for a STAT MRI and possible steroids. The MRI revealed a “3.9 cm suprasellar mass… characteristics suggestive of heterogeneous proteinaceous content and is favored to represent a craniopharyngioma.” She was admitted to the hospital and started on IV solumedrol. The mass was resected through an endoscopic transsphenoidal transtuberculum approach after 3 days. Her post-op course was complicated by SIADH and a pulmonary embolism, but she otherwise did well. The day after surgery, there was improvement in her visual fields and her acuity was 20/40 OU. Pathology showed “superficial eosinophilic membranous material suggestive of the wall of a cysticercal cyst, and scattered microcalcifications consistent with calcareous corpuscles…consistent with a parasitic helminthic infection, such as the necrotic stage of neurocysticercosis.” Serum Cysticercus and Echinococcal antibodies were negative. She was started on Albendazole. The remained of her hospital course was unremarkable and she was discharged after 2 weeks. At her 5-month follow-up, her vision had returned to baseline. She had best-corrected visual acuities of 20/20 OU, with no rAPD or dyschromatopsia. Her discs were notable for bilateral trace temporal pallor. Her visual fields showed only mild, nonspecific depression. Follow-up MRIs have shown no recurrence of disease.

Struggle/Dilemma of the Clinical Presentation Description: This is a case in which a clinical diagnosis could not have been sufficient. The MRI was highly suggestive of a neoplastic process with no features to suggest a parasitic infection. Her social history was also completely unrevealing and put her at low-risk for exposure. In this case, her pretest probability was so low that even with pathology results, it required multiple reviews of images and conversations with experts to confidently make this diagnosis.

Keywords: Infectious disease, Vision loss binocular, Supranuclear palsies

References: None provided.

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“Multiple sclerosis Treatment Goes Viral”

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History & Exam: A 25-year-old male of mixed Turkish and English heritage, with a diagnosis of relapsing-remitting Multiple Sclerosis (RRMS) presented with a four-week history of bilateral progressive vision loss. He had been receiving Ocrelizumab (anti-CD20) infusions, with his third dose administered two months prior. He had no other relevant past medical history, drug or family history. His childhood history included a full vaccination schedule and no significant illnesses. He began experiencing blurry vision in both eyes starting on October 11, 2023, whilst in Turkey. He subsequently returned to the UK to see his MS Neurologist and vision had deteriorated to counting fingers (CF) in both eyes. He was treated as an outpatient for presumed bilateral optic neuritis with oral Methylprednisolone 500mg once a day for five days and was referred to our Neuro-ophthalmology unit. A subsequent contrast enhanced MRI (Nov, 17 2023) showed stable non-enhancing white matter lesions but additionally asymmetric diffuse T2/ FLAIR changes seen in cortical and subcortical, bilateral temporal occipital lobes more prominent on the right side, concerning for Posterior reversible encephalopathy syndrome (PRES). On November 15, 2023, on first consultation with Neuro-ophthalmology, his visual acuity had further reduced to hand movements (HM) in the right eye and perception of light (PL) in the left eye (MRI Dec, 15 2023). Visual fields to confrontation were grossly depressed centrally in both eyes. There was no RAPD. Occasional vitreous cells were noted in both eyes. The fundal exam showed white-yellow outer retinal necrotic lesions at the maculae with subretinal fluid, in addition to smaller extramacular lesions (OCT + fundus images) . There was no disc oedema or pallor in either eye. A diagnostic procedure was performed.

Financial Disclosures: The authors had no disclosures.

Grant Support: None

"Multiple sclerosis Treatment Goes Viral"

Answer

Final Diagnosis: Rapidly progressive bilateral sequential Acute Retinal Necrosis (ARN) leading to a fatal diagnosis of Subacute Sclerosing Panencephalitis (SSPE), precipitated by the use of Ocrelizumab for Multiple Sclerosis

Summary of Case: This the case of a young patient who developed a rapidly progressive and ultimately blinding retinal necrosis alongside subacute sclerosing panencephalitis (SSPE). This is a measles virus driven phenomenon, and was suspected to have been precipitated by immunosuppressive therapy. Measles-related retinal involvement is exceptionally rare in the western world, and this is the first known case in the context of disease modifying treatment for MS. Fundal examination was initially highly suspicious for a progressive outer retinal necrosis due to a herpesvirus, however vitreous PCR testing was negative. Blood workup conducted for various infections, including Syphilis, HIV, and Hepatitis were negative and measles IgG titres were consistent with serological immunity. However, diagnosis was made by targeted PCR testing for measles virus on vitreous and retina, and subsequently confirmed by genetic sequencing to be the rare D6 subtype. This subtype had not been seen nationally for 20 years and therefore may support the possibility that the patient contracted the virus before completing his MMR vaccination schedule, aged 5. The patient was commenced on antiviral therapy, including oral Inosine Pranobex and Ribavirin alongside weekly pegylated IFN-2a. Despite early identification and aggressive treatment his visual and neurological condition deteriorated. His visual acuity was reduced to perception of light (PL) in the right eye and no perception of light (NPL) in the left. Multiple opinions from across the world were sought and it was agreed at a National Encephalitis multi-disciplinary meeting to proceed with brain biopsy for transcriptomics to better characterize the disease and guide treatment. Unfortunately, the patient developed status epilepticus and succumbed to his illness very soon after this decision and a post-mortem was declined by the family.

Struggle/Dilemma of the Clinical Presentation Description: Modern DMTs such as Ocrelizumab, have revolutionized MS management. However, in this case, complex downstream effects on the immune system may have accounted for re-activation of the D6-subtype of Measles virus. As this strain was not seen for 20 years, it was suspected to have been acquired before the vaccination schedule was completed as a child. Unusually, the viral cause of the patient's fatal neurological disorder was identified through intraocular sampling and retinal biopsy.

Keywords: Multiple sclerosis (MS), Bilateral vision loss, Infectious disease, Neurologic disorders, Retinal disorders

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“Under the Surface”

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History & Exam: A 14-year-old male with history of autism spectrum disorder and pica presented to the emergency room for 3 weeks of lethargy, decreased PO intake, ataxia, and incontinence. At baseline, the patient had limited verbal communication but was independent in activities of daily living. On physical exam, he was afebrile with normal vital signs, disoriented, nonverbal aside from occasional echolalia, with left upper and lower extremity weakness, left facial droop, and left gaze preference. MRI brain and spine with and without contrast showed multiple foci of T2/FLAIR hyperintensity in the subcortical, periventricular, and deep white matter along the posterior fossa involving the cerebellum bilaterally, and right greater than left thalamus with associated patchy enhancement. There were extensive patchy T2/FLAIR hyperintensities throughout the spinal cord without associated enhancement. CSF studies showed mild pleocytosis (RBC 143, WBC 7 with 76% lymphocytes, 9% monocytes, 15% eosinophils), normal glucose and protein, and positive oligoclonal bands. CSF paraneoplastic/encephalitis panel was negative. Serum labs showed peripheral eosinophilia (14.7%, ULN < 4%), normal CMP, and mildly low complement levels (C3 84, C4 17). He tested positive for Monospot; EBV VCA IgG was positive, but EBV VCA IgM and serum EBV PCR were negative. Additional testing showed elevated lead levels (7.1) and positive Mycoplasma pneumoniae IgG (1.76 U/L). Stool parasite testing, cysticercosis antibodies, Toxocara antibodies, and Quantiferon Gold were negative. He was diagnosed with ADEM and completed a 5-day course of intravenous methylprednisolone without improvement. Ophthalmologic exam showed poor fixation to light OU, left relative afferent pupillary defect, normal vestibulo-ocular reflex with full horizontal ductions, and weak left orbicularis oculi function. Sensorimotor exam was limited by cooperation but the patient appeared orthotropic. There was mild disc edema OS>OD and diffuse macular edema OS on limited dilated fundus examination. Additional examination and serum tests were performed.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“Under the Surface”

Answer

Final Diagnosis: Diffuse unilateral subacute neuroretinitis with neural larva migrans

Summary of Case: Repeat dilated exam with fundus photos 2 days after initial exam showed a partially coiled subretinal nematode inferonasal to the disc. The patient underwent exam under anesthesia. The right eye was unremarkable. The left eye had mild disc pallor and curvilinear RPE changes in the macula and equatorial regions. A live, writhing nematode was identified in the inferonasal quadrant approximately 2-3 disc diameters from the disc. Laser ablation of the roundworm was performed with the green diode laser. The patient was started on albendazole 400mg BID for a 6-week course and a prolonged oral steroid course with slow taper. Repeat MRI brain 3 weeks after initial presentation showed decreased extent of posterior fossa edema and decreased enhancement throughout the supratentorium. Serum samples sent to the CDC to test for antibodies to recombinant Baylisascaris antigen returned positive. The patient’s siblings also received a 10-day course of 20 mg/kg albendazole. Baylisascaris procyonis (racoon roundworm) is transmitted by the fecal-oral route, and may cause neural, ocular, and visceral larva migrans [1]. Clinicians should have a high index of suspicion in cases of eosinophilic meningoencephalitis, particularly in young children and those with developmental disorders that may be associated with pica. Early detection and treatment may ameliorate neurological and ophthalmologic sequelae [2,3].

Struggle/Dilemma of the Clinical Presentation Description: In this case, the patient was initially diagnosed with post-infectious ADEM although imaging features were atypical. He did not improve on steroids, and other neuroinflammatory diseases such as vasculitis, genetic immune dysregulation, systemic rheumatologic disease with CNS manifestations, and infections such as neurocysticercosis, toxocariasis, and neural larva migrans were considered. CSF and serum eosinophilia raised suspicion for a parasitic process, and visualization of the nematode in the retina was key in establishing the diagnosis.

Keywords: Neuroretinitis, Acute disseminated encephalomyelitis

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“No Worming Our Way Out of This One”

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History & Exam: A 12-year-old male presented with syncopal episodes, gait ataxia, headache with photophobia and 30-pound weight loss over 2 months. Exam showed papilledema, ataxic gait and clusters of excoriated papules over the torso and extremities. MRI revealed diffuse leptomeningeal enhancement with no focal lesions. CT chest, abdomen and pelvis was negative for systemic disease. Serial lumbar punctures revealed elevated OP with an eosinophilic pleocytosis in both CSF and serum. He underwent definitive CSF diversion with placement of a ventriculoperitoneal shunt for hydrocephalus. Extensive infectious, autoimmune, and oncologic work-up was negative. He underwent three serial biopsies of the sphenoid rostrum, lumbar nerve root, and right frontal dura and subjacent parenchyma with pathology revealing non-specific eosinophilic perivascular inflammation, concordant with CSF studies suggesting an eosinophilic meningitis. He deteriorated neurologically with altered mental status and left upper and lower facial weakness. A repeat LP showed evidence of malignancy on cytology, and he returned to the OR for biopsy of the posterior fossa leptomeninges which again returned inconclusive. He continued to decline, now with poor arousal, dysfluent speech, bilateral INO with complete bilateral adduction and subtle abduction deficits, V-pattern exotropia, truncal ataxia, and intermittent myoclonus. Serial imaging showed severe cerebral and spinal cord atrophy and nearly one year after presentation, repeat MRI revealed a discrete, contrast-enhancing lesion in the right parietal convexity. He underwent a 5th neurosurgical biopsy.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“No Worming Our Way Out of This One”

Answer

Final Diagnosis: The patient is diagnosed with malignant hematopoietic neoplasm with a mixed myeloid and T cell phenotype and loss of SMARCB1 expression suggestive of a new disease entity, independently confirmed by the NIH. Similar cases have recently been reported with similar genetic alteration and immunophenotype in the pediatric population. These cases show partial and aberrant T cell antigen expression (CD3 and CD7) suggesting a possible T cell lineage derivation with variable myeloid marker expression.

Summary of Case: The patient presented with progressive neurologic decline in the setting of an eosinophilic meningitis with diffuse leptomeningeal disease and CNS atrophy. Extensive infectious, autoimmune, and oncologic work-up were inconclusive despite numerous CNS and systemic biopsies until a repeat MRI revealed a focal, discrete intracranial lesion which could be accessed. Pathology showed atypical cells positive for CD7, CD43, CD45, and CD117 and focal positivity for CD30 and EMA favoring a hematopoietic neoplasm. Next-generation sequencing and comprehensive genomic profiling revealed cells with a T cell lineage derivation with variable myeloid marker expression, constituting a new disease entity. The patient was started on chemotherapy though progressed through escalations in care, including craniospinal radiation and immunotherapy. He was palliatively extubated after developing respiratory failure from neurologic decline. Next-generation sequencing and genomic profiling ultimately revealed a hematopoietic malignancy that was initially thought to be consistent with a myeloid sarcoma, though CNS involvement is a rare occurrence (0.4%), and disease confined only to the CNS disease is exceptionally rare.1 When the latter occurs, studies suggests the disease universally evolves into acute myelogenous leukemia within one year, which did not occur in this patient and contributed to diagnostic uncertainty. His final diagnosis was ultimately determined after FoundationOne Heme next generation sequencing confirmed loss of SMARCB1 expression and concurrent absence of INI-1, the protein encoded by SMARCB1, confirming neoplasm within a mixed population of myeloid and T cells, suggestive of a fundamentally distinct disease.2 - 1. Cervantes, G. M. & Cayci, Z. Intracranial CNS manifestations of myeloid sarcoma in patients with acute myeloid leukemia: Review of the literature and three case reports from the author’s institution. J. Clin. Med. 4, 1102–1112 (2015). - 2. Kinnaman, M. D. et al. Aggressive hematopoietic malignancy characterized by biallelic loss of SMARCB1. JCO Precis. Oncol. 4, 1280–1284 (2020).

Struggle/Dilemma of the Clinical Presentation Description: There were two turning points in this case. The first was the development of a discrete intracranial lesion which could be successfully biopsied. Repeated systemic and CNS biopsy attempts came as a joint multidisciplinary recommendation in the face of progressive clinical decline despite numerous empiric treatments. The second was genomic clarity regarding the immunophenotype of his hematopoietic malignancy. Chemotherapy was initiated on this basis despite an exceedingly rare presentation of a leptomeningeal SMARCB1-/- neoplasm.

Keywords: Tumor, 3rd nerve palsy, 6th nerve palsy, Chemotherapy, CSF shunt

References: 1. Cervantes, G. M. & Cayci, Z. Intracranial CNS manifestations of myeloid sarcoma in patients with acute myeloid leukemia: Review of the literature and three case reports from the author’s institution. J. Clin. Med. 4, 1102–1112 (2015). 2. Kinnaman, M. D. et al. Aggressive hematopoietic malignancy characterized by biallelic loss of SMARCB1. JCO Precis. Oncol. 4, 1280–1284 (2020).

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“A Kid, a Fever, and a Whole Lot of Optic Nerve Drama”

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History & Exam: An 8-year-old male with no prior medical history was found unconscious at home following an acute fever and gastroenteritis. He was intubated, with hypotension and laboratory findings of acute kidney injury, metabolic acidosis, hyponatremia, and moderate pancytopenia. Brain imaging revealed diffuse cerebral edema with cerebellar herniation on CT (figure 1,2). An MRI brain showed nonspecific bilateral subcortical white matter hyperintense lesions on T2 FLAIR, with partial resolution of edema (figure 3). A diagnosis of probable meningoencephalitis was made, and the patient received mannitol, broad-spectrum antibiotics, antivirals, Solumedrol, and hypertonic saline. His recovery was rapid, and he was discharged. A follow-up MRI (figure 4,5,6) revealed bilateral longitudinally extensive, non-enhancing, hyperintense signals along the optic nerves, chiasm, and optic tracts, raising concern for demyelinating lesions. Ophthalmologic evaluation showed visual acuity (VA) of 20/30 in the right eye and counting fingers at 2 meters in the left, with left RAPD, color vision deficits, and marked bilateral visual field (VF) loss. Fundus examination demonstrated diffuse bilateral optic disc pallor, and OCT revealed severe RNFL and GCL thinning. Treatment with IV Methylprednisolone and plasmapheresis led to minimal improvement. Comprehensive workup, including spinal cord MRI and serum tests for Anti-MOG, Anti-AQP4, Anti-NMDA antibodies, ANCA, ACE, ANA was negative. Lumbar puncture did not detect an infectious cause and oligoclonal bands were negative too. Subsequent MRI identified additional lesions in the brainstem and area postrema, suggestive of seronegative Neuromyelitis Optica (NMO). The patient was treated with monthly IVIG for one year, resulting in subjective and objective improvements. Final ophthalmologic assessment showed VA of 20/25 right eye and 20/400 left eye, with improvement in bilateral visual fields. Follow-up MRI (figure 7,8,9) showed new frontal lobe swelling, with stable lesions in the brainstem and visual pathways. A diagnostic test was done…

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“A Kid, a Fever, and a Whole Lot of Optic Nerve Drama”

Answer

Final Diagnosis: X-linked Cerebral Adrenoleukodystrophy

Summary of Case: Due to the unusual presentation, next generation sequencing-based gene panel for inborn errors of metabolism was done and surprisingly a known pathogenic mutation in ABCD1 gene was found. An abnormal very long chain fatty acids (VLCFAs) pattern in serum confirmed the diagnosis of X-linked adrenoleukodystrophy (ALD). He had an abnormal ACTH stimulation test and was commenced with hormone replacement therapy. The cascade screening in seemingly healthy brothers led to the diagnosis of ALD in his younger brother. There was no previously known family history of ALD. ALD is an X-linked recessive disorder caused by mutations in the ABCD1 gene, leading to the accumulation of VLCFAs in tissues. Diagnosis is confirmed by elevated VLCFA levels and genetic testing for ABCD1 mutations. [1-2] Ophthalmic manifestations in ALD include optic nerve atrophy and retinal nerve fiber layer thinning detectable also by OCT imaging. [3-4] Visual loss is usually a prominent early symptom, particularly in the childhood cerebral form of ALD, and is associated with demyelination of the optic nerves. [3][5] Multidisciplinary approach is essential in managing ALD. Our patient’s care involved collaboration among ophthalmologic, metabolic, radiologic, endocrinologic and neurologic teams to ensure accurate diagnosis and comprehensive treatment. The patient then underwent a successful bone marrow transplant. Allogeneic hematopoietic stem-cell therapy or autologous hematopoietic stem-cell ex vivo gene therapy is approved for cerebral-ALD in early-stage, although it does not reverse existing neurological damage. [6-8] Visual functions including acuity, color vision and field of vision improved markedly as compared to first presentation.

Struggle/Dilemma of the Clinical Presentation Description: 1. Initial misdiagnosis as seronegative NMO? Atypical presentation raises the question of whether this is just cALD or cALD triggered by an infectious/inflammatory process. 2. Severe optic atrophy and significant vision loss at presentation to ophthalmology raised uncertainty about the potential benefit of steroid pulse therapy and the yield of plasmapheresis or IVIG. 3. Family initially declined genetic testing due to religious beliefs.

Keywords: Bilateral vision loss, Optic atrophy, Afferent pupillary defect, Neuromyelitis Optica (NMO), Magnetic resonance imaging (MRI)

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“Dancing with “Peggy””

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History & Exam: A previously healthy 21-year-old man presented with one week of worsening headache, fever, bilateral leg weakness, and cognitive-behavioral changes, including psychomotor agitation and auditory and visual hallucinations. Initially, he self-medicated for three days, but as his headache worsened and he sought care at an outside hospital, where he was treated with a migraine cocktail and fluids, providing temporary relief. However, the headache progressed into the "worst headache of his life," prompting his return to the emergency department (ED) the next day. En route to the ED, he developed stroke-like symptoms, including difficulty speaking, slurred speech, and numbness in his left arm and leg. The patient, a farmer with frequent exposure to chemicals, reported no recent travel, sick contacts, or illicit drug use, though he drinks socially and uses marijuana nightly. He also has many pets. During his clinical course, he developed oscillopsia and spontaneous limb jerking two weeks after symptom onset. Neurological examination revealed encephalopathy, spastic paraparesis, hyperreflexia in the lower extremities, bilateral Babinski signs, and spontaneous limb myoclonus exacerbated by posture and movement. Neuro-ophthalmic findings included pupillary hippus and spontaneous, multiplanar eye movements, more pronounced in extreme gaze and with convergence. Strabismus and afferent visual function were otherwise normal. A series of diagnostic tests were performed.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“Dancing with “Peggy””

Answer

Final Diagnosis: Human Pegivirus (HPgV)-associated encephalomyelitis with opsoclonus-myoclonus.

Summary of Case: This 21-year-old farmer presented with a febrile illness of unknown origin, meningismus, encephalopathy, spastic paresis, myoclonus, oscillopsia, pupillary hippus, and spontaneous eye movements. MRI revealed FLAIR hyperintensities in the medulla, pons, dentate nuclei, and midbrain, with longitudinally extensive myelitis (LETM) on spine MRI. A cytotoxic lesion of the corpus callosum (CLOCC) was detected on DWI/ADC imaging. Post-contrast T1 imaging showed diffuse leptomeningeal enhancement from the brain to the cauda equina. CSF analysis demonstrated lymphocytic pleocytosis (50 WBCs/µL), hyperproteinorrachia (160 mg/dL), and normal glucose, consistent with encephalomyelitis and opsoclonus-myoclonus (OM). The differential diagnosis included infections targeting the brainstem and spinal cord (e.g., Listeria, flaviviruses) and atypical infections like COVID-19 and Whipple’s disease (1,2). Autoimmune causes, such as Bickerstaff encephalitis, paraneoplastic syndromes (e.g., IGLON5, anti-Hu, Ma2), sarcoidosis, and Neuro-Behçet's disease, were also considered. Imaging findings like LETM and CLOCCs raised concerns for demyelinating conditions (ADEM, NMOSD, MOGAD) and lymphoma (1,3). CLOCCs are also associated with metabolic disturbances and infections, reinforcing suspicion of infectious etiologies (4). Pupillary hippus is a non-specific finding, but could suggest an underlying encephalopathy. A comprehensive diagnostic workup, including blood tests, EEG, PET/CT, CSF studies, viral PCRs, cultures, cytology, and paraneoplastic panels, was inconclusive. However, metagenomic next-generation sequencing (mNGS) of CSF, confirmed by reverse-transcriptase PCR, established the final diagnosis (5). Empiric treatment with acyclovir was ineffective, but a 5-day course of intravenous immunoglobulin (IVIg) led to significant clinical improvement, including resolution of opsoclonus-myoclonus and mental status recovery, with pupillary hippus disappearing. At the 8-month follow-up, the patient remained symptom-free.

Struggle/Dilemma of the Clinical Presentation Description: Encephalomyelitis and opsoclonus-myoclonus (OM) have broad differential diagnoses, including infectious, autoimmune, and paraneoplastic causes. Longitudinally extensive myelitis (LETM) raised concern for NMOSD and other demyelinating diseases. CLOCCs further complicated the case, being associated with seizures, metabolic disturbances, toxins, infections, and lymphoma. Despite extensive testing, no common cause was identified. Metagenomic sequencing (mNGS) confirmed an infectious etiology, supported by reverse-transcriptase PCR. IVIg treatment significantly improved OM, suggesting immune involvement, with sustained resolution without long-term immunosuppression.

Keywords: Opsoclonus, Infectious disease, Brain stem syndromes, Complications of infections

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“TRUE FANS will stand by you, no MATTER what!”

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History & Exam: 15-year-old male presented with recent onset squinting of both eyes to general ophthalmology clinic. His medical history includes Fanconi anemia (FA) s/p bone marrow transplantation (BMT), congenital kidney disease, inflammatory bowel disease on vedolizumab, and autism spectrum disorder. In-clinic, he demonstrated fixate/follow vision in both eyes. Due to cooperation, he underwent an eye exam under anesthesia (EUA) which demonstrated a OD-white cataract and OS-Salzmann nodular degeneration and dense posterior subcapsular cataract. Posterior exam was limited. B-scan did not reveal any vitreous, retinal, and choroidal abnormalities. After routine cataract extraction in the right eye, patient underwent post-operative EUA, which revealed severe optic nerve edema with significant exudation and retinal disc hemorrhages (Fig1). For concerns of endophthalmitis, an anterior chamber tap was performed to test for HSV VZV, and CMV, and intravitreal injections of foscarnet and ganciclovir were administered. PCR testing for viral retinopathies was negative. Neuro-ophthalmology was consulted. Emergent MRI brain demonstrated bifrontal ring-enhancing lesion centered on corpus callosum. Nodular foci were noted in the posterior fossa and left occipital lobe (Fig 2-4). Differential diagnosis was included malignancy (higher risk in FA), infection (BMT), and/or inflammatory process. Multi-disciplinary evaluation determined that the clinical history and neuroimaging were characteristic of Fanconi Anemia Neuroinflammatory Syndrome (FANS), a novel and rare syndrome that has been observed at tertiary centers in recent years (1). Intracranial biopsy was deferred due to the high risk of hemorrhage that had been noted during previous attempts in similar cases (Fig6). Plasma and urine PCR and antibody serologies for JC virus were sent. While PCR negative; antibody serologies were positive. Patient was admitted for a two-week regimen of high-dose IV dexamethasone followed by slow taper regimen. Serial EUA and MRI showed resolution of optic nerve edema and improvement of the inflammatory lesions on serial imaging (Fig 7-10).

Financial Disclosures: Hyun Jun Kim: No; Laura Coyne: No; Parinda Mehta: No; Stella Davies: No; Blaise Jones: Yes; Christine Fuller: No; Veeral Shah: No

Grant Support: None.

“TRUE FANS will stand by you, no MATTER what!”

Answer

Final Diagnosis: A pediatric case of Fanconi Anemia Neuroinflammatory Syndrome, or FANS

Summary of Case: 15-year-old male with FA s/p BMT, IBD on vedolizumab, and severe ASD presented to clinic with initial symptoms of squinting in both eyes. After routine cataract surgery in the right eye, postoperative EUA demonstrated severe optic edema. He underwent empiric treatment for viral retinopathies and PCR testing was negative. Brain MRI demonstrated a large ring-enhancing lesion centered on the corpus callosum with extension to the bilateral frontal lobes. Differential considerations for a large ring-enhancing lesion in an immunosuppressed child with Fanconi Anemia include primary neoplasm (glioblastoma) and infection/abscess. The multiplicity of lesions argues against glioblastoma and the clinical presentation did not support an acute bacterial infection. Furthermore, the presence of a large lesion accompanied by multiple satellite lesions were also observed in other cases of FANS. Neuroimaging characteristics of FANS include the presence of a dominant periventricular mass, multiple small lesions (many with ring-enhancement and/or calcification), and involvement of the cerebellum and brainstem. The diagnosis of FANS was made based on the clinical context of the patient. Biopsy was deferred due to the high risk of hemorrhage. FANS is a novel clinical entity that cause multifocal, ring-enhancing lesions that are waxing and waning and usually involve the cerebellum. The condition usually presents in older patients with FA and can be observed in both transplant and non-transplant patients. Immunohistochemical staining of biopsy tissue positive JC virus (1). It is believed cells of the CNS have defective selective autophagy (2). This differs from the pathophysiology observed in progressive multifocal leukoencephalopathy, another condition associated with JC virus re-activation where the primary defect implicates T-cell function. Lesions can cause neurologic deficits. Biopsy of these lesions are associated with high risk of hemorrhage. Dexamethasone is used to treat the underlying edema. Rarely, patients can develop a exudative retinopathy (3).

Struggle/Dilemma of the Clinical Presentation Description: This case of Fanconi Anemia Neuroinflammatory Syndrome (FANS), a novel syndrome that associated with JC virus re-activation from impaired selective autophagy of viruses (2). This case illustrates the difficulty of differentiating FANS from neoplastic and infectious etiologies. While a clinical diagnosis of FANS was determined, there are no similar cases in the literature, or guidelines for navigating this diagnostic challenge. Management and optimum treatment also remain undefined.

Keywords: Papilledema, Disc edema, Systemic disorders, JC virus, Ring-enhancing lesions

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“The Eyes Have It”

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History & Exam: 46 year old male with h/o HTN, renal insufficiency who presented to the emergency room after suffering a seizure while at work. He was confused with difficulty with his memory. He complained of left sided weakness and some difficulty seeing to the left side. An urgent MRI showed a large right frontal lobe mass with ring enhancement and with significant midline shift and compression of the right lateral ventricle. The process was thought most consistent with a malignancy. Ophthalmic exam showed 20/30 vision OU, 12/14 color plates OU, normal IOP and unremarkable anterior segment. Fundus exam of the right eye showed a sharp optic nerve, mildly attenuated vessels with vasculature tortuosity and AV nicking, inferior arcade arterial copper wiring, mottled pigmentary changes in the mid periphery, and a few pigmentary changes in the macula. Fundus exam of the left eye showed a sharp optic nerve, peripheral vascular ischemia, occasional dot blot heme in the periphery, mild pigmentary changes in the mid peripheral retina, attenuated vessels with AV nicking. An urgent biopsy and resection of the brain mass was performed.

Financial Disclosures: Raghu Mudumbai: Clinical Trial Support: Stoke Therapeutics, Viridian Therapeutics, Nicox; Daniel Child: No; Kasra Rezaei: No

Grant Support: None.

“The Eyes Have It”

Answer

Final Diagnosis: Retinal Vasculopathy with Cerebral Leukoencephalopathy and Systemic manifestations (RVCL-S)

Summary of Case: 46 yo male with h/o HTN, renal insufficiency with new onset seizure and some difficulty seeing to the left side. Imaging was most consistent with an aggressive tumor like glioblastoma. Biopsy showed brain parenchyma with extensive necrosis and evidence of vasculopathy. Small parenchymal vessels displayed markedly thickened walls with “onion skin” appearance and luminal thrombi. There was no evidence of vasculitis. Mural PAS-positive deposits found in CADASIL were not identified. There were no signs of infection. Beta Amyloid stain was negative for cerebral amyloid angiopathy. Subsequent Fluorescein Angiography demonstrated in the right eye an enlarged foveal avascular zone with peripheral retinal ischemia, and a few vessels notable for staining in the nasal periphery. The left eye showed significant temporal retinal ischemia with a few vessels notable for staining in the nasal periphery. OCT in both eyes showed blunting of the foveal contour and extensive atrophic inner retina. There was mild scarring in the fovea. When the patient became more lucid, he was able to provide a family history of many similarly affected relatives across several generations who presented with seizure, brain mass on imaging, biopsy negative for a tumor. Affected relatives were not given a definitive diagnosis and had early mortality. The pathologic profile, along with the ophthalmic findings and the strong family history raised suspicion for TREX1 mutation associated with Retinal Vasculopathy with Cerebral Leukoencephalopathy and Systemic manifestations (RVCL-S). Gene testing revealed the patient had a TREX1c.a29A>T,pLys277 variant, which results in a premature termination codon, consistent with a diagnosis of RCVL-S. 8 months after presentation, the patient’s seizure significantly worsened along with severely worsened mental status. His family elected for hospice care and the patient met his demise.

Struggle/Dilemma of the Clinical Presentation Description: RVCL-S is a rare disease which remained a mystery until the TREX1 mutation was described in 2007. Approximately 60 families have been identified. Brain imaging can be misleading and be suggestive of a high-grade malignancy. Pathology can demonstrate that the patient does not have a tumor and a vasculopathy of unclear etiology. Retinal findings and family history remain critical to pursue screening for the TREX1 gene to identify this condition.

Keywords: Vasculopathy, Ring-enhancing lesions, Fluorescein angiography, Intracranial tumors, Optical coherence tomography (OCT), HRT, GDX

References: 1. Richards A, van den Maagdenberg AM, Jen JC, Kavanagh D et al C-terminal truncations in human 3'-5' DNA exonuclease TREX1 cause autosomal dominant retinal vasculopathy with cerebral leukodystrophy. Nat Genet. 2007 Sep;39(9):1068-70. 2. Wang WX, Spiegelman D, Rao PK, Ford AL, Apte RS. Crizanlizumab for retinal vasculopathy with cerebral leukoencephalopathy in a phase II clinical study. J Clin Invest. 2024 May 7;134(12):e1809 3. de Boer I, Steenmeijer SR, Pelzer N, Al-Nofal M, Dijkman G, Notting IC, Terwindt GM. Spectral Domain Optical Coherence Tomography in Retinal Vasculopathy With Cerebral Leukoencephalopathy and Systemic Manifestations: A Monogenic Small Vessel Disease. J Neuroophthalmol. 2022 Mar 1;42(1):e130-e136. 4. Hedderich DM, Lummel N, Deschauer M, Kümpfel T, Schuh E, Patzig M, Zimmer C, Huber T. Magnetic Resonance Imaging Characteristics of Retinal Vasculopathy with Cerebral Leukoencephalopathy and Systemic Manifestations. Clin Neuroradiol. 2020 Jun;30(2):229-236.

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Descriptive Posters: Meet the Author – March 16, 2025 (Sunday)

Poster #	Submission Title	Author	Category
1	A Zebra From Kentucky	Tyler S. Osborne (he/him/his)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
2	A Curious Case of Optic Neuropathy	Thomas C. Dunn (he/him/his)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
3	Case series of optic perineuritis in a tertiary medical referral center	Stephanie B. Syc-Mazurek	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
4	Normal Visual Fields in Chiasmal Compression: Use a Smaller Spot Size	Nicole Tsai	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
5	Seeing the Unexpected: A Unique Case of NAION with Temporal Vision Loss As a Periprocedural Complication of Cerebral Angiography	Tejasvi Paturu (she/her/hers)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
6	Transient Monocular Vision Loss With Paracentral Acute Middle Maculopathy (PAMM) On OCT: Beware Of Giant Cell Arteritis (GCA)!	George Alencastro	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
7	Crouzon Syndrome Optic Neuropathy with Retinitis	Katherine G. O'Neill	Disorders of the Anterior Visual

	Pigmentosa Causing Progressive Vision Loss		Pathway (Retina, Optic Nerve, and Chiasm)
8	Radiation-Induced Optic Neuropathy Following Proton Beam Radiation: Experiences of a Single Tertiary Care Center	Mohamad R. Hassoun	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
9	Does Metformin Alter The Course Of Type 2 Leber Hereditary Optic Neuropathy?	Shenoda Abd Elmaseh (he/him/his)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
10	Ba Da Boom	Kathleen Louis- Gray (she/her/hers)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
11	Uncommon Cause of Vision Loss	Mangayarakarasi Thandampallayam Ajjeya Gowder (she/her/hers)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
12	Efficacy and Safety of Lenadogene Nolparvovec Gene Therapy for Leber Hereditary Optic Neuropathy in the Real-Life Setting	Mark L. Moster	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
13	Description of a Novel Pathogenic Variant in the OPA1 Gene With Significant Intrafamilial Phenotypic Variability	Thomas Louis Perron (he/him/his)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
14	Optic Atrophy and Type I Diabetes: A Case Report on Mitochondrial Disease	Chia Wei Hsu (she/her/hers)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
15	Sildenafil induced Maculopathy	Etienne Bénard-Séguin	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)

16	Clinical Presentation and Visual Outcomes in Leber's Hereditary Optic Neuropathy Associated with the Novel 4171C>A Mutation: A Retrospective Case Series	Sally Al Hassan	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
17	The sensitivity and specificity of angiotensin converting enzyme (ACE) in the diagnosis of optic neuropathy due to sarcoidosis	Emily Daly	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
18	Until I'm Blue in the Hips - Optic Neuropathy from Cobalt Toxicity	Michael Carper	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
19	Central Retinal Artery Occlusion Associated With Myelin Oligodendrocyte Glycoprotein Antibody Disease	Brendan K. Tao (he/him/his)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
20	Smoke, Not Smoking, As A Risk Factor Triggering Conversion in Leber’s Hereditary Optic Neuropathy	Nutsa Pargalava (she/her/hers)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
21	An Atypical Case of Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD) Optic Neuritis Following COVID-19 Infection	Mohammed Mehdi Shahid (he/him/his)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
22	Intraocular Hemorrhage as a Complication of Empiric Thrombolysis in Patients Misdiagnosed as Having Central Retinal Artery Occlusion (CRAO)	Daniel Adamkiewicz	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
23	A Case of Retinal Migraine Exacerbated by Temporomandibular Joint Dysfunction	Cecilia Villanueva Boone	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)

24	Hemorrhagic Stroke Associated With Intravenous Tissue Plasminogen Activator In A Patient Receiving Adjuvant Hyperbaric Oxygen For The Treatment Of Central Retinal Artery Occlusion	Oluwatoyosi Arogbokun (she/her/hers)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
25	A Rare Presentation of Desmoplastic Small Round Cell Tumor Resulting in Post-Operative Vascular Induced Optic Atrophy	Akash Maheshwari	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
26	Spontaneous Visual Recovery in Toxic and Nutritional Optic Neuropathy After Years of Vision Loss	Peter L. Felton (he/him/his)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
27	Optic Nerve Metastasis from Non-Small Cell Lung Cancer Leading to Vision Loss	Prerna Das (she/her/hers)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
28	Whole Genome Sequencing of 10 Families with Optic Disc Drusen	Alvilda H. Steensberg (she/her/hers)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
29	Case Series: Two Patients Using Semaglutide Presenting with Bilateral NAION	Daniel Elefant	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
30	A Complicated Case of Late-Onset Leber's Hereditary Optic Neuropathy	Alberto Distefano	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
31	Age-related changes in optic disc drusen visibility and their anatomical correlates	Morten Jørgensen	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)

32	Post-operative Vision Loss in Shoulder Surgery: A Case Series and Review of the Literature	J. Anthony. Chacko (he/him/his)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
33	Progression Of Amaurosis Fugax To Retinal Artery Occlusion With Anterior Migration Of Retrobulbar "Spot Sign"	Ari August (she/her/hers)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
34	Resilient Pituicytoma: A 30-Year Journey	Logan C. Rademacher (he/him/his)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
35	Cotton Wool Spots in Classic Migraine: Is the Eye a Window to the Microangiopathic MRI Findings?	Madhura Shah (she/her/hers)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
36	Acute worsening central and peripheral vision in patient with hereditary optic neuropathy ... 30 years after diagnosis.	Natalie Brossard Barbosa	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
37	Non-Arteritic Anterior Ischemic Optic Neuropathy In The Setting Of Glucagon-like Peptide-1 Agonist Use	Jeremy Nortey (he/him/his)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
38	Three Cases of Nonarteritic Anterior Ischemic Optic Neuropathy in Patients Prescribed Semaglutide	Yue Li (she/her/hers)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
39	Post-traumatic Intracranial Hypotension with Concurrent Bilateral Optic Disc Edema and Abducens Nerve Palsies	Sonia C. Francone	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
40	Leukemic and Lymphomatous Optic Nerve Infiltration	Emily Eng	Disorders of the Anterior Visual Pathway (Retina,

	Treatment: A Case Series And Review Of The Literature		Optic Nerve, and Chiasm)
41	Metastatic Melanoma Masquerading as Giant Cell Arteritis	William M. Clark	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
42	Dural Tails Tell No Tales: A Case of Nonarteritic Anterior Ischemic Optic Neuropathy With Progressive Visual Loss and Concomitant Incidental Frontal Meningiomas	Dustin A. Hines (he/him/his)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
43	Association Between GLP-1 Agonist Use and NAION: A Two-Year Retrospective Chart Review at a Tertiary Eye Care Center	Yonah Levy (he/him/his)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
44	A treatment dilemma in primary vitreoretinal lymphoma without extraocular involvement: case report	Roswaldo Vilchez (he/him/his)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
45	Reversible homonymous hemianopsia secondary to hyperglycemia-induced occipital lobe seizures	Jacquelyn N. Hamati (she/her/hers)	Disorders of the Posterior Visual Pathway and Visual Processing
46	A Case of Visual Snow Following Systemic Ozone Therapy	Maxwell Wilberding (he/him/his)	Disorders of the Posterior Visual Pathway and Visual Processing
47	Bilateral Posterior Ischemic Optic Neuropathy as Sequela of Sepsis Induced Hypotension	Kiah McSwain	Disorders of the Posterior Visual Pathway and Visual Processing
48	Seeing Clearly: Early Neuro-Ophthalmological Symptoms Can Delay the Diagnosis of Progressive Multifocal Leukoencephalopathy	Daniela Vultorius (she/her/hers)	Disorders of the Posterior Visual Pathway and Visual Processing
49	Cortical blindness as a migraine aura mimicker	Samantha Blum (she/her/hers)	Disorders of the Posterior Visual

			Pathway and Visual Processing
50	The Varieties of Junctional Scotoma: 17 cases, a review, and a taxonomy	Gulce Ozturan	Disorders of the Posterior Visual Pathway and Visual Processing
51	Eagle Syndrome: A Secondary Cause Of Intracranial Hypertension	Fernando Nunez (he/him/his)	Idiopathic Intracranial Hypertension (IIH)
52	Earlier mortality for patients with Pseudotumor cerebri syndrome	Coby Soule (he/him/his)	Idiopathic Intracranial Hypertension (IIH)
53	More Than Meets The Eye	Carly Pappo (she/her/hers)	Idiopathic Intracranial Hypertension (IIH)
54	Evaluating Long-term Outcomes of Venous Sinus Stenting in Idiopathic Intracranial Hypertension	Sabrina Poonja	Idiopathic Intracranial Hypertension (IIH)
55	Diagnosis and Etiologic Classification of Optic Tract Syndrome	Natalie Chen (she/her/hers)	Miscellaneous
56	Bilateral Fixed Dilated Pupils: Uncommon Presentation in Acute Basilar Artery Thrombosis with Positive Recovery	Anya Rahman	Miscellaneous
57	Optimization of Ptosis Crutch Design Using Additive Manufacturing	Emily J. Scircle (she/her/hers)	Miscellaneous
58	Advancing Techniques to Produce Novel 3D Images of Human Orbital and Optic Nerve Vasculature	Drenushe Krasniqi	Miscellaneous
59	The Hijacked Ophthalmic Artery: Preoperative Embolization of a Giant Olfactory Groove Meningioma	Mura Abdul-Nabi	Neuro-Imaging
60	Artery of Percheron Infarct with Multiple Cranial Nerve Palsies and Horner Syndrome	William A. Sanfelippo (he/him/his)	Neuro-Imaging
61	The Third Nerve in Hindsight	Eve F. Moll	Neuro-Imaging

62	A Case of Curious Bilateral Disc Edema	Amani Khaled. Alsaidat (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
63	Increased Opening Pressure in Patients with Multiple Sclerosis and Neuromyelitis Optica	Sydney R. Roston (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
64	Anti Ganglioside Antibody Mediated Relapsing Cranial Nerve Palsies Mimicking Microvascular Cranial Nerve Palsies	Elizabeth D. Madison-Cowan (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
65	MRI-negative optic myelitis and bilateral disc swelling due to myelin oligodendrocyte glycoprotein antibody disease : A Case Report	Alvin WJ. Teo (they/them/theirs)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
66	Unveiling Misdiagnosis: Rethinking Seronegative NMOSD as a Distinct Entity	Mary V.. Lang (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
67	Nonarteritic Anterior Ischemic Optic Neuropathy with Antithrombin III Deficiency in Early Pregnancy: A Case Report	Kyra Singh* (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
68	Incidence of Thymoma in Patients with Ocular Myasthenia Gravis	Kambiz Ameli Zamani (he/him/his)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
69	Rare Neuro-Ophthalmic Manifestations of Syphilis Infection	Jennifer Drechsler (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
70	Between a Chiasm and a Hard Place: A Biopsy-Heavy Search for the Missing Diagnosis	Sara Krachmalnick (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
71	Not All Headaches are Migraine	Irene C. Yator	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases

72	Increase In Retinal Nerve Fiber Myelination In A Patient With Multiple Sclerosis: Ocular Evidence Of Remyelination?	Neringa Jurkute	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
73	Dupilumab-Induced Eosinophilic Granulomatosis With Polyangiitis Mimicking Giant Cell Arteritis	Alex L. Jin (he/him/his)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
74	Acetazolamide Induced thrombocytopenia in a patient with Idiopathic Intracranial Hypertension	Sarah Anderson	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
75	Cemiplimab in Squamous Cell Carcinoma with Perineural Invasion and Ophthalmoplegia	Marina Shenouda	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
76	A Case of Diffuse Large B-Cell Lymphoma Masquerading as Cavernous Sinus Syndrome	Kristen Park	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
77	Atypical Guillain-Barré Syndrome with Miller Fisher Variant: Acute Ophthalmoplegia and Hemiparesis	Sangeethabalasri Pugazhendhi (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
78	Fear of the Occult: A Case of GCA Presenting as Sequential Vision Loss	Caroline Tipton (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
79	Eosinophilic Granulomatosis with Polyangiitis Presenting with Optic Neuropathy	Mallika Tyagi (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
80	My, Oh, My	Amanda Wong	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
81	Diffuse Large B-cell Lymphoma Presenting as Multiple Cranial Nerve Palsies	Ayat H. Alni'mat (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases

82	Visual Field Defects with Posterior Cerebral Artery Stroke as a Complication of Anterior Temporal Lobectomy for Medically Intractable Seizures: Case Reports	Syeda Amel Safi (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
83	Recurrent Subconjunctival Hemorrhage Following Efgartigimod Treatment in Ocular Myasthenia Gravis: A Unique Case Report	Kayla Kendall	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
84	CV2/CRMP5 Antibody-Associated Retinopathy Linked to Immune Checkpoint Inhibitor Therapy	Christian Tallo (he/him/his)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
85	3460 Leber's Hereditary Optic Neuropathy In A 42 Year Old Female Masquerading As A Junctional Scotoma	Luke Barrick	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
86	An Unusual Optic Neuropathy	Rebecca F. Silverman (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
87	Acetylcholine receptor blocking antibodies of questionable diagnostic utility for Neuro-Ophthalmologists	Carleigh Bruce (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
88	A Rare Case of Bilateral Fourth Cranial Nerve Palsy Secondary to Hydrocephalus	Hoang-Viet Tran (he/him/his)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
89	An atypical case of Miller Fisher syndrome presenting with bilateral ptosis and total external ophthalmoplegia	Hak Seung Lee (he/him/his)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
90	Calciphylaxis: A Rare Cause of Ischemic Vision Loss	Mary-Grace R. Reeves	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
91	MOGAD Optic Neuritis in Older Adults : A Case Series	Yakira P. Mishan (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases

92	Phenylketonuria and Visual Symptoms: The Impact of Dietary Control on Neurological and Ophthalmic Outcomes	Sari Yordi	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
93	CNS White Matter Lesions and Progressive Optic Neuropathy in a Child with Craniopharyngioma after Resection and Proton Beam Radiation	Stephen Chai (he/him/his)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
94	"Brainzy"	Somya Chowdhary (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
95	Trapped In My Head	Padmaja Sudhakar (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
96	Wernicke Encephalopathy and Optic Neuropathy: Rare Conditions	Agni Kakouri	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
97	Collapsin Response-Mediator Protein 5 Paraneoplastic Syndromes – A Descriptive Case Series	jessica Kraker (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
98	Clinical features and prognosis of orbital fungal infection	Hyeshin Jeon (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
99	Bilateral Enophthalmos in Parry-Romberg Syndrome: A Case Report of Novel Disease Manifestation	Rachel A.H.. Bielling (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
100	Ophthalmic complications associated with the antidiabetic drugs semaglutide and tirzepatide	Bradley J. Katz (he/him/his)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
101	Bilateral optic nerve atrophy as the presenting symptom of chronic cerebral venous sinus	Pareena Sharma (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases

	thromboses in autoimmune hemolytic anemia		
103	A Case of Treatment with Efgartigimod PH20 SC in a Patient with Ocular Myasthenia Gravis	Julie Dela Cruz	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
104	Glial Fibrillary Acidic Protein Astrocytopathy Presenting as Asymptomatic Bilateral Optic Disc Edema with Normal Neuroimaging	Kristina Lin	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
105	Keep your Eye on the Ball	Zachary R. Barry (he/him/his)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
106	Vision Loss in Giant Cell Arteritis Treated with Tocilizumab	Bardia Abbasi	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
107	Neuro-ophthalmologic Characteristics Of Idiopathic Hypertrophic Pachymeningitis	Aurel Nagy (he/him/his)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
108	Cerebral Polyopia Due To Paraneoplastic Monoclonal IgG4-Related Hypertrophic Pachymeningitis	Casey Judge (he/him/his)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
109	Understanding the Myelin Oligodendrocyte Glycoprotein Optic Neuritis: Balancing Steroid Dependence and Immunosuppression	Shikha Talwar. BASSI	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
110	Novel Management of Herpes Zoster Ophthalmicus with Optic Neuritis and Cavernous Sinus Involvement	Nathan A. Lambert-Cheatham (he/him/his)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
111	Neurosyphilis with Disc Edema	Akash Gupta	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases

112	WFS1- Associated optic neuropathy in a predominantly Asian population	Jasmine G. Ge (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
113	A Visionary Approach: Last-Minute Rescue with Fractional Radiotherapy for Progressive Occipital Edema and Visual Loss from Lupus Cerebritis	Ayatalla Ahmed	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
114	Leber Hereditary Optic Neuropathy (LHON) Peer-to-Peer Mental Health Booklet	Malinda Marsh (she/her/hers)	Neuro-Ophthalmic Practice
115	As You Can See, The Mouth Speaks For Itself	Joseph M. Acierno	Neuro-Ophthalmic Practice
116	Not all Altitudinal Visual Field Defects are NAION	Varsha Pramil	Neuro-Ophthalmic Practice
117	Utilizing Social Media for Neuro-Ophthalmology Education, Outreach, and Pipeline Development	Jennifer K. Dunnigan (she/her/hers)	Neuro-Ophthalmic Practice
118	Radiologic-clinical correlation study of patients with stroke-Induced Isolated or Predominant Third Nerve Palsy	Tian Tian	Neuro-Ophthalmic Practice
119	Neuro-ophthalmic complications of molecular targeted therapies. Two case reports and review of literature.	Inbal Man Peles	Neuro-Ophthalmic Practice
120	Improved Visual Outcomes in Pediatric Optic Disc Drusen-Associated Neovascularization: A Systematic Review	Anas Alkhabaz	Neuro-Ophthalmic Practice
121	Acute Acquired Comitant Esotropia Secondary to a Large Foramen Magnum Meningioma	sasha narain (she/her/hers)	Neuro-Ophthalmic Practice
122	What is the visually enhanced vestibulo-ocular reflex and how can I use it to localize and diagnose?	Kaitlyn Druyor (she/her/hers)	New Diagnostic Measurement Techniques

123	Quantification Of Metabolic Stress In Optic Nerve Ischemia Using Flavoprotein Fluorescence Imaging And The Impact Of Optic Disc Edema	Rishita Pujari (she/her/hers)	New Diagnostic Measurement Techniques
124	Virtual Reality: Transforming Experiences For Young Astrocytoma Patients	Paul R. Clifford (he/him/his)	New Diagnostic Measurement Techniques
125	Bilateral Lateral Rectus Tendonitis Associated with Fluoroquinolone Use	Raquel Pinto	Ocular Motility Disorders and Nystagmus
126	Opsoclonus-Myoclonus Syndrome Secondary To West-Nile Virus Infection In A 24 Year Old Female With Medial Cerebellar Atrophy	Abdulaziz Al Abdulghani	Ocular Motility Disorders and Nystagmus
127	Trochlear Schwannomas In The Absence Of Systemic Neurofibromatosis: A Case Series	Adam Snowden (he/him/his)	Ocular Motility Disorders and Nystagmus
128	Progressive Ophthalmic Findings of an Intracranial Lesion	Yael Steinberg (she/her/hers)	Ocular Motility Disorders and Nystagmus
129	IgG4 Related Hypertrophic Pachymeningitis in a Child	Michael Seleski	Ocular Motility Disorders and Nystagmus
130	Downbeat Nystagmus and Causes of Diplopia in SCA27B: A Newly Described, Novel yet Common, Entity with Unique Neuro-Ophthalmologic Presentations	Janet Rucker (she/her/hers)	Ocular Motility Disorders and Nystagmus
131	Ocular Neuromyotonia After Peribulbar Block	Jia Jia Zhang (she/her/hers)	Ocular Motility Disorders and Nystagmus
132	Take a HINT[S] (exam): Posterior circulation stroke misdiagnosed as migraine	Sabrina J. Wirth (she/her/hers)	Ocular Motility Disorders and Nystagmus
133	Vertigo on the Hunt: Downbeat Nystagmus During Angiography in Bow Hunter's Syndrome	Claire Allen	Ocular Motility Disorders and Nystagmus

134	Late-onset AGRN-associated Congenital Myasthenic Syndromes Presenting With Diplopia	Yan Yan (he/him/his)	Ocular Motility Disorders and Nystagmus
135	Occult Saccadomania	Sunjay Parmar	Ocular Motility Disorders and Nystagmus
136	A case of thalamic lesion casing vertical one and a half syndrome	Chaoyi Feng (she/her/hers)	Ocular Motility Disorders and Nystagmus
137	Iatrogenic CCF's: A Case of Bilateral CCF's Spawned by Tamoxifen Therapy	Sannah Vasaya (she/her/hers)	Ocular Motility Disorders and Nystagmus
138	Lamotrigine Induced Downbeat Nystagmus and Oculogyric Crisis: A Case Report	Alexa Rothenberg (she/her/hers)	Ocular Motility Disorders and Nystagmus
139	Progressive Internuclear Ophthalmoplegia Secondary To Hypertrophic Olivary Degeneration Of To Be Determined Etiology	Rachelle Srinivas	Ocular Motility Disorders and Nystagmus
140	Centripetal Nystagmus: Why is it so rare and does it have diagnostic value?	Isabel Torres (she/her/hers)	Ocular Motility Disorders and Nystagmus
141	Downbeat Nystagmus (DBN) as a Sign of Myoclonic Status Epilepticus in a Patient With Anoxic Brain Injury	Max Parker (he/him/his)	Ocular Motility Disorders and Nystagmus
142	Presentation of Eight-And-A-Half Syndrome with Contralateral Hemiparesis Due to a Pontine Hemorrhage	Sanjana Marikunte (she/her/hers)	Ocular Motility Disorders and Nystagmus
143	Windmill nystagmus in blindness	Daniel Gold	Ocular Motility Disorders and Nystagmus
144	Artificial Intelligence and Machine Learning in Neuro-Ophthalmology	Paul Chong	Ocular-Imaging
145	Sarcoidosis-Related Myogenic Blepharoptosis with Direct Levator Palpebrae Superioris Involvement	Kim Firn	Orbital and Eyelid Disorders

146	Therapeutic Management of Oculomotor Nerve Palsy Ptosis and Mydriasis with Topical Oxymetazoline and Pilocarpine	Sehajpreet Kaur	Orbital and Eyelid Disorders
147	Acute Bilateral Compressive Optic Neuropathy Secondary to Fibrous Dysplasia of Skull Base in Adult	Harsh Parekh (he/him/his)	Orbital and Eyelid Disorders
148	The Necessity Of Biopsy In Differentiating Between Spheno-orbital Meningioma And Orbital Diffuse Large B-Cell Lymphoma	Carly Garvin	Orbital and Eyelid Disorders
150	A Battle of Wills: A Resilient CCF in a Noncompliant Patient	Sarah Kazemeini	Orbital and Eyelid Disorders
151	Dangerous Giant Cell Arteritis Mimicker - Mucormycosis	Philippe Ortiz	Orbital and Eyelid Disorders
152	Bilateral Optic Disc Edema and Orbital Inflammation in a Child with Trisomy 21 and B-ALL Following CAR-T Cell Therapy	Anis Hilal (he/him/his)	Pediatric Neuro-Ophthalmology
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155	Cryptic Suprasellar Germinoma Presenting as Autoimmune Hypophysitis in a Pediatric Patient	Humza Zaidi	Pediatric Neuro-Ophthalmology
156	Is That Nerve Swollen? A Systematic Literature Review and Our Proposed Paediatric Pathway	Alan Hopkins (he/him/his)	Pediatric Neuro-Ophthalmology
157	Neuromyelitis Optica Spectrum Disorder in a Young Patient with Shwachman-Diamond Syndrome.	Sergio A.. Garces (he/him/his)	Pediatric Neuro-Ophthalmology
158	Clinical Presentation of Homozygous Pathogenic Mutations in the CLN3 Gene in a 9-Year-Old Caucasian Male	Somya Chowdhary (she/her/hers)	Pediatric Neuro-Ophthalmology
159	Unveiling A TNF-Receptor Associated Factor 7 Mutation	Michael Miltich (he/him/his)	Pediatric Neuro-Ophthalmology

	Resulting In Optic Nerve Sheath Meningiomas Through A Pediatric Case		
160	Benign Path to Blindness	Rafaella C. Penteado (she/her/hers)	Pediatric Neuro-Ophthalmology
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163	Presumed Graft-Versus-Host-Disease (GVHD) of the Extraocular Muscles in a Teenager with Leukemia and Systemic GVHD	Mark J. Phillips (he/him/his)	Pediatric Neuro-Ophthalmology
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165	Exploring the Hidden Autoimmunity Link in Ross Syndrome	Axel L. Rivas (he/him/his)	Pupillary Disorders
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167	Hyperhidrosis With Associated Pupillary Lag: Questionable Horner's Syndrome	Fiona Steinmetz (she/her/hers)	Pupillary Disorders
168	The Intermittently Outstanding Pupil: A Case of Isolated Unilateral Episodic Mydriasis from Oculomotor Schwannoma	Ashley Zhou (she/her/hers)	Pupillary Disorders
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1
A Zebra From Kentucky

Tyler Osborne [1], Padmaja Sudhakar [1], Flavius Raslau [1], Mangayarkarasi Ajjeya [1]

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Introduction:
Here we describe a rare case of optic nerve sheath meningioma (ONSM) which was previously mistaken for optic neuritis.

Description of Cases:
A 48-year-old woman presented to the emergency department with left eye pain. She has had 4 worsening episodes over the last 25 years of left eye pain and exotropia which were treated as optic neuritis and idiopathic orbital inflammatory disease (IOI) with corticosteroids during each episode. On exam, her visual acuity was 20/25 right eye (OD), counting fingers left eye (OS) with relative afferent pupillary defect (RAPD) OS. Fundus examination showed normal optic disc OD and optic disc pallor OS. Magnetic resonance imaging (MRI) of orbits was consistent with optic nerve sheath meningioma with extension to left optic canal and extending along the posterior wall of the sphenoid sinus and left anterior clinoid process. Over the next 4 months visual acuity in the left eye progressively decreased likely due to optic nerve compression. Due to the rapid progression and symptomatic nature of the tumor, patient underwent left-sided pterional craniotomy for sub frontal approach for resection of tuberculum sella meningioma, extensive decompression of the optic nerve and canal.

Conclusions, including unique features of the case:
Our case highlights the difficulty in diagnosing ONSM when presented with acute visual loss in association with painful eye movements mimicking optic neuritis. Lack of recovery or progressive loss of vision should prompt the clinician to explore alternative diagnoses other than typical demyelinating optic neuritis. Finally selecting the appropriate imaging protocol in the setting of progressive loss of vision, particularly high-resolution contrast MRI of the orbit with fat-suppression sequences, can be crucial in making the correct diagnosis.

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Keywords: Tumors, Optic neuritis, Neuroimaging, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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2

A Curious Case of Optic Neuropathy

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Introduction:
Optic neuropathy has a very broad differential. Here we present an unusual case.

Description of Cases:
70 y.o male with a h.o CVA secondary to vascular malformation, no past ocular history presented with one week of progress painless vision loss OS. Visual acuity was 20/20 OD, FC OS, + rAPD OS. Anterior and posterior segment unremarkable. Optic nerves without pallor or edema. Optic nerve OCT unremarkable. Visual field was full OD and showed severe global depression OS. LP, CXR, CRP, ESR, CBC, syphilis, HIV, QuantiFERON, ACE, anti MOG, anti AQP4, anti CRMP-5, SSA, SSB ordered. MRI demonstrated enhancement and swelling of the intracranial segment of the left optic nerve and left aspect of the chiasm. Initial lab work up was normal. Anti MOG, NMO and CRMP-5 had not yet resulted. CSF was unremarkable. Started IV Methylprednisolone 1g daily for a working diagnosis of atypical optic neuritis. Discharged on prednisone 1250mg daily to complete 5-day course. CSF studies: VDRL, Adenovirus, WNV, Enterovirus, Meningitis/encephalitis, VZV, HSV1/HSV2, cytology/flow cytometry, CDS1, oligoclonal bands result WNL. Repeat MRI was unchanged. At follow up vision is HM, exam unchanged. Plasmapheresis recommended. Anti-NMO, AQP4 and CRMP-5 antibodies result and are negative. On day 5 of plasmapheresis visual acuity worsens to LP. CT chest ordered for sarcoid/malignancy screen and is unremarkable. Discharged after plasmapheresis. Repeat MRI demonstrated enlargement of the area of enhancement. At follow up vision is NLP. Admitted for whole body PET scan. ANCA, Lyme, Bartonella are negative. SPEP and paraneoplastic panel are negative. Repeat LP unremarkable. PET scan is performed and is WNL. Biopsy demonstrated high-grade glioma with molecular features of glioblastoma.

Conclusions, including unique features of the case:
There is a broad differential of optic neuropathy that varies widely in morbidity. When an older patient with atypical optic neuritis does not improve with plasmapheresis there must be a high index of suspicion for malignancy.

References: None provided.

Keywords: Optic neuropathy, Optic neuritis

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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3

Case series of optic perineuritis in a tertiary medical referral center

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Introduction:
Optic perineuritis is an uncommon condition of inflammatory infiltration of the optic nerve sheath. Optic perineuritis can occur as a primary ocular entity or secondary to a systemic disease. This study evaluates the clinical and radiologic characteristics of patients with optic perineuritis.

Description of Cases:
This is a preliminary retrospective case series of patients at a tertiary care medical center from 2010-2024 who consented to record review for research. Patients were included if they had visual symptoms or eye discomfort and had post-contrast gadolinium images with fat saturation with linear appearance of the optic nerve sheath on axial imaging (“tram track" appearance) or circular appearance on coronal imaging (“doughnut” appearance). Patients with optic nerve sheath meningiomas were excluded. Seventeen patients were included [median age, 65 (range 37-93); 53% female]. Presenting symptoms included vision loss in 12/17 (76%) and eye pain in 9/17 (53%). Visual acuity was 20/20 in 6/17 (35%) and was 20/200 or worse in 4/17 (24%). Clinically, 4/17 (24%) had disc edema, 4/17 (24%) had a relative afferent pupillary defect, 2/17 (12%) had proptosis, and 2/17 (12%) had diminished motility. Radiographically, enhancement was bilateral in 7/17 (41%) cases and unilateral in 10/17 (59%). In addition to the optic nerve sheath enhancement, 9/17 (53%) had enhancement of the periorbital fat. The etiology was idiopathic in 9/17 (53%), related to a systemic inflammatory process in 4/17 (24%, Crohn’s ileocolitis, sarcoidosis, immune check point toxicity, giant cell arteritis), infectious process in 2/17 (12%, both varicella zoster virus), local inflammatory syndrome in 1/17 (6%, biopsy proven localized small-vessel vasculitis), and demyelinating disease in 1/17 (6%, MOGAD). Steroids were given to 11/17 patients with improvement in symptoms in 9/11 (82%).

Conclusions, including unique features of the case:
Optic perineuritis occurred in patients with systemic inflammatory conditions, infection, and demyelinating disease. A broad workup should be considered in the patients presenting with perineuritis.

References: None provided.

Keywords: Optic neuropathy, Neuroimaging

Financial Disclosures: Stephanie Syc-Mazurek; Deena Tajfirouz; Kevin Chodnicki; M. Tariq Bhatti; Eoin Flanagan: The institution of Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Alexion. Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Genentech. Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Horizon Therapeutics. The institution of Dr. Flanagan has received personal compensation in the range of $10,000-$49,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Roche. Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Speakers Bureau for Pharmacy times. The institution of Dr. Flanagan has received personal compensation in the range of $5,000-$9,999 for serving on a Speakers Bureau for UCB. The institution of Dr. Flanagan has received research support from Viela Bio. The institution of Dr. Flanagan has received research support from UCB. The institution of Dr. Flanagan has received research support from Roche. Dr. Flanagan has received publishing royalties from a publication relating to health care. Dr. Flanagan has a non-compensated relationship as a Member of medical Advisory Board with The MOG Project. Dr. Flanagan has a non-compensated relationship as a Editorial board member with Journal of The Neurologic Sciences. Dr. Flanagan has a non-compensated relationship as a Editorial board member with Neuroimmunology Reports. Dr. Flanagan has a non-compensated relationship as a Editorial Board Member with Neurology, Neuroimmunology Neuroinflammation (N2) Journal.; John Chen

Grant Support: R01NS113828

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4

Normal Visual Fields in Chiasmal Compression: Use a Smaller Spot Size

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Introduction:
Compressive lesions of the optic chiasm classically present with bitemporal hemianopia. However, Humphrey visual field (HVF) testing with a standard stimulus size III (0.43°) spot sometimes fails to show a deficit in patients with chiasmal compression [1-4]. No prior studies have examined whether the use of a smaller size stimulus can increase the sensitivity of HVF testing in such patients.

Description of Cases:
A 21-year-old man presented for surveillance of a suprasellar tumor. CT imaging at age 16 after minor head trauma showed a partially calcified mass. Subsequent MR imaging revealed a heterogenous lesion containing fatty components, felt to be a dermoid tumor. The tumor thinned and displaced the optic chiasm superiorly. Multiple 24-2 HVF tests conducted over 5 years with a stimulus size III spot remained normal. However, a Zeiss ganglion cell analysis showed macular ganglion cell-inner plexiform layer (mGCIPL) thinning to 69 µm in the inferonasal sectors. Given this discrepancy between normal visual fields and mGCIPL thinning, we decided to perform further HVF testing using smaller test spots. Stimulus size I and II spots both revealed a superior temporal field defect in each eye that was missed by the standard stimulus size III spot.

Conclusions, including unique features of the case:
Our findings demonstrate that HVF testing using stimulus size I or II spots can reveal a visual field defect that was missed when using a standard size III test spot. We therefore recommend routinely performing HVF testing in patients with known chiasmal compression with a stimulus size I or II spot, when testing with a stimulus size III spot is negative. Although it has been proposed that a substantial fraction of ganglion cells must be lost before a visual field defect becomes detectable [5], our results suggest that with use of a more sensitive testing paradigm, this mismatch between anatomy and function may be mitigated.

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Keywords: Visual fields, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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5

Seeing the Unexpected: A Unique Case of NAION with Temporal Vision Loss As a Periprocedural Complication of Cerebral Angiography

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Introduction:
Non-arteritic anterior ischemic optic neuropathy (NAION) is a relatively common cause of acute monocular visual loss. NAION is typically due to optic disc ischemia in older patients with vascular risk factors including hypertension, diabetes, smoking, hyperlipidemia, or obstructive sleep apnea. NAION often presents with altitudinal field loss. Here, we describe an case of periprocedural NAION in a young patient with isolated temporal field loss.

Description of Cases:
A 46-year-old female with history of migraines and hypertension presented for elective diagnostic cerebral arteriogram for evaluation of Moyamoya disease. Immediately following the procedure, the patient reported a painless visual disturbance in the temporal field of the right eye including blurriness, photopsias, and colors. The positive visual phenomena resolved but temporal field loss in the right eye persisted. MRI brain and orbits with and without contrast demonstrated right optic disc edema. At neuro-ophthalmology follow-up 3 months later, exam demonstrated a right relative afferent pupillary defect and nasal pallor of the right optic disc. Automated kinetic visual field of the right eye demonstrated a 70 degree defect extending from the blind spot temporally. Ocular computed tomography of the right retinal nerve fiber layer (RNFL) demonstrated isolated nasal thinning with retrograde RNFL thinning in the nasal retinal periphery. Macular RNFL and ganglion cell layer was within normal limits. Fluorescein angiography (FA) was obtained to assess for ocular ischemic syndrome which revealed no retinal or choroidal filling defects and a normal arteriovenous transit time of 24 seconds.

Conclusions, including unique features of the case:
We present a case of periprocedural NAION suffered during cerebral angiogram. Atypical features include isolated nasal RNFL thinning with absence of generalized RFNL abnormality or damage to the macular GCL layer. Isolated nasal RNFL loss with temporal field defect is highly unusual in NAION and may suggest an atypical etiology such as posterior ciliary artery micro-embolism or vasospasm.

References: None provided.

Keywords: Optic neuropathy, Stroke

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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6

Transient Monocular Vision Loss With Paracentral Acute Middle Maculopathy (PAMM) On OCT: Beware Of Giant Cell Arteritis (GCA)!

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Introduction:
Acute vision loss from optic nerve retinal or choroidal ischemia can result from giant cell arteritis (GCA). Transient monocular vision loss (TMVL) from GCA is particularly challenging to diagnose in emergency departments (ED). Paracentral acute middle maculopathy (PAMM) has been described in GCA patients, typically with other ocular findings such as cotton wool spots, anterior ischemic optic neuropathy, or central retinal or cilioretinal artery occlusions. We describe a patient evaluated in the ED for TMVL with PAMM demonstrated on OCT as the only objective ocular finding of biopsy-proven GCA.

Description of Cases:
An 80-year-old woman presented to our ED 4 days after a 2-hour episode of a grey band in the central vision OD, which spontaneously resolved. She had history of polymyalgia rheumatica treated with oral prednisone, discontinued 2 months prior. She noted jaw claudication for 1 month. In the ED, non-mydriatic color fundus photographs were normal, but OCT showed a macular lesion with increased hyperreflectivity at the level of the inner nuclear layer, remotely identified as PAMM by ophthalmology. She immediately received IV-methylprednisolone for presumed TMVL from GCA. Subsequent examination in the eye clinic showed normal visual function with no RAPD. Funduscopic examination and automated perimetry were normal. Fluorescein/ICG angiography were normal without choroidal hypoperfusion. ESR was 20 and CRP was 27 (normal < 10). Temporal artery biopsy one day later confirmed the diagnosis of GCA.

Conclusions, including unique features of the case:
PAAM is a hyperreflective band-like lesion on macular OCT corresponding to ischemia of the middle retinal layers. Most reported GCA patients with PAMM also had permanent vision loss and other obvious funduscopic findings. Our patient had TMVL and a normal ophthalmic examination, including full HVF and normal ICG/FA. Immediate macular OCT revealing PAMM in TMVL patients older than 50 should suggest GCA and prompt immediate treatment in the ED prior to in-person ophthalmic examination.

References: Pellegrini F, Mairot K, Cuna A, Lee AG. Paracentral acute middle maculopathy in giant cell arteritis. Retin Cases Brief Rep. 2024 May 1;18(3):285-289.

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

Financial Disclosures: George Alencastro; Valérie Biousse: Consultant for Topcon which commercializes fundus cameras. The current research is completely independent from Topcon and is not funded by the company.; Etienne Bénard-Séguin

Grant Support: None.

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Crouzon Syndrome Optic Neuropathy with Retinitis Pigmentosa Causing Progressive Vision Loss

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Introduction:
Crouzon Syndrome is the most common craniosynostosis disorder and results from the premature fusion of cranial sutures either in-utero or postnatally. This rare branchial arch disorder is due to a mutation of the FGFR2 gene. Patients with Crouzon Syndrome develop ophthalmic manifestations resulting in visual impairment such as: amblyopia, optic atrophy, and strabismus. Retinitis pigmentosa, a group of congenital disorders causing the degeneration of the photoreceptors and retinal pigment epithelium, is a rare concomitant finding seen in association with Crouzon Syndrome(1).

Description of Cases:
A 31-year-old woman with a history of Crouzon Syndrome presented for progressive bilateral vision loss over ten years. At the age of six months, she experienced bilateral optic neuropathy, presumably due to elevated intracranial pressure and was subsequently treated with a ventriculoperitoneal shunt. Surgical history consisted of Chiari malformation decompression and multiple craniosynostosis reconstructions. Her visual acuity has progressively decreased from 20/200 in childhood to count fingers presently. Serial imaging revealed bilateral orbital optic canal narrowing and atrophy but no active compression. Ventriculoperitoneal shunt patency and lack of hydrocephalus was confirmed with imaging. She had significant retinal pigmentary changes bilaterally, and full field electroretinogram(ffERG) was performed. ffERG revealed flat contour with photopic and scotopic undetectable A and V waves, consistent with retinitis pigmentosa. The patient has previously undergone genetic testing to assess for gene mutations associated with retinitis pigmentosa.

Conclusions, including unique features of the case:
The management of the ocular findings in Crouzon include correction of refractive errors, timely treatment of strabismus, and patching to prevent or treat amblyopia. Although optic atrophy is a known finding in Crouzon syndrome, concomitant retinitis pigmentosa with or without optic atrophy has also been described. Ophthalmologists should recognize the potential for coexistence of both conditions in Crouzon syndrome to avoid recommending unnecessary decompressive craniectomy for visual loss due to retinopathy rather than compressive or post-papilledema related optic neuropathy.

References: 1. Gray, T, et al. “Ophthalmic sequelae of Crouzon syndrome.” Ophthalmology, vol. 112, no. 6, June 2005, pp. 1129–1134, https://doi.org/10.1016/j.ophtha.2004.12.037.

Keywords: Genetic disease, Optic neuropathy, Retina, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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8

Radiation-Induced Optic Neuropathy Following Proton Beam Radiation: Experiences of a Single Tertiary Care Center

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Introduction:
Compared to traditional radiation therapies, proton beam therapy (PBT) is often considered safer because it is thought to reduce the volume of irradiated tissue outside the tumor target, which theoretically reduces toxicity to surrounding structures. In patients undergoing radiation treatment for tumors near the optic nerve, a worrisome complication is radiation-induced optic neuropathy (RION), which has no proven effective treatment. Our study seeks to better understand RION occurring after PBT.

Description of Cases:
We analyzed all cases at a single tertiary center from 2014 to 2023 of patients who underwent PBT for chordomas, central nervous system tumors, nasopharyngeal tumors, or sinonasal tumors with ≥ 25 Gy at either the optic chiasm or optic nerve. A total of 555 unique patients met the inclusion criteria. Of these patients, 1.4% (8) developed RION following PBT. The median age at the time of RION diagnosis was 70.5 years (IQR 51 to 76 years), and the median duration between completing PBT and being diagnosed with RION was 1.35 years (IQR 0.63 to 2.18 years). The median physical dose delivered to the optic nerve or optic chiasm was 53.1 Gy (IQR 49.8 to 63.2 Gy), with no reported cases of RION in patients receiving less than 47.5 Gy. The median final visual acuity was light perception (IQR 20/200 to no light perception). Of note, two patients received multiple rounds of radiation with a total radiation dose of 73.6 Gy and 135.3 Gy. The tumors being treated in these cases consisted of three clival chordomas, one craniopharyngioma, one meningioma, one nasopharyngeal squamous cell carcinoma, one pterygopalatine adenoid cystic carcinoma, and one sinonasal melanoma.

Conclusions, including unique features of the case:
RION is a vision threatening complication of radiation therapy. In our study, the incidence of RION following PBT was 1.4%. Further studies are warranted to further elucidate risk factors and predictive parameters for RION.

References: None provided.

Keywords: Chemotherapy and radiation injury, Optic nerve trauma and treatment, Optic neuropathy, Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Does Metformin Alter The Course Of Type 2 Leber Hereditary Optic Neuropathy?

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Introduction:
Leber's hereditary optic neuropathy (LHON) is a maternally inherited disorder caused by missense mutations in mitochondrial DNA (mtDNA) genes encoding subunits of respiratory complex I in the electron transport chain (ETC). Metformin, a biguanide derivative, is primarily used to treat type 2 diabetes (T2D) and has shown potential benefits in various conditions, including cancers, cardiovascular disease (CVD), liver diseases, obesity, neurodegenerative diseases, and renal disorders.

Description of Cases:
We report a case of a postmenopausal woman with type 2 LHON with mitochondrial mutation 11778. She exhibited significant improvement in her visual field following metformin treatment. Previously, she had undergone idebenone, hormone replacement therapy, and NAD+, all without improvement. Upon diagnosis of diabetes mellitus, her internist prescribed metformin. After 8 months of treatment, her mean deviation in visual fields improved from -32 to -25 in both eyes.

Conclusions, including unique features of the case:
Three mechanisms may explain this patient's visual improvement: metformin's role in reducing reactive oxygen species production, suppressing inflammation and autophagy, and the intriguing second site suppression theory. In conclusion, metformin may influence the molecular mechanisms underlying complex I function, potentially altering the course of type 2 LHON in affected patients.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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10
Ba Da Boom

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Introduction:
A 73-year-old man presented with painless progressive vision loss OD for six weeks. Medical history included Waldenstrom's macroglobulinemia, or WM) in remission since last treatment in 2021.

Description of Cases:
Our examination disclosed visual acuities of 20/100 OD, 20/20 OS, a right APD, Ishihara color plates 0/11 OD, 7/11 OS, and bilateral disc edema. Visual fields showed generalized defects OU with mean deviations of -23.28 DB OD, -9.38 OS. MRI orbits showed bilateral long segment optic nerve enhancement. MRI spine showed enhancement of multiple cauda equina nerve roots. NMO and MOG were negative. Serum protein electrophoresis and immunofixation showed an IgM kappa M-protein that was too small to quantify, consistent with effective treatment of WM. Serum viscosity was normal. Lumbar puncture showed a normal opening pressure, 28 WBCs (99% lymphocytes), protein 42, glucose 46 (simultaneous blood glucose 97). Cytology was negative for carcinoma. Flow cytometry showed a small population of kappa restricted B cells without aberrant T cells or blast cells. CSF MYD 88 L265P was positive, confirming the diagnosis of Bing Neel Syndrome (BNS), warranting treatment with zanubrutinib, a Bruton's tyrosine kinase (BTK) inhibitor used effectively in BNS1,2. Seven weeks after treatment began, visual acuities had improved to 20/50 OD, 20/25 OS and mean deviations to -15.09 dB OD, -4.60 dB OS.

Conclusions, including unique features of the case:
WM is a rare B-cell non-Hodgkin lymphoma, and BNS is a rare complication of this disorder, which occurs when lymphoplasmacytic lymphoma cells colonize the CNS. Our patient had a history of WM in remission since 2021. Was the optic neuropathy due to BNS, even though the protein electrophoresis showed only a small IgM kappa M-protein? The MYD88 L265P mutation recovered from CSF allowed robust confirmation of the diagnosis of BNS without need for a bone marrow biopsy. Prompt treatment with zanubrutinib could then commence.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

11
Uncommon Cause of Vision Loss

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Introduction:
Here we present a unique case of optic neuropathy and neovascular glaucoma associated with chronic sphenoid sinusitis.

Description of Cases:
33-year-old female presented with left sided headache and progressive vision loss in the left eye. On examination, her visual acuity was 20/20 in the right eye (OD) and hand movements in the left eye (OS). Intraocular pressure 21 mmHg in OD and 28 mm Hg in OS. 3+ APD and inferior neovascularization of the iris (NVI) were noted in the left eye. Fundus showed normal optic disc in OD and optic disc pallor with scattered dot-blot hemorrhages in the mid-periphery in OS. She was started on Dorzolamide/Timolol eye drops for the neovascular glaucoma in the left eye. MRI Brain with and without contrast showed chronic left sphenoid sinusitis. CT orbits showed bony erosion along the lateral wall of the left sphenoid sinus, adjacent to the optic canal, suggestive of erosion from sinusitis. MRI orbits with and without contrast showed volume loss of left optic nerve but no abnormal enhancement. Labs including fungal work up were normal except for mild eosinophilia. ESR and CRP were normal. She underwent left total ethmoidectomy with sphenoidotomy. Culture from the drained purulent material was suggestive for bacterial sinusitis. She received Amoxicillin-Clavulanate 875/125 for 14 days. In 4 weeks follow up, neuro-ophthalmology evaluation revealed best corrected visual acuity 20/20 OD 20/200 OS, resolution of NVI OS, normal optic disc OD and optic disc pallor OS.

Conclusions, including unique features of the case:
The association between sphenoethmoid sinusitis (SES) and optic neuropathy with posterior segment ischemia and neovascular glaucoma has not been reported so far. The mechanisms of optic nerve damage include direct spread of infection, occlusive vasculitis or vaso-occlusive ischemic optic neuropathy. Delay in sino-orbital imaging and recognition of SES can lead to a worse visual prognosis.

References: None provided.

Keywords: Optic neuropathy, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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12

Efficacy and Safety of Lenadogene Nolparvovec Gene Therapy for Leber Hereditary Optic Neuropathy in the Real-Life Setting

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Introduction:
Early access programs (EAPs) provide efficacy and safety data on the use of lenadogene nolparvovec gene therapy (LNGT) in real-life conditions in patients with Leber hereditary optic neuropathy (LHON) due to the m.11778G>A ND4 mutation.

Description of Cases:
LNGT was provided based on unsolicited requests and its use was authorized by local regulations in 4 countries (France, Italy, UK and US). Patients received LNGT as a unilateral or bilateral intravitreal injection (9E10 viral genomes/eye). Intermediate analysis was performed on August 29, 2024. A total of 63 ND4-LHON patients received LNGT in EAPs, mainly in France (35 [55.6%]) and the US (18 [28.6%]). Most (42 [66.7%]) patients received a bilateral injection. At the time of the first injection of LNGT, patients were on average (SD) 33.7 (16.6) years old, with 6 (9.5%) children aged 13 or 14 years. The mean (SD) duration of disease at the first injection was 11.4 (9.6) months. Most (84.1%) patients were treated with idebenone therapy at or after LNGT injection, for a mean (SD) duration of 36.1 (14.6) months. BCVA values at 1 year were obtained from 53 patients; the mean (SD) change in BCVA from nadir to 1 year was -0.42 (0.54) LogMAR (+21 ETDRS letters equivalent). Clinically relevant recovery (CRR) from nadir was observed in 42.9% of treated eyes within 12 months of disease onset, and in 76.5% of treated eyes after 12 months of disease onset. The safety of LNGT was comparable to those of the 189 patients from clinical studies, with no difference in the incidence of intraocular inflammation between patients treated bilaterally and unilaterally (51.2% vs 52.4%).

Conclusions, including unique features of the case:
Preliminary analyses show that injection of LNGT in the real-life setting was associated with a clinically meaningful improvement in visual acuity from nadir and a favorable safety profile similar to that observed in the clinical studies.

References: None provided.

Keywords: Optic neuropathy

Financial Disclosures: Mark Moster: Mark L. Moster is a consultant for GenSight Biologics and has received research support from GenSight Biologics.; Catherine Vignal-Clermont: Catherine Vignal-Clermont is a consultant for GenSight Biologics and has received research support from Santhera Pharmaceuticals.; Valerio Carelli: VC is a consultant for GenSight Biologics, Chiesi, Stoke, and Pretzel.; Chiara La Morgia: Chiara La Morgia is a consultant for Chiesi Farmaceutici, Gensight Biologics, Regulatory PharmaNet and Thenewway srl. She received speaker honoraria and/or financial support for meetings from Santhera Pharmaceuticals, Chiesi Farmaceutici, Gensight Biologics, Regulatory PharmaNet, Thenewway srl, First Class srl and Biologix.; Robert Sergott: Robert C. Sergott is a consultant for GenSight Biologics.; Sarah Thornton; Sean Donahue; Patrick Yu-Wai-Man: Consulting: GenSight Biologics, Stoke Therapeutics, Transine Therapeutics; Speaker honoraria and/or financial support: GenSight Biologics, Santhera Pharmaceuticals; Hélène Dollfus; Thomas Klopstock: Thomas Klopstock received research support and/or personal compensation for presentations and/or consulting from GenSight Biologics and Chiesi Farmaceutici.; Claudia Priglinger; Rabih Hage; Vasily Smirnov; Catherine Cochard; Marie-Bénédicte Rougier; Emilie Tournaire-Marques; Pierre Lebranchu; Caroline Froment; Frédéric Pollet-Villard; Marie-Alice Laville; Claudia Prospero Ponce; Scott Walter; Francis Munier; Pauline Zoppe; Magali Taiel: MT is an employee of GenSight Biologics.; José-Alain Sahel: JAS is a consultant/contractor for Avista Therapeutics and Tenpoint; has financial interests (stock/stock options) in GenSight Biologics, Sparing Vision, Prophesee, Chronolife, Tilak Healthcare, VegaVect, Inc., Avista, Tenpoint, SharpEye, Celanese and Netramind; is owner/co-owner/founder/co-founder for Gensight Biologics, Sparing Vision, Avista, Tenpoint, Prophesee, Chronolife, Tilak Healthcare, SharpEye, Celanese, Vegavect and Netramind; participates in scientific advisory board for Gilbert Foundation, Foundation Fighting Blindness, Institute of Ophthalmology Basel and Senses Institute Lausanne; is an observer at Gensight Biologics, SparingVision, Avista and Vegavect; is President of Fondation Voir et Entendre (Paris) and StreetLab (Paris); has patent for allotopic expression, rod-derived cone viability factor and related patents; is a recipient for patent royalties and GenSight Biologics.

Grant Support: None.

Contact Information: None provided.

13

Description of a Novel Pathogenic Variant in the OPA1 Gene With Significant Intrafamilial Phenotypic Variability

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Introduction:
Dominant optic atrophy (DOA) is an inherited mitochondrial disease caused in approximately 70% of cases by a mutation in the OPA1 gene on chromosome 3. Since the initial descriptions of families with childhood-onset progressive bilateral visual loss with autosomal dominant inheritance in the 1950s, more than 400 distinct pathogenic variants in the OPA1 gene have been identified and considerable intrafamilial and interfamilial variability in the expression of the disease has been reported. Evidence is lacking to explain such heterogeneity, although the type of mutation and its localization on the protein appears to represent one of the underlying mechanisms.

Description of Cases:
We report a novel pathogenic variant identified in the OPA1 gene (c.2804T>C) and describe the clinical findings of eight affected individuals in four generations of a French-Canadian family. Patients identified with this missense mutation have isolated optic neuropathies of variable severity, ranging from subclinical decreased visual acuity of 20/25 at 74 years old to childhood-onset color vision defect with decreased visual acuity progressing to 20/400. Every patient's optical coherence tomography shows a mitochondrial pattern of optic atrophy, involving initially the temporal peripapillary retinal nerve fiber layer. We also describe the type and localization of this mutation on the OPA1 gene. Finally, we discuss the possible pathogenic mechanisms and review the different hypotheses proposed in the literature to explain the phenotypic variability of the disease.

Conclusions, including unique features of the case:
DOA is a complex mitochondrial optic neuropathy with significant intrafamilial phenotypic variability, as seen in a French-Canadian family affected by a novel pathogenic variant in the OPA1 gene. This finding adds to the growing number of pathogenic variants identified in the OPA1 gene and could be used in future genotype-phenotype correlation analyses

References: Ham, Han, Osann, Smith, Kimonis, Meta-analysis of genotype-phenotype analysis of OPA1 mutations in autosomal dominant optic atrophy. Mitochondrion. Volume 46, Page 262-269, 2019. Amati-Bonneau, Milea, Bonneau, Chevrollier, Ferré, Guillet, et al. OPA1-associated disorders: Phenotypes and pathophysiology. The International Journal of Biochemistry & Cell Biology. Volume 41(10), Pages 1855-1865, 2009. Amati-Bonneau, Valentino, Reynier, Gallardo, Bornstein, Boissiere, et al. OPA1 mutations induce mitochondrial DNA instability and optic atrophy "plus" phenotypes. Brain. Volume 131, Page 338-351, 2008. Lenaers, Neutzner, Le Dantec, Jüschke, Xiao, Decembrini, et al. Dominant optic atrophy: Culprit mitochondria in the optic nerve. Progress in Retinal and Eye Research. Voume 83, Article 100935, 2021.

Keywords: Genetic disease, Optic neuropathy, Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Optic Atrophy and Type I Diabetes: A Case Report on Mitochondrial Disease

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Introduction:
Mitochondrial diseases are a clinically and genetically heterogenous group of disorders that lead to a diverse phenotypic spectrum. Accurate genetic counseling requires the identification of the underlying causative genetic mutation.

Description of Cases:
A 22-year-old Asian female pharmacy student presented with one year of bilateral decreased vision. Notably, she was diagnosed with type I diabetes after presenting in ketoacidosis 6 months prior. Examination showed acuity of counting fingers in both eyes, with bilateral optic disc pallor. Cecocentral scotomas were present in both eyes on formal visual field testing. Toxic and nutritional work up was unremarkable. Magnetic resonance imaging (MRI) of the brain and orbit showed increased signal in the right optic nerve without compressive lesions or abnormal enhancement. Initially, given the presentation, there was suspicion for Wolfram syndrome; however, her optic atrophy nuclear panel (including WFS1, as well as other nuclear genes associated with optic atrophy) was negative. At this point, mitochondrial sequencing and deletion/duplication analysis was performed and identified a pathogenic variant in the MT-ND3 gene, m.10191T>C (p.S45P), at approximately 71% heteroplasmy.

Conclusions, including unique features of the case:
The 10191T>C mutation in MT-ND3 is often associated with Leigh syndrome, a subacute necrotizing encephalomyelopathy seen in pediatric patients. Interestingly, adult presentations of this mitochondrial mutation may present with cognitive impairment and optic atrophy that is not observed in the pediatric cohort. While this specific mutation has not been previously reported to be associated with diabetes, other mutations in MT-ND3 have. This case highlights both the varied phenotypes for a given gene mutation, as well as the overlap in phenotype among different gene mutations, in that this patient's presentation mimicked the autosomal dominant condition, Wolfram syndrome. When mitochondrial optic neuropathy is suspected, confirmation of the underlying genetic mutation allows for genetic counseling and may, in the future, allow for opportunities for gene therapy.

References: None provided.

Keywords: Optic neuropathy, Genetic disease

Financial Disclosures: Chia Wei Hsu; Amanda Henderson: None related to this submission: Horizon Therapeutics/Amgen.

Grant Support: None.

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15
Sildenafil induced Maculopathy

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Introduction:
Sildenafil is an oral phosphodiesterase-5 (PDE-5) inhibitor used to treat male erectile dysfunction. Approved dosages range from 25-100mg. In vitro studies have shown that sildenafil can have a weak inhibitory effect on PDE-6, which is found in the retinal photoreceptors and plays a key role in phototransduction.

Description of Cases:
We present a case of a 48-year-old man who was referred to neuro-ophthalmology for acute bilateral vision changes from presumed bilateral optic neuropathies after ingesting 120 x 100mg (12,000mg) of Sildenafil pills in a suicide attempt 10 days prior. On presentation, his visual acuity was 20/70 OD and 20/70 OS. Pupils were equal and reactive to light with no RAPD. Color plates were 11/14 OD and 11/14 OS. HVF 24-2 showed a central scotoma OU (MD -6.54 dB OD and -7.57 dB OS). Dilated fundus examination was unremarkable with no optic disc edema or pallor. OCT Macula showed nodular thickening of the ellipsoid zone with possible choriocapillaris vessel dilation and thickening. 3 months later, the patient was seen in neuro-ophthalmology follow up. Visual acuity was 20/25 OD and 20/20 OS. Color plates were 14/14 OD and 14/14 OS. HVF 24-2 showed almost completed resolution of his central scotomas. Dilated fundus examination was normal. His OCT Macula showed improvement of his ellipsoid zone loss. Multifocal ERG showed diminished response in the macula OD greater than OS.

Conclusions, including unique features of the case:
To our knowledge, this is the single largest dose of Sildenafil ingested by a human. Sildenafil maculopathy has rarely been described in the literature and presents similarly to our case. OCT Raster show diffuse nodular thickening and irregularities of the central ellipsoid zone associated with thinning and poor delineation of the inter-digitation zone. Multifocal electroretinogram often shows reduced amplitudes in the macula. Visual recovery is variable.

References: None provided.

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

Financial Disclosures: Etienne Bénard-Séguin; Kevin Ferenchak; Nancy Newman: Consultant for GenSight, Chiesi, Neurophth (all involved with the treatment of Leber hereditary optic neuropathy. Research support as PI to my institution from GenSight for clinical trials.; Valérie Biousse: Consultant for Topcon which commercializes fundus cameras. The current research is completely independent from Topcon and is not funded by the company.

Grant Support: None.

Contact Information: None provided.

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Clinical Presentation and Visual Outcomes in Leber's Hereditary Optic Neuropathy Associated with the Novel 4171C>A Mutation: A Retrospective Case Series

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Introduction:
The rare 4171C>A mutation presents unique clinical features. This retrospective chart review explores four related patients and one unrelated patient with the mutation.

Description of Cases:
Case 1: An 18-year-old female presented in November 2018 with bilateral painless vision loss. Genetic testing confirmed the 4171C>A mutation. Her presenting visual acuity was CF at 1 meter (OD) and CF at 1.5 meters (OS). After two years on idebenone and fampridine, her vision improved to 20/400 OD and 20/300 OS. Visual field testing showed central scotomas in both eyes. Case 2: A 54-year-old maternal aunt of Case 1 experienced vision loss at age 10. Her presenting visual acuity was 20/125 OD and 20/250 OS. Visual field testing showed a central scotoma in the left eye and nonspecific defects in the right eye. Case 3: A 53-year-old maternal uncle of Case 1 reported vision loss at age 11. His presenting visual acuity was 20/60 OD and 20/100 OS. Visual field testing demonstrated central and inferior deficits. Case 4: A 64-year-old male cousin of Case 1 reported vision loss at age 14. His presenting visual acuity was CF near the face in both eyes. Visual field testing revealed complete visual field loss. Case 5: A 62-year-old male (unrelated) developed vision loss at age 53. His presenting visual acuity was 20/50 OD and 20/40 OS, deteriorating to 20/250 OD and CF at 1 meter OS. OCT showed bilateral optic nerve atrophy. Visual field testing revealed central scotomas in both eyes. Optic disc atrophy was noted in Cases 3 and 5. RNFL thinning was noted on Optical Coherence Tomography in all cases.

Conclusions, including unique features of the case:
This case series highlights the variability in onset age, progression, and visual outcomes of LHON with the 4171C>A mutation. Maintaining a low threshold for LHON diagnosis is crucial to prevent unnecessary treatments and to provide genetic counseling.

References: None provided.

Keywords: Genetic disease, Optic neuropathy, Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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The sensitivity and specificity of angiotensin converting enzyme (ACE) in the diagnosis of optic neuropathy due to sarcoidosis

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Introduction:
Sarcoidosis is a rare but important cause of optic neuropathy. It is estimated that between 1 and 5% of sarcoidosis patients have anterior visual pathway involvement, and in some patients, optic neuropathy may be the first clinical manifestation of the disease1. While there are multiple tests that can be used to help diagnose sarcoid optic neuropathy, there is no established protocol. Angiotensin converting enzyme (ACE), has been reported to have relatively high sensitivity in the setting of pulmonary sarcoidosis2,3, but variable utility in the setting of neuro-ophthalmic presentations of sarcoid 1,4. The utility of serum ACE has not been systematically studied in the specific setting of sarcoid optic neuropathy. With this study we set out to determine the sensitivity and specificity of ACE for the diagnosis of sarcoid optic neuropathy.

Description of Cases:
Methods: We conducted a single-institution retrospective chart review of adult patients seen in our Neuro-ophthalmology clinics from January 2012 through June 2023. We included patients with a Neuro-ophthalmologist-confirmed optic neuropathy diagnosis, available serum ACE level, and sufficient work-up/follow-up. For the diagnosis of “Probable” or “Definite” sarcoid optic neuropathy, we used a modified version of previously published consensus criteria for the diagnosis of neuro-sarcoidosis5. Results: The charts of 1052 patients were reviewed. 340 patients did not meet inclusion criteria and were excluded. 20 cases meeting criteria for a diagnosis of “Probable” or “Definite” sarcoid optic neuropathy were identified. In the diagnosis of sarcoid optic neuropathy, ACE had a sensitivity of 25% and a specificity of 97.0%.

Conclusions, including unique features of the case:
These results indicate that ACE has a low sensitivity, but high specificity in the diagnosis of sarcoid optic neuropathy. Thus, ACE may not be the most optimal choice as a screening test for sarcoid optic neuropathy, however, it can be valuable for helping to rule in the diagnosis when ACE is elevated in suspected cases.

References: 1. Frohman LP, Guirgis M, Turbin RE, Bielory L. Sarcoidosis of the anterior visual pathway: 24 new cases. J Neuroophthalmol. 2003 Sep;23(3):190-7. doi: 10.1097/00041327-200309000-00002. PMID: 14504590. 2. Prior C, Barbee RA, Evans PM, Townsend PJ, Primett ZS, Fyhrquist F, Grönhagen-Riska C, Haslam PL. Lavage versus serum measurements of lysozyme, angiotensin converting enzyme and other inflammatory markers in pulmonary sarcoidosis. Eur Respir J. 1990 Nov;3(10):1146-54. PMID: 1965306. 3. Hosoya S, Kataoka M, Nakata Y, Maeda T, Nishizaki H, Hioka T, Mori Y, Ejiri T, Shiomi K, Ueoka H, et al. Clinical features of 125 patients with sarcoidosis: Okayama University Hospital review of a recent 10-year period. Acta Med Okayama. 1992 Feb;46(1):31-6. doi: 10.18926/AMO/32676. PMID: 1561903. 4. Henderson AD, Tian J, Carey AR. Neuro-Ophthalmic Manifestations of Sarcoidosis. J Neuroophthalmol. 2021 Dec 1;41(4):e591-e597. doi: 10.1097/WNO.0000000000001108. PMID: 33110001. 5. Stern BJ, Royal III W, Gelfand JM et al. Definition and consensus diagnostic criteria for neurosarcoidosis. From the Neurosarcoidosis Consortium Consensus Group. JAMA Neurology. 2018 Dec 1;75(12):1546-1553. doi: 10.1001/jamaneurol.2018.2295.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Until I'm Blue in the Hips - Optic Neuropathy from Cobalt Toxicity

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Introduction:
Cobalt (Co) toxicity has been associated with hip replacement surgery, pertinently metal-on-metal articulation, resulting in frictional release of Co ions into circulation. While ocular toxicity (among other systemic toxicities) is a rare outcome, an estimated 60% of all hip replacements require replacement due to wear. This case details an atypical case of this rare outcome, while also illustrating the importance of awareness for a complication of a very common procedure.

Description of Cases:
55M presenting with progressive significant vision loss, with history of Afib, COPD, SCFE, multiple pulmonary emboli (PE's). He is s/p L hip arthroplasty. Spontaneous onset of vision loss began March 2022 with asymmetric, but gradual progression in the absence of eye pain, headaches, or other focal neurologic symptoms. He had mild reduction in VA on initial exam with optic nerve pallor and concern for possible ischemic optic neuropathy. Infectious, inflammatory, and genetic testing was negative. He continued to progress to count finger vision, 1/11 colors and severe RNFL/GCL thinning bilaterally. Updated labwork revealed elevated Cobalt level of 4.5 g/dL (0.0-0.9) raising concern for cobalt neurotoxicity. Orthopedic evaluation raised concern for metal-on-metal articulation and metallosis. L THA revision was completed with pathology revealing fragmented foreign material in bone/marrow samples.

Conclusions, including unique features of the case:
In the setting of profound optic neuropathy and vision loss with negative extensive workup, Cobalt toxicity was of high suspicion as the underlying etiology. The asymmetric progression confounded the workup for toxic causes, and Co levels were unfortunately not obtained at the time of onset. This etiology was supported by ongoing L hip pains where his prior L THA was completed with a now-recalled product, and evidence of metallosis by orthopedics on revision of his arthroplasty. Interestingly, the patient had also undergone extensive non-revealing workup for multiple PE's and chronic GI upset, which also can be attributed to systemic Co toxicity.

References: Garcia, M et al; Cobalt toxic optic neuropathy and retinopathy: Case report and review of the literature, American Journal of Ophthalmology Case Reports, Volume 17, #100606, 2020. Catalani S, Rizzetti MC, et al. Neurotoxicity of cobalt. Human & Experimental Toxicology. 31(5):421-37, May 2012.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: N/A

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Central Retinal Artery Occlusion Associated With Myelin Oligodendrocyte Glycoprotein Antibody Disease

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Introduction:
To describe a patient with a history of myelin oligodendrocyte glycoprotein antibody disease optic neuritis (MOGAD-ON) and venous stasis retinopathy in their right eye, who subsequently developed a central retinal artery occlusion in their left eye.

Description of Cases:
A 43-year-old female with a history of concurrent venous stasis retinopathy and MOGAD-ON (diagnosed six years prior and managed with long-term immunosuppression and oral steroids) in her right eye presented with a new five-hour history of pain and blurry vision in her left eye. Examination of the left eye revealed a visual acuity (VA) of 20/80, a cherry red spot (without a visualized embolus), and a new generalized visual field defect. Ocular coherence tomography (OCT) revealed diffuse retinal edema in her left eye with inner layer hyper-reflectivity. An MRI orbits and brain with contrast showed enhancement of the anterior part of the intraorbital optic nerve near its insertion into the left globe. She was referred to stroke neurology and continued oral steroid therapy. At six-month follow-up, her VA had markedly improved to 20/30 in her left eye, and she had stable OCT parameters.

Conclusions, including unique features of the case:
This unique case demonstrates sequential venous stasis retinopathy and central retinal artery occlusion in opposite eyes, which were associated with recurrent MOG-ON flares, where inflammation co-local with retinal vasculature may have facilitated retinal venous stasis and artery occlusion. Unlike with their prior VSR presentation, the patient was on long-term oral steroid therapy, which likely reduced the severity of their MOGAD-ON recurrence and associated CRAO visual outcome. This case supports the use of steroids in a patient with a CRAO that is associated with MOGAD. Further research is needed to better elucidate the role of MOGAD in vascular occlusive events and whether this relationship may be arteritic in etiology.

References: None provided.

Keywords: Retina, Optic neuritis, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Smoke, Not Smoking, As A Risk Factor Triggering Conversion in Leber's Hereditary Optic Neuropathy

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Introduction:
Leber's hereditary optic neuropathy (LHON) is a maternally inherited mitochondrial disorder characterized by oxidative stress, leading to retinal ganglion cell degeneration. LHON is classified into Type I, typically converting around age 20, and Type II, which often develops after age 40 and is more often associated with environmental factors like smoke exposure.

Description of Cases:
We present four cases of LHON carriers from the Bay Area, California, who were exposed to wildfire smoke and experienced vision loss within 3 to 6 weeks. All had a family history of LHON and reported rapid, bilateral, painless vision loss, with baseline vision of 20/20 prior to exposure. The visual loss was, similar to that previously reported in both eyes respect to timing at trigger. Case I showed a 33-year-old female carrier (m.11778 G>A/MT-ND4) with decreased VA (20/200, 20/20), RNFL (107µm,122 µm), bilateral VF scotomas (-5dB). Case II a 45-year-old male converted carrier (m.3460G>A/MT-ND1), VA (20/200, 20/400), VF (-5 dB, -9dB) Case III a 26-year-old female carrier (m.11778 G>A/MT-ND4) decreased VA (20/25, 20/30), RNFL (107 µm, 106µm) bilateral central VF scotomas (-1 dB, -2 dB). Case IV a 60-year-old male carrier (m.4171>C/MT-ND1), VA (20/100, 20/20), VF (-17 dB, -9 dB), RNFL (74µm, 70µm).

Conclusions, including unique features of the case:
Our findings suggest that environmental smoke exposure may act as a trigger for both Type I and Type II LHON, with a lag time of approximately one month before vision loss occurs. Clinicians should advise LHON carriers to minimize exposure to all forms of smoke as part of their disease management strategy. Larger cohort studies are required to confirm these findings and assess the broader impact of environmental smoke on LHON progression.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: no

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21

An Atypical Case of Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD) Optic Neuritis Following COVID-19 Infection

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Introduction:
Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is an autoimmune demyelinating disease usually associated with optic neuritis (ON) which is often relapsing. COVID-19 has been implicated as a neurotoxic trigger for autoimmune demyelinating injuries including MOGAD-ON.

Description of Cases:
A 67-year-old female presented with moderate painless vision loss (20/20 OD; 20/50 OS) progressing over 2 weeks, an afferent pupillary defect (APD) and mild optic disc edema with peripapillary cotton wool spots in the left eye. Six weeks prior, she had COVID-19 with upper respiratory symptoms and frontal headaches. Inflammatory markers were unremarkable, and she had no microvascular risk factors. Visual field (VF) testing showed a predominantly inferotemporal visual field defect OS. OCT showed mild edema OS and bilateral ganglion cell thinning. Prior non-contrast MRI showed no optic nerve T2 hyperintensity. She received two days of empiric high-dose steroids for possible giant cell arteritis (GCA) pending temporal artery biopsy which was negative. Three weeks later (5 weeks after vision loss), her vision improved (OS 20/40) with trace APD, no residual disc edema and progression of ganglion cell thinning on OCT. MRI Orbits with gadolinium showed longitudinally extensive left optic nerve enhancement. MOG IgG was positive at 1:1000 titer. The patient deferred further steroid treatment given vision improvement and prior side effects. On examination at both 3 and 7 months after vision loss, her vision improved (20/25 OU) and she had temporal disc pallor OS with ganglion cell thinning.

Conclusions, including unique features of the case:
Infectious agents like COVID-19 frequently cause bilateral cases of MOGAD-ON with moderate to severe disc edema. Unilateral presentations of MOGAD optic neuritis with mild disc edema, such as this case, suggest a different pathophysiology. Although MOGAD-ON is a relapsing condition strongly associated with eye pain and often steroid dependent, this case highlights our evolving understanding of its clinical characteristics and treatment responses.

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

Financial Disclosures: Mohammed Mehdi Shahid; Natalie Brossard Barbosa; Zoë Williams: I was a site principal investigator for the QRK207 trial

Grant Support: None.

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22

Intraocular Hemorrhage as a Complication of Empiric Thrombolysis in Patients Misdiagnosed as Having Central Retinal Artery Occlusion (CRAO)

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Introduction:
Diagnosis of acute CRAO is commonly delayed in emergency departments (ED). Alternatives to ocular funduscopic examination, including point-of-care-ultrasound (POCUS) to rule-out vitreous hemorrhage and retinal detachment as causes of acute vision loss are often used in EDs prior to stroke work-up, sometimes with subsequent empiric thrombolysis treatment. We describe two cases of intraocular hemorrhage following intravenous thrombolysis in the ED for presumed, but ultimately misdiagnosed CRAO.

Description of Cases:
Case 1 A 65-year-old woman presented to an ED within 3 hours of sudden painless vision loss OS. Pupils were normal and no fundus examination was performed. POCUS and head-CT were reportedly normal. She was treated for presumed CRAO with IV-alteplase @4.5 hours. Vision worsened within 30 minutes of thrombolysis. Patient was transferred and vision was hand-motion OS, with a large horseshoe tear and vitreous hemorrhage, without CRAO. Case 2 A 51-year-old man presented to an ED within one hour of sudden painless vision loss OD. Head-CT was read as unremarkable. He was treated for presumed CRAO with IV-tenecteplase @98 minutes. Vision immediately worsened with right eye pain from ocular hypertension (84mmHg). Patient was transferred and vision was light-perception, with dense vitreous/anterior chamber hemorrhage. Review of the pre-tenecteplase head-CT showed focal hyperdensity in the right retina consistent with spontaneous hemorrhage (initial vision loss). Limited retinal examination during pars-plana vitrectomy showed fibrotic bands in the posterior pole and possible retinal vasculitis, without CRAO.

Conclusions, including unique features of the case:
Two patients developed severe intraocular hemorrhage after receiving IV-thrombolysis for presumed CRAO. Both patients had been misdiagnosed in an ED, one despite POCUS, and should not have received thrombolysis. We identified 15 cases where thrombolysis given for stroke, cardiac ischemia, pulmonary embolus, or CRAO resulted in intraocular hemorrhage. Five patients had pre-existing retinal conditions that bled, emphasizing that thrombolysis for CRAO should never be administered without confirmation of CRAO causing vision loss.

References: Chorich LJ, Derick RJ, Chambers RB, et al. Hemorrhagic ocular complications associated with the use of systemic thrombolytic agents. Ophthalmology. 1998;105(3):428-431. doi:10.1016/S0161-6420(98)93023-8

Keywords: Vascular disorders, Retina, Stroke

Financial Disclosures: Daniel Adamkiewicz; Christian Leal; Sruthi Arepalli; Kevin Ferenchak; Etienne Bénard-Séguin; Nancy Newman: Consultant for GenSight, Chiesi, Neurophth (all involved with the treatment of Leber hereditary optic neuropathy. Research support as PI to my institution from GenSight for clinical trials.; Valérie Biousse: Consultant for Topcon which commercializes fundus cameras. The current research is completely independent from Topcon and is not funded by the company.

Grant Support: None.

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23

A Case of Retinal Migraine Exacerbated by Temporomandibular Joint Dysfunction

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Introduction:
Retinal migraine is a rare form of migraine involving transient monocular visual disturbances, such as scotomas or temporary blindness, often followed by headaches. The exact mechanisms remain unclear, with proposed theories including vasospasm, ischemia, and trigeminovascular involvement [1]. Previous studies have indicated an increased risk for migraine with temporomandibular joint (TMJ) dysfunction, and suggest that adequate treatment of TMJ may serve as prophylactic migraine treatment [2], [3]. However, this remains understudied in the literature.

Description of Cases:
A 37-year-old female presented with persistent monocular visual disturbances without associated headaches. On initial presentation, she had normal structural eye exams and negative imaging studies which ruled out other potential etiologies including demyelinating disease, compressive lesions, or optic neuritis. Over two years, her symptoms worsened despite treatment with verapamil, erenumab (Aimovig), and nonpharmacologic interventions, developing facial and jaw pain related to TMJ dysfunction. Imaging confirmed mandibular hypoplasia and TMJ misalignment, which led to surgical intervention. Post-surgery, her facial pain and migraine frequency significantly decreased, and the patient was able to manage her residual symptoms with carbamazepine. This highlights the role TMJ dysfunction played in exacerbating retinal migraine and suggests that retinal migraine aura can be suppressed and provide relief from retinal migraine attacks.

Conclusions, including unique features of the case:
This case demonstrates the complex interplay between retinal migraine, vascular dysregulation, and mechanical triggers like TMJ dysfunction. The trigeminal thalamic occipital cortex pathway is presumed to be involved in this patient's migraine. The patient's partial response to verapamil and erenumab, successful response to carbamazepine, and notable improvement after TMJ surgery suggest a central acting mechanism for both her aura and her pain. Ultimately, a multidisciplinary approach addressing both vascular and mechanical components proved essential. Further investigation into the role of structural abnormalities in retinal migraine is needed to better formulate tailored intervention and treatment.

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Keywords: Retina, High intracranial pressure/headache, Visual fields, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Hemorrhagic Stroke Associated With Intravenous Tissue Plasminogen Activator In A Patient Receiving Adjuvant Hyperbaric Oxygen For The Treatment Of Central Retinal Artery Occlusion

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Introduction:
Central retinal artery occlusion (CRAO) is an ophthalmic emergency equivalent to cerebral ischemic stroke. Current AHA/ASA guidelines suggest intravenous (IV) tissue plasminogen activator (tPA) may be an effective treatment for CRAO (1). To our knowledge, there are no published reports of intracranial hemorrhage (ICH) following IV-tPA for CRAO. We report the first case of ICH in a patient treated with IV-tPA and adjuvant hyperbaric oxygen (HBO) for CRAO.

Description of Cases:
A 60-year-old male with a history of ischemic stroke 3 years prior was diagnosed with CRAO following one hour of sudden, painless vision loss in his right eye. Visual acuity on admission was hand motion (HM). Head CT demonstrated old right middle cerebral artery (MCA) stroke, but no acute ICH. IV-tPA was administered 148 minutes after symptom onset. A standardized protocol of twice daily, 90-minute HBO treatments was initiated. Roughly 90 minutes after IV-tPA administration and 51 minutes into HBO therapy, he developed a severe headache. Emergent head CT after HBO decompression revealed a large right hemispheric cerebral ICH. Despite inpatient rehabilitation, he continued to have limited left upper extremity function. Visual acuity remained HM.

Conclusions, including unique features of the case:
While IV-tPA is currently considered a safe treatment for CRAO in eligible patients, prospective data are not yet published. A limited number of studies suggest no increased risk when treating myocardial infarction or ischemic stroke with IV-tPA+HBO, but this has not been studied prospectively in CRAO (2). Although the ICH occurred within an area of previous infarct, only a prior infarct within 3 months is a tPA contraindication (3). While IV-tPA is endorsed by the AHA/ASA as a low-risk measure that improves outcomes in CRAO, further studies are needed to clarify the safety and efficacy of IV-tPA+HBO for CRAO, particularly in patients with a history of ischemic stroke.

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Keywords: Stroke, Vascular disorders, Optic neuropathy, Retina

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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A Rare Presentation of Desmoplastic Small Round Cell Tumor Resulting in Post-Operative Vascular Induced Optic Atrophy

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Introduction:
Desmoplastic small round cell tumor (DSRCT) is an uncommon neoplastic sarcoma that occurs more frequently in young males and most commonly in the abdominal region. We report a unique case of intracranial desmoplastic small round cell tumor that resulted in bilateral optic atrophy following resection.

Description of Cases:
A 9-year-old female presented to the emergency department with headaches, emesis, and altered mental status. CT imaging of the brain demonstrated a 6.5cm x 4.7cm x 4.5cm mass in the left medial frontal lobe. The patient underwent left frontal craniotomy with gross total resection of the lesion; pathological analysis revealed high grade small round cell sarcoma with increased mitotic activity, necrosis, lack of normal neuropil, compact nests and Homer Wright rosettes. The mass was highly vascularized and profusely bled during resection; a large branch of the anterior cerebral artery required coagulation. One month following resection, the patient began proton beam radiation therapy. Two weeks after beginning radiation treatment, the patient noticed a decline in vision and memory. Exam demonstrated bilateral visual acuity of 20/200, moderate dyschromatopsia, bilateral central scotoma, and bilateral temporal optic nerve atrophy.

Conclusions, including unique features of the case:
Due to the rarity of DSRCT as well as the uncommon intracranial presentation of DSRCT in a pediatric female, the presented case of vision loss is unique. Although the differential diagnosis for the patient's presentation of optic atrophy included pre-operative elevated intracranial pressure, side effects of radiation therapy, and malignancy recurrence, vascular insult was found to be the most probable diagnosis given that the anterior cerebral artery, which typically supplies the superior group of vessels that perfuse the optic chiasm, required intraoperative coagulation during mass resection. DSRCT has been observed with hemorrhagic, necrotic, and degenerative changes; vascular insult of the anterior cerebral artery during intracranial resection provides a unique anatomic correlate for bilateral optic atrophy.

References: None provided.

Keywords: Vascular disorders, Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Spontaneous Visual Recovery in Toxic and Nutritional Optic Neuropathy After Years of Vision Loss

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Introduction:
Toxic and nutritional optic neuropathy can cause permanent visual impairment. This case report describes a rare instance of substantial spontaneous visual recovery in a patient with toxic and nutritional optic neuropathy marked by temporal nerve atrophy and central and binasal visual field losses.

Description of Cases:
We present a 39-year-old female with multiple risk factors for toxic and nutritional optic neuropathy, including history of bariatric surgery with possible vitamin deficiency, alcoholism, and exposure to metronidazole and disulfiram. She originally presented with reduced visual acuity (20/400) and progressive central and nasal visual field deficits. Temporal retinal nerve fiber atrophy was appreciated on imaging. As advised, she stopped taking metronidazole and disulfiram and appropriate vitamins were repleted. Yet for several years, as she intermittently relapsed with alcohol abuse, her vision continued to deteriorate. Remarkably however, after a 5-year period of sobriety, she experienced an impressive visual recovery. Her visual acuity improved to 20/15 with near-complete restoration of visual fields, except for slight central depression and loss of color discrimination.

Conclusions, including unique features of the case:
The patient's unexpected improvement suggests dormant nerve fibers capable of regeneration or reactivation. This case highlights neural plasticity in the visual system and underscores the importance of continued monitoring and reassessment in optic neuropathy cases. The dramatic improvement of visual acuity and fields, despite stable optic atrophy, provides valuable insights into neural recovery mechanisms.

References: None provided.

Keywords: Optic neuropathy, Optic nerve trauma and treatment, Visual fields, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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27

Optic Nerve Metastasis from Non-Small Cell Lung Cancer Leading to Vision Loss

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Introduction:
We present a rare case of intra-orbital optic nerve involvement with concurrent choroid involvement, without an obvious choroidal mass, from primary non-small cell lung cancer. Our objective is to better define the presentation and complications of optic nerve metastasis, aiming to raise awareness and improve understanding of this unique condition.

Description of Cases:
A 67-year-old male with a history of non-small cell lung cancer, diagnosed approximately two years prior, had known metastases to the choroid treated with external beam radiation at that time. He presented with one week of new eye pain and progressive vision loss over the past year, with no light perception (NLP) at presentation. Initial work-up revealed neovascular glaucoma, but no intraocular masses were identified. At the patient's request, enucleation was performed to alleviate pain. Notably, post-enucleation pathology confirmed extensive metastatic involvement of the optic nerve, including the optic nerve sheath, as well as the choroid, retina, and sclera.

Conclusions, including unique features of the case:
This presentation highlights a rare case of intra-orbital optic nerve involvement with concurrent choroidal involvement from primary non-small cell lung cancer. Notably, our patient experienced gradual vision loss without an obvious mass on fundoscopic exam or B-scan imaging. This differs from other reported cases, where patients typically presented with choroidal or optic disc lesions, retinal hemorrhage, or papilledema. While metastases are the most common adult intraocular tumors, optic nerve involvement remains relatively rare. Additionally, optic nerve metastatic disease may indicate a poorer prognosis due to its association with central nervous system involvement.

References: None provided.

Keywords: Neuroimaging, Tumors, Orbit

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Whole Genome Sequencing of 10 Families with Optic Disc Drusen

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Introduction:
Optic disc drusen (ODD) are deposits in the optic nerve head that affects 2% of the general population. A genetic predisposition is suspected, with family studies suggesting an autosomal dominant inheritance pattern with incomplete penetrance. In cases of seemingly sporadic ODD, screening of apparently healthy family members revealed that nearly two-thirds were familial. The prevalence is also higher in certain genetic disorders, such as pseudoxanthoma elasticum and retinitis pigmentosa. This study aimed to identify candidate genes involved in the development of ODD.

Description of Cases:
We included 10 families, each with two to five affected members. All participants underwent OCT imaging of the optic nerve head, and blood samples were collected for genetic analysis. DNA was sequenced using next-generation sequencing on the Illumina NovaSeq 6000 platform. Single nucleotide variants (SNVs) were identified with the Genome Analysis Toolkit (GATK) and filtered in VarSeq using a population frequency threshold of 1%. For families with more than two affected members, we conducted a genome-wide analysis. For families with only two affected members, we used gene panels linked to potential ODD pathogenesis, together with a panel including variants identified in the genome-wide analysis. Variants with an ACMG classification score of two or less were excluded, resulting in the identification of nine variants across eight genes: ABCC6, DDX50, TREX1, PLCB4, PTPRQ, LBR, RP1L1, and KRT3. Of particular interest is ABCC6, due to its role in inhibiting ectopic calcification.

Conclusions, including unique features of the case:
We identified a list of candidate genes associated to ODD after applying manual filter criteria. The genes show a wide range of functions and are associated with different disorders with ABCC6 being of particular interest. Studies including larger ODD families will be necessary to identify robust candidate genes.

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Keywords: Optic neuropathy, Genetic disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Case Series: Two Patients Using Semaglutide Presenting with Bilateral NAION

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Introduction:
Nonarteritic anterior ischemic optic neuropathy (NAION) is characterized by acute painless vision loss, optic disc edema, and new visual field (VF) defects, primarily affecting adults over 50. Bilateral involvement may occur, typically several months apart. We present two cases of bilateral NAION in patients who recently started or increased their semaglutide dosage.

Description of Cases:
Case 1: A 64-year-old male presented with acute, painless right superior VF loss. His only recent medication change was starting semaglutide seven months prior. Visual acuity was 20/50 OD and 20/20 OS. An afferent pupillary defect (APD) was noted OD. Fundoscopic examination revealed optic disc edema with inferior predominance OD > OS. VF testing showed a superior altitudinal defect OD and subtle superior defect OS respecting horizontal midline. Optical coherence tomography (OCT) indicated average retinal nerve fiber layer (RNFL) thickening OD > OS. ESR and CRP were normal, and contrast-enhanced MRI showed no optic nerve enhancement. Lumbar puncture revealed a slightly elevated opening pressure of 26 cm H2O, which is atypically associated with marked disc swelling or altitudinal VF defects. CSF analysis and infectious/inflammatory workup were unrevealing. Case 2: A 46-year-old male presented with acute, painless vision loss OS two months after increasing his semaglutide dose to 2mg/week. Visual acuity was 20/20 OU, and an APD was noted OS. Fundoscopic examination showed superior sectoral disc edema OD and superior > inferior edema OS. OCT demonstrated RNFL thickening OS > OD and VF testing showed bilateral inferior altitudinal defects OS > OD. Contrast-enhanced MRI showed no optic nerve enhancement, and lumbar puncture showed normal opening pressure.

Conclusions, including unique features of the case:
We present two patients, one under 50, using or recently increasing semaglutide dosage, presenting with bilateral NAION. Given the recently reported association between semaglutide use and NAION, this atypical bilateral presentation suggests the possibility of more severe presentation in patients using this medication.

References: None provided.

Keywords: Stroke, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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A Complicated Case of Late-Onset Leber's Hereditary Optic Neuropathy

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Introduction:
Leber's Hereditary Optic Neuropathy (LHON) is a rare mitochondrial disorder typically affecting young adults, leading to rapid, bilateral vision loss. However, cases of late-onset LHON are uncommon and present unique diagnostic challenges, especially in patients with pre-existing ophthalmic conditions. We report the case of an elderly patient diagnosed with LHON after already experiencing significant vision loss due to unrelated ocular pathology.

Description of Cases:
A 79-year-old man presented with a subacute decline in vision over days to weeks in both eyes. He has a complicated ocular history with chronic uveitis since childhood managed with intermittent steroids. About 18 months prior, he experienced recurrent bouts of intraocular pressure elevation in the right eye only, which was eventually managed with a glaucoma shunt about six months later. The left eye did not experience pressure elevation. He noticed vision continued to decline over the next six months in both eyes. He underwent bilateral cataract extraction without improvement. Ophthalmic exam revealed bilateral optic disc pallor and retinal nerve fiber layer atrophy with preserved outer retina. ERG was grossly normal. MRI was unrevealing. Lab work including MOG, NMO, VDRL, paraneoplastic panel were all negative. Mitochondrial genetic testing was obtained and found a mutation of mt-ND4 11778 associated with Leber's Hereditary Optic Neuropathy. The patient was already started on idebenone.

Conclusions, including unique features of the case:
This case illustrates that Leber's Hereditary Optic Neuropathy can cause vision loss even in older age, and should be considered in patient's presenting with sudden vision loss. Exam and work-up when other ocular co-morbidities are present complicate the work-up and can delay obtaining diagnosis.

References: None provided.

Keywords: Genetic disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Age-related changes in optic disc drusen visibility and their anatomical correlates

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Introduction:
The visibility of optic disc drusen (ODD) increases with age, yet the anatomical changes related to this finding has not been established. Enhanced-depth imaging optical coherence tomography (EDI-OCT) provides a detailed imaging modality to evaluate the anatomical location of ODD within the optic nerve head. The aim of this study was to determine the factors contributing to the age-related increased visibility of ODD using EDI-OCT.

Description of Cases:
A retrospective observational study was conducted on patients with an ODD diagnosis confirmed and systematically phenotyped using EDI-OCT from November 2017 to December 2023. Data on ophthalmoscopic ODD visibility, OCT based anatomical location, with superficial ODD being above and deep ODD being below Bruch's Membrane Opening (BMO), peripapillary retinal nerve fiber layer (RNFL) thickness and macular ganglion cell layer (GCL) volume were collected and analyzed.

Conclusions, including unique features of the case:
A total of 411 eyes were included for analysis. ODD visibility increased significantly with age, with 6 percent being visible in the first decade of life and 90 percent being visible in patients over 70 years of age. The anatomical location of ODD remained stable throughout life. RNFL thickness exhibited an age-related decline, with a mean thickness of 153 µm in the first decade decreasing to 70 µm in patients over 70 years of age. In 17 percent of cases, ODD were classified as buried on fundus photography despite being superficial on OCT. Our study revealed that with age, ODD become more visible while their anatomical location in the optic nerve head remains stable and the peripapillary RNFL thickness decreases. This suggests that RNFL thinning is the primary contributor to the age-related increased ODD visibility.

References: None provided.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Post-operative Vision Loss in Shoulder Surgery: A Case Series and Review of the Literature

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Introduction:
Post-operative vision loss (POVL) after shoulder surgery is a serious condition that can result in permanent vision loss, visual field deficits, and/or visual disturbances. We present a case series of POVL after shoulder surgery and provide a review of the literature. In addition, we propose an alternate form of eye protection during shoulder surgery to avoid inadvertent pressure on the globe. We hope to promote provider and patient awareness of this infrequent yet devastating complication.

Description of Cases:
We present three cases of post-operative vision loss (POVL) after shoulder surgery in the beach chair position and propose a simple preventative intervention. Our first patient underwent right arthroscopic rotator cuff repair. The patient's eyes were protected by goggles, and he remained normotensive. However, he developed bilateral POVL with visual field (VF) deficits and abnormal electroretinogram (ERG). Our second patient underwent a left total shoulder arthroplasty. There was no intraoperative hemodynamic instability (IOHI) and no mention of eye protection. He developed POVL OS. Our third patient underwent a right arthroscopic rotator cuff repair. Protective eye goggles were used, and there was no IOHI. Post-operative vision loss OS occurred with a macular-sparing central retinal artery occlusion. In all three cases, we believe that the eye goggles and head positioning with tight padded head straps could cause inadvertent compression and ocular ischemia. Although POVL is likely multifactorial, we propose the use of soft foam eye protection that we use in retina surgery and a more relaxed yet secure padded head strap to decrease the risk of POVL.

Conclusions, including unique features of the case:
Post-operative vision loss after shoulder surgery is rare and likely multifactorial. However, it is important to minimize risks and optimize patient positioning and eye protection to promote patient safety and favorable outcomes.

References: None provided.

Keywords: Optic neuropathy, Retina, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease, Vascular disorders, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Progression Of Amaurosis Fugax To Retinal Artery Occlusion With Anterior Migration Of Retrobulbar "Spot Sign"

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Introduction:
Orbital ultrasound (US) and color Doppler imaging (CDI) are useful in the evaluation of sudden monocular vision loss, providing information on etiology which may guide management. We present two cases of amaurosis fugax progressing to retinal artery occlusion (RAO) associated with migration of a hyperechoic particle within the central retinal artery (CRA) and altered vascular dynamics found on US with CDI.

Description of Cases:
Both patients presented with amaurosis fugax and US with CDI revealed a hyperechoic particle 2.8 mm from the optic nerve head. Patient 1 was found to have severe aortic stenosis and a thoracic aortic aneurysm and was managed with dual antiplatelet therapy (DAPT) while awaiting evaluation for cardiothoracic surgical repair. Ten days later, Patient 1 represented with a central RAO, and repeat US with CDI showed 1.0 mm of anterior migration with reduced CRA blood velocity and an increased resistivity index. Patient 2 was managed with DAPT and oral corticosteroids; symptoms recurred during steroid taper, necessitating a prolonged course. Systemic complications required reduction of steroid dosing, and the patient developed a branch RAO six months after initial presentation. Repeat US with CDI revealed 0.9 mm of anterior migration of the embolus, and increased CRA blood velocity and resistivity index. Thrombolysis and resumption of steroids did not result in visual improvement.

Conclusions, including unique features of the case:
Anterior migration of a hyperechoic particle on US and CDI parameters may correlate with clinical progression of embolic retinal ischemia. Visualization of an embolus may predict nonresponse to coagulation-based treatment. These findings suggest unique implications of imaging on disease mechanism, course, and potential future treatments.

References: None provided.

Keywords: Vascular disorders, Retina, Stroke, Orbit/ocular pathology, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Resilient Pituicytoma: A 30-Year Journey

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Introduction:

Pituicytomas are rare tumors originating from the glial cells of the posterior pituitary, often misdiagnosed as pituitary adenomas, requiring histopathological confirmation 1,2 . These tumors typically present with pituitary dysfunction and vision loss 2,3 . While they can be effectively treated with resection, incomplete removal may lead to recurrence 4 . Here, we present a case of recurrent pituicytomas over 30 years, a duration not previously documented in the scientific literature.

Description of Cases:

An 82-year-old female with a history of recurrent pituicytoma presented due to rapidly progressive vision loss. She was first diagnosed with a pituicytoma in 1994 after experiencing several months of peripheral vision loss. The tumor recurred in 2007, presenting similarly, and required resection. In both instances, she achieved full visual recovery. In 2020, she underwent radiation therapy after the tumor was presumed to have returned, accompanied by vision loss, which subsequently improved. By 2022, she developed binocular diplopia, relieved with prisms, along with left vision loss. An exploratory surgery was performed, revealing no tumor but scar tissue, which was successfully removed. In 2024, she presented to our facility with rapidly progressive bilateral vision loss. An MRI revealed a newly enhancing large suprasellar tumor with mass effect on the optic chiasm, which had not been present on an MRI conducted five months earlier. She underwent endoscopic transsphenoidal resection of the mass, resulting in improved vision. Initially thought to be a pituitary adenoma on histopathology, a second opinion revealed findings consistent with pituicytoma recurrence.

Conclusions, including unique features of the case:

Although pituitary adenomas and pituicytomas are distinct entities histopathologically, their clinical and radiographic characteristics often overlap, leading to potential misdiagnosis. Reports of recurrent pituicytoma are rare in the scientific literature. Clinicians should be aware of this prolonged 30-year course marked by repeated recurrences of pituicytoma, as appropriate treatment can significantly enhance the prognosis for visual recovery.

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Keywords: Optic neuropathy, Neuroimaging, Tumors, Visual fields, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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35

Cotton Wool Spots in Classic Migraine: Is the Eye a Window to the Microangiopathic MRI Findings?

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Introduction:
White matter lesions are frequently observed in migraine as hyperintensities on MRI in the deep cerebral white matter or periventricular areas. These findings are thought to reflect small-vessel ischemia, microvascular dysfunction, or altered cerebral autoregulation. This case series examines the occurrence of retinal cotton wool spots in migraine patients and proposes a potential connection between these retinal findings and the cerebral white matter hyperintensities.

Description of Cases:
We describe three patients with a history of classic migraine who sought medical attention just after having a visual aura. Ophthalmic evaluations led to the recognition of a monocular scotoma on automated perimetry and cotton wool spots corresponding to the area of visual deficit. All three patients were female, under age of 40, without systemic vascular risk factors; evaluations did not identify a plausible explanation for the cotton wool spots or hypercoagulability. Subsequent testing of one patient showed resolution of the scotoma.

Conclusions, including unique features of the case:
Migraine is a diagnosis of exclusion when there are persistent neural or visual deficits. Our patients had monocular scotomas which occurred in temporal association with otherwise typical visual auras. Cotton wool spots in the retina, which signify localized small vessel-induced retinal ischemia, may provide insight into the microvascular cerebral pathology which when observed on MRI are often categorized as being non-specific. Prior reports of migraine-induced retinal ischemia have suggested vasospasm as culprit, but vasospasm would presumably tend to cause a larger region of retinal ischemia.

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Keywords: Retina, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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36

Acute worsening central and peripheral vision in patient with hereditary optic neuropathy ... 30 years after diagnosis.

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Introduction:
This case explores the diagnostic and management challenges associated with spontaneous cerebrospinal fluid (CSF) leaks in patients with no history of headaches in a setting of hereditary optic neuropathy.

Description of Cases:
A 44-year-old male with a history of type 1 diabetes mellitus (DMT1) and hypertension (HTN) and poor vision since childhood was evaluated for 2 years of worsening vision (from 20/40 OU to 20/200 OU). On exam, there was bilateral optic atrophy and cecocentral field defects, no RAPD. The history of DMT1 raised suspicion for Wolfram syndrome, however, this would not explain his more recent visual deterioration. He was asymptomatic otherwise. MRI head revealed evidence of intracranial hypotension (ICH) with diffuse pachymeningeal thickening and midline structure slumping as well as pituitary stalk thickening, raising concerns for infiltrative or inflammatory etiologies for which he tested negative. Lumbar puncture revealed an opening CSF pressure of 8 cm H2O and mildly elevated CSF protein. Cytology was negative. He then added postural headaches and was referred for neurosurgical repair. Spontaneous ICH (SICH) is an uncommon disorder that is often misdiagnosed due to its variable clinical manifestations, especially in the absence of postural headache. A case series by Horton and Fishman described two patients with visual field loss and worse central vision in the setting of SICH. The authors postulated that the visual field defects were likely related to compression or vascular congestion of the intracranial portions of the optic nerve.

Conclusions, including unique features of the case:
This case illustrates that SICH can be a cause of worsening vision. It can also cause pituitary stalk thickening (an underreported finding) which can also be seen associated with T1DM and visual field defects in other conditions such as germinoma, lymphoma or sarcoidosis making this case especially challenging. Collaboration with neurology, and neurosurgery is essential for comprehensive evaluation and management.

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Keywords: Optic neuropathy, Neuroimaging

Financial Disclosures: Natalie Brossard Barbosa; Zoë Williams: I was a site principal investigator for the QRK207 trial; Edward Margolin

Grant Support: None.

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Non-Arteritic Anterior Ischemic Optic Neuropathy In The Setting Of Glucagon-like Peptide-1 Agonist Use

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Introduction:
61-year-old male with history of well-controlled hyperlipidemia and BMI 26 presented to neuro-ophthalmology clinic for acute evaluation of unilateral optic disc edema. After recent initiation of Tirzepatide (5 weeks prior, for modest weight loss), he endorsed acute vision changes. He was found to have disc edema with peripapillary hemorrhages along with a contralateral disc-at-risk. The presumed diagnosis was an acute ischemic optic neuropathy in the setting of new Tirzepatide use.

Description of Cases:
The patient initially presented to the emergency room for subtle vision changes three weeks after starting the medication. He noted inferior visual field deficits along with some dyschromatopsia in that eye. On ROS, patient had been on the same medication and dosage for hyperlipidemia for six years. He had a borderline elevated hemoglobin a1c (5.7%) and no history of hypertension or OSA (formal testing completed). Neuroimaging did not demonstrate any acute pathology, and ESR/CPR were within normal limits (as was QuantiFERON, RPR). Patient endorsed 10-lb (4%) weight loss over the preceding five weeks, while on Tirzepatide. He was advised to discontinue the medication during this acute event.

Conclusions, including unique features of the case:
A large retrospective study by Hathaway, et al, brought to light the possible associations between semaglutide (Glucagon-like peptide-1/GLP-1 agonist) and NAION. As in this case with tirzepatide (another GLP-1 agonist), there were other possible confounding factors including patient being male, overweight with recent weight loss, and having hyperlipidemia. To our knowledge, this is the first case report regarding an association between Tirzepatide and NAION; however, it should be noted that the patient's disc-at-risk could have contributed to this presentation as well as the multiple other variables above. More work needs to be conducted to assess the relationship between the variety of GLP-1 agonists and NAION; this is particularly important as GLP-1 agonist use continues to rise.

References: Hathaway JT, Shah MP, Hathaway DB, Zekavat SM, Krasniqi D, Gittinger JW Jr, Cestari D, Mallery R, Abbasi B, Bouffard M, Chwalisz BK, Estrela T, Rizzo JF 3rd. Risk of Nonarteritic Anterior Ischemic Optic Neuropathy in Patients Prescribed Semaglutide. JAMA Ophthalmol. 2024 Aug 1;142(8):732-739. Mollan SP. Semaglutide and Nonarteritic Anterior Ischemic Optic Neuropathy. JAMA Ophthalmol. 2024 Aug 1;142(8):740-741. doi: 10.1001/jamaophthalmol.2024.2514. PMID: 38958953

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Three Cases of Nonarteritic Anterior Ischemic Optic Neuropathy in Patients Prescribed Semaglutide

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Introduction:
A recent study linked semaglutide to an increased risk of nonarteritic anterior ischemic optic neuropathy (NAION). Here we present three cases of NAION in patients prescribed semaglutide—two bilateral and one unilateral—who visited our neuro-ophthalmology clinic between April and September 2024.

Description of Cases:
All three patients were male, aged 55 to 76 years. Their medical histories included type 2 diabetes (2/3), well-controlled hypertension (3/3), hyperlipidemia (3/3), obesity (2/3), and sleep apnea (1/3). Each had received weekly subcutaneous semaglutide injections for at least seven months prior to symptom onset; one also took oral semaglutide for two years before switching to injections. One patient stopped semaglutide two months prior due to gastrointestinal side effects. All three denied symptoms of temporal arteritis or intracranial hypertension. Presenting symptoms included blurred vision (1/3) or spots/shadows in vision (2/3). Visual acuity was good (20/20 bilaterally in 2/3, 20/25 and 20/30 in 1/3), color vision was normal (3/3). A RPAD was noted in the symptomatic eyes (3/3). HVF showed bilateral (2/3) or unilateral (1/3) arcuate or altitudinal defects. Anterior segment exams were unremarkable (3/3). Fundus exams revealed bilateral optic disc edema (3/3) with bilateral (2/3) or unilateral (1/3) peripapillary hemorrhage. OCT confirmed RNFL swelling and retinal GCL loss corresponding to the visual field defects (3/3). All neuroimaging and laboratory tests were non-diagnostic, including contrast MRI brain/orbit (3/3), MRV or CTV (2/3), lumbar punctures with CSF studies (1/3), and blood work for inflammatory, autoimmune, and infectious panels (1/3). The overall impression was bilateral (2/3) or unilateral (1/3) NAION.

Conclusions, including unique features of the case:
The association between NAION and semaglutide is not well understood. Recent reports indicate that GLP-1 receptor expression in the optic nerve and increased sympathetic activity from GLP-1 RAs may impact optic nerve head perfusion, potentially raising the risk of NAION. Further studies are needed.

References: 1. Hathaway JT, Shah MP, Hathaway DB, Zekavat SM, Krasniqi D, Gittinger JW Jr, Cestari D, Mallery R, Abbasi B, Bouffard M, Chwalisz BK, Estrela T, Rizzo JF 3rd. Risk of Nonarteritic Anterior Ischemic Optic Neuropathy in Patients Prescribed Semaglutide. JAMA Ophthalmol. 2024 Aug 1;142(8):732-739. doi: 10.1001/jamaophthalmol.2024.2296. 2. Mollan SP. Semaglutide and Nonarteritic Anterior Ischemic Optic Neuropathy. JAMA Ophthalmol. 2024 Aug 1;142(8):740-741. doi: 10.1001/jamaophthalmol.2024.2514.

Keywords: Optic neuropathy, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: n/a

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Post-traumatic Intracranial Hypotension with Concurrent Bilateral Optic Disc Edema and Abducens Nerve Palsies

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Introduction:
Intracranial hypertension has many etiologies and is a known cause of ocular pathologies including papilledema, compressive optic neuropathy, and cranial nerve palsies. There are fewer reports of ophthalmological manifestations seen with intracranial hypotension.

Description of Cases:
A 27-year-old Asian female developed loss of vision and diplopia two months after significant blunt head trauma. CT Head without contrast revealed large, mixed density bilateral subdural hygromas. MRI brain/orbits with and without contrast did not have evidence of an acute stroke or hemorrhagic process, however bilateral optic nerve discs were protruded with distended optic nerve sheaths. Initial evaluation revealed a visual acuity of 20/400 in the right eye and light perception with an afferent pupillary defect in the left eye. She had bilateral abducens nerve palsies with 20 prism diopters of esotropia in primary gaze. Dilated funduscopic exam showed scattered intraretinal hemorrhages in both eyes with grade 4 and 5 optic disc edema in the right and left eyes, respectively. OCT studies were consistent with bilateral optic disc edema with no macular edema. She underwent a myelogram showing contrast extravasation at L3-L4 thought to reflect abnormal cerebrospinal fluid leakage as the likely source of her intracranial hypotension. She was treated with an epidural blood patch after which visual acuity improved to 20/70 in the right eye and hand motion in the left eye. Repeat evaluation showed ongoing grade 4 and 5 optic disc edema however there was notable improvement in the severity of optic disc protrusion after blood patching.

Conclusions, including unique features of the case:
While optic disc edema is most commonly seen in patients with intracranial hypertension, this is a case of significant bilateral optic disc edema in a patient with intracranial hypotension presumably from the compressive effect of cerebrospinal fluid along the bilateral optic nerve sheaths.

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Keywords: Optic nerve trauma and treatment, Orbit/ocular pathology, Trauma, Ocular motility, Retina

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Leukemic and Lymphomatous Optic Nerve Infiltration Treatment: A Case Series And Review Of The Literature

Emily Eng [1], Sachin Patel [1], Kristina Lin [1], Steve Braunstein [1], Siavash Assar [1], Michael Trainer [1], Rabih Hage [1], Marc Levin [1], Nailyn Rasool [1]

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Introduction:
Leukemic and lymphomatous optic nerve (ON) infiltration is a neuro-ophthalmic emergency that is difficult to treat due to rapid vision loss and devastating treatment complications. Treatment regimens are varied and have significant side effects. Studies report partial or unsuccessful treatment with chemotherapy alone due to poor penetration of the ON and necessitating treatment with radiation, the dose of which is often center and provider dependent. Side effects of radiation alone include optic neuropathy, orbital compartment syndrome, and leukoencephalopathy.

Description of Cases:
A retrospective review from 2019-2024 of patients with ON infiltration from leukemia or lymphoma at one institution was performed. Eight patients were identified, ranging from 13 to 81 years old with 14 affected eyes. Six patients had acute lymphoblastic leukemia (ALL), one had mantle cell lymphoma and one had diffuse-large B cell lymphoma. CSF cytology was positive in four patients. Pre-treatment visual acuities (VA) ranged from 20/20 to NLP. 14 eyes underwent fractionated ON radiation ranging from 8 to 30 Gy. Seven patients receiving radiation were pre-treated with high dose IV methylprednisolone (five to eight days). One patient received low-dose IV steroids. Three months post-treatment, VA improved in 75% (all ≥20/40) and remained stable in 25% of eyes treated with high dose IV steroids and radiation. Vision worsened in the patient treated with low-dose IV steroids and radiation.

Conclusions, including unique features of the case:
ON infiltration is a rare complication of cancer that represents worsening disease with poor prognosis. Given the high variability of success of treatments reported, we propose a protocol that includes pre-treatment with high dose IV methylprednisolone followed by radiotherapy and chemotherapy to preserve vision and reduce complications.

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Keywords: Chemotherapy and radiation injury, Optic neuropathy

Financial Disclosures: Emily Eng; Sachin Patel; Kristina Lin; Steve Braunstein; Siavash Assar; Michael Trainer; Rabih Hage; Marc Levin: Unrelated financial compensation as: consultant, Jazz Pharmaceuticals; consultant, Vanda Pharmaceuticals; royalties, University of California; Nailyn Rasool

Grant Support: None.

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Metastatic Melanoma Masquerading as Giant Cell Arteritis

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Introduction:
A 55-year-old Caucasian female presented to the emergency department with complete vision loss in the right eye preceded by one day of temporal and periocular headaches. She also reported fever, night sweats, and generalized fatigue

Description of Cases:
Physical exam revealed no light perception vision in the right eye with pallid disc edema concerning for anterior ischemic optic neuropathy. She had significantly elevated inflammatory markers, with erythrocyte sedimentation rate of 55 and C-reactive protein of 3.4 mg/dl. Magnetic resonance imaging (MRI) of the orbits demonstrated mild right retrobulbar optic nerve enhancement. Given concern for possible giant cell arteritis (GCA), she was started on empiric 1g/day methylprednisolone, and a temporal artery biopsy (TAB) was performed. Pathology of the arterial segment revealed mild lymphohistiocytic infiltration suggestive of possible early GCA, and she was continued on 1mg/kg/day oral prednisone. The neurology service obtained MRI of the spine to rule out demyelinating disease and imaging of the thoracic spine incidentally demonstrated the presence of a liver lesion felt to be benign. The patient returned to the emergency department two weeks later with subacute vision loss in the previously unaffected left eye to 20/200. Her exam revealed multiple foci of cream-colored subretinal lesions in the left macula with a normal left optic nerve, suggestive of paraneoplastic retinopathy. Upon further questioning, the patient reported a history of anal melanoma status post total resection with clean surgical margins and normal positron emission tomography scan within the previous year. Dedicated MRI liver protocol revealed multifocal hepatic lesions suggestive of metastatic disease, and a diagnosis of metastatic malignant melanoma was confirmed by needle biopsy

Conclusions, including unique features of the case:
Metastatic disease may closely mimic GCA based on symptom profile, presence of vision loss, and elevation of inflammatory markers; as such, a thorough oncologic history should be obtained on all patients presenting suspects for GCA

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Dural Tails Tell No Tales: A Case of Nonarteritic Anterior Ischemic Optic Neuropathy With Progressive Visual Loss and Concomitant Incidental Frontal Meningiomas

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Introduction:
Vision loss, whether static or progressive, raises an acute concern about preserving vision and preventing further visual deficits. A common cause of sudden vision loss in an older individual is anterior ischemic optic neuropathy (AION). One subset of AION is nonarteritic anterior ischemic optic neuropathy (NAION). This condition is characterized by painless monocular vision loss that occurs over hours to days. However, it is predominately a stable phenomenon with no progression. This case study highlights that the medical course can be progressive and even present with meningiomas near the orbit.

Description of Cases:
The case presentation is composed of a 66-year-old female with no vascular risk factors who experienced sudden, painless, monocular vision loss OD that worsened over two weeks. This was preceded by two weeks of scalp tenderness occurring two to three months before the onset of visual symptoms. Lab work including ESR and CRP were unremarkable. MRI Brain and Orbits was significant for a calcified dural-based 2 x 1.3 mass lesion in the right frontal lobe abutting the medial wall of the right orbit with an adjacent medial parasagittal 1.8 x 1.6 cm mass. Temporal artery biopsy (TAB) was negative. Neuro-ophthalmological exam was significant for disc edema OD with a decreased cup-to-disc ratio in the fellow eye. With an inability to completely rule out giant cell arteritis (GCA), treatment included high-dose steroids for three days followed by a steroid taper. The patient's vision stabilized upon subsequent evaluation with minimal benefit from steroid therapy.

Conclusions, including unique features of the case:
The case presented emphasizes that NAION can be a progressive process. Additionally, the case uniquely showcases two intracranial masses near the orbit without affecting the optic nerve. The case stresses that NAION should be on the differential for sudden vision loss with both a static and progressive disease course.

References: None provided.

Keywords: Optic neuropathy, Tumors, Neuroimaging, Orbit/ocular pathology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Association Between GLP-1 Agonist Use and NAION: A Two-Year Retrospective Chart Review at a Tertiary Eye Care Center

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Introduction:
Glucagon-like peptide-1 (GLP-1) agonists are increasingly being used as adjunct therapy in the treatment of type 2 diabetes mellitus and obesity. A potential association between the use of semaglutide and the development of non-arteritic ischemic optic neuropathy (NAION) was recently described (Rizzo). We seek to further characterize any potential association of GLP-1 agonist use and the development of NAION in this retrospective chart review.

Description of Cases:
An EPIC query using the terms “glucagon-like peptide-1” and “non-arteritic ischemic optic neuropathy” from September 2022 to September 2024 identified 30 patients. Clinical parameters including visual acuity, commonly used GLP-1 analog, other comorbid risk factors for NAION, glycosylated hemoglobin, body mass index, high-risk medication use, and Heidelberg Spectralis-OCT RNFL data were investigated. 18 eyes of 14 patients met the inclusion criteria for NAION following the initiation of a GLP-1 agonist. Of these, 4 patients experienced sequential NAION. The agent mostly commonly used was semaglutide. The average age was 58, with 9 males and 5 females, average body mass index (BMI) was 33.62 kg/m² and average glycosylated hemoglobin at the time of presentation was 7.25. An analysis of comorbid risk factors showed that 10 had hypertension, 13 had hyperlipidemia, 8 had obstructive sleep apnea, and 5 had coronary artery disease. Four patients were on high-risk medications: amiodarone (1), alpha-1 antagonist (1), and phosphodiesterase-5 (PDE-5) inhibitors (2). Additionally, one patient developed pancreatitis after starting a GLP-1 agonist. The average global retinal nerve fiber layer (RNFL) thickness at presentation was 152.4 μm.

Conclusions, including unique features of the case:
As the use of GLP-1 agonists continues to rise, there is a potential increased risk of developing non-arteritic anterior ischemic optic neuropathy (NAION) in individuals with high risk factors. To confirm these case-based findings and enhance the generalizability of the results, further research involving larger and more diverse study cohorts is required.

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Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: none

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A treatment dilemma in primary vitreoretinal lymphoma without extraocular involvement: case report

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Introduction:
Primary vitreoretinal lymphoma (PVRL) is a rare type of primary central nervous system lymphoma (PCNSL). 15–25% of patients with PCNSL present as vitreoretinal lymphoma. Treatment options include both local ocular therapy and systemic treatments. What approach to choose remains controversial as no current guidelines exist. We present a case that brings the treatment dilemma of whether patients with PVRL without extraocular involvement will need local versus systemic treatment.

Description of Cases:
59 y.o. Female who presented with insidious onset of blurry vision OU for the past 6 months associated with progressively worsening conjunctival hyperemia and inflammation of the OD and eventually the OS. She was diagnosed with cataracts and was started on Difluprednate. B-Scan ocular ultrasound showed OD: PVD with dense vitreous hemorrhage, OS: vitreous hemorrhage with tractional vitreous membranes, and Hemorrhagic retinal detachment with multiple areas of subretinal hemorrhages. MRI brain revealed OU uveitis with OS retinal detachment and subretinal hemorrhage with no other CNS involvement. CSF flow cytometry negative. OU diagnostic vitrectomy with pathology demonstrated diffuse large B-cell lymphoma in OD, no extraocular involvement was identified. She was started on intravitreous methotrexate therapy.

Conclusions, including unique features of the case:
PVRL mortality is between 9% and 81%. The prognosis depends, to a large extent, on whether the CNS is involved. The optimal treatment of PVRL remains controversial and undefined as there is limited data and no current guidelines exist. Studies report varying rates of effectiveness of local versus systemic treatments, with reasonable ocular remission rates but high rates of recurrence and CNS progression. Some experts believe that early systemic therapy for PVRL may prevent CNS progression, but Riemens et al showed no difference in CNS progression between patients treated with local ocular treatment or systemic treatment. Optimal treatment would include not only the eradication of the ocular disease but also prevention of CNS progression. Future studies are needed.

References: Riemens A., Bromberg J., Touitou V., Sobolewska B., Missotten T.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: none

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45

Reversible homonymous hemianopsia secondary to hyperglycemia-induced occipital lobe seizures

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Introduction:
Seizures involving the occipital lobe of the brain can lead to a variety of visual disturbances, including visual field defects, such as partial or complete loss of vision in certain areas. The nature and extent of the visual impairment depend on the specific areas of the occipital lobe affected during the seizure activity. We present a case of homonymous hemianopia as the presenting feature in a patient with undiagnosed diabetes mellitus causing occipital seizures.

Description of Cases:
A 60-year-old man with history of hypertension and hyperlipidemia presented to the clinic with 2 months of right sided vision loss with photopsias. Confrontational visual field testing revealed a macular-sparing right homonymous hemianopsia. 24-2 Humphrey Visual Field testing reaffirmed this finding. Fundus examination demonstrated lattice degeneration without retinal tears and myopic optic nerves. He was sent to the emergency department for stroke workup. Lab work was remarkable for blood sugar of 460. Glycated hemoglobin was >18.0. MRI brain demonstrated restricted diffusion with T2 hypointense signal within the affected left occipital lobe, favored to represent sequelae of occipital seizure. EEG was normal. He was diagnosed with type 2 diabetes mellitus during the hospitalization. At follow up visit 2 months later, patient reported subjective improvement in peripheral vision. 24-2 HVF demonstrated full field in left eye and mild persistent supero-temporal defect in right eye. Blood sugar levels was around 100 and repeat A1c was 6.5.

Conclusions, including unique features of the case:
1. Occipital lobe seizures are a rare manifestation of hyperglycemia, frequently resolving with treatment of underlying metabolic abnormalities though sometimes requiring short-term anti-epileptic drugs as well. 2. Visual symptoms, such as positive visual phenomena and hemianopsia, secondary to occipital seizures improve with treatment, sometimes resolving entirely. 3. Although rare, we should maintain seizures in the differential when patient has new homonymous hemianopsia.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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A Case of Visual Snow Following Systemic Ozone Therapy

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Introduction:
39-year-old female with a new history of migraines one year prior presented to the neuro-ophthalmology clinic for new visual disturbances. Upon further discussion, patient noted that the visual disturbances started and worsened throughout several treatments of intravenous, systemic ozone therapy (OT). Though OT is understudied, prior reports show visual and neurological side effects including cortical blindness, amnesia, dysphasia, and others. The patient's symptoms were akin to visual snow, a disorder of central visual processing resulting in a perturbed perception of constant bilateral whole-visual field flickering or pixelation.

Description of Cases:
In the neuro-ophthalmology clinic, patient had full Humphrey visual fields; vision was 20/20, and examination was unremarkable. Patient described countless transluscent spots throughout her vision, most apparent in bright light settings. Though patient endorsed a 1-year history of migraines, patient was 11 weeks pregnant and endorsed resolution of headaches with current pregnancy. Patient reports she started intravenous OT from a medical spa for symptoms of fatigue and stress; she received this treatment one to two times per week for a total of five weeks. Symptoms started after the second treatment and worsened with each subsequent treatment. Patient identified images of pixelation and visual snow as representative of her symptoms. MRI at onset of new migraines was within normal limits. Per patient preference, medications were deferred during pregnancy.

Conclusions, including unique features of the case:
Limited data exists on the side-effects and management of OT. While there is some literature supporting visual impact through "ozone-induced encephalopathy" or air emboli, no prior reports discuss visual snow. Our patient experienced acute onset of visual snow that has persisted during current pregnancy. This case presents a unique picture of a central visual processing dysfunction potentially related to an increasingly popular medical spa treatment option. More case reports and further data around this treatment option is crucial to educate patients and practitioners.

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Keywords: Non-organic visual disorders, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: N/a

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Bilateral Posterior Ischemic Optic Neuropathy as Sequela of Sepsis Induced Hypotension

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Introduction:
Posterior ischemic optic neuropathy (PION) is an optic neuropathy caused by ischemia to the retrobulbar portion of the optic nerve. We present a case of bilateral PION due to sepsis resulting in profound irreversible vision loss.

Description of Cases:
A 70 year-old-man with a past medical history of hypertension, diabetes, and prostate cancer presented to the emergency department with altered mental status. On presentation, he was in septic shock with a blood pressure of 83/45. Upon stabilization the patient reported acute bilateral vision loss. Visual acuity was no light perception in both eyes. Pupils were dilated and fixed. Further examination revealed an old central retinal artery occlusion in the right eye. Intraocular examination of the left eye was unremarkable. There was no significant optic nerve head edema in either eye. Diffusion-weighted magnetic resonance imaging demonstrated restricted diffusion within the optic nerves extending from the optic chiasm bilaterally and a new temporal lobe ischemic infarct. Laboratory studies revealed positive pseudomonas blood cultures, C-reactive protein of 176mg/L, and an erythrocyte sedimentation rate of 51mm/hr. Temporal artery biopsy was negative for arteritis. MOG and AQP4 antibody testing were also negative. Further infectious, rheumatologic, and toxicologic workup were unremarkable. The patient's painless, severe vision loss was ultimately attributed to non-arteritic posterior ischemic optic neuropathy in the setting of sepsis induced hypotension.

Conclusions, including unique features of the case:
Many bilateral cases of PION are related to systemic hypotension in the setting of spinal surgery. Here, we describe a rare but devastating case of bilateral non-arteritic posterior ischemic optic neuropathy in a patient with hypotension due to septic shock. While PION is a less common form of ischemic optic neuropathy, it may have devastating visual outcomes. This case demonstrates a unique etiology of bilateral non-arteritic PION and establishes septic shock as a potential risk factor for severe and irreversible blindness.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Seeing Clearly: Early Neuro-Ophthalmological Symptoms Can Delay the Diagnosis of Progressive Multifocal Leukoencephalopathy

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Introduction:
Progressive multifocal leukoencephalopathy (PML) is a rare and debilitating disease of the central nervous system (CNS) caused by the JC virus (JCV). PML is characterized by progressive neurological symptoms, multifocal lesions on MRI, and JCV DNA in the CNS (1). While anterior visual pathways are unaffected by JCV, visual symptoms are common in PML (2). Visual manifestations, especially early in the disease course, can often be misinterpreted for ocular pathologies and may delay PML diagnosis (3).

Description of Cases:
Clinical data from 127 PML patients were reviewed for neuro-ophthalmological symptoms documented at the time of their initial admission. 61/127 patients (48%), either self-reported or were found to have visual findings on physical exam, including visual field cuts (44%), blurred vision (33%), difficulty reading (16%), diplopia (21%), cortical visual impairment (12%), abnormal pupillary response (3%), cortical blindness (3%), nystagmus (36%), and impaired color perception (3%). MRI reports of the 127 patients were also reviewed. Lesions in the occipital lobes were reported in 52/127 (41%) patients, with 26/52 (50%) predominately in the occipitoparietal lobe and 15/52 (29%) predominately in the occipitotemporal lobe. Among the 61 patients, 20 (33%) had a delayed diagnosis of 4 months on average due to several factors including misinterpretation of visual symptoms as ocular pathologies and multiple consultations.

Conclusions, including unique features of the case:
No FDA-approved therapies are available for PML. Factors associated with survival include early detection of PML and reversal of underlying immunosuppression. Unfortunately, the broad constellation of neurological signs and symptoms, low incidence, and unfamiliarity among most physicians make PML diagnosis challenging. The median time from symptom onset to diagnosis is reported to be 74 days (4). Further delays in diagnosis may occur when only visual symptoms predominate early in the clinical course. In conclusion, early recognition of the visual manifestations of PML may contribute to earlier diagnosis and better prognosis.

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Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Demeylinating disease, Higher visual functions

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Cortical blindness as a migraine aura mimicker

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Introduction:
We report a case of bilateral occipital strokes in a young healthy patient presenting with vision loss in both eyes and headache.

Description of Cases:
A 38 year old male with a history of migraine with visual aura, asthma, and anxiety (recently started on a new SSRI) presenting with headache, tinnitus, and vision loss in both eyes. Humphrey visual field (24-2) notable for a left homonymous hemianopia and right superior quadrantanopia. CTA revealed severe stenosis of the right PCA and MRI head showed large bilateral PCA territory infarcts. History and neuroimaging findings raised suspicion for RCVS likely induced by SSRI use resulting in acute ischemic strokes. The patient was treated with a calcium channel blocker for 3 months. Repeat Humphrey visual fields 1 year later showed significant improvement from his initial fields though with persistent left superior quadrantanopia and right superior altitudinal-like defect. The patient received a second opinion at another institution with regard to the etiology of his stroke. TEE revealed a large PFO and bilateral lower extremity Dopplers were suggestive of May-Thurner syndrome. Given new concern for possible cardioembolic source of prior strokes, the patient ultimately underwent PFO closure.

Conclusions, including unique features of the case:
This is a case about a young healthy patient with a history of migraine with visual aura who presented with headache and visual disturbances which were very different from his usual aura. This case demonstrates the importance of collecting a detailed history and performing a careful neuro-opthalmological examination for informing next steps in work-up. This case serves as a reminder that we should have a high degree of clinical suspicion for causes of secondary headaches, particularly in patients with a prior history of primary headache disorder.

References: None provided.

Keywords: Higher visual functions, Neuroimaging, Stroke, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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The Varieties of Junctional Scotoma: 17 cases, a review, and a taxonomy

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Introduction:
The hemi-decussation at the optic chiasm creates the potential for crossed and uncrossed fibers to be affected in isolation or in various combinations of nerve, chiasm and tract damage, with patterns that reflect the retinotopic arrangement of axons. While the junctional scotoma and the junctional scotoma of Traquair are well known, more patterns are possible.

Description of Cases:
We present seventeen cases that illustrate the variety of complex field defects from this region and review the literature, to create a taxonomy of junctional visual field defects with nine possible categories. The first is the complete junction defect, with only a nasal hemifield left in one eye. In the classic junctional scotoma, a superior hemifield defect is accompanied by blindness, a central scotoma, or other patterns such as arcuate or altitudinal defects in the other eye. The less frequent atypical junctional scotoma involves the lower temporal hemifield more and has a higher frequency of non-compressive pathology. There are monocular temporal hemifield defects ('junctional scotoma of Traquair') and the rarer monocular nasal hemifield pattern. Highly asymmetric bitemporal defects with or without a central scotoma and the paradoxical junctional scotoma all can be explained by medial or lateral extension of the lesion causing the junctional scotoma of Traquair. The posterior junction defect occurs from combined damage to the optic chiasm and optic tract. Finally, there are other, more complex combinations.

Conclusions, including unique features of the case:
Recognizing these various junctional patterns is important clinically as, relative to bitemporal hemianopia, junctional field defects are being encountered more, yet they have the same localizing implications as bitemporal hemifield defects.

References: None provided.

Keywords: Neuroimaging, Perimetry, Tumors, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None

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Eagle Syndrome: A Secondary Cause Of Intracranial Hypertension

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Introduction:

Eagle Syndrome is a rare, poorly understood condition that presents with a multitude of nonspecific symptoms associated with an abnormally long or disfigured styloid process. Though the etiology is debatable, in Eagle syndrome there is compression of local neurovascular structures by the stylohyoid complex. The condition can result in various clinical presentations depending on the affected structures: cranial nerves (e.g. dysphagia, pharyngeal foreign body sensation, otalgia, orofacial and cervical pain), internal carotid artery (e.g. TIA, syncope, periorbital pain, vision disturbances), or internal jugular vein (e.g. headaches, vomiting, papilledema, tinnitus, dizziness).

Description of Cases:

A 30 year old female presented to the ED after being referred by her optometrist for evaluation of bilateral optic disc edema. She endorsed headaches, TVOs, and pulsatile tinnitus. Her ophthalmic exam was notable for 2+ disc edema and otherwise unremarkable. MRI/MRV revealed signs of increased intracranial pressure and a lumbar puncture was performed with elevated opening pressure of 38 cm H2O without CSF abnormalities. She was presumed to have idiopathic intracranial hypertension and discharged on acetazolamide. Her papilledema resolved and symptoms improved with therapy; however, she was unable to successfully taper off the medication. She was separately evaluated by ENT for symptoms of right neck pressure, throat pain and ear fullness. A CT neck showed bilateral abutment and slight compression of the jugular veins by elongated styloid processes. Patient was diagnosed with Eagle Syndrome and underwent subsequent bilateral styloidectomy with ENT, which resulted in significant decompression of adjacent neurovascular components and improvement of her symptoms, allowing her to successfully taper off acetazolamide.

Conclusions, including unique features of the case:

Eagle Syndrome can cause secondary intracranial hypertension by compression of jugular veins by styloid processes. Eagle syndrome should be considered when evaluating patients with elevated intracranial pressure especially in atypical cases without known risk factors for Idiopathic Intracranial Hypertension.

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Keywords: High intracranial pressure/headache, Skull base, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Earlier mortality for patients with Pseudotumor cerebri syndrome

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Introduction:

Pseudotumor cerebri syndrome (PTCS) is divided into primary idiopathic intracranial hypertension (IIH) or secondary (PTC related to medication, venous sinus disease, etc.). It is characterized by normal imaging, elevated intracranial pressure (ICP), and normal spinal fluid. PTCS has significant health and visual impacts. All-cause mortality in patients with IIH is reported as increased (1). The purpose of this study is to review the number and causes of death in our patients with PTCS.

Description of Cases:

Methods: A retrospective review was conducted of our center's database of 907 patients diagnosed with PTCS between 1999 and 2024. Inclusion criteria were based on established diagnostic criteria for PTCS. Data collection included patient age, sex, age at death, and time between diagnosis and death. Cause of death from death certificates or hospital records was reviewed. Results: Our 26 deceased patients included 24 females and 2 males. IIH had been diagnosed in 19 patients and PTC in 7. Comorbidities included obesity (18), depression/anxiety (17), migraines (17), hypertension (12), and diabetes (8). Causes of death included vascular disease (10), cancer (4), external (3), endocrine (2), suicide (2), respiratory disease (1), and hepatic disease (1). 3 deaths were of unknown cause. Average age of death for IIH was 50.4 ± 13.4 years and for PTC was 43.7 ± 16.4 years. Average time from diagnosis to death for IIH was 11.5 ± 7.7 years and for PTC was 9.14 ± 6.6 years.

Conclusions, including unique features of the case:

Patients with IIH are dying 27.1 years earlier and with PTC 33.8 years earlier than the national average of 77.52 (2). Circulatory disease-related deaths were more common in both IIH and PTC. Suicide rate was 0.22 % in IIH patients compared with national average of 0.0142%. (3) Further research is needed to analyze cause of death trends in patients with PTCS, especially the rate of suicide.

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

Financial Disclosures: Coby Soule; Cade ONeill; Jacqueline Shaia: JKS National Eye Institute: T32 EY024236 (Jacqueline Shaia) P30EY025585(BA-A), Research to Prevent Blindness (RPB) Challenge Grant, Cleveland Eye Bank Foundation Grant honorarium: Impact Education - Regeneron Pharmaceuticals, Inc. RPS reports personal fees from Apellis, Iveric Bio, Eyepoint, Regenxbio, Genentech, Bausch and Lomb, Zeiss, Alcon, and Regeneron, and research grants from Jannsen. KET: Alimera (consultant), Apellis (consultant), Bausch and Lomb (consultant), Eyepoint (consultant), Genentech (consultant, speaker's bureau), Iveric Bio (speaker's bureau), Regeneron (research), Regenxbio (research), Zeiss (research); Michael Newman; Judith Warner; Kathleen Digre

Grant Support: Supported in part by an unrestricted grant from Research to Prevent Blindness, Moran Eye Center, Department of Ophthalmology and Visual Sciences, University of Utah

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More Than Meets The Eye

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Introduction:
A 25-year-old male with morbid obesity (BMI 44) presented to an outside hospital with one month of blurred vision and bifrontal headaches. Teleneurology exam was normal. MRI brain without contrast was normal; MRV revealed a hypoplastic left transverse and sigmoid sinus. LP showed an OP of 40, WBC 30 (59% lymphocytes), RBC 9, glucose 16, and protein >200. Infectious, inflammatory, and neoplastic work-up was unrevealing. CT chest/abdomen/pelvis were negative. He was discharged with outpatient ophthalmology follow-up for presumed IIH vs chronic aseptic meningitis.

Description of Cases:
Two weeks later, ophthalmology observed bilateral grade 3 papilledema. Repeat LP demonstrated an OP of 67 cm H20, WBC 31 (monocytes 79%), RBC 3, glucose 3, and protein >200. MRI brain with/without contrast noted optic nerve sheath fluid, an empty sella, and leptomeningeal enhancement, thought to be sequela of LP vs aseptic meningitis. An area of cerebellar enhancement was interpreted as venous infarct from elevated pressure. He underwent a VP shunt and right optic nerve sheath fenestration by outside providers. One month later, he presented to our institution with neck stiffness, confusion, imbalance, urinary retention, and weight loss (30 pounds). Exam showed decreased grip strength, right upper extremity dysmetria, and a T1 sensory level. Toes were up-going. MRI spine revealed disseminated nodular enhancement throughout the leptomeninges. CSF cytology showed clusters of atypical cells. Biopsy of an intradural lumbar lesion revealed WHO Grade 4 medulloblastoma. The patient was treated with whole brain and spine radiation, followed by Packer protocol.

Conclusions, including unique features of the case:
1. It is rare for medulloblastoma to present in adults (0.6 per one million people per year). 2. There were several issues of anchoring and confirmation bias. 3. Initially negative cytology can be falsely reassuring. Repeat LPs may be required, as sensitivity increases from 60% to 90% after the second sample. Biopsies may be appropriate even with negative cytology.

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Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Neuroimaging, Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: N/a

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Evaluating Long-term Outcomes of Venous Sinus Stenting in Idiopathic Intracranial Hypertension

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Introduction:
IIH (idiopathic intracranial hypertension) is a condition affecting young individuals, predominantly women. Studies have shown that venous sinus stenting (VSS) is effective in treating IIH-associated papilledema, but long-term outcomes are not well described. This study aimed to describe long-term benefit and safety of VSS in IIH.

Description of Cases:
Methods: A single-center retrospective chart review was performed for patients with IIH who underwent VSS between May 2015 and October 2021 with >36 months of follow-up. Data were collected pre-VSS and from two time points representing short and long duration measures: (1) within the first 12 months post-VSS, and (2) >36 months post-VSS. We evaluated the presence of headache, pulse-synchronous tinnitus, IIH-related medications, and need for additional procedures. Neuro-ophthalmic exam and testing including optical coherence tomography and visual fields were reviewed for patients at all three time points. VSS-related complications were also noted. Results: Of 81 patients who underwent VSS, 38 (47%) had >36 months follow-up. Median follow-up was 53 months (IQR 46-61). Median papilledema grade pre-VSS was 1 (IQR 0.3-3) with 25 patients (66%) having grade 1 papilledema or worse. At the most recent visit, median papilledema grade was 0 (IQR 0-0.5) and 22 patients (58%) were off all IIH medications. Ten patients (26%) underwent additional procedures after initial VSS, including repeat VSS, bariatric surgery, or ventriculoperitoneal shunt placement for any indication. Four patients (11%) underwent additional procedures for persistent or worsening papilledema. Complications within the first 12 months post-VSS were seen in 3 patients (8%) including pain, post-operative seizure, and femoral hematoma. A single patient (3%) had delayed stent thrombosis (non-occlusive), but no other delayed complications were noted in the cohort.

Conclusions, including unique features of the case:
This study offers longitudinal post-VSS follow-up on a relatively large IIH cohort. It echoes the findings of earlier smaller studies that VSS can offer a safe treatment option with sustained benefit.

References: None provided.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Interventional neuroradiology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Diagnosis and Etiologic Classification of Optic Tract Syndrome

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Introduction:
There is limited literature regarding the diagnosis of optic tract syndrome (OTS) using modern methods, which incorporate peripapillary retinal nerve fiber layer (ppRNFL) and ganglion cell complex (GCC) analysis. This retrospective case series aims to describe the diverse clinical and diagnostic imaging manifestations of patients with OTS.

Description of Cases:
All patients with OTS seen at two tertiary neuro-ophthalmology practices from 2014 to 2024 were reviewed. Inclusion criteria were: 1) signs associated with OTS (homonymous hemianopia (HH), relative afferent pupillary defect (RAPD) and/or characteristic atrophy of ppRNFL or GCC); and 2) radiographically confirmed optic tract lesion. Fifty-six patients were identified. Mean age was 49.4 ± 16.7 years, and 66% of patients were women. Etiologies included space-occupying lesions (45%), demyelination (20%), ischemia/hemorrhage (16%), non-specific optic tract atrophy (14%), perinatal insult (4%), and trauma (2%). Visual field defects were observed in 98% of patients. Amongst these patients, 20% demonstrated complete hemianopia while 80% demonstrated incomplete hemianopia, of which 95% were incongruent. Contralateral HH or quadrantanopia was observed in 88% of all patients. Of the 54 patients with ppRNFL findings, 39% had contralateral band atrophy and ipsilateral hourglass atrophy. Forty-eight percent of the 46 patients who underwent GCC analysis had homonymous thinning. These findings of ppRNFL and GCC analysis were essential in making the diagnosis when field defects were subtle. Of the 51 patients with available data, only 29% had contralateral RAPD. Patients with demyelinating lesions tended to present earlier with less atrophy observed on ppRNFL.

Conclusions, including unique features of the case:
While OTS can present heterogeneously, a high index of suspicion should be maintained in patients with subtle homonymous defects, especially in the presence of pattern ppRNFL atrophy or homonymous GCC thinning. Patients with clinical features that align with OTS but normal ppRNFL should be investigated for a demyelinating etiology.

References: None provided.

Keywords: Visual fields, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Bilateral Fixed Dilated Pupils: Uncommon Presentation in Acute Basilar Artery Thrombosis with Positive Recovery

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Introduction:
Bilateral blown pupils are often associated with poor prognosis in the neuro-critical care setting. To our knowledge, isolated bilateral oculomotor nerve palsy has seldom been reported. We present a rare case in which a patient presented acutely after cardiac PCI with bilateral fixed dilated pupils due to a basilar artery occlusion.

Description of Cases:
A 59-year-old man was transferred to our hospital due to decreased responsiveness following left heart catheterization for NSTEMI. Initial CT angiogram of head and neck from an outside hospital showed acute nonocclusive basilar artery thrombosis. The patient received tenecteplase prior to transfer. Upon arrival, he was intubated with fixed, midline, and dilated pupils (6 mm) with limited movement in the left lower extremity. CT perfusion showed an ischemic penumbra in posterior circulation. Due to recanalization of the patient's acute basilar artery thrombus following thrombolytic therapy, neuro-endovascular intervention was not indicated. MRI brain showed multifocal ischemic injuries in the vertebrobasilar system, and MRA of head showed significant recanalization of basilar artery with residual occluded right PCA. He was started on IV Cangrelor and Aspirin. Despite bilateral ptosis and fixed pupils, he was extubated 2 days later with motor recovery in four limbs. However, his pupils remained bilaterally fixed, dilated, and non-reactive to light. He had bilateral ptosis, due to which his hospital course was complicated by disturbed sleep wake cycles and multiple falls.

Conclusions, including unique features of the case:
Bilateral blown pupils in acute basilar artery occlusion are typically associated with severe brain injury. However, this case demonstrates that such findings may not always predict catastrophic outcomes. The patient's deficits, localized to the central caudal nucleus of the oculomotor complex, were isolated, lacking global impairments. This rare presentation underscores the importance of correlating cranial nerve III anatomy with clinical findings for accurate evaluation and prognosis in cases with bilateral blown pupils.

References: None provided.

Keywords: Ocular motility, Stroke, Pupil, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Optimization of Ptosis Crutch Design Using Additive Manufacturing

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Introduction:
When surgical intervention is not safe or desired by patients, ptosis crutches offer an alternative for functional improvement in ptosis. Initial models of ptosis crutches were wire attachments to spectacles that provide elevation in the eyelid. This study aimed to create optimized custom crutch models utilizing alternatives designs and materials to improve functionality and comfort.

Description of Cases:
Additive manufacturing (3D printing) was used to generate the design dimensions and models of the ptosis crutches. Using Autodesk Fusion 2.0.18477 x86_64 macOS 12.6.2 (21G320) on MacBookPro12, the models were designed then sliced using version 5.4.0 of Ultimaker Cura. The designs were transmitted to the Ultimaker S5 for printing. A right-angle design and 180-degree (semi-circle) design were created. Attachment to a generic pair of eyeglasses was attempted for both designs. Two separate model designs were created. A semi-circle design was created with measurements of 41.00 x 24.74 mm and a hinge width of 5.0 mm dimensions using polylactic acid (PLA) filament. A right-angle design was created with 38.0 x 27.16 mm with a hinge width of 5.03 mm using thermoplastic polyurethane (TPU) 95A filaments. The semi-circle model was unable to affix to the glasses without breaking at the hinge. The right-angle model was easily affixed to a pair of glasses.

Conclusions, including unique features of the case:
It is important to have various models available for ptosis crutches, not only for patient comfort, but to accomodate for glasses frame thickness and allowance for more natural blinking. Based on our initial models, we found the right-angle model to be more flexible for a larger spectacle frame size compared to a 180-degree (semi-ciricle) model. We also found the material TPU 95A was more flexible in nature, which would likely correlate to increased patient comfort.

References: None provided.

Keywords: Miscellaneous, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Advancing Techniques to Produce Novel 3D Images of Human Orbital and Optic Nerve Vasculature

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Introduction:
Non-arteritic anterior ischemic optic neuropathy (NAION) is the second most common optic neuropathy in adults. Despite extensive research, the precise cause of NAION remains elusive, although the consensus is that ischemia involving the vascular distribution of one or more paraoptic posterior ciliary arteries is the culprit. Remarkably, there have been no prior depictions of the 3D volumetric architecture of the human orbital and optic nerve arteries derived from confluent anatomical landmarks. Light sheet fluorescence microscopy (LSFM) now allows high-resolution (up to 5 microns) 3D imaging of intact tissues, addressing the challenges posed by the orbit's complex volume and dense vasculature. This study presents optimized methods for visualizing the optic nerve vasculature in 3D.

Description of Cases:
We adapted and modified a tissue clearing protocol from Darche (2023) to better suit the delicate neuronal and connective tissues of the human orbit. Initially, our procedure involved dehydration, 10% hydrogen peroxide bleaching for 10 days, and delipidation with dichloromethane for 2-3 days until specimens floated. However, bleaching proved too harsh for optic nerve tissues, and we altered the delipidation step to minimize dye damage. These adjustments improved tissue preservation while maintaining the transparency required for LSFM imaging. Our modified approach has produced detailed 3D renderings of the optic nerve vasculature highlighting key vascular connections that are presumably relevant for NAION.

Conclusions, including unique features of the case:
The application of LSFM, combined with optimized tissue clearing protocols, provides detailed 3D visualizations of the optic nerve vasculature. Our approach offers significant advantages over traditional 2D imaging, especially by rendering a comprehensive, digitized data set of vascular and neuronal structures. We plan to leverage our data sets to develop a software-based, parameterizable model of optic nerve blood flow, which will have the potential to provide insight into our understanding of the vascular dynamics underlying NAION and possibly some forms of glaucoma.

References: None provided.

Keywords: Orbit, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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The Hijacked Ophthalmic Artery: Preoperative Embolization of a Giant Olfactory Groove Meningioma

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Introduction:
Olfactory groove meningiomas (OGM) are rare, slow-growing tumors originating from the anterior cranial base that comprise approximately 5-18% of all intracranial meningiomas. OGMs may present with headaches, anosmia, personality changes and visual disturbances. Treatment goals include gross total surgical resection along with frontal lobe and cranial nerve preservation. As an adjunct to surgical treatment, preoperative tumor embolization is associated with reduced blood loss, decreased length of surgery, as well as reduced risk of damage to surrounding structures. However, as OGMs are commonly vascularized by parasitized branches from the ophthalmic artery (OA) and anterior ethmoidal artery (AEA), liquid embolization poses an increased risk of blindness due to inadvertent occlusion of the central-retinal artery (CRA).

Description of Cases:
We present the case of a 64F who presented with confusion, anosmia, intermittent diplopia, slurred speech, and ataxic gait over the preceding 2-3 months. A CT-angiogram of the head demonstrated a well vascularized, 6.4 x 6.6 x 5.3 cm anterior cranial fossa midline mass – confirmed to be an OGM – with mass effect on the bilateral frontal lobes and ventricles causing a 1.1 cm left-to-right midline shift. Angiography confirmed the presence of parasitized branches off the right and left OAs, with the majority of the tumor's blood supply originating from a parasitized branch off the left AEA. Liquid embolization of the latter was performed with 0.2 mL of an ethylene-vinyl-alcohol copolymer until reflux was visualized. Subsequent angiography confirmed diminished blood supply to the parasitized branch, with preservation of the OA and CRA.

Conclusions, including unique features of the case:
OGMs with large ethmoidal feeders can be safely and successfully embolized prior to surgical resection. Here, we present a case of successful embolization of a giant OGM with preservation of the OA and CRA. Patient recovered well with preservation of vision.

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Keywords: Tumors, Interventional neuroradiology, Neuroimaging, Skull base

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Artery of Percheron Infarct with Multiple Cranial Nerve Palsies and Horner Syndrome

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Introduction:
The artery of Percheron is a rare variant of posterior cerebral circulation that supplies both paramedian thalamic zones in addition to variably supplying the midbrain. Infarction of the artery of Percheron is exceedingly rare accounting for less than 2% of all thalamic strokes and can present with multiple different symptoms. Classically, the symptoms of infarct include drowsiness progressing to coma, upward gaze palsy, cognitive impairment, aphasia, dysarthria, motor deficits, and cerebellar signs.

Description of Cases:
A 65 year old man originally presented to the hospital after acutely suffering double vision, weakness of his left side, and then losing consciousness. He was successfully treated with thrombolytic tenecteplase. Six days after suffering a stroke, the patient was seen in the ophthalmology clinic where he was noted to have right hypertropia on primary gaze, incomplete fascicular right oculomotor palsy, bilateral complete downgaze/partial upgaze paresis, and left incomplete Horner syndrome with positive apraclonidine test. A partial cranial nerve VII palsy was also noted on the left side. In total the patient experienced bilateral vertical gaze paresis, incomplete left Horner syndrome, right-sided cranial nerve VI palsy, and partial left-sided cranial nerve VII palsy. MRI of the brain revealed an infarct in the left thalamus, infarct along the anteromedial right thalamus, and infarct of the right medial midbrain. Structures affected within the midbrain include the red nucleus, midbrain medial longitudinal fasciculus, and periaqueductal gray matter. Based on the findings of the infarction pattern, the patient was diagnosed with an infarct of the artery of Percheron.

Conclusions, including unique features of the case:
This case represents a previously unknown presentation of an artery of Percheron infarct. Artery of Percheron infarcts can be difficult to diagnose based on variant symptoms; however, rapid evaluation of symptoms including multiple ophthalmic manifestations and mental status changes is essential for timely treatment with thrombolysis.

References: None provided.

Keywords: Neuroimaging, Ocular motility, Stroke

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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The Third Nerve in Hindsight

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Introduction:
Arachnoid cysts are benign, usually congenital, lesions that develop due to splitting between layers of membrane within the arachnoid during embryogenesis. They are usually asymptomatic, but classically cause cranial nerve deficits, interruptions to cerebral spinal fluid flow, or headache when symptomatic. They are relatively common, in nearly 1% of the population, with a predilection for the middle cranial fossa. Few cases have been described in the prepontine space.

Description of Cases:
Mr. M is a previously healthy 20 year old male with a history of partial left third cranial nerve palsy since age six months, reportedly due to an inflammatory response to childhood vaccination. He has undergone two strabismus surgeries (2014, 2022) for his amblyopia. He presented to the ED with acute severe left frontal headache with photophobia, phonophobia, vomiting, and worsening of baseline left ptosis. His exam revealed color plates 11/11 OU, full visual fields, decreased visual acuity OS (20/100+2), normal visual acuity OD (20/20), no afferent pupillary defect OD, fixed dilated pupil OS, marked ptosis OS, and a normal fundus exam OU. He had full extraocular movements OD, 0/4 adduction and 2/4 abduction OS. A noncontrast head CT revealed a cystic lesion anterior to the pons. A MRI Brain/Orbit revealed a cystic lobulated lesion 1.9x1.5cm along the left oculomotor triangle extending to the interpeduncular cistern consistent with an arachnoid cyst. Upon review of childhood imaging, this lesion was appreciable in retrospect.

Conclusions, including unique features of the case:
This presentation is unique in that we reviewed imaging from this patient from the age of 6 months, one year, seven years, and now at twenty years of age, with new insights. Our workup represented a large diagnostic paradigm shift for this patient and his family after two decades. It allows the appreciation of the natural history and radiographic evolution of this congenital process, arachnoid cyst, in a rare locale.

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Keywords: Pediatric neuro-ophthalmology, Neuroimaging, Adult strabismus with a focus on diplopia, Ocular motility, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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A Case of Curious Bilateral Disc Edema

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Introduction:
Most stomach cancers are adenocarcinomas. Signet ring cell histology represents an aggressive subtype. We report a case of infiltrative optic neuropathy secondary to signet ring gastric adenocarcinoma.

Description of Cases:
A 65-year-old male presented with sudden onset blurred vision in both eyes, visual acuity was 20/100 OD, 20/70 OS with no RAPD. Extraocular motility revealed mild restricted abduction (-0.5) in both eyes. Fundoscopy showed bilateral disc edema. His GVF showed enlarged blind spots in each eye and temporal constriction in the right eye. Patient was admitted for additional workup and an MRI orbit revealed flattening of posterior sclera as well as enhancement of the optic nerve heads in each eye – initially described as possibly secondary to papilledema, except his lumbar puncture had a normal opening pressure of 21cmH2O. Infectious causes were excluded, and meningitis / encephalitis workup was normal. He received 5 days of IV solumedrol with subsequent improvement in vision to BCVA 20/70 OD, 20/50 OS. Initial discussion of etiology included possibly chemotherapy induced vs paraneoplastic vs metastasis. We thought it would be highly atypical for metastasis to occur at only the bilateral optic nerve heads. He was discharged on a steroid taper and chemotherapy was discontinued. At follow-up his vision had improved to 20/40 OD, 20/50 OS and his disc edema improved. Unfortunately, he was admitted again 4 weeks later for syncope and collapse. He complained of headache but denied other symptoms of increased intracranial pressure or worsening vision. CSF cytology from a second spinal tap showed numerous atypical cells with cytomorphology highly suggestive of signet cell carcinoma. MRI spine with contrast revealed abnormal linear and nodular leptomeningeal enhancement throughout spine, suggesting leptomeningeal carcinomatosis.

Conclusions, including unique features of the case:
This pattern of metastasis is extremely rare, it is associated with a poor prognosis due to disabling symptoms and a scarcity of treatment options.

References: None provided.

Keywords: Optic neuropathy, Paraneoplastic syndromes, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Chemotherapy and radiation injury, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Increased Opening Pressure in Patients with Multiple Sclerosis and Neuromyelitis Optica

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Introduction:
Increased intracranial pressure (ICP) is increasingly recognized in myelin oligodendrocyte glycoprotein antibody-associated disease. While there are isolated case reports of raised ICP in neuromyelitis optica spectrum disorder (NMOSD) and multiple sclerosis (MS), systematic studies are lacking. This project examines the incidence and features of increased ICP in NMOSD and MS.

Description of Cases:
This cross-sectional study included NMOSD (AQP4-IgG positive) and MS patients with documented lumbar puncture (LP) opening pressure (OP) within 30 days of a clinical attack. Demographics, attack phenotype, and cerebrospinal fluid (CSF) constituents were collected. Patients with raised OP (>250 mmH2O in adults or >280 mmH2O in children) were reviewed for headaches, disc edema, abducens nerve palsy, pulsatile tinnitus, transient visual obscurations, and neuroimaging signs of increased ICP (partially empty sella, posterior globe flattening, perioptic subarachnoid space distention, transverse venous sinus stenosis). Of the 297 NMOSD patients, 41 met the inclusion criteria. The mean age at LP was 51.24 ± 17.61 years, 78% were female, and median OP was 170 (range 80-550). Of the 232 MS patients, 37 met the inclusion criteria. The mean age at LP was 37.00 ± 14.01 years, 73% were female, and median OP was 170 (range 86-290). Raised OP was identified in 7 (17%) NMOSD patients (OP 252-550) with optic neuritis (3), transverse myelitis (1), acute diencephalic syndrome (1), and mixed phenotype (2). Raised OP was identified in 4 (11%) MS patients (OP 250-290) with optic neuritis (1), supratentorial syndrome (2), and mixed phenotype (1). None had disc edema or abducens nerve palsy. Headaches were documented in 1 NMOSD and 2 MS patients. Only 2 NMOSD patients had neuroimaging signs of increased ICP (distended perioptic subarachnoid space). None had leptomeningeal enhancement.

Conclusions, including unique features of the case:
Raised OP was occasionally observed in acute NMOSD and MS attacks, but these patients were largely asymptomatic.

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

Financial Disclosures: Sydney Roston; Melanie Quick; Nanthaya Tisavipat; Laura Cacciaguerra; Deena Tajfirouz; Kevin Chodnicki; Jan-Mendelt Tillema; Sean Pittock: Sean J. Pittock has received personal compensation for serving as a consultant for Roche/Genentech, Sage Therapeutics, Arialys and Astellas. He has received personal compensation for serving on scientific advisory boards or data safety monitoring boards for F. Hoffman-LaRoche AG, Genentech, Arialys and UCB. His institution has received compensation for serving as a consultant for Astellas, Alexion, and Viela Bio/MedImmune. All compensation is paid to Mayo Clinic. He has received research support from Alexion, Viela Bio/MedImmune, Roche/Genentech and Adimmune. He has a patent, Patent# 8,889,102 (Application#12-678350, Neuromyelitis Optica Autoantibodies as a Marker for Neoplasia)—issued; a patent, Patent# 9,891,219B2 (Application#12-573942, Methods for Treating Neuromyelitis Optica (NMO) by Administration of Eculizumab to an individual that is Aquaporin-4 (AQP4)-IgG Autoantibody positive)-issued and from which he has received royalties and a patent for GFAP-IgG; Septin-5-IgG; MAP1B-IgG; Kelch-like protein 11; PDE10A pending. He is working as a consultant in the Mayo Clinic Neuroimmunology laboratory clinical service. The Mayo Clinic Neuroimmunology Laboratory commercially offers MOG-IgG testing, but revenue accrued does not contribute to salary, research support, or personal income; Eoin Flanagan: The institution of Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Alexion. Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Genentech. Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Horizon Therapeutics. The institution of Dr. Flanagan has received personal compensation in the range of $10,000-$49,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Roche. Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Speakers Bureau for Pharmacy times. The institution of Dr. Flanagan has received personal compensation in the range of $5,000-$9,999 for serving on a Speakers Bureau for UCB. The institution of Dr. Flanagan has received research support from Viela Bio. The institution of Dr. Flanagan has received research support from UCB. The institution of Dr. Flanagan has received research support from Roche. Dr. Flanagan has received publishing royalties from a publication relating to health care. Dr. Flanagan has a non-compensated relationship as a Member of medical Advisory Board with The MOG Project. Dr. Flanagan has a non-compensated relationship as a Editorial board member with Journal of The Neurologic Sciences. Dr. Flanagan has a non-compensated relationship as a Editorial board member with Neuroimmunology Reports. Dr. Flanagan has a non-compensated relationship as a Editorial Board Member with Neurology, Neuroimmunology Neuroinflammation (N2) Journal.; John Chen

Grant Support: NA

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Anti Ganglioside Antibody Mediated Relapsing Cranial Nerve Palsies Mimicking Microvascular Cranial Nerve Palsies

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Introduction:
Guillain Barre syndrome (GBS) is a group of acute immune mediated inflammatory polyneuropathies and involves cranial nerves in 45-75% of patients (1,2). Microvascular cranial nerve palsies (MCNP) are presumed with spontaneous resolution over 3-6 months in patients with vascular risk factors. Further workup is pursued when multiple cranial nerve palsies develop, or resolution does not occur in the expected time frame (3). We present two unique cases where cranial nerve predominant GBS with anti-ganglioside antibody positivity presented as multiple relapsing MCNPs in patients with microvascular ischemic disease (MID) and multiple vascular risk factors.

Description of Cases:
Case 1: 62-year-old male, presented 07/2022 with diplopia, MID, and vascular risk factors of diabetes and hypertension. Alignment measurements mapped to a left CN6 palsy which spontaneously resolved in 2-3 months. Additional right CN7 and left CN3 palsies prompted infectious/inflammatory work up revealing elevated antiGM2 ab. PLEX in 12/2022 resolved diplopia and CN3 and CN7 palsies. In 11/2023 he presented with a right CN3 palsy resolved by IVIG therapy in 12/2023. He is being maintained on IVIG every 8 weeks. In 06/2024 all cranial nerve palsies were resolved in support of the diagnosis of cranial nerve predominant GBS with antiGM2 positivity. Case 2: 67-year-old male, presented 10/2023 with diplopia and MID on brain MRI. Past medical history includes hypertension, hyperlipidemia, diabetes, smoking, and OSA. Alignment measurements were consistent with a left CN4 palsy. Diplopia resolved 01/2024, he returned 08/2024 with diplopia consistent with a partial CN3 palsy. Infectious/inflammatory/compressive workup was unrevealing. By 09/2024 his diplopia persisted, and ganglioside antibodies returned elevated GD1A ab, GD1b ab, and GQ1b ab. Patient is currently on IVIG awaiting follow up.

Conclusions, including unique features of the case:
In cases of multiple cranial nerve palsies, GBS with cranial nerve involvement and anti-ganglioside antibody positivity should be ruled out in workup despite typical characteristics of MCNP.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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MRI-negative optic myelitis and bilateral disc swelling due to myelin oligodendrocyte glycoprotein antibody disease : A Case Report

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Introduction:
Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is an inflammatory central nervous system disease that is increasingly recognized. Its clinical features, distinct neuroimaging characteristics and increasing availability of cell-based assays to detect myelin Oligodendrocyte glycoprotein (MOG) antibody have led to greater understanding of this condition and led to the recent proposed criteria for MOGAD. This requires the presence of a core clinical inflammatory event, a positive MOG-IgG test and supporting MRI features such as optic neuritis, transverse myelitis or brain, brainstem, or cerebral syndrome(1).In this report, we present a MOG-positive patient who had clinical features of myelitis but normal neuroimaging. He also had bilateral disc swelling without clinical and radiological features of optic neuritis.

Description of Cases:
We present a case report of a 20 year old Chinese gentleman with MRI negative MOG after presenting with urinary incontinence and visual disturbance. This young gentleman with a past medical history of obesity and untreated severe obstructive sleep apnoea presents with a weeklong history of headache, fever and acute urinary retention. Examination revealed bilateral papilledema. Magnetic resonance imaging (MRI) of the brain, spine and cerebral venogram were unremarkable. Lumbar puncture revealed pleocytosis. With his signs suggestive of conus medullaris pathology, a typical feature of MOGAD, MOG antibody was tested. Immunofluorescence assay revealed raised MOG titres. He was treated with pulsed methylprednisolone followed by a taper of oral steroids which led to clinical recovery.

Conclusions, including unique features of the case:
Clinicians should be aware of MRI-negative MOGAD and should investigate for MOG antibodies if there are clinical symptoms which strongly suggest its presence.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Unveiling Misdiagnosis: Rethinking Seronegative NMOSD as a Distinct Entity

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Introduction:
The international 2015 diagnostic criteria for neuromyelitis optica spectrum disorder (NMOSD) divided patients into seropositive (AQP4-IgG positive) and seronegative NMOSD. Since then, myelin oligodendrocyte glycoprotein antibodies (MOG-IgG) have emerged, accounting for another group of patients with NMOSD-like phenotypes. However, some patients remain negative for both AQP4-IgG and MOG-IgG, presenting a unique diagnostic challenge. Diagnosis in these cases relies heavily on clinical and radiological criteria due to the lack of definitive serological markers. The 2015 NMOSD diagnostic criteria aid in such cases, yet misdiagnosis, including conflation with conditions like multiple sclerosis (MS), remains common. This study aimed to determine the frequency of incorrect use of the term seronegative NMOSD among referring providers to a tertiary center.

Description of Cases:
We retrospectively reviewed 33 patients with negative AQP4-IgG and MOG-IgG tests referred for seronegative NMOSD evaluation at a tertiary academic center from January 1, 2018, to December 31, 2023. Two blinded evaluators determined if patients met the 2015 criteria for seronegative NMOSD, resolving disagreements with the principal investigator. Initial evaluations showed 94% consensus. Of the 33 identified patients, only one met the 2015 diagnostic criteria for seronegative NMOSD; an additional patient was suspected of having seronegative NMOSD without meeting the criteria. The most common mimicking conditions included MS (37%), idiopathic optic neuritis (15%), and non-neurologic pathologies like functional vision loss (12%). Common presentations were recurrent optic neuritis (39%) and transverse myelitis (19%).

Conclusions, including unique features of the case:
Our data suggest that up to 97% of patients referred for seronegative NMOSD may have alternative or idiopathic conditions. Distinguishing between seronegative NMOSD and MS appears to be particularly challenging in patients with recurrent optic neuritis or transverse myelitis. This study highlights the importance of strict application of the 2015 diagnostic criteria and underscores the need for careful diagnosis and consideration of alternative explanations in those patients that do not fulfill criteria.

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

Financial Disclosures: Mary Lang; Grant Welk; Deena Tajfirouz; Kevin Chodnicki; Sean Pittock: Sean J. Pittock has received personal compensation for serving as a consultant for Roche/Genentech, Sage Therapeutics, Arialys and Astellas. He has received personal compensation for serving on scientific advisory boards or data safety monitoring boards for F. Hoffman-LaRoche AG, Genentech, Arialys and UCB. His institution has received compensation for serving as a consultant for Astellas, Alexion, and Viela Bio/MedImmune. All compensation is paid to Mayo Clinic. He has received research support from Alexion, Viela Bio/MedImmune, Roche/Genentech and Adimmune. He has a patent, Patent# 8,889,102 (Application#12-678350, Neuromyelitis Optica Autoantibodies as a Marker for Neoplasia)—issued; a patent, Patent# 9,891,219B2 (Application#12-573942, Methods for Treating Neuromyelitis Optica (NMO) by Administration of Eculizumab to an individual that is Aquaporin-4 (AQP4)-IgG Autoantibody positive)-issued and from which he has received royalties and a patent for GFAP-IgG; Septin-5-IgG; MAP1B-IgG; Kelch-like protein 11; PDE10A pending. He is working as a consultant in the Mayo Clinic Neuroimmunology laboratory clinical service. The Mayo Clinic Neuroimmunology Laboratory commercially offers MOG-IgG testing, but revenue accrued does not contribute to salary, research support, or personal income; Eoin Flanagan: The institution of Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Alexion. Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Genentech. Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Horizon Therapeutics. The institution of Dr. Flanagan has received personal compensation in the range of $10,000-$49,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Roche. Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Speakers Bureau for Pharmacy times. The institution of Dr. Flanagan has received personal compensation in the range of $5,000-$9,999 for serving on a Speakers Bureau for UCB. The institution of Dr. Flanagan has received research support from Viela Bio. The institution of Dr. Flanagan has received research support from UCB. The institution of Dr. Flanagan has received research support from Roche. Dr. Flanagan has received publishing royalties from a publication relating to health care. Dr. Flanagan has a non-compensated relationship as a Member of medical Advisory Board with The MOG Project. Dr. Flanagan has a non-compensated relationship as a Editorial board member with Journal of The Neurologic Sciences. Dr. Flanagan has a non-compensated relationship as a Editorial board member with Neuroimmunology Reports. Dr. Flanagan has a non-compensated relationship as a Editorial Board Member with Neurology, Neuroimmunology Neuroinflammation (N2) Journal.; John Chen

Grant Support: None.

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Nonarteritic Anterior Ischemic Optic Neuropathy with Antithrombin III Deficiency in Early Pregnancy: A Case Report

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Introduction:
Nonarteritic anterior ischemic optic neuropathy (NAION) is an acute optic neuropathy commonly resulting in irreversible vision loss in the affected eye. There is minimal literature linking NAION with thrombophilia and pregnancy, which limits guidance on screening and prevention. We present a unique case of NAION during early pregnancy in a thrombophilic patient who may have benefited from preventative intervention.

Description of Cases:
A 39-year-old 12-week pregnant woman with a history of type II diabetes and obesity developed sudden vision loss. Ophthalmologic examination revealed 20/25 visual acuity in the right eye and 20/20 in the left eye, with normal intraocular pressures. Fundoscopy revealed optic disc edema in the right eye and a disc-at-risk in the left. Non-contrast enhanced MRI Brain/Orbits and MRV were unrevealing and infectious/inflammatory workup was negative, suggesting NAION. Thrombophilia screening revealed an antithrombin III deficiency and a heterozygous prothrombin G20210A mutation, and she was started on Enoxaparin. At her 3-month follow-up, superior optic disc pallor in the right eye and bilateral small, crowded discs were noted. Humphrey visual field testing revealed a dense inferior altitudinal defect in the right eye corresponding to superior nerve fiber layer thinning on optical coherence tomography. Her NAION was monitored throughout pregnancy without further changes.

Conclusions, including unique features of the case:
While several systemic risk factors for NAION are well established, the association with inherited thrombophilias remains controversial. Moreover, NAION in pregnancy is rare, typically occurring in late pregnancy or postpartum. In our case, pregnancy may have served as a trigger for NAION in a patient with underlying prothrombotic conditions, highlighting the potential role of thrombophilia screening and the importance of proper counseling for at-risk pregnant patients. Further research on the etiology of NAION would help improve guidance for screening and counseling.

References: None provided.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Incidence of Thymoma in Patients with Ocular Myasthenia Gravis

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Introduction:
Myasthenia gravis (MG) can be divided into two relatively distinct categories: ocular (OMG) and generalized (GMG) disease. OMG involves signs and symptoms limited to the extraocular muscles. Incidence of thymoma in patients with OMG has been reported to range from 4.3% to 15.4% based on histopathological reviews of thymectomized patients. However, we hypothesized that the incidence in our population is lower than these reported rates.

Description of Cases:
We conducted a retrospective chart review of all patients diagnosed with MG from 2000 to 2024. A total of 236 patients were identified, of whom 77 were excluded due to either conversion to GMG or the absence of chest CT imaging. The remaining 159 patients consisted of 63 females (39.6%) and 96 males (60.4%), with an average age of 67 ± 16 years. The majority were white (130, 81.8%), followed by African American patients (10, 6.3%). Of the 159 patients who underwent chest CT, four were found to have an enlarged thymus, suspicious for thymoma. Among these four patients, only one was histologically confirmed to have an invasive thymoma. Additionally, two other patients underwent thymectomy due to treatment failure despite having an unremarkable chest CT. Of these two, none had thymomas. Of the five non-thymomatous patients, two patients had follicular hyperplasia, and two patients had normal thymus tissue. One patient didn't have a histologic report, but she was told her thymectomy report was “benign”.

Conclusions, including unique features of the case:
The incidence of thymoma in patients with OMG may be significantly lower than previously reported, 0.6% (1/159) in our report. This raises the question of whether routine chest CT is recommended for all individuals diagnosed with stable OMG.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Rare Neuro-Ophthalmic Manifestations of Syphilis Infection

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Introduction:
Syphilis is a sexually transmitted infection caused by Treponema pallidum. According to the World Health Organization, in 2022, there were approximately eight million adults diagnosed with syphilis.(1) Syphilis is divided into four stages: primary, secondary, latent, and tertiary.(2) Tertiary can present with cardiovascular or neurologic findings. We present two unusual neuro-ophthalmic presentations of syphilis: optic neuropathy and third nerve palsy.

Description of Cases:
The first case is a 52-year-old man referred for unilateral left optic disc edema with central scotoma. Laboratory testing revealed reactive T. pallidum antibodies. The patient reported recent prior treatment for syphilis with intramuscular (IM) penicillin. Lumbar puncture was obtained and cerebrospinal fluid (CSF) showed reactive VDRL. The patient was treated for neurosyphilis with a 14-day course of intravenous (IV) penicillin, with subsequent resolution of optic disc edema. The second case is a 47-year-old woman who presented with two weeks of painless worsening right eye vision and binocular diplopia. On examination, the right pupil was dilated and minimally reactive, and ocular motility showed limitation of supraduction, infraduction, and adduction, consistent with pupil-involving third nerve palsy. MRI showed “questionable subtle asymmetric enhancement of right cranial nerve III,” and laboratory testing was positive for T. pallidum antibodies. The patient underwent lumbar puncture with reactive VDRL in the CSF. She received a 10-day course of IV penicillin followed by an IM dose prior to returning to her home country.

Conclusions, including unique features of the case:
Syphilis can cause numerous ophthalmic manifestations including retinitis, uveitis, perineuritis, optic neuritis, or papilledema and has been described as “the great mimicker.” Our two cases of rare neuro-ophthalmic manifestations of syphilis demonstrate the importance of consideration in any unexplained inflammatory cranial neuropathy.

References: 1. “Data on Syphilis.” World Health Organization, World Health Organization, www.who.int/data/gho/data/themes/topics/data-on-syphilis. Accessed 20 Oct. 2024. 2. French P. Syphilis. BMJ (Clinical research ed.), 334(7585), 143–147. 2007. https://doi.org/10.1136/bmj.39085.518148.BE

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

Financial Disclosures: Jennifer Drechsler; Yash Shah; Raquel Pinto; Alberto Distefano; Rudrani Banik: Omni Actives Health Technologies: Lecture Fees/Speakers Bureau Rupa Health: Lecture Fees/Speakers Bureau Optomed USA, Inc.: Consultant/Advisor, Lecture Fees/Speakers Bureau GenSight Biologics: Research Support Viridian Therapeutics: Research Support; Valerie Elmalem: Amgen: speaker for Tepezza

Grant Support: None.

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Between a Chiasm and a Hard Place: A Biopsy-Heavy Search for the Missing Diagnosis

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Introduction:
Peripheral T-cell lymphoma is a rare subtype of non-Hodgkin's lymphoma and an exceptionally rare cause of optic pathway infiltration. While optic nerve involvement in lymphoma has been documented, extensive optic pathway infiltration, including the chiasm, bilateral optic nerves, and tracts, is unprecedented. This case underscores the diagnostic and management challenges posed by rare optic nerve lesions.

Description of Cases:
A 44-year-old man presented with progressive bilateral vision loss over four weeks, following severe nausea, vomiting, and a 50-pound weight loss. Initial visual acuity was 20/60 (right eye) and count fingers (left eye), with no optic disc edema. Imaging revealed a uniformly enhancing lesion of the optic chiasm, tracts, and nerves. Extensive serologic and CSF evaluations for infectious, inflammatory, and autoimmune etiologies were negative. Nutritional deficiencies were corrected but deemed incidental. CT-guided biopsies of retroperitoneal lymph nodes and an ileocecal mass were inconclusive, suggesting non-Langerhans histiocytosis. Despite empiric steroids, vision declined further. A PET scan and bone marrow biopsy revealed no definitive diagnosis. Finally, a cervical lymph node biopsy confirmed peripheral T-cell lymphoma with T-cell clonality six months after symptom onset. The patient underwent chemotherapy and autologous stem cell transplantation, achieving radiographic resolution of the lesion. Vision partially improved to 20/300 in the right eye, while the left eye showed no improvement and remained at count fingers with stable optic atrophy in both eyes.

Conclusions, including unique features of the case:
This case highlights the need for multidisciplinary, iterative approaches to complex optic nerve lesions when standard workups and biopsies are inconclusive. Early CNS biopsy carries significant risks, including permanent vision loss, and multiple peripheral biopsy sites should be prioritized before pursuing optic nerve or chiasm biopsies. This unique case demonstrates extensive optic pathway infiltration by peripheral T-cell lymphoma and the importance of strategic diagnostic planning to minimize treatment delays and optimize outcomes.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Not All Headaches are Migraine

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Introduction:
Cavernous sinus thrombosis is a rare and life-threatening disorder. Early identification is important to increase chances of good outcome as it can be fatal.

Description of Cases:
47-year-old male with history of hypertension, substance use disorder on suboxone presented with 2 weeks of headache, worsening left eye pain and proptosis. He made several ED visits for severe headache and was attributed to migraine. Neurology was consulted in his 3rd visit to ED when he developed left eye swelling. Examination showed temperature of 102.4, left eye proptosis and complete ptosis, frozen globe, 4+chemosis and trace optic disc edema. Right eye had pupil sparing partial cranial nerve 3 and 6 palsy. Visual acuity (VA) was 20/25 on both eyes. CTA head/neck showed chronic sinusitis of multiple facial sinuses, proptosis left>right, enlarged extraocular muscles (EOM) left>right, superior ophthalmic vein thrombosis left>right, bilateral cavernous sinus thrombosis, right sigmoid and bilateral jugular vein thrombosis. MRI head showed multiple subacute infarcts in the right cerebellum and vermis. WBC was 32. Lumbar puncture was not attempted due to concern of herniation. He was diagnosed with bilateral cavernous thrombosis and extensive cerebral venous thrombosis secondary to acute bilateral rhinosinusitis. ENT performed bilateral sphenoidotomy, ethmoidectomy and maxillary antrostomy. He was started on heparin infusion and antibiotics (vancomycin, cefepime, metronidazole). Hospital course was complicated by worsening cerebellar edema resulting in development of hydrocephalus. Family decided on comfort care due to worsening exam and he eventually died on 7th day of his hospital admission.

Conclusions, including unique features of the case:
This is an interesting case of bilateral cavernous sinus thrombosis secondary to rhinosinusitis and patient eventually died. Early recognition is critical for a good outcome and high index of suspicion is recommended as mortality is approximately 8-13 % despite antibiotics.

References: None provided.

Keywords: Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Increase In Retinal Nerve Fiber Myelination In A Patient With Multiple Sclerosis: Ocular Evidence Of Remyelination?

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Introduction:
Myelinated retinal nerve fiber layer (MRNF) is a largely congenital condition characterized by the presence of abnormally myelinated axons within the retina. Acquired retinal myelination has been reported but it is exceptionally rare. Myelination process of the anterior visual pathways starts centrally at the lateral geniculate body, followed by optic tracts, chiasm and optic nerve. Myelination reaches the lamina cribrosa and terminates at term (although in some cases the myelination may continue for a short period after birth). When the process extends beyond the lamina cribrosa, MRNF can be observed on ocular examination. Optic neuritis (ON) is an inflammatory condition affecting the optic nerve, and it may be associated with multiple sclerosis (MS). Episodes of optic neuritis can exacerbate damage to the optic nerve, leading to significant demyelination and vision impairment. Recent studies suggest the possibility of remyelination in the central nervous system, including the optic nerve, raising the question of whether similar processes can occur within the retina in MS patients.

Description of Cases:
A 54-year-old female was seen in the neuro-ophthalmology clinic following concerns raised by an optician about an increase in MRNF. Eight years ago, she experienced sequential bilateral vision loss. While no significant pain was reported at the time of vision loss, she did have a severe headache three days prior to the onset of her visual symptoms. Further investigations confirmed MS diagnosis and since initial diagnosis she had a several relapses (RRMS) with progressive white matter lesions. Fundus examination revealed florid MRNF, which has increased following the optic neuritis attack.

Conclusions, including unique features of the case:
The observation of increase in MRNF following optic neuritis in a patient with RRMS provides additional evidence of remyelination process in optic neuritis. Although evidence for this phenomenon is limited and it requires further investigations.

References: None provided.

Keywords: Demeylinating disease, Optic neuritis, Retina, Miscellaneous

Financial Disclosures: Neringa Jurkute: No relevant financial relationships. Neringa Jurkute has received consultancy and research fees, as well as speaker honoraria from Chiesi.; Anthony Robson; Ahmed Toosy: No relevant financial relationships. Ahmed Toosy has received speaker honoraria from Merck, Biomedia, Sereno Symposia International Foundation, Bayer and At the Limits and meeting expenses from Merck, Biogen Idec and Novartis. He was the UK PI for two clinical trials sponsored by MEDDAY pharmaceutical company (MD1003 in optic neuropathy [MS-ON - NCT02220244] and progressive MS [MS-SPI2 - NCT02936037]). He has been supported by recent grants from the MRC (MR/S026088/1), NIHR BRC (541/CAP/OC/818837) and RoseTrees Trust (A1332 and PGL21/10079). He is an associate editor for Frontiers in Neurology – Neuro-ophthalmology section and on the editorial board for Neurology and Multiple Sclerosis Journal.

Grant Support: None.

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Dupilumab-Induced Eosinophilic Granulomatosis With Polyangiitis Mimicking Giant Cell Arteritis

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Introduction:
Eosinophilic granulomatosis with polyangiitis (EGPA) is an anti-neutrophil cytoplasmic antibody (ANCA)-associated small-medium vessel vasculitis. Dupilumab (Dupixent) is a human IgG4 monoclonal antibody against the interleukin (IL)-4Rα and is used for atopic dermatitis, asthma, and chronic rhinosinusitis with nasal polyps (CRSwNP). Recently, there have been reports of EGPA associated with dupilumab administration. We report a case of a patient with dupilumab-induced EGPA with ocular involvement that presented mimicking giant cell arteritis (GCA).

Description of Cases:
A 62-year-old Caucasian female with medical history of CRSwNP, asthma, allergic rhinitis, and eosinophilia presented to the emergency department with episodes of painless monocular transient vision loss and a "patchy" appearance to the vision. Two months prior, she received dupilumab injections for CRSwNP, after which she began to experience headache, jaw claudication, myalgias, and constitutional symptoms. Inpatient workup was significant for elevated inflammatory markers and bilateral perineural enhancement on MRI. She was admitted for IV steroids due to concern for GCA. Temporal artery biopsy later returned negative. On outpatient follow up, visual acuity was 20/20 in the right eye (OD) and 20/40 in the left eye (OS) with trace relative afferent pupillary defect OS. Dilated fundus exam showed multiple large cotton wool spots OS. Optical coherence tomography of the macula was consistent with paracentral acute middle maculopathy. The constellation of symptoms and findings raised concern for a systemic vasculitis, so she was referred to rheumatology and was diagnosed with seronegative EGPA, likely associated with dupilumab administration.

Conclusions, including unique features of the case:
The relationship between dupilumab administration and the potential onset of EGPA remains unclear, whether via the unmasking of a present condition or initiation of disease development. This case describes ophthalmic manifestations of EGPA in the setting of dupilumab use. Clinicians should be aware of this association between dupilumab and EGPA and that it may present mimicking GCA.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None

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Acetazolamide Induced thrombocytopenia in a patient with Idiopathic Intracranial Hypertension

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Introduction:
Acetazolamide is a carbonic anhydrase inhibitor of sulfonamide origin commonly used in patients with idiopathic intracranial hypertension. Although rare in occurrence, there have been multiple case reports documenting acetazolamide induced blood dyscrasias. These include aplastic anemia, thrombocytopenia, and agranulocytosis. We report a case of presumed acetazolamide induced thrombocytopenia.

Description of Cases:
A 17 year old obese female presented with blurred vision in the left eye and occipital headaches. On evaluation she had non-vision threatening bilateral optic disc edema. An MRI and MRV were notable for signs of elevated intracranial pressure. A lumbar puncture revealed an opening pressure of 25 cm H20 with normal CSF constituents. The patient was started on acetazolamide 250 mg twice daily for idiopathic intracranial hypertension. Three months after diagnosis, the patient presented to the emergency department with generalized petechiae and ecchymoses on the extremities and trunk. Laboratory studies revealed platelets < 5, Hemoglobin 10.1, Hematocrit 30.1, WBC 5.6, INR 1.1, PTT 333. There was no recent trauma, illness, or family history of autoimmune disease. Bone marrow aspirate was consistent with peripheral destruction and/or sequestration of platelets. Notable labs included negative autoimmune workup (ANA, dsDNA, SSA, SSB), negative HIV. Thorough hematologic work up resulted in a diagnosis of Immune Thrombocytopenia Purpura (ITP) thought to be secondary to acetazolamide use. The acetazolamide was discontinued, and the patient had improved optic disc edema with focus on weight management. Platelets recovered after further platelet transfusion, dexamethasone, and IVIG.

Conclusions, including unique features of the case:
A unique feature of this case is that blood dyscrasias are a rare, yet serious side effect of acetazolamide. They typically occur within 6 months of starting medication and are dose independent.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Cemiplimab in Squamous Cell Carcinoma with Perineural Invasion and Ophthalmoplegia

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Introduction:
Cutaneous squamous cell carcinoma (SCC) infrequently may lead to perineural invasion, which is considered a poor prognostic indicator. Cemiplimab is a monoclonal antibody that targets programmed cell death protein 1 (PD-1), a checkpoint inhibitor, and was approved for recurrent or metastatic squamous cell carcinoma of the head and neck in 2021. We present a challenging case of SCC with extensive skull base perineural invasion treated successfully with cemiplimab.

Description of Cases:
A 73-year-old male with a history of squamous cell carcinoma of the left scalp that was surgically resected and chemically treated in 2018 was referred for new-onset left facial numbness and double vision. Examination showed left pupil involvement and paralysis of cranial nerves III, V, and VI. Neuroimaging revealed perineural spread involving the left subcutaneous scalp, left supraorbital and infraorbital foramens, left cavernous sinus, and superior orbital fissure to the interpeduncular cistern as well as left cranial nerves V2 and III. Biopsy confirmed squamous cell carcinoma, and the patient was initiated on cemiplimab with significant improvement. He has experienced no adverse effects on his current treatment regimen with plans to continue cemiplimab therapy for at least an additional year.

Conclusions, including unique features of the case:
This case presents significant challenges due to the extensive SCC involvement of the skull base. Surgical resection and radiation are associated with high morbidity in these cases. As such, cemiplimab emerges as a well-tolerated alternative treatment option. Limited reports exist on its effectiveness for SCC with perineural invasion and associated ophthalmoplegia. The current case adds to the limited literature and supports the effectiveness of cemiplimab for SCC of the head and neck with perineural invasion.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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A Case of Diffuse Large B-Cell Lymphoma Masquerading as Cavernous Sinus Syndrome

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Introduction:
Cavernous sinus syndrome includes any disease process that affects the cavernous sinus, often presenting with painful ophthalmoplegia.1

Description of Cases:
A 73 year old woman with a history of diabetes and hypothyroidism presented to the hospital after experiencing three weeks of right-sided headache, jaw pain, right eye swelling, and binocular diplopia that started after an upper respiratory infection. Her initial exam was notable for complete ophthalmoplegia with a visual acuity of 20/30 (right) and 20/25 (left). MRI imaging of the orbits demonstrated enhancing soft tissue from the right middle cranial fossa extending into the posterior right orbit via the superior orbital fissure. Ophthalmology, neurology, infectious disease, and hematology/oncology were consulted, and subsequent inflammatory, neoplastic, and infectious work-up was unremarkable. Based on her significant ocular pain and unrevealing work-up, the patient was thought to have Tolosa-Hunt Syndrome and underwent a round of IV steroids with no improvement in symptoms. The patient then developed an acute worsening of visual acuity to counting fingers, and ophthalmology was re-consulted. We noted that compared to the initial complete blood count (CBC) that was notable only for a leukocytosis of 33, the subsequent CBC four days later was notable for multiple hematologic abnormalities: leukocytosis of 18.7, mild anemia with a hemoglobin of 13.1, and thrombocytopenia with a platelet level of 93,000. As such, a bone marrow biopsy was performed, which revealed a diagnosis of diffuse large B-cell lymphoma. The patient is currently undergoing chemotherapy and radiation and has had improvement in her visual acuity to 20/400 (right) and 20/40 (left).

Conclusions, including unique features of the case:
Tolosa-Hunt Syndrome is a diagnosis of exclusion, and there should be a high index of suspicion for a different etiology of symptoms if there is worsening or no improvement after initiation of steroid treatment.

References: None provided.

Keywords: Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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77

Atypical Guillain-Barré Syndrome with Miller Fisher Variant: Acute Ophthalmoplegia and Hemiparesis

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Introduction:
Miller Fisher syndrome (MFS) is a rare variant of Guillain-Barré syndrome that typically presents with ophthalmoplegia, ataxia and areflexia.[1-3] MFS is often preceded by viral infection (84%) of the gastrointestinal or respiratory tract, or post-vaccinations.[4,5] We present an atypical case of MFS featuring acute eye symptoms, dysphagia, dysarthria and hemiplegia.

Description of Cases:
A healthy 20-year-old woman presented to the ER with double vision and left-sided weakness that began upon waking. Examination revealed diffuse restriction of extraocular movement in left eye, moderate abduction deficit in right eye, left eyelid ptosis, hoarseness of voice, dysarthria, left hemiplegia, global hyporeflexia and left-steppage gait. MRI brain was negative and lumbar puncture revealed no pleocytosis, normal protein (28.1mg/dl) and glucose (45 mg/dl) levels. Consideration of GBS including MFS variant, prompted GQ1b antibody testing (send out labs in our institution). The following day, patient's dysarthria worsened, and she developed difficulty swallowing. When dysphagia heightened case urgency, myasthenia gravis (MG) was considered and treatment with IVIG, prednisone and pyridostigmine was started. After five days of IVIG, she was discharged for clinic follow-up. Subsequently, her MG workup returned negative for Ach receptor binding, modulating and blocking antibodies, and MuSk antibody. However, her serum GQ1b antibody was elevated at 1:800 titer, confirming Guillain-Barré Syndrome with Miller Fisher syndrome (GBS-MFS). Pyridostigmine was discontinued, and steroids were tapered off. Her diplopia resolved after four months of follow-up in ophthalmology clinic.

Conclusions, including unique features of the case:
We feature a GBS-MFS case with unusual presentation: acute eye symptoms, voice/speech changes, and left-sided weakness. This highlights the importance of maintaining broad differentials for oculomotor and neuromuscular issues. Dysphagia and dysarthria misdirected the team to a neuromuscular junction disorder. However, her initial symptoms of ophthalmoplegia, weakness, and areflexia prompted testing for peripheral nerve autoimmunity (LP and GQ1b antibodies). Thorough examination and avoiding diagnostic anchoring ultimately led to uncovering the correct diagnosis.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Ocular motility, Non-organic visual disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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78

Fear of the Occult: A Case of GCA Presenting as Sequential Vision Loss

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Introduction:
Giant cell arteritis (GCA) is a potentially preventable cause of blindness, which requires clinicians to be sensitive to subtle evidence of the disease. Vision loss, elevated ESR/CRP, systemic symptoms, and/or positive biopsy should prompt further evaluation for GCA due to the increased risk of further damage in untreated patients.

Description of Cases:
A 76 year old male reported 5 days of sudden, painless vision loss in the left eye. He denied cardiac history, shoulder stiffness, scalp tenderness, fevers, or muscle/jaw pain. At an outside hospital the preceding day, he was diagnosed with a central retinal artery occlusion (CRAO). Subsequent work-up, including ESR and platelets, was normal aside from mildly elevated CRP and mild calcification of the left carotid artery on CTA. On initial evaluation, the diagnosis of CRAO was confirmed and outpatient TTE was verified. Eight days later, the patient returned to the clinic with new vision loss in the fellow eye. He again denied systemic symptoms and was diagnosed with a sequential right CRAO. Repeat work-up again showed only mildly elevated CRP and ESR. On suspicion of occult GCA, the patient was started on pulse steroids and scheduled for temporal artery biopsy, which was subsequently positive for active arteritis.

Conclusions, including unique features of the case:
This case highlights the difficulties of diagnosing occult GCA and the vision-threatening dangers of a missed diagnosis. Almost all (94.4%) cases of occult GCA manifest as AION. Occult GCA is a diagnosis of exclusion, as patients will not demonstrate classic systemic symptoms. Additionally, ESR and CRP levels are lower compared to classic GCA. This case highlights that an abnormal CRP level should prompt suspicion for GCA regardless of degree of elevation. As approximately 20% of GCA attributable vision loss is due to occult GCA, careful evaluation of all patients over 50 years old must be accomplished.

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Keywords: Vascular disorders, Retina, Stroke

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Eosinophilic Granulomatosis with Polyangiitis Presenting with Optic Neuropathy

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Introduction:
Eosinophilic Granulomatosis with Polyangiitis (eGPA) is a systemic small vessel necrotizing vasculitis diagnosed in the presence of clinical criteria such as obstructive airway disease, nasal polyps, and mononeuritis. Laboratory criteria consists of eosinophilia (>1 x 109/liter), negative cytoplasmic antineutrophil cytoplasmic antibodies (c-ANCA) assay, hematuria and biopsy indicated eosinophilic-predominant inflammation on biopsy [1]. We present three cases of eGPA and review the current literature on the condition's association with optic neuropathy.

Description of Cases:
Case One: An 86-year-old man presents with past medical history (PMHx) significant for asthma, interstitial lung disease, prostate cancer and lung nodules developed acute bilateral visual loss. The patient reports sensorimotor polyneuropathy and previous biopsy revealed extravascular eosinophilia. Laboratory evaluation identified eosinophilia of 18.1% and atypical ANCA titer of 1:40. The patient is stable and currently managed on rituximab and steroids. Case Two: A 41-year-old woman with PMHx significant for asthma, allergic conjunctivitis and eosinophilia of 16.9%. Patient presented with a history of an acute, painful, left-sided ophthalmoplegia that was steroid responsive. MRI revealed enhancement of the cavernous sinus and the diagnosis of Tolosa Hunt Syndrome was made. The patient is being managed on mepolizumab for treatment-resistant asthma with control of symptoms. Case Three: A 54-year-old woman with PMHx significant for chronic sinopulmonary disease, nasal polyposis, peripheral neuropathy and eosinophilia ranging from 6.0-15.7%. Past ocular history is significant for acute painless unilateral vision loss in the right eye leading to optic atrophy in the right eye. The patient's condition remains stable and controlled on dupilumab.

Conclusions, including unique features of the case:
eGPA associated optic neuropathy is an extremely rare manifestation warranting further investigation. When evaluating ocular symptoms in the presence of obstructive airway disease, nasal polyps, mononeuritis multiplex, and in particular eosinophilia, we should consider further evaluation for the diagnosis of eGPA.

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

Financial Disclosures: The authors had no disclosures.
Grant Support: None.

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My, Oh, My

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Introduction:
Moyamoya disease is a cerebrovascular disorder resulting from progressive narrowing and stenosis of the internal carotid artery.(1) We present a unique case of a patient with Alport Syndrome who presented with bilateral optic nerve edema and Moyamoya with stroke.

Description of Cases:
A 40-year-old woman presented with one week of blurred vision. Visual acuity was 20/150 in the right eye and 20/80 in the left eye. Dilated fundus exam showed Frisen grade 5 optic nerve edema with diffuse peripapillary hemorrhages bilaterally. Her blood pressure was elevated at 270/140. The patient became lethargic, and was intubated for airway protection. MRI brain showed an expansile T2/FLAIR hyperintensity within the left cerebral hemisphere that did not enhance with gadolinium, and a somewhat radial pattern on coronal scan, possibly following the vasculature. There was medialization of the left temporal lobe with subfalcine herniation. Lab work showed signs of renal failure with elevated creatinine, hypokalemia, and hyponatremia. The patient underwent left frontal stereotactic needle biopsy, which showed demyelinating changes with macrophages. Digital subtraction angiography showed severe vasculopathy of the supraclinoid right internal carotid artery that appeared chronic. Findings were consistent with Moyamoya disease.(1) A renal biopsy was performed, which was compatible with chronic thrombotic microangiopathy and Thin Glomerular Basement Membrane Disease/Alport Syndrome.(2) Four months later, blood pressure remained under control. Visual acuity was 20/70 in the right eye and 20/30 in the left eye, and optic nerve edema had resolved.

Conclusions, including unique features of the case:
This case is unique due to its presentation of Alport Syndrome presenting with bilateral optic nerve edema and Moyamoya with stroke. This case emphasizes the importance of timely follow-up, coordination of care, and having high suspicion in patients with unexplained optic nerve edema along with other systemic findings to prevent the progression of underlying systemic diseases.

References: 1. Gonzalez NR, Amin-Hanjani S, Bang OY, et al. Adult Moyamoya Disease and Syndrome: Current Perspectives and Future Directions: A Scientific Statement From the American Heart Association/American Stroke Association. Stroke, 54(10):e465-e479. 2023. doi:10.1161/STR.0000000000000443 2. Kashtan CE. Alport Syndrome: Achieving Early Diagnosis and Treatment. Am J Kidney Dis, 77(2):272-279. 2021. doi:10.1053/j.ajkd.2020.03.026

Keywords: Vascular disorders, Optic neuropathy, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Diffuse Large B-cell Lymphoma Presenting as Multiple Cranial Nerve Palsies

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Introduction:
DLBL presenting as isolated or multiple cranial nerve palsies represent a diagnostic challenge. The rarity of this form of presentation warrant attention from health care providers. The authors present a case of sequential seventh and third cranial nerve palsies secondary to DLBL with complete improvement after chemotherapy.

Description of Cases:
A 72 y.o. male with medical history significant for hypertension and Atrial Fibrillation presented to emergency department with left sided lower motor neuron facial palsy. He was diagnosed with bell's palsy and discharged on Valtrex and steroids. One week later, he returned with severe generalized weakness, headache and partial pupil sparing left third nerve palsy. MRI acoustic and orbit protocol with contrast was within normal limits. Work-up for infectious, autoimmune and malignancy including CT chest/abdomen/pelvis was negative. Lumbar puncture (LP) was not possible immediately as patient was on anticoagulant. Miller Fisher variant of Guillain-Barre was considered after EMG showed pattern for possible demyelinating neuropathy in upper extremities. Empirical treatment with IVIG was given for 5 days but patient worsened with progression to left complete oculomotor nerve palsy. After anti-coagulation was stopped for 5 days, LP was done which showed abnormal findings of elevated CSF protein 72, lymphocytic predominance of 16 WBCs and flow cytometry positive for CD10/CD23 cells. MRI of entire spine revealed lesions concerning for metastasis to thoracic vertebrae and sacrum. Bone marrow (BM) biopsy showed Diffuse Large B-cell lymphoma. Patient was started on chemotherapy with full improvement in both 3rd and 7th cranial nerve palsies.

Conclusions, including unique features of the case:
. DBL can present as multiple cranial nerve involvement . MRI brain may be negative for pathologies affecting skull base. High index of suspicion is needed for the diagnostic possibilities based on patient's presentation. . CSF with Flow cytometry and BM biopsy is the key to diagnosis of B-cell lymphoma

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Visual Field Defects with Posterior Cerebral Artery Stroke as a Complication of Anterior Temporal Lobectomy for Medically Intractable Seizures: Case Reports

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Introduction:
Visual field defects (VFDs) following anterior temporal lobectomy (ATL) typically affect the superior quadrant due to anterior optic radiation damage. However, posterior cerebral artery (PCA) strokes after ATL are rare and can result in more extensive VFDs. This case series presents two patients with PCA infarcts after ATL for intractable epilepsy, resulting in contralateral superior quadrantanopia and hemianopia.

Description of Cases:
A 34-year-old man developed left superior quadrantanopia and homonymous left inferior scotoma after right ATL for low-grade glioma. MRI revealed a right PCA infarct sparing the calcarine fissure. A patent foramen ovale was noted in an echocardiogram and is under investigation as a potential contributor to his PCA stroke. A 27-year-old man developed left homonymous hemianopia, hemiparesis, and hemi-neglect after right ATL for mesial temporal sclerosis. MRI revealed a complete PCA occlusion. No clear underlying factors were identified, but medical history included a childhood diagnosis of type 1 diabetes. Both were managed conservatively, with negligible improvement in VFDs long-term.

Conclusions, including unique features of the case:
To mitigate the risk of ATL neurological complications, including ischemic events, careful intraoperative handling of vascular structures is required. These cases emphasize the need for thorough preoperative risk discussions and postoperative monitoring for managing and recognizing these rare PCA strokes post-ATL, as they can lead to significant, irreversible VFDs.

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Keywords: Visual fields, Stroke

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Recurrent Subconjunctival Hemorrhage Following Efgartigimod Treatment in Ocular Myasthenia Gravis: A Unique Case Report

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Introduction:
Efgartigimod is generally well-tolerated, treatment for refractory myasthenia, with most adverse events being mild to moderate. The ADAPT MG trial reported headaches and urinary or respiratory infections as common side effects, with no ophthalmological side effects. We report a unique case of a 75-year-old female with ocular MG who developed recurrent subconjunctival hemorrhage (SCH) after efgartigimod infusion, an undocumented event.

Description of Cases:
A 75-year-old female with ocular MG, idiopathic SCH, osteoporosis, and recurrent diplopia on prolonged steroids was started on Efgartigimod therapy due to intolerance to other immunosuppressants. Shortly after each infusion she developed subconjunctival hemorrhage (SCH) at varying intervals—within an hour, 2 days, and 3 days following the first, second, and third infusions, respectively. The SCH presented both bilaterally and unilaterally, which resolved after discontinuing the treatment. SCH can be linked to factors like age, diabetes, blood disorders, anticoagulation therapy, ocular malignancies, ocular inflammation, and Valsalva maneuver; none of which she had. Transient blood pressure elevation during the first infusion may have contributed to hemorrhagic episodes. However, normal blood pressure during subsequent infusions with persistent SCH ruled out elevated blood pressure as the cause. Her long-term prednisone (10 mg daily only) use was also considered, however in her 5 years of prednisone use, no SCH was noted. With presence of FcRn in the cornea, retina, conjunctiva and other ocular neurovascular structures, we hypothesize that FcRn inhibition may impact vascular integrity in these areas, although the mechanism still remains unclear.

Conclusions, including unique features of the case:
While the mechanism remains unelucidated, this case highlights the first instance SCH has been reported as an adverse event following efgartigimod infusion, warranting further investigation into the long-term effects of FcRn inhibitors on blood vessel integrity. It highlights the potential need to include SCH alongside other hemorrhagic events including hemodynamic instability as exclusion criteria in the administration of efgartigimod.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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CV2/CRMP5 Antibody-Associated Retinopathy Linked to Immune Checkpoint Inhibitor Therapy

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Introduction:
The CV2/CRMP5 (Collapsin response-mediator protein-5) antibody is known to be linked to paraneoplastic neurologic syndromes and can present with many neurologic manifestations. Although rare, ophthalmic presentations include optic neuritis, retinitis, vitritis, and uveitis. Such ophthalmic presentations have rarely been reported to be associated with immune checkpoint inhibitors (ICIs). We report a rare case of CV/CRMP5 antibody-associated encephalopathy, optic neuropathy, and retinal vasculitis related to the ICI, pembrolizumab.

Description of Cases:
A 72-year-old man with Merkel cell carcinoma on pembrolizumab presented with two weeks of mental status changes, hallucinations, weakness, and appetite loss. He was diagnosed with autoimmune encephalitis, he was treated with high-dose IV methylprednisolone, improving his mental status. He later developed bilateral vision loss and was diagnosed with paraneoplastic autoimmune retinopathy, subsequently being treated with monthly IVIG for 6 months. After treatment cessation, severe photophobia persisted, prompting neuro-ophthalmologic referral. Neuro-ophthalmology exam revealed severe bilateral visual acuity decline with a significantly constricted visual field, disc edema/hyperemia, pan uveitis, and retinal pigment epithelium loss bilaterally. Retinal vasculitis was noted on Fluorescein angiogram, peripapillary photoreceptor loss on OCT retina. Electroretinography demonstrated generalized photoreceptor dysfunction. Lumbar puncture revealed elevated protein and lymphocytosis. Further investigation revealed mild gliosis with scattered perivascular lymphocytes infiltration on right dural biopsy and a positive CRMP-5 antibody. He was treated with oral steroids and rituximab, with improvement of the optic neuropathy and retinal vasculitis.

Conclusions, including unique features of the case:
This case highlights a unique presentation of CRMP5 sequelae, including encephalopathy, retinitis, optic neuropathy, and vasculitis. His mental status changes and ocular symptoms developed after starting pembrolizumab. The introduction of this ICI likely triggered the formation of CRMP5 antibodies, resulting in a myriad of neurologic and ocular inflammatory signs and symptoms. In such cases, discontinuing the ICI and considering alternative immunotherapies is advisable. Early and aggressive immunotherapy remains strongly recommended for better prognosis.

References: None provided.

Keywords: Paraneoplastic syndromes, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Retina, Optic neuritis, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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3460 Leber's Hereditary Optic Neuropathy In A 42 Year Old Female Masquerading As A Junctional Scotoma

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Introduction:
Leber's Hereditary Optic Neuropathy (LHON) is a rare mitochondrial disease which causes subacute painless blindness, typically affecting both eyes sequentially. Male individuals are affected at a rate of 5 to 1 compared to women, with features of the disease typically arising between ages 19-55. This report discusses the rare occurrence of a woman with m.3460G< A LHON with a presentation consistent with a junctional scotoma.

Description of Cases:
A 42 year old Caucasian female presented with two months of evolving bilateral loss of central vision of an undetermined etiology. Visual acuity was initially 20/60 OD and 20/70 OS, Ishihara color plates were 5/8 OD and 6/8 OS, and optic nerve head pallor was present OS. Humphrey fields revealed a central scotoma OD and a superior nasal quadrantanopia OS (extending slightly beyond the horizontal and vertical meridians) suggesting a bilateral optic nerve lesion or an atypical chiasm area lesion. The work up for a chiasm area mass was negative. Her vision rapidly deteriorated to 20/400 OU over the span of three months. Genetic testing confirmed the diagnosis of m.3460G< A LHON.

Conclusions, including unique features of the case:
This case highlights the importance of incorporating LHON in the differential diagnosis of woman presenting with an evolving optic neuropathy of unknown etiology, despite the strong male predilection of this disease. We determined the female incidence of a primary affected carrier of m.3460G< A to be 13 in 25 million. These values may be skewed given the presumably low genetic testing rate for LHON in young women because of its already reported rarity. This case highlights the role of genetic testing for this rare mitochondrial disease including woman with atypical optic neuropathy.

References: None provided.

Keywords: Genetic disease, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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An Unusual Optic Neuropathy

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Introduction:
Primary diffuse large B-cell lymphoma involving the optic nerve as the presenting diagnosis of primary CNS lymphoma.

Description of Cases:
76 year old male presented to our emergency room with progressive blurry vision of left eye. He had been admitted to an outside hospital one month prior where he was diagnosed and treated for 'optic neuritis'. He presented to us when vision started to decline again after steroid taper. Exam showed an afferent pupillary defect in the left eye with dyschromatopsia and light perception (LP) vision. Exam was otherwise normal. Blood work and evaluation of CSF for infection, inflammation, and abnormal cells was all negative. MRI orbits showed enhancement along pre-chiasmatic left optic nerve. The patient was admitted for IV steroids, and vision improved to 20/400-2 after five days. Plasmapheresis was then initiated as NMO and MOG lab work were pending – after five days of PLEX his vision was counting fingers in affected eye. At four week follow-up his vison had dropped to hand motion (HM) in the left eye with unchanged optic nerve appearance. Patient began to develop field cut in right side while on steroids: the decision was then made to biopsy optic nerve on left side. Initial biopsy was inconclusive, and a second biopsy was performed via craniotomy which demonstrated a diffuse large B-cell lymphoma.

Conclusions, including unique features of the case:
Here, we report a case of a 76 year old male who had progressive vision loss with some steroid response and repeatedly negative blood work, cerebrospinal fluid evaluation, and progressive enhancing lesions on MRI. He eventually lost all vision in that eye and a biopsy was performed demonstrating the presence of diffuse large B-cell lymphoma, leading to a diagnosis of primary central nervous system lymphoma (PCNSL). This presentation of PCNSL is very rare and is reported in only case reports and series.

References: None provided.

Keywords: Neuroimaging, Chemotherapy and radiation injury, Optic neuropathy, Skull base, Tumors

Financial Disclosures: Rebecca Silverman; Saif Hamdan; Danijel Pericic; Sarah Thornton; Robert Sergott: Robert C. Sergott is a consultant for GenSight Biologics.; Shruthi Harish

Grant Support: None.

Contact Information: None provided.

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Acetylcholine receptor blocking antibodies of questionable diagnostic utility for Neuro-Ophthalmologists

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Introduction:
Myasthenia gravis (MG) is an autoimmune neuromuscular disease caused by autoantibody binding at postsynaptic membranes impeding neuromuscular transmission. MG commonly affects eye muscles, leading to diplopia and ptosis. Diagnostic testing for MG includes Acetylcholine Receptor (AChR) binding, blocking, and modulating antibodies (Abs), differentiated by the sites that they target on the surface of the AChRs. In a prior study from 1987, there were no patients (out of 349 patients with MG) in whom the AChR blocking antibody was positive, without also having positive AChR binding or modulating Abs detected.1 It nevertheless remains common in clinical practice for providers to test for AChR blocking antibodies. We endeavored to study our own experience with AChR Abs in this setting.

Description of Cases:
We performed a single-center, retrospective review of a cohort of adult patients presenting to a Neuro-Ophthalmology Clinic and diagnosed with MG between January 1, 2018, to January 1, 2023. Patients were excluded if they did not have AChR antibody lab work up or were not diagnosed with MG.

Conclusions, including unique features of the case:
There were 176 patients who met our inclusion criteria. There were 57 (32%) patients with AChR blocking antibody positivity with other seropositivity for AChR modulating antibody and/or AChR binding antibody positivity. There were 0 (0%) patients with AChR blocking antibody positivity without other seropositivity. AChR blocking Abs were never positive without other concomitant AChR Abs seropositivity in patients with MG presenting to Neuro-ophthalmology clinics. As such we found that checking AChR blocking Ab is no significant additional value as a diagnostic test in this setting. Our study was limited to a single center and five years of clinical practice. Based on our results, we believe omitting AChR blocking Abs from the work-up of suspected myasthenic patients presenting to Neuro-ophthalmology clinics may be an opportunity to decrease unnecessary health care costs while not sacrificing diagnostic accuracy.

References: Howard Jr, FRANK M., et al. "Clinical correlations of antibodies that bind, block, or modulate human acetylcholine receptors in myasthenia gravis." Annals of the New York Academy of Sciences 505 (1987): 526-538.

Keywords: Myasthenia

Financial Disclosures: The authors had no disclosures.

Grant Support: None

Contact Information: None provided.

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A Rare Case of Bilateral Fourth Cranial Nerve Palsy Secondary to Hydrocephalus

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Introduction:
Bilateral fourth nerve palsy is most commonly caused by head trauma. However, hydrocephalus is an exceedingly rare etiology. Here, we present a rare case of bilateral fourth nerve palsy secondary to hydrocephalus and will discuss the radiological findings and clinical challenges in its management.

Description of Cases:
The patient is a 27-year-old female with a history of bacterial meningitis, complicated by hydrocephalus. While in the hospital, she developed progressive headaches and diplopia. Neuro-ophthalmic examination revealed a small-angle right hypertropia and small-angle esotropia increasing in downward gaze. Double Maddox rod testing revealed excyclotorsion of 10 degrees in the right eye, 7 degrees in the left eye, and 15 degrees in the bilateral test, consistent with bilateral fourth nerve palsy. CT imaging demonstrated dilated 3rd and 4th ventricles. The patient underwent ventriculoperitoneal (VP) shunt placement, which improved her headaches but did not resolve her diplopia. Follow-up MRI revealed stable ventricular size, ruling out shunt malfunction. Given the torsional nature of the diplopia, prism correction was not feasible. The patient was advised to use intermittent eye patching, with surgical correction considered if symptoms persisted beyond six months.

Conclusions, including unique features of the case:
This case illustrates the rare development of bilateral fourth nerve palsy due to hydrocephalus, likely caused by compression of the dilated ventricles on the fourth nerve nuclei in the dorsal midbrain region. The persistence of diplopia despite shunt placement requires continued monitoring and a potential need for surgical intervention. This case underscores the importance of considering hydrocephalus in the differential diagnosis of cranial nerve palsies, especially in patients with a history of intracranial infections.

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Keywords: Ocular motility, Adult strabismus with a focus on diplopia, High intracranial pressure/headache, Neuro-ophth & infectious disease (eg, AIDS, prion), Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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An atypical case of Miller Fisher syndrome presenting with bilateral ptosis and total external ophthalmoplegia

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Introduction:
Miller Fisher syndrome (MFS) is a rare entity of Guillain-Barré syndrome (GBS) characterized by the triad of external ophthalmoplegia, ataxia, and areflexia. MFS arises from an antecedent infectious event that initiates the process of molecular mimicry. Diplopia (78%) and ataxia (48%) are prevalent symptoms of MFS, while ophthalmoplegia accounts for almost 34%. MFS diagnosis is a clinical one. Cerebrospinal fluid (CSF) studies, electrodiagnostic studies, and serologic analysis help confirm the diagnosis. Here we describe an atypical case of MFS presenting with bilateral ptosis and total external ophthalmoplegia without laboratory evidence.

Description of Cases:
A 42-year-old previously healthy male presented with rapidly developing diplopia and dizziness for 2 days. Neurological examination was remarkable for bilateral ptosis and total external ophthalmoplegia without areflexia. The remainder of the exam was negative. Neuroradiological imaging, including magnetic resonance imaging (MRI) with and without contrast of the brain and the cervical and lumbar spine, did not show any acute process or abnormal enhancement. Lumbar puncture revealed cerebrospinal fluid (CSF) with elevated protein and normal cell count. Extended serological workup including anti-GQ1b IgG, anti-GM1 IgM/IgG, anti-Aquaporin4 IgG and MOG antibody revealed negative findings. He received a course of IV immunoglobulin (2 g/kg over 5 days) and had complete recovery in 2 months.

Conclusions, including unique features of the case:
There are many incomplete or atypical forms of MFS. Recognition of its various clinical presentations is essential for early diagnosis and optimal management. Further investigation is needed to elucidate the role of serological workup and laboratory test including nerve conduction study in the pathogenesis of MFS patients.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Calciphylaxis: A Rare Cause of Ischemic Vision Loss

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Introduction:
Calciphylaxis is a life-threatening condition that can cause vision loss due to anterior ischemic optic neuropathy and chorioretinal ischemia. In addition to a review of 18 published cases, we present two new cases of optic neuropathy and one of chorioretinal ischemia due to biopsy-proven calciphylaxis.

Description of Cases:
Case 1 A 70-year-old male with ESRD on HD, CAD, HTN, HLD, and T2DM described 3 weeks of central scotoma OS. Vision was 20/20- in each eye. There was pallor of the optic disc OS and Grade I edema OD. ESR and CRP were elevated. Urgent TAB revealed extensive calcium deposition consistent with calciphylaxis. His dialysate solution was adjusted. Two months later, vision was stable with resolution of optic disc edema. Case 2 A 73-year-old female with diffuse large B cell lymphoma in remission, CHF, Afib on warfarin, HTN, and T2DM presented with four days vision loss OD. Vision was 20/40 OD and 20/20 OS. Exam showed Grade II disc edema OD. She had painful leg wounds which showed vascular calcifications on biopsy. TAB also demonstrated calcification consistent with calciphylaxis. The etiology of her non-uremic calciphylaxis was most likely due to warfarin use. Despite initiation of sodium thiosulfate, her non-healing skin wounds quickly progressed and she passed away. Case 3 A 62-year-old female with HTN, T2DM, and bilateral internal carotid artery stenosis presented for acute vision loss OD weeks prior. Vision was 20/70 OD, 20/20 OS. Cotton wool spots were noted along the arcades OD. FA revealed profound choroidal perfusion delay OD. Urgent TAB demonstrated calciphylaxis. Her exam improved in follow up. This non-uremic calciphylaxis was likely due to extensive occlusion of the internal carotid vessels.

Conclusions, including unique features of the case:
Calciphylaxis remains a potentially fatal diagnosis with non-uremic calciphylaxis being especially rare. Ophthalmologists must act swiftly in obtaining diagnosis (preferably by TAB) and coordinating care with the patient's internist.

References: None provided.

Keywords: Optic neuropathy, Retina, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: Mary-Grace Reeves is the recipient of the Vitreo-Retinal Surgery Foundation Research Award, supporting her research during 2023-2025. This work was additionally supported by an unrestricted grant from Research to Prevent Blindness.

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MOGAD Optic Neuritis in Older Adults : A Case Series

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Introduction:
Optic neuritis (ON) is an atypical etiology for vision loss with optic disc edema in patients over 65 (1). Further, Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disorder (MOGAD), a common cause of ON in the pediatric population, is a rare etiology for ON in older adults (2,3). We present a case series of two males over 65 years old presenting with MOGAD ON.

Description of Cases:
Patient 1 is a 70-year-old male with subacute left eye blurred vision, urinary retention and left arm weakness. Examination found a left afferent pupillary defect (APD), optic disc edema, a T2 dermatomal sensory level, and hyperreflexia. MRI showed left optic nerve, T1-T3, and conus medullaris enhancement. Symptoms improved with IV methylprednisolone and plasma exchange. One month later, he re-presented with right blurred vision and retrobulbar pain. MRI revealed right optic nerve enhancement. He received intravenous methylprednisolone and intravenous immunoglobulin, with substantial clinical improvement. MOG antibodies were positive at 1:10,000 by serum live cell-based assay. Patient 2 is a 68-year-old male with two days of progressive blurred vision and moderate retrobulbar pain. Examination showed left eye optic disc edema, APD and 20/200 vision. MRI revealed left optic nerve enhancement. MOG antibodies were positive at 1:100 by serum live cell-based assay. He had complete symptomatic resolution with intravenous methylprednisolone and a steroid taper.

Conclusions, including unique features of the case:
Epidemiological studies found that < 5% of new onset MOGAD cases present in patients over 50 (2). In patients over 45 with unilateral vision loss and optic nerve edema, Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION) has a 51-fold higher incidence than MOGAD ON (4). A multicenter study of MOGAD ON in patients over 45 found a mean age of 56 (IQR 49.8-60.9) and a 70% female predominance (4). This highlights the atypical nature of this case series presenting two men with new-onset MOGAD ON over age 65.

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Keywords: Demeylinating disease, Optic neuritis

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Phenylketonuria and Visual Symptoms: The Impact of Dietary Control on Neurological and Ophthalmic Outcomes

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Introduction:
A 42-year-old woman with a medical history including phenylketonuria (PKU), visual snow syndrome (VSS), fibromyalgia (FM), and migraines presented to the neurology clinic with bilateral spots in her visual fields, blurry vision, and recurrent migraines.

Description of Cases:
Initial Visit: The patient reported constant small spots across her visual field bilaterally for the past nine months. She also experienced paresthesias in her distal lower extremities. Her migraines recurred with increased severity and frequency over the past six months, accompanied by photophobia, nausea, and fatigue. Her physical examination revealed a visual acuity of 20/25 with normal color vision, slit lamp examination, OCT, and Humphrey visual fields. Neurological exam revealed decreased temperature and vibration sensation distally, but otherwise unremarkable. Laboratory tests were normal except for low B1 and B12, which were corrected with oral supplementation. MRI showed small hyperintensities in the right frontoparietal region and bilateral occipital white matter. The patient was started on Lamotrigine for VSS and Galcanezumab for migraines. Four Years Later: Our patient presented back to clinic and stated that her migraines and paresthesias had resolved. However, she continued to experience VSS, photophobia, and developed new persistent decreased energy, worsening fibromyalgia, and blurry vision bilaterally. Lab work and visual examination remained unremarkable. Afterwards, she started a strict PKU diet which required maintaining a low-protein diet and controlled intake of phenylalanine-rich foods. To her delight, on follow up, she reported significantly clearer vision and decreased light sensitivity, allowing her to reduce lens tint from 80% to 50%. She also reported improved energy and fibromyalgia symptoms. Interestingly, repeat MRI brain showed subtle improvement of the hyperintense lesions noted in prior imaging.

Conclusions, including unique features of the case:
This case underscores the importance of PKU dietary management in mitigating neurological and ophthalmic symptoms. The improvement following metabolic control suggests a therapeutic role for diet in managing visual symptoms in PKU patients.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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CNS White Matter Lesions and Progressive Optic Neuropathy in a Child with Craniopharyngioma after Resection and Proton Beam Radiation

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Introduction:
Radiation therapy (XRT) for brain tumors has been associated with risks including radiation necrosis and radiation-induced optic neuropathy. XRT has rarely been associated with demyelinating lesions simulating multiple sclerosis (MS). We report a case of a child with white matter lesions suggestive of MS in association with unilateral optic neuropathy after XRT for craniopharyngioma.

Description of Cases:
A 15-year-old boy with delayed puberty and intermittent headaches underwent a brain MRI and was found to have a suprasellar mass involving the optic chiasm, consistent in appearance with a craniopharyngioma. On initial ophthalmologic exam, he was 20/20 in both eyes with normal optic nerves. He underwent subtotal resection and subsequently developed cystic recurrence, which was treated by proton beam radiation. Four months later, his visual acuity decreased to 20/25 in the left eye, with a new RAPD, mild thinning on the OCT RNFL, and nonspecific visual field defects. There was a concern for tumor recurrence, and he underwent repeat MRI. This revealed tumor shrinkage, no enhancement of the optic nerves, and periventricular T2/FLAIR hyperintense white matter lesions, some of which were enhancing. He had no systemic neurologic symptoms. There was a concern for radiation necrosis, and he underwent hyperbaric oxygen therapy and a course of dexamethasone, without improvement. Lumbar puncture showed elevated IgG index and oligoclonal bands, and AQP4 and MOG antibodies were negative. At ten months post-radiation, his left eye visual acuity stabilized at 20/50, with a stable OCT RNFL average thickness of 78 µm. His white matter lesions remained asymptomatic and were largely resolved on repeat MRI scan.

Conclusions, including unique features of the case:
This case suggests that radiation damage to oligodendrocytes can result in a pattern of demyelination similar to MS, while simultaneously causing presumed radiation optic neuropathy. Unlike MS, the white matter lesions may be asymptomatic and resolve spontaneously.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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"Brainzy"

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[1] West Virginia University, [2] University of Pennsylvania

Introduction:
Retinal vasculopathy with cerebral leukoencephalopathy (RVCL) in a 42-year-old Caucasian male, secondary to TREX 1 mutation.

Description of Cases:
A 42-year-old male presented to the emergency room with severe headaches and confusion. A CT scan revealed a left frontoparietal white matter lesion extending into the left basal ganglia and thalamic regions, causing mass effect on the left lateral ventricle and a rightward midline shift. He was diagnosed with acute encephalopathy due to a left-sided frontoparietal lesion and associated vasogenic edema. His medical history was significant for multiple substance use disorder. Initially, the lesion was suspected to be an abscess or tumefactive multiple sclerosis, and he was treated with broad-spectrum antibiotics, but there was no improvement. A CTA of the intracranial and extracranial vessels showed no evidence of vasculitis. To rule out malignancy, he underwent surgical resection of the brain lesion, which revealed a macrophage-predominant inflammatory process. His best-corrected visual acuity of 20/20 in the right eye and 20/25 in the left. Color vision was normal. Examination revealed mild optic nerve pallor and peripheral retinopathy in the right eye, as well as peripheral avascular retina in the left eye. Visual fields showed inferior depression in both eyes, and optical coherence tomography revealed global retinal nerve fiber layer (RNFL) thinning with ganglion cell analysis showing inferior temporal wedge defects bilaterally. Fluorescein angiography (FA) demonstrated peripheral neovascularization in the right eye, and peripheral neovascularization in the left eye for which he was treated with laser photocoagulation. On further questioning, he reported a family history of retinal vasculopathy with cerebral leukodystrophy (RVCL) in his father, paternal grandmother, and other paternal relatives. A complete rheumatological evaluation was conducted, and genetic testing confirmed a pathogenic TREX1 mutation (c.802del p.(R268Gfs*9)

Conclusions, including unique features of the case:
We describe the spectrum of disease in RVCL (TREX -1 (c.802del p.(r268gfs*9) mutation) in this young patient.

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

Financial Disclosures: Somya Chowdhary; Monique Leys; Han Peng Cheng; Jonathan Miner: Heads the RVCL research center in Pennysylvania

Grant Support: none

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Trapped In My Head

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Introduction:
Camurati- Engelman disease is a rare autosomal dominant disease, produced by mutations in the TGFB1 gene. It is associated with bilateral symmetric diaphyseal hyperostosis of the long bones with progressive involvement of the metaphysis We describe a gentleman with this disease who presented with bilateral proptosis and bilateral optic neuropathy associated with bilateral sensory neural hearing loss.

Description of Cases:
A 52 year old non-obese gentleman with hypertension and h/o radial keratotomy presented in neuro-ophthalmology for evaluation of bilateral optic disc elevation. He has bilateral hearing loss. Reported pulsatile tinnitus but denied headache or vision loss. On exam visual acuity was 20/20 OD and 20/25 OS , had normal color vision, no afferent pupillary defect, had bilateral proptosis, bilateral lagophthalmos and bilateral lower eyelid retraction. Anterior segment showed radial keratotomy marks OU. Fundus exam showed elevated optic discs OU that seemed longstanding. HVF 24-2 OU was unremarkable but retinal nerve fiber layer thinning was seen OU with intact ganglion cell analysis. Reported longstanding history of muscle weakness of all extremities and bony abnormality since he was a child. He was diagnosed with Camurati–Engelmann disease around age 8. MRI head with contrast 2 years ago was unremarkable. Denied progressive visual loss. Never had a spinal tap. He was recommended another MRI head and orbits to monitor the optic neuropathy.

Conclusions, including unique features of the case:
Ocular manifestations are rare in this rare genetic disease. There is bony overgrowth of the orbit and optic canal stenosis. Orbital bone involvement may result in proptosis, rarely globe subluxation and optic nerve compression. Cranial base involvement leads to foraminal sclerosis and raised intracranial pressure, producing papilledema. Facial palsy, hearing loss and epiphora may occur.

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Keywords: Genetic disease, Miscellaneous, Optic neuropathy, High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Wernicke Encephalopathy and Optic Neuropathy: Rare Conditions

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Introduction:
Wernicke syndrome is a result of thiamine deficiency that typically presents with ophthalmoplegia, nystagmus, ataxia, altered mental status, and rarely presents with optic neuropathy. We report a case of optic disc edema and vision loss associated with Wernicke's encephalopathy in the setting of semaglutide-induced GI disturbance. This case highlights a unique manifestation of thiamine deficiency, which is highly treatable.

Description of Cases:
A 41-year-old woman presented with four days of bilateral progressive painless vision loss and six weeks of diarrhea, paresthesia, and emesis following the initiation of semaglutide for weight loss. On examination, vision was 20/400 bilaterally with normal intraocular pressure, full motility, and no rAPD. Dilated ophthalmoscopy revealed bilateral temporal optic disc edema with a few macular hemorrhages in the right eye. MRI brain showed symmetric, bilateral diffusion restriction and hyperintensity on T2-weighted FLAIR within medial thalami, mammillary bodies, periaqueductal grey matter as well as areas of nodular enhancement in the periaqueductal gray matter, hypothalamus, and medial thalami consistent with Wernicke encephalopathy. She received intravenous thiamine, stopped semaglutide, and experienced a rapid 4 days, significant, and sustained improvement of her acuity to 20/20 with persistent paracentral visual field defects and the development of mild, bilateral optic atrophy.

Conclusions, including unique features of the case:
Wernicke's syndrome, typically associated with chronic alcoholism, can be induced by any cause of thiamine deficiency. While uncommon, optic neuropathy has been a manifestation of thiamine deficiency, often accompanied by optic disc edema. Semaglutide is a long-acting GLP-1 receptor agonist, with a frequent side effect of dose-related nausea and diarrhea. To our knowledge, this is the first documented case of bilateral optic disc edema caused by thiamine deficiency precipitated by the side effects of semaglutide. Our case highlights the importance of early detection of visual changes due to thiamine deficiency and rapid treatment as prompt initiation of therapy can prevent severe, permanent neurological manifestations.

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Keywords: Optic neuropathy, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Collapsin Response-Mediator Protein 5 Paraneoplastic Syndromes – A Descriptive Case Series

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Introduction:
Collapsin response-mediator protein 5 immunoglobulin G (CRMP5-IgG) associated paraneoplastic syndromes can cause the triad of bilateral papillitis, vitritis, and/or retinitis.(1) Due to the rarity of the disease and extensive testing required for a diagnosis, there is a paucity of data on ocular manifestations of CRMP5-IgG syndromes. Most studies to date focus on the papillitis aspect of the phenotype, with only case reports describing associated electroretinogram (ERG) changes, which are variable across studies.(2-5) Therefore, we aim to report the details of retinopathy in our cohort of CRMP5-IgG associated disease.

Description of Cases:
Out of 76 patients with CRMP5 autoimmunity, we identified 7 (9%) patients with subacute bilateral vision loss and retinopathy. Of the 7 patients, 5 had coincident papillitis, vitritis, and systemic neurologic symptoms, while the remaining 2 had retinitis as their sole manifestation of the disease. In the patients with retinitis, there was ellipsoid zone disruption and photoreceptor loss on optical coherence tomography. Visual fields showed variable patterns including central scotomas, ring scotomas, and peripheral constriction. Fluorescein angiography showed perivenular, optic nerve head, and macular leakage. Full field and multifocal ERG showed variable patterns of predominant cone dysfunction, mixed cone-rod dysfunction, and predominant rod dysfunction. One patient had different ERG phenotypes in each eye. Underlying cancer was found in 5 of 7 patients (4 small-cell lung cancer, 1 ductal carcinoma), 4 of whom had improvement with immunotherapy.

Conclusions, including unique features of the case:
CRMP5-IgG paraneoplastic syndrome, although classically associated with bilateral papillitis, can also manifest as retinopathy though this aspect of the phenotype is underreported in the literature. Our cohort of patients with CRMP5-associated retinitis display varied patterns of photoreceptor dysfunction on ERG testing. Therefore, there is not a single phenotype that should prompt CRMP5 testing and it can be considered in any patient with autoimmune retinopathy especially if there are coinciding neurologic symptoms, papillitis, and/or vitritis.

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Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Neuroimaging, Optic neuritis, Paraneoplastic syndromes, Retina

Financial Disclosures: jessica Kraker; Devon Cohen; Flanagan Eoin; Sean Pittock: Sean J. Pittock has received personal compensation for serving as a consultant for Roche/Genentech, Sage Therapeutics, Arialys and Astellas. He has received personal compensation for serving on scientific advisory boards or data safety monitoring boards for F. Hoffman-LaRoche AG, Genentech, Arialys and UCB. His institution has received compensation for serving as a consultant for Astellas, Alexion, and Viela Bio/MedImmune. All compensation is paid to Mayo Clinic. He has received research support from Alexion, Viela Bio/MedImmune, Roche/Genentech and Adimmune. He has a patent, Patent# 8,889,102 (Application#12-678350, Neuromyelitis Optica Autoantibodies as a Marker for Neoplasia)—issued; a patent, Patent# 9,891,219B2 (Application#12-573942, Methods for Treating Neuromyelitis Optica (NMO) by Administration of Eculizumab to an individual that is Aquaporin-4 (AQP4)-IgG Autoantibody positive)-issued and from which he has received royalties and a patent for GFAP-IgG; Septin-5-IgG; MAP1B-IgG; Kelch-like protein 11; PDE10A pending. He is working as a consultant in the Mayo Clinic Neuroimmunology laboratory clinical service. The Mayo Clinic Neuroimmunology Laboratory commercially offers MOG-IgG testing, but revenue accrued does not contribute to salary, research support, or personal income; Brittni Scruggs; Kevin Chodnicki; Deena Tajfirouz; John Chen

Grant Support: None.

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Clinical features and prognosis of orbital fungal infection

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Introduction:
Fungal infection is a serious disease that can be life threatening if not properly treated, but diagnosis is often delayed because the first symptoms are often non-specific. Appropriate biopsy is essential to determine the treatment. This study was to investigate the clinical features and prognosis of orbital fungal infection.

Description of Cases:
Medical records of patients who were diagnosed as orbital fungal infection via histological or cultural results and underwent anti-fungal treatment. Patients with positive were included. Ophthalmic features and type of anti-fungal treatment was analyzed. Fifteen patients (17 eyes) were included. The mean age was 66.9 ± 8.4 years. Thirteen patients had diabetes while there was no immunocompromised patient. Two patients had a previous history of sinusitis surgery. Confirmed pathogen was Aspergillus in 13 patients. Patients could be classified into five categories based on the clinical features. (1) Optic neuropathy in 5 patients (2) Pan orbital disease in 4 patients (3) Orbital apex syndrome in 5 patients (4) Anterior-orbital disease (5) other. All patients showed radiological abnormality correlated with clinical symptoms. Vision prognosis varied from NLP to 20/20.

Conclusions, including unique features of the case:
Orbital fungal infection showed various clinical features depending on the region of invasion. MRI and active biopsy of the suspected lesion are helpful in diagnosis.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Bilateral Enophthalmos in Parry-Romberg Syndrome: A Case Report of Novel Disease Manifestation

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Introduction:
Parry-Romberg syndrome (PRS) is a rare condition predominantly affecting children and young adults, characterized by progressive unilateral hemifacial atrophy. Ocular involvement in PRS is uncommon, however enophthalmos, a posterior displacement of the eyes due to retrobulbar fat atrophy or globe shrinkage, has been reported. Isolated bilateral enophthalmos in a patient with exclusively unilateral signs is undocumented in the literature. We treated a patient with bilateral enophthalmos and midface atrophy, warranting consideration of PRS subtype.

Description of Cases:
A 64-year-old female presented to clinic in complaint of transient diplopia, blurry vision, and a 15-year history of periodic generalized muscle weakness without bulbar symptoms. On examination, a striking facial asymmetry was noted due to right midface wasting, which the patient did not believe to be a long-standing issue. Old photos corroborate this statement, as midface atrophy was progressive. Facial asymmetry showed right midfacial wasting with narrowing of the right palpebral and reduced right lid movement. Despite muscle wasting, bilateral pterygoid strength was full, and masseter bulk was found to be symmetrical. Physical examination revealed diffuse generalized muscle weakness. Muscle bulk in the upper and lower extremities was symmetrical. Acetylcholine receptor antibody titers were negative. EMG of upper and lower extremities did not show evidence of disordered neuromuscular transmission, myopathy, or lower motor neuron disease. MRI was remarkable for bilateral enophthalmos as well as an incidental finding of Chiari I Malformation.

Conclusions, including unique features of the case:
Hemifacial muscle wasting is not common and warrants a consideration in the differential diagnosis. It is plausible that the development of progressive hemifacial atrophy and bilateral enophthalmos represent a rare variant of PRS.

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Keywords: Orbit/ocular pathology

Financial Disclosures: The authors had no disclosures.

Grant Support: N/A

Contact Information: None provided.

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Ophthalmic complications associated with the antidiabetic drugs semaglutide and tirzepatide

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Introduction:
Nearly 2% of the US population received a prescription for semaglutide in 2023. There has been recent concern that this drug and other, similar medications may be associated with ophthalmic complications. In a retrospective cohort study of NAION and semaglutide use at a single institution, an increased risk of NAION was demonstrated with a hazard ratio of 7.64. In this retrospective case series, we describe five women and four men, ages 37-77 years with ocular complications temporally associated with the use of GLP-1 receptor agonists.

Description of Cases:
We report seven cases of non-arteritic anterior ischemic optic neuropathy, one case of sequential papillits, and one case of PAMM in patients using GLP-1 receptor agonists (semaglutide, dulaglutide, tirzepatide) for type 2 diabetes (T2D) and/or weight loss. In all cases, these complications occurred after initiation or dose escalation of these medications. Visual presentations ranged from painful vision loss to painless scotomas or shadows, typically upon awakening. Most cases involved optic nerve swelling and scotomas, with some progressing to optic nerve atrophy. Visual acuity ranged from 20/15 to counting fingers, with significant defects on perimetry. Neuroimaging showed features typical of non-arteritic anterior ischemic optic neuropathy. Treatments included steroid administration and discontinuation of the medication, leading to either stabilization or partial recovery of visual function. Atypical features included sequential ischemic optic neuropathy, bilateral disc swelling at presentation, and progressive vision loss. Diagnostic workups excluded common causes like MOGAD, NMOSD, and increased intracranial pressure. These findings suggest a potential association between GLP-1 receptor agonists and ocular complications, warranting further investigation.

Conclusions, including unique features of the case:
It is not possible to determine if there is a causal link between these drugs and the ophthalmic complications reported. In some cases, we hypothesize that it may be the rapid correction of hyperglycemia induced by these drugs, rather than a toxic effect, that caused the ophthalmic complication.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: Supported in part by a grant from Research to Prevent Blindness, New York, NY, USA to the Department of Ophthalmology and Visual Sciences, University of Utah Health, Salt Lake City, UT, USA

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Bilateral optic nerve atrophy as the presenting symptom of chronic cerebral venous sinus thromboses in autoimmune hemolytic anemia

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Introduction:
Cerebral venous sinus thrombosis (CVST) is a rare but life-threatening condition that can be difficult to diagnose. We present a 41-year-old Burmese female with a history of autoimmune hemolytic anemia who presented with chronic CVST and progressive vision loss. Her symptoms began a decade prior to moving to the United States from Burma. Imaging revealed severe bilateral optic atrophy with chronic intracranial venous congestion and marked dilation of the extracranial venous system.

Description of Cases:
A 41-year-old female with autoimmune hemolytic anemia (AIHA), headache, hypertension, and diabetes presented with progressive bilateral vision loss. Notable medications included prednisone, azathioprine, and mycophenolate. The patient reported previously taking an unknown medication for her vision and headaches in Burma for an undiagnosed neurological condition, which she had stopped after her vision improved ten years prior. Subsequently, she experienced significant deterioration in her vision. Her vision on exam was 20/400 OU. Pupillary exam revealed no RAPD. Dilated fundus exam showed bilateral optic atrophy with signs of gliosis. MRI orbits and MRV of the head and neck identified extensive intracranial dural venous sinus thromboses, with an extensively distended extracranial cortical venous system and collateral venous pathways of the face and scalp. Laboratory evaluations showed leukocytosis and thrombocytosis. A lumbar puncture revealed elevated intracranial pressure of 23 cmH2O and otherwise normal CSF contents. Optical coherence tomography confirmed bilateral optic nerve thinning on the peripapillary retinal nerve fiber layer and macular ganglion cell analysis with signs of permanent visual loss indicating a poor outcome. AIHA may have predisposed this patient to CVST.

Conclusions, including unique features of the case:
We highlight the end-stage ocular manifestations of longstanding CVST, despite collateralization of the extracranial cortical venous system. Headaches and progressive visual symptoms should prompt clinicians to investigate neuro-ophthalmic causes. Venous phase imaging of the head should always be performed in patients with papilledema or bilateral optic neuropathy.

References: None provided.

Keywords: Neuroimaging, High intracranial pressure/headache, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Vascular disorders, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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A Case of Treatment with Efgartigimod PH20 SC in a Patient with Ocular Myasthenia Gravis

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Introduction:
The objective is to describe the effect of efgartigimod PH20 SC in a case of ocular myasthenia gravis (oMG). oMG is a form of myasthenia gravis (MG) in which ocular muscles are easily fatigued and weakened, causing symptoms including diplopia and ptosis. 12-80% of patients presenting with only ocular symptoms develop generalized myasthenia gravis (gMG). Efgartigimod is a human IgG1 antibody Fc-fragment that reduces total IgG levels, including pathogenic IgG autoantibodies, through neonatal Fc receptor blockade. Because Efgartigimod IV and SC have demonstrated tolerability and efficacy in patients with gMG, including ocular symptoms associated with gMG, we hypothesized that this patient would benefit from efgartigimod.

Description of Cases:
Patient's oMG treatment followed this dosing scheme: efgartigimod PH20 SC 1000mg administered subcutaneously in cycles of 4 once-weekly injections followed by 6 weeks between cycles, with initiation timing of subsequent cycles determined by clinical judgement. 58-year-old male first experienced diplopia April 2022 and presented to the hospital with diplopia May 2023. Baseline MG-ADL score was 5 (constant diplopia, daily ptosis). Patient is AChR-Ab positive and MGFA class I. Initiation of oral prednisone resulted in monocular vision changes leading to discontinuation. Pyridostigmine has provided incomplete symptom relief. Patient worries about job stability due to disease progression. Current oMG treatment includes efgartigimod PH20 SC and pyridostigmine 60mg as needed. Clinical improvements were observed one month after the last dose of patient's first cycle (MG-ADL 2: diplopia 2, ptosis 0). MG-ADL reassessment in March 2024 was 3 (diplopia 1, ptosis 2). Current MG-ADL is 2 (diplopia 1, ptosis 1). Current MG symptoms include diplopia (only in weeks between cycles), minor ptosis, and deconjugate gaze in left eye only. No adverse effects reported with efgartigimod PH20 SC.

Conclusions, including unique features of the case:
This case demonstrates potential for symptomatic improvement of oMG when treated with efgartigimod PH20 SC, though further study is warranted.

References: None provided.
Keywords: Myasthenia, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: Julie Dela Cruz: JDC is an employee of argenx.; J. Douglas Miles: Currently or within the past two years, I have received personal compensation from a commercial interest for serving as a consultant. Please see the following for more information: - Argenx US, Inc. Title: consultant. Year(s): 2023. Dollar range: $500-4,999. Recipient: myself. Paid to: individual. - UCB, Inc. Title: consultant. Year(s): 2024. Dollar range: $500-4,999. Recipient: myself. Paid to: individual. - Alexion Pharmaceuticals, Inc. Title: consultant. Year(s): 2024. Dollar range: $500-4,999. Recipient: myself. Paid to: individual. Currently or within the past two years, I or my Immediate Family Member have received research support from a Commercial Interest, Non-Profit Organization, or Government Entity serving as a principal investigator. Please see the following for more information: - HMSA Center of Learning Innovation. Role in research project: Principal Investigator. Year(s): 2023. Dollar range: $500-4,999. Recipient: myself. Paid to: individual Currently or within the past two years, I or my Immediate Family Member have received publishing royalties from a publication relating to Health Care. Please see the following for more information: - Elsevier. Description: Book royalties. Year(s): 2019-2024. Recipient: myself Currently or within the past two years, I or my Immediate Family Member have NOT - received personal compensation from a commercial Interest or Non-Profit Organization (does not include private-practice, academic, or hospital-based settings, see above definitions) for serving as an employee (requires filing of an IRS Form W-2) - received personal compensation from a commercial Interest for serving on a Scientific Advisory or Data Safety Monitoring Board - received personal compensation from a commercial interest for serving on a Speakers Bureau - received personal compensation from a commercial interest or Non-Profit Organization for serving as an officer or Member of a Board of Directors - received personal compensation from a commercial interest or Non-Profit Organization for serving as an editor, associate editor, or editorial advisory board member - received personal compensation from a commercial interest for serving as an expert witness - owned Stock or an Ownership Interest (excluding mutual funds)from a commercial interest - held Patents, Royalties, or Other Intellectual Property Interests with a Discovery or Technology relating to Health Care received personal compensation from a commercial interest, Non-Profit Organization, or Government Entity for serving in other capacity

Grant Support: None.
Contact Information: None provided.

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Glial Fibrillary Acidic Protein Astrocytopathy Presenting as Asymptomatic Bilateral Optic Disc Edema with Normal Neuroimaging

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Introduction:
Glial Fibrillary Acidic Protein (GFAP) astrocytopathy is an autoimmune, steroid-responsive CNS condition associated with encephalitis, meningitis, and/or myelitis. This new disease entity has no specific clinical signs but presents with broad meningoencephalitis symptoms. MRI characteristically shows perivascular radial brain enhancement and/or longitudinal spinal enhancement. Visual involvement documented ranges from asymptomatic disc edema to severe vision loss, without elevated intracranial pressure. The pathophysiology of optic disc edema in GFAP astrocytopathy remains uncertain. Its incidence has been reported in up to 50% of cases investigated with fundoscopy. Relapse occurs in 20-50% after one course of steroids and is more common in patients with visual involvement.

Description of Cases:
A previously healthy 68-year-old male presented with subacute-onset fatigue, lower extremity pain, and floaters. Neuro-ophthalmic exam demonstrated isolated bilateral optic disc edema with normal visual acuity, visual fields, extraocular motility, and pupil testing. Fluorescein angiography and indocyanine green angiography showed bilateral optic disc staining and leakage without vasculitis. Brain/orbits neuroimaging was unrevealing, and cervical spinal MRI showed degenerative changes without enhancement. CSF opening pressure was normal, but CSF analyses revealed elevated protein and lymphocytic pleocytosis. Extensive serologic and CSF workup of infectious, inflammatory, demyelinating, and paraneoplastic etiologies was negative, as were chest CT and whole-body PET CT. GFAP-IgG antibodies were positive in CSF and not in serum. With oral corticosteroid treatment, optic disc edema resolved.

Conclusions, including unique features of the case:
We present a case of bilateral optic disc edema without associated vision loss in the setting of normal ICP and lymphocytic pleocytosis due to GFAP astrocytopathy. Although GFAP astrocytopathy characteristically shows perivascular brain or longitudinal spine enhancement, our case did not have such findings. Therefore, we believe GFAP astrocytopathy should be added to the differential in bilateral asymptomatic optic disc swelling, without elevated ICP, in patients with normal neuroimaging. GFAP-IgG-related disc edema can be treated with corticosteroids, which may preserve visual function.

References: None provided.

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

Financial Disclosures: Kristina Lin; Rabih Hage; Michael Trainer; Nailyn Rasool; Marc Levin: Unrelated financial compensation as: consultant, Jazz Pharmaceuticals; consultant, Vanda Pharmaceuticals; royalties, University of California; Emily Eng; Siavash Assar

Grant Support: None.

Contact Information: None provided.

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Keep your Eye on the Ball

Zachary Barry [1], Nicholas Levergood [2], Kevin Lai [2], Robert Bell [3], Devin Mackay [4], Melissa Ko [2]

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Introduction:
A 50-year-old man presented with episodic diplopia, which developed into a right partial oculomotor palsy. Neurological findings included right-sided hyperreflexia, decreased temperature sensation in his right hand, and a dilated right pupil. Initial MRI, MRA/CTA, and MRV were reported normal. Cerebrospinal fluid (CSF) studies including cytology, serum metabolic, myasthenic and inflammatory studies were normal. Initial neuro-ophthalmic evaluation was stable, but over eight weeks he developed left eye abduction/adduction deficits, right facial sensory changes, and right foot drop. Repeat neuroimaging was normal, but lumbar puncture (LP) revealed a new lymphocyte-predominant pleocytosis, elevated protein, and elevated opening pressure with negative cytology. Review of initial MRIs revealed subtle cisternal enhancement of the right oculomotor nerve.

Description of Cases:
Extensive investigation of this patient's history disclosed two years of right hemiscrotum swelling. Positron emission tomography demonstrated an enlarged right retroperitoneal lymph node, and biopsy confirmed stage IIA testicular seminoma. Treatment was initiated with high-dose intravenous methylprednisolone, immunoglobulin, and chemotherapy. CSF studies for paraneoplastic disease were negative at this time. As his condition worsened, repeat imaging finally showed bilateral oculomotor and facial nerve enhancement and transverse myelitis. Treatment with rituximab and steroids were initiated for presumed paraneoplastic disorder. Testing at an outside institution identified Leucine Zipper 4 antibody (LUZP4). Testicular seminoma has been previously linked to antibodies to KLHL11 and Ma2.2-4 LUZP4 is a novel antigen strongly associated with testicular seminoma.5,6 He had some visual symptom improvement with cancer treatment and immunotherapy, but the patient remained wheelchair-bound.

Conclusions, including unique features of the case:
This patient developed a progressive bilateral cranial polyneuropathy and myelitis. Initial work up with neuroimaging, CSF analysis, and infectious/inflammatory/toxic labs were reported as unremarkable. Neuro-ophthalmic examination revealed a history of scrotal swelling, leading to diagnosis of testicular seminoma with positive paraneoplastic biomarkers. The patient displayed limited improvement despite cancer treatment and immunotherapy. Exhaustive series of testing discovered underlying antibody-positive paraneoplastic disorder.

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Keywords: Paraneoplastic syndromes

Financial Disclosures: The authors had no disclosures.

Grant Support: None

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Vision Loss in Giant Cell Arteritis Treated with Tocilizumab

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Introduction:
Neuro-ophthalmic relapses of giant cell arteritis (GCA) have rarely been reported on tocilizumab,[1-3] so the timing, extent, and reversibility of visual involvement remains incompletely characterized. We describe four cases of vision loss on maintenance doses of tocilizumab.

Description of Cases:
Case 1: An 80-year-old woman presented with central retinal artery occlusion OS; temporal artery biopsy was positive, and she was started on tocilizumab. Three months later, she developed "tunneling" of her vision OS upon tapering prednisone to 5 mg daily that resolved with high-dose steroids. Case 2: A 53-year-old woman presented with peripheral vision loss OS; temporal artery biopsy was negative, but she developed a supraduction limitation OS and worsening headaches upon weaning prednisone. MRI brain was unrevealing, prompting initiation of tocilizumab for biopsy-negative GCA. Four months later, after tapering prednisone to 10 mg daily, she developed headaches and peripheral field constriction OD with pallid disc edema; MRI, PET-CT, and lumbar puncture were unrevealing, and her vision loss remained stable. Case 3: A 76-year-old woman with polymyalgia rheumatica developed headaches and jaw pain; temporal artery biopsy was positive, prompting treatment with tocilizumab. One year later, she developed blurred vision OD with 20/25 central acuity, a relative afferent pupillary defect, dyschromatopsia, and disc pallor. MRI was negative, and her optic neuropathy remained stable. Case 4: A 78-year-old man presented with bilateral anterior ischemic optic neuropathy; temporal artery biopsy was positive, and he was started on tocilizumab. Three months later, he developed intermittent "darkening" vision after weaning prednisone to 20 mg daily, prompting addition of methotrexate. Eighteen months later, he developed worsening, painless vision loss OD that subsequently remained stable.

Conclusions, including unique features of the case:
Although rare, transient or permanent vision loss can occur during treatment with tocilizumab. The highly variable time to onset, severity, and reversibility of visual involvement presents a challenge to accurate retrospective assessment of relapse frequency.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Neuro-ophthalmologic Characteristics Of Idiopathic Hypertrophic Pachymeningitis

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Introduction:
Idiopathic hypertrophic pachymeningitis (IHP) is a devastating neurologic disease caused by inflammatory thickening of the dural meninges of the brain and spinal cord. Neuro-ophthalmologic manifestations include vision loss, extraocular motility deficits, and papilledema (1–5). Immunosuppression is initiated after the exclusion of infectious etiologies, but delayed treatment, side effects of long-term steroid use, and incomplete response increase patient morbidity. Here we present a case series of dural biopsy-confirmed IHP.

Description of Cases:
A single-center retrospective analysis of all dural biopsies submitted to UCSF Neuropathology (2012-2024) was performed. 14 patients were identified (8 female, 6 male, mean age 50) with biopsy-confirmed pachymeningitis, diffuse dura matter enhancement on T1-weighted gadolinium enhanced magnetic resonance imaging (MRI) at presentation, and negative work-up for inflammatory, infectious, neoplastic, and infiltrative etiologies. Presenting symptoms included transient (2) or sustained (3) vision loss, cranial neuropathies (6), chronic headache (8), encephalitis (1), and compressive spinal symptoms (2). Presenting visual acuities (VA) ranged from 20/20 to NLP. MRI abnormalities were restricted to cranial or spinal dura in 4 cases -- extradural pathology was noted in orbit (4), cavernous sinus (4), central venous sinuses (2), mastoid processes (2), pituitary (1), brain parenchyma (1), and nasopharyngeal sinuses (1) in the remaining 10 patients. In eyes with VA worse than 20/100, acuity returned to baseline in compressive optic neuropathy or papilledema-associated vision deficits with steroid and intracranial pressure reducing treatments in all but 3 eyes. Orbital apex pathology with concomitant diminished VA and extraocular motility deficits were a poor prognostic marker for visual recovery.

Conclusions, including unique features of the case:
IHP is a poorly understood clinical entity that can present with neuro-ophthalmologic deficits. We identify simultaneous motility deficts and VA decline below 20/100 as predictors of poor visual prognosis. There is no standardized treatment regimen and ocular outcomes remain highly variable, justifying further investigation of this enigmatic pathology to protect vision.

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

Financial Disclosures: Aurel Nagy; Emily Eng; Kristina Lin; Siavash Assar; Marc Levin: Unrelated financial compensation as: consultant, Jazz Pharmaceuticals; consultant, Vanda Pharmaceuticals; royalties, University of California; Rabih Hage; Nailyn Rasool

Grant Support: None.

Contact Information: None provided.

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Cerebral Polyopia Due To Paraneoplastic Monoclonal IgG4-Related Hypertrophic Pachymeningitis

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Introduction:
Cerebral polyopia is the perception of multiple images from a single stimulus associated with occipital lobe lesions from trauma, stroke, seizures, tumors, or inflammatory disease. IgG4-related disease (IgG4-RD) is a fibroinflammatory condition which can rarely affect central nervous system. We describe a case of cerebral polyopia due to paraneoplastic monoclonal IgG4 hypertrophic pachymeningitis associated with small-cell lung cancer (SCLC).

Description of Cases:
A 66-year-old female with a history of Sjogren's syndrome presented with 4 months of episodic multiplication of images. She reported up to six to eight images revolving around a central image. Symptoms were similar with either eye open and persisted with pinhole. She had no headaches and denied history of migraine. Her neurological and ophthalmological exams were within normal limits. MRI of the brain with and without contrast demonstrated left hemispheric and falcine pachymeningeal thickening and enhancement. EEG was within normal limits. IgG4 was elevated at 406 mg/dL (normal < 86 mg/dL). SPEP demonstrated monoclonal gammaglobulinemia with an M spike of 1.43. CSF analysis revealed no WBCs and a protein of 52 mg/dL. CSF electrophoresis confirmed presence of monoclonal gamma globulin. PET/CT was concerning for malignancy in the lingula with mediastinal metastasis. Bronchoscopy with biopsy was consistent with undifferentiated SCLC. Malignancy was treated with chemotherapy and local radiation. For presumed IgG4-mediated hypertrophic pachymeningitis, she received three days of 1 gram IV methylprednisolone followed by a 6-week prednisone taper. Repeat IgG4 level was 89 mg/dL. Follow-up MRI prior to completion of chemotherapy demonstrated near resolution of pachymeningeal enhancement. Patient also reported resolution of visual symptoms.

Conclusions, including unique features of the case:
This patient presented with cerebral polyopia that ultimately resulted in a diagnosis of paraneoplastic monoclonal IgG4-RD associated with SCLC. This case is the first known association between SCLC and IgG4-RD. Treatment with corticosteroids led to clinical and radiographical improvement, reinforcing their utility in atypical cases.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Understanding the Myelin Oligodendrocyte Glycoprotein Optic Neuritis: Balancing Steroid Dependence and Immunosuppression

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Introduction:
Myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease is a demyelinating disorder often presenting with optic neuritis. It is diagnosed by detecting MOG antibodies through a live cell-based assay. While corticosteroids are effective initially, relapses are common, especially with quick tapering. Ongoing research aims to improve treatment strategies and predict relapses.

Description of Cases:
A 27-year-old woman presented with painful vision loss in the right eye, diagnosed as optic neuritis. Initially treated with intravenous methylprednisolone (IVMP) followed by oral steroids, her symptoms recurred after stopping steroids, necessitating the restart of 30 mg Omnacortil (prednisolone). Magnetic resonance imaging (MRI) revealed T2 hyperintense signals in the right intraorbital optic nerve and periventricular demyelinating patches. Best corrected visual acuity (BCVA) was 6/5 in both eyes, with normal color vision, fundus, and visual field tests, although early ganglion cell complex (GCC) thinning was detected. Blood tests confirmed MOG antibodies, indicating MOG-antibody-associated disease. Due to recurrent optic neuritis, she was treated with rituximab and instructed to taper her steroids. Despite immunosuppression, a third attack occurred when her methylprednisolone dose was reduced to 8 mg, causing her vision to decline to 6/7.5 with visual field constriction. She was treated with a second dose of rituximab, intravenous immunoglobulin (IVIG), and mycophenolate mofetil. However, steroid side effects, including moon facies, buffalo hump, and acne, developed. Steroids were tapered to 5 mg, but she experienced a nasal visual field defect in the right eye, requiring further IVMP treatment to control the recurrence.

Conclusions, including unique features of the case:
This case highlights the challenges of managing steroid-dependent optic neuritis in patients with MOG antibodies. Recurrent episodes correlated with steroid tapering and significant side effects underscore the need for alternative immunosuppressive therapies to improve long-term outcomes while tapering steroids.In retrospect, prolonged treatment with 10 mg of oral steroids with immunosuppressive for 3 months initially could have prevented the relapses.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Novel Management of Herpes Zoster Ophthalmicus with Optic Neuritis and Cavernous Sinus Involvement

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Introduction:
Optic neuropathy is a rare complication of Herpes Zoster Ophthalmicus (HZO). In the literature, these cases are typically treated with IV Acyclovir/Valacyclovir and, controversially, IV corticosteroids. Despite these treatments, most patients have significant irreversible vision loss.

Description of Cases:
55-year-old female presented to the emergency department with right sided facial pain and afterwards developed a rash in the right trigeminal V1 distribution characteristic of HZO. MRI Brain/Orbits with and without contrast at that time was unremarkable. She was treated with Acyclovir and Valacyclovir with visual acuity of 20/50 in the involved eye secondary to corneal disease. During follow-up, roughly 1 month after symptom onset, the patient's visual acuity abruptly decreased to hand motion and she developed extraocular movement restrictions. Repeat MRI Brain/Orbits showed obvious right optic nerve and cavernous sinus enhancement. The patient was treated with a 14-day course of IV ganciclovir 340mg twice daily and a 5-day course of 1 gram Methylprednisolone daily. During follow-up the patient's best corrected visual acuity improved to 20/25 in the involved eye with a small superior visual field defect on perimetry.

Conclusions, including unique features of the case:
This report demonstrates a rare case of HZO optic neuropathy with cavernous sinus involvement who made a dramatic improvement after treatment with an unconventional therapeutic approach including systemic ganciclovir and IV corticosteroids.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Neurosyphilis with Disc Edema

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Introduction:
Neurosyphilis can be a vision threatening and potentially life-threatening complication of an infection by the spirochete Treponema pallidum. We describe two cases of patients presenting with vision changes as the first manifestation of syphilis.

Description of Cases:
1) 58-year-old male presented with four months of blurry vision in his right eye. Examination showed Frisen grade 2 optic disc edema in both eyes. MRI/MRV brain and orbits showed numerous microhemorrhages throughout the brain. LP was considered but in the meantime Syphilis testing came back positive with titer of 1:512. Infectious disease recommended not acquiring a lumbar puncture given ocular symptoms with elevated titers was diagnostic. 2) 55-year-old male presented with gray spots in right eye for 1 week. Examination showed VA of 20/25 right eye and 20/30 left eye with acute disc edema with hemorrhages and exudates in both eyes. MRI brain and MRV head was negative. Lumbar puncture showed opening pressure of 10.5 with negative CSF VDRL. A syphilis screen was obtained which resulted positive with RPR titers of 1:128. Both patients were started on penicillin G IV 4 million units every four hours for two weeks. In patient 1 repeat syphilis titers ten months later demonstrated a >4-fold decrease in titers (1:32), and he was asymptomatic at 1 year follow up with mild disc pallor. In patient 2, at 1 month follow up, exam showed improvement in disc edema in right eye and stable swelling in left eye, repeat syphilis titers pending.

Conclusions, including unique features of the case:
• Cases of syphilis surged during HIV/AIDS epidemic (1980s-early 1990s), decreased with public health interventions, but have risen again since the 2000s.1,2 • 37% of patients with ocular syphilis will develop neurosyphilis which can be life-threatening.3 • Prompt diagnosis and treatment is needed to save patient's vision and life in ocular syphilis.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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WFS1- Associated optic neuropathy in a predominantly Asian population

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Introduction:
Wolfram Syndrome Type 1 (WFS1) has been traditionally described to cause a constellation of symptoms collectively known as DIDMOAD (diabetes insipidus, diabetes mellitus, optic atrophy, and deafness). In recent years however, it has been found that Wolfram Syndrome Type 1 can manifest a diverse range of phenotypes. However, isolated optic atrophy in WFS1 patients with no other systemic involvement is rare.

Description of Cases:
We report a short case series of WFS1 related optic atrophy in a predominantly Asian population. These patients were identified as having pathogenic WFS1 mutations when they underwent whole exome sequencing as part of a larger study to diagnose hereditary optic neuropathy in patients with bilateral optic neuropathy of unknown cause despite extensive investigations. Four patients were found to have pathogenic mutations in WFS1. Of these, three were Chinese, with ages at WS diagnosis ranging from 18 to 41 years. All patients presented with insidious onset bilateral blurring of vision and had bilateral optic atrophy. Only one had a positive family history. Two patients had only bilateral optic atrophy clinically indifferentiable from OPA1 dominant optic atrophy, and no other syndromic features of WFS1. Genotyping confirmed autosomal recessive Wolfram Syndrome in all 4 patients and 3 of these were compound heterozygotes for distinct pathogenic WFS1 variants.

Conclusions, including unique features of the case:
Consistent with previous reports, autosomal recessive Wolfram Syndrome has a variable phenotype. Uniquely, we present the first and largest case series in Singapore with WS, of which two of the four patients had isolated optic atrophy with no other systemic manifestations, and only two of the four having diabetes. This expanded understanding underscores the complexity of Wolfram syndrome, and further research will help us understand this elusive disease better.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: NIL

Contact Information: None provided.

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A Visionary Approach: Last-Minute Rescue with Fractional Radiotherapy for Progressive Occipital Edema and Visual Loss from Lupus Cerebritis

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Introduction:
Systemic lupus erythematosus (SLE) is a multifaceted autoimmune disorder that can affect various organ systems, including the central nervous system (CNS), which can lead to neurologic and neuro-ophthalmic manifestations as well (10-30% of cases). Prompt recognition of CNS involvement is critical, as it is associated with increased mortality and often necessitates an elaborate and complex treatment regimen to manage effectively.

Description of Cases:
A 62-year-old right-handed female with history of SLE on prednisone, leflunomide, and mycophenolate, migraine, and central venous thrombosis who presented to the Neuro-ophthalmology clinic with multiple episodes of abrupt transient bilateral vision loss, worsening headaches, photophobia, and scalp tenderness. The initial examination revealed a right homonymous visual field defect. MRI Brain identified a corresponding left occipital mass extending both supra- and infra-tentorially. Cerebrospinal fluid analysis (CSF) showed lymphocytic pleocytosis, and dural biopsies ultimately confirmed lupus cerebritis. Despite treatment with immunomodulatory agents, the patient's symptoms worsened aggressively, with an increasing homonymous altitudinal field defect and progressive enlargement of the occipital mass on MRI. This led to the addition of rituximab along with high-dose steroids. However, her condition continued to decline, presenting with new-onset weakness and gait instability, necessitating hospitalization and pulse-steroid therapy. Although there was initial stabilization, her headaches and vision deteriorated, and a repeat MRI revealed further progression of the occipital mass, raising concerns for potential herniation. An interdisciplinary team decision was made to initiate fractionated radiotherapy. Two months later, the patient experienced significant symptomatic relief, and follow-up MRI showed a marked reduction in both the mass burden and meningeal involvement.

Conclusions, including unique features of the case:
Progressive Lupus cerebritis involving the occipital lobe in this case caused significant altitudinal visual loss, refractory to multiple anti-inflammatories and immunomodulators. Fractionated radiotherapy was initiated, showing impressive clinical improvement and brain lesion regression. Radiotherapy is a considerable option for patients with refractory lupus cerebritis.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Leber Hereditary Optic Neuropathy (LHON) Peer-to-Peer Mental Health Booklet

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Introduction:
A non-profit organization established to support patients and promote science for LHON, partnered with a licensed clinical psychologist to create a booklet to be used by mental health providers working with the LHON community.

Description of Cases:
The purpose of the LHON Peer-to-Peer Mental Health Booklet is twofold. Its primary purpose is to provide mental health clinicians with a greater understanding of this rare disease and how it affects not only the individual who has lost central vision, but also others associated to the affected individual such as moms, dads, siblings and spouses/partners. The secondary purpose of this booklet is to serve as a resource for medical specialists who see these patients, but do not specialize in the mental health support that is also needed. A clinical psychologist interviewed members of the LHON community who represent fourteen unique roles related to an LHON diagnosis. From these interviews, a peer-to-peer mental health booklet was created that shares commonly experienced mental health challenges for each role within the LHON community and guides mental health professionals to understand the unique mental health challenges different individuals with different relationships to LHON may encounter. The booklet was completed in October 2024.

Conclusions, including unique features of the case:
A newly affected individual with LHON will often receive their diagnosis from a neuro-ophthalmologist. This booklet can be a part of the toolkit offered to patients and their families by the neuro-ophthalmologist who will be sharing this diagnosis, its prognosis and the fact that there is no cure yet for the vision loss that will or already has been rapidly lost.

References: None provided.

Keywords: Genetic disease, Optic neuropathy, Pediatric neuro-ophthalmology, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: This booklet was supported by a grant from Global Genes.

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As You Can See, The Mouth Speaks For Itself

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Introduction:
Introduction: Acromegaly, a rare condition, of excess growth hormone (GH) and insulin-like growth factor (IGF-1) production due to an adenoma of the pituitary gland.1,2 This condition is characterized by physical changes and symptoms of headaches and visual loss. Acromegaly is often undiagnosed until cranial features become clinically prominent. Its orofacial features can significantly impact one's quality of life; hence, physicians need to recognize changes in jaw size.

Description of Cases:
Description: 28 year old male with 4 year history of headache, snoring, and ill-fitting retainers. His dentist was unable to properly fit him with a retainer. Due to concerns for jaw prognathism, referral for medical examination. Endocrine blood studies included insulin-like growth factor-1 (IGF-1) 801, prolactin 9.94, thyroid-stimulating hormone (TSH) 1.28, thyroxine (T4) 1.07, cortisol 4.8, adrenocorticotropic hormone (ACTH) 7.8, testosterone 303, free testosterone 2.75 and contrasted MRI brain revealed sella enlargement by a hypoenhancing homogeneous pituitary gland lesion. Additionally he had increasing hand and ring size and blurry vision. Neuro-ophthalmic examination demonstrated intact visual acuity and visual field testing. The patient underwent transsphenoidal hypophysectomy.

Conclusions, including unique features of the case:
Conclusions: Orofacial symptoms of acromegaly include frontal bossing, lip thickening, mandibular prognathism, widening of nose, macroglossia, teeth separation, aperthognathia, malocclusions, and palatal tissue hypertrophy.3,4 Our patient had total resection of the pituitary adenoma with resolving acromegalic signs and symptoms specifically, improvement in jaw size. The clinical diagnosis of severe condylar hyperplasia is straightforward. Reversal of endocrine-based orofacial changes prove to positively impact the patient's quality of life. Thus, it's important for dentists and the multidisciplinary specialty team to have a keen awareness and recognition of a patient's early changes in jaw size. This may lead to sooner diagnosis of a functioning pituitary tumor and, for some, preventable visual loss.5 Sometimes, the mouth speaks for itself and allows neurologists and ophthalmologists to focus accordingly.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: N/A

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Not all Altitudinal Visual Field Defects are NAION

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Introduction:
Non-arteritic ischemic optic neuropathy (NAION) is the most common cause of painless optic neuropathy in adults over 50 years of age with associated vascular risk factors. Visual function is generally preserved. Optic nerve head swelling must be present, and altitudinal visual field defects are common. We present a patient with a large meningioma mimicking bilateral sequential NAION.

Description of Cases:
A 52-year-old Cantonese-speaking man with a history of hypertension and sleep apnea developed acute onset painless visual field loss in the right eye upon awakening in September 2023. He saw a doctor in China who diagnosed him with glaucoma and prescribed eye drops. Around March 2024 he had milder left eye vision loss. On examination at our clinic in June 2024, visual acuities were 20/300 OD and 20/25 OS. There was a mild relative afferent pupillary defect and decreased color vision OD. Automated visual field showed inferior altitudinal visual field defects OU with bilateral retinal nerve fiber layer thickening and diffusely decreased ganglion cell complex layer on OCT. Brain MRI demonstrated a large enhancing extra-axial mass with extensive vasogenic edema throughout the right hemisphere, midline shift and right uncal herniation. In July 2023, he underwent resection of a sphenoid wing meningioma. His visual field improved and his visual acuities were 20/70 OD and 20/25 immediately post-surgery.

Conclusions, including unique features of the case:
Bilateral sequential NAION is rare. Therefore, one should have a high index of suspicion for compressive, infiltrative and inflammatory causes in patients showing clinical deterioration over time. Optic nerve head swelling initially appreciated on funduscopic examination and optical coherence tomography usually resolves within 11 weeks. Persistent swelling should raise consideration of an alternative diagnosis. NAION has no treatment, but processes like inflammatory optic neuropathy, and tumors can be treated to prevent progression and recover visual function. The mechanism of the loss of vision may have been papilledema.

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Keywords: Optic neuropathy, Tumors, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Utilizing Social Media for Neuro-Ophthalmology Education, Outreach, and Pipeline Development

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Introduction:

Social media in neuro-ophthalmology has the potential to improve patient and physician education; to advance subspecialty advocacy and promote professional networking; and develop outreach, marketing, and a pipeline for recruitment to our field. We review the advantages of specific platforms and report on specific metrics over time for the use of the video-sharing website, YouTube. We also address potential ethical considerations and concerns regarding misinformation. The aim is to provide clinicians, patients, and educators with a comprehensive, up-to-date overview of the role of social media in neuro-ophthalmology.

Description of Cases:

Methods: A review of recent literature and surveys was conducted to assess the usage patterns and effectiveness of social media platforms in neuro-ophthalmology. A PubMed search for the terms “social media” AND “neuro-ophthalmology” as well as “social media” AND “ophthalmology” was performed. Inclusion criteria required full-text publications in scholarly journals. The analytics and metrics for one neuro-ophthalmology site from YouTube, NODAL (Neuro-ophthalmology with Dr. Andrew Lee) were reviewed. Results: The literature search produced over 50 articles and as expected most were published in the last 4 years (2020-2024). Outcome measures included engagement analysis, Altmetric analysis, and utilization surveys. Since inception on June 4, 2017, the NODAL YouTube site has produced 813 videos, has 87.7K subscribers, and over 7 million views. Reviews of the guidelines from the American Academy of Neurology (AAN), American Academy of Ophthalmology (AAO), and North American Neuro-Ophthalmology Society (NANOS) were also reviewed.

Conclusions, including unique features of the case:

Social media offers significant benefits for neuro-ophthalmologists but requires careful management to address misinformation and maintain content quality, underscoring the need for responsible usage. We believe that specific platforms (e.g., YouTube) have the potential to promote neuro-ophthalmology as a specialty; increase awareness about the field among the lay patient and medical provider populations; and create interest and enthusiasm for the field to develop a pipeline for future trainees.

References: None provided.

Keywords: Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Radiologic-clinical correlation study of patients with stroke-Induced Isolated or Predominant Third Nerve Palsy

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Introduction:
Third nerve palsy is an unusual manifestation of stroke. This study aims to describe the clinical features and underlying mechanisms of patients with stroke-induced third nerve palsy.

Description of Cases:
We identified 10 stroke patients with third nerve palsy as the predominant symptom. Magnetic resonance imaging or computed tomography, and in most cases, angiography, were performed. The clinical and neuroimaging features of these patients was analyzed. Six males and four females were included. The ages ranging from 11 to 69 years (mean, 56.1 years). Seven patients had cerebral infarctions, while three had hemorrhagic strokes. Nine patients exhibited ptosis, with bilateral ptosis in one case. Pupillary dilation were observed in four patients. Various patterns of weakness in extraocular muscles innervated by the oculomotor nerve were noted. Notably, medial rectus weakness was predominant when compared to other ocular muscles. Ataxia was the most common neurologucal symptom. Patients were classified into groups based on the extent of midbrain lesions: isolated and combined. The anteromedial territory was the region most commonly affected in this group. Pathogenesis analysis indicated large vessel disease and artery-to-artery embolism in combined infartion, small vessel disease in isolated midbrain infarction, and cavernous hemangioma or hypertension in hemorrhagic strokes.

Conclusions, including unique features of the case:
In this patient cohort, the medial rectus muscle fibers were commonly affected, and ataxia was the most prevalent neurological symptom. The anteromedial territory emerged as the most frequently affected region. This study contributes to a better understanding of the clinical and neuroimaging features of stroke-induced third nerve palsy.

References: None provided.

Keywords: Stroke, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Neuro-ophthalmic complications of molecular targeted therapies. Two case reports and review of literature.

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Introduction:
The following cases represent the increasing number of patients presenting with neuro-ophthalmic side effects of biologic therapeutics.

Description of Cases:
Case number 1 41 years old female, treated with Alemtuzumab (CD-52 monoclonal antibody) for Multiple sclerosis, developed both Thyroid orbitopathy and ocular Myasthenia gravis (MG). Co-occurrence of all three diseases is possible but very rare. Thyroid autoimmunity is a common (17% -34%) side effect of Alemtuzumab. Thyroid eye disease is noticed in >2% and MG was also reported (1-5). Case number 2 75 years old male, treated with Ipilimumab and Nivolumab for metastatic Melanoma, complained of fatigue, ptosis and diplopia due to new onset Myasthenia gravis. Immune checkpoint inhibitors are associated with both orbital myositis and ocular myasthenia gravis (6).

Conclusions, including unique features of the case:
Molecular targeted therapies, including monoclonal antibodies and small molecule inhibitors, are now widely used to treat oncologic and inflammatory diseases. The number of such agents and its approved indications is rapidly increasing. Reports of wide variety of ophthalmic adverse effects are also rising. Neuro-ophthalmologists might encounter optic neuritis, optic disc edema, oculomotor nerve palsies, immune-related myasthenia gravis and posterior reversible encephalopathy syndrome (7-8). Most ophthalmic adverse effects can be treated with specific ocular therapy or corticosteroids without discontinuation of cancer treatment, but some life-threatening or vision-threatening events may require therapy cessation in consultant with the oncologist (5-8).

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Improved Visual Outcomes in Pediatric Optic Disc Drusen-Associated Neovascularization: A Systematic Review

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Introduction:
Optic disc drusen (ODD) are calcified deposits in the anterior optic nerve associated with visual field loss and vascular complications. ODD-associated choroidal neovascularization (ODD-CNV) is a rare complication of ODD that causes prominent vision loss. Treatment has not been standardized, particularly in the younger population. We aim to integrate current evidence to report visual outcomes in ODD-CNV patients managed differently. We conducted a systematic review of all published ODD-CNV cases from 1974 to 2024 in three different databases (PubMed, EMBASE, and Web of Science). Only studies reporting baseline visual acuity, follow-up visual acuity, and an intervention were included. Methodological quality was assessed using the Newcastle–Ottawa Scale for case series and case reports.

Description of Cases:
A total of 71 eyes (62 patients) were identified from 45 eligible articles. The median age of the subjects was 13.5 years (range: 3-75). 64.8% were females. Only 32.8% of CNV cases occurred bilaterally. CNVs were mainly peripapillary, with 43.3% of them progressing to involve the macula. On average, the eyes had a follow-up period of 21.7 months. Overall, treatment (of any type) showed better outcomes (0.52 LogMAR improvement, >3 lines on Snellen chart) compared to observation only (0.09 LogMAR improvement). Anti-VEGF injections and laser photocoagulation, the most frequently used interventions, showed 0.63 and 0.19 LogMAR improvement, respectively. Among 22 pediatric eyes, anti-VEGF showed 0.74 LogMAR improvement with minimal side effects and recurrence in one eye only. When stratified by age, pediatric patients experienced a greater LogMAR improvement compared to adults, even when adjusting for anti-VEGF treatment ($p = 0.0279$).

Conclusions, including unique features of the case:
Our findings highlight the importance of intervention in ODD-CNV patients, particularly in the younger population as they tend to be more responsive to treatment. Anti-VEGF demonstrates great efficacy and safety profile in the pediatric population.

References: None provided.

Keywords: Optic neuropathy, Vascular disorders, Pediatric neuro-ophthalmology, Retina

Financial Disclosures: Anas Alkhabaz; Rishita Pujari; Yaping Joyce Liao: Consulting: Stoke Therapeutics

Grant Support: None.

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Acute Acquired Comitant Esotropia Secondary to a Large Foramen Magnum Meningioma

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Introduction:
Acute acquired comitant esotropia (AACE) is characterized by sudden onset of comitant esotropia with diplopia, often in older children or adults. Neurological examination and imaging are required to determine the etiology of AACE, although in many cases, no etiology can be identified. Here, we introduce a patient with AACE, presumably secondary to a foramen magnum meningioma.

Description of Cases:
A 73-year-old woman presented with acute onset of binocular diplopia that started 2 days prior to presentation. Diplopia was horizontal and occurred only at distance. She denied any other neurologic problems such as headache or any pain, weakness, paresthesia, or mental change. Her past medical history was significant for Sjogren's disease, treated with hydroxychloroquine. On neuro-ophthalmic exam, the patient's best corrected visual acuity was 20/30 OD and 20/20-2 OS. Pupils were equal and reactive to light without afferent pupillary defect. Anterior and posterior segment exams were normal. Strabismus exams showed an esotropia of 25 prism diopters in the primary position and other cardinal positions with a full range of motion consistent with AACE. MRI of the brain with and without contrast revealed an enhancing extramedullary mass at the C1 level. This suspected meningioma 2.5 x 1.6 x 1.8 cm caused mass effect on the cervicomedullary junction and moderate to severe foramen magnum stenosis. MRI of the orbits and the screening blood tests for thyroid eye disease and myasthenia gravis were within normal limits. A neurosurgery consult recommended observing the mass with surveillance imaging and avoiding surgery due to the high-risk location.

Conclusions, including unique features of the case:
AACE has been reported in association with various diseases in the posterior fossa, including medulloblastoma, cerebellar astrocytoma, Chiari malformation, and others. This paper highlights a novel case of AACE, presumably due to meningioma at the foramen magnum and compression of the cervicomedullary junction that has not been previously reported.

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Keywords: Orbit/ocular pathology, Skull base, Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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What is the visually enhanced vestibulo-ocular reflex and how can I use it to localize and diagnose?

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Introduction:
The visually enhanced VOR (vVOR) is a combination of both VOR and smooth pursuit. In conjunction with the head impulse test (HIT) and VOR suppression (VORS), this battery of ocular motor tests quickly evaluates the integrity of the vestibular and cerebellar systems. Herein, we describe these tests and demonstrate their utility in patients with 1) normal vestibular and cerebellar systems, 2) isolated unilateral vestibular loss (UVL), 3) isolated bilateral vestibular loss (BVL), 4) isolated cerebellar ataxia, and 5) cerebellar ataxia with BVL (e.g., cerebellar ataxia, neuropathy, and vestibular areflexia syndrome [CANVAS], and spinocerebellar ataxia [SCA] 27B).

Description of Cases:
vVOR: vVOR is a combination of pursuit and VOR. If either of these is intact, then the vVOR will be normal. If the vVOR is saccadic, both pursuit and VOR are impaired. Pursuit: A saccadic appearance is a consequence of reduced gain (saccadic amplitude/target amplitude < 1) in the pursuit system, resulting in saccades to reach the target. Cerebellar ataxia is a common reason for impairment. HIT: This rapid head movement isolates the VOR as the pursuit system fails at high speeds. If a catch-up saccade is present, this is an abnormal result. VORS: Smooth pursuit and VORS are almost always both normal or both abnormal. However, when pursuit is saccadic and VORS is normal, this implies there is no VOR present to suppress so vestibular loss must be present.

Conclusions, including unique features of the case:
When the vVOR is saccadic, the examiner can quickly conclude both the vestibular and cerebellar systems are impaired. Furthermore, an abnormal vVOR allows the examiner to quickly and accurately predict the results of smooth pursuit, HIT, and VORS tests. The vVOR should be evaluated in all patients presenting with downbeat nystagmus, oscillopsia, dizziness, or imbalance because, when abnormal, the differential can be narrowed to disorders causing concomitant vestibulopathy and cerebellopathy (e.g., CANVAS and SCA27B).

References: 1.Leigh, R. John, and David S. Zee. The Neurology of Eye Movements. Buch R. John Leigh ; David S. Zee. 4th ed., Oxford Univ. Press, 2006. 2.Gold, Daniel. Neuro-Ophthalmology and Neuro-Otology: A Case-Based Guide for Clinicians and Scientists. Springer International Publishing AG, 2022. 3.Halmágyi, Gábor M et al. “The visually enhanced vestibulo-ocular reflex in CANVAS.” Journal of neurology vol. 269,1 (2022): 490-492. doi:10.1007/s00415-021-10755-8 *Poster will include a table describing each test result (x axis) by each patient scenario described above (1-5, y axis).*

Keywords: Vestibular disorders, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Ocular manifestations of vestibular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Quantification Of Metabolic Stress In Optic Nerve Ischemia Using Flavoprotein Fluorescence Imaging And The Impact Of Optic Disc Edema

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Introduction:
Endogenous flavoprotein fluorescence (FPF) imaging is a novel technique to image accumulation of oxidized flavoprotein in living mitochondria – an indicator of metabolic stress. We present 3 patients with nonarteritic anterior ischemic optic neuropathy (NAION) who had serial optic disc FPF imaging to assess the evolution of acute to chronic phases of NAION, which is associated with significant optic disc swelling acutely and thinning of the optic nerve axons chronically.

Description of Cases:
Case 1 is a 67-year-old woman with right NAION with visual acuity of 20/125. Disc FPF signal was normal 2 weeks after onset, when there was severe optic disc edema. Her FPF increased at 1-month, when disc edema was reduced with pseudonormalization of the peripapillary retinal nerve fiber layer (pRNFL). At 3-months, FPF was even higher, with resolution of optic disc edema and thinned pRNFL. At 6-months, FPF and pRNFL remained stable. Case 2 is a 71-year-old man with left NAION with 20/250 visual acuity. Disc FPF was normal 1-week after onset, when there was severe disc edema. Repeat imaging at 6-months when there was no optic disc edema, revealed increased FPF. Case 3 is an 86-year-old woman with left NAION with 20/70 visual acuity. At 3-months, there was still some disc edema, and disc FPF was normal. At 6-months, disc FPF was increased, when disc edema resolved along with severe optic atrophy. In chronic phase of NAION in all 3 cases, temporal disc had the highest FPF signal, corresponding with the papillomacular bundle. Representation of disc FPF signal using Garway-Heath map revealed high correspondence of the disc FPF with that of static perimetry.

Conclusions, including unique features of the case:
Optic disc edema masks disc FPF signal in acute NAION. As edema resolves, axonal mitochondrial stress is unmasked, peaking at 3 months and remaining stable at 6 months.

References: None provided.

Keywords: Optic neuropathy, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Visual fields

Financial Disclosures: Rishita Pujari; Jamie Zhang; Ping Zhu; Sangeethabalasri Pugazhendhi; Collin Rich: I am an employee and shareholder of OcuSciences, Inc.; Yaping Joyce Liao: Consulting: Stoke Therapeutics

Grant Support: None.

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Virtual Reality: Transforming Experiences For Young Astrocytoma Patients

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Introduction:
VisuALL, a portable perimeter that employs virtual reality for various ophthalmic examinations including visual acuity measurement and visual field testing, provides frequent monitoring of patients' visual functions outside the clinical setting. In this study, we present the case of a pediatric patient with a brain tumor who used the portable perimeter for at-home monitoring of visual acuity and visual field.

Description of Cases:
An 8-year-old boy with an astrocytoma suffered a complete loss of vision in his right eye due to the tumor's compressive effects. He required monthly office visits to monitor his healthy left eye closely. Due to the patient's immunosuppressed state from cancer treatment and increased risk of infection during the COVID-19 pandemic, it was deemed unsafe for him to make such frequent visits. Therefore, he was advised to use the portable perimeter for at-home monitoring. For consecutive visits, visual acuity and visual field tests were conducted using the portable perimeter and standard in-office techniques (Snellen chart and Humphrey field analyzer). The mean difference and degree of agreement were calculated. Bland-Altman analysis indicated good agreement between the results.

Conclusions, including unique features of the case:
The VisuALL portable perimeter, as well as standard in-person examinations, produced similar results. Additionally, the patient found the virtual reality experience to be more engaging and less intimidating, particularly advantageous for pediatric patients. These findings suggest that portable perimetry with virtual reality technology could be considered an alternative to in-person examinations for pediatric patients requiring continuous visual assessment. Further research will objectively determine the benefits of these new technologies.

References: None provided.

Keywords: Visual fields, Perimetry, Pediatric neuro-ophthalmology, Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Bilateral Lateral Rectus Tendonitis Associated with Fluoroquinolone Use

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Introduction:
Fluoroqiunolones are commonly prescribed to treat a variety of infections. Treatment is not without risk, and adverse effects should be considered. Fluoroquinolones can rarely cause diplopia. Recognition allows for a change in therapy to promote healing.

Description of Cases:
A 54-year-old man presented with five days of diplopia. A week, the patient and his family were on a ski trip where the whole family became sick with upper respiratory infection and fevers. Everyone was positive for Influenza Type A. COVID was negative. The patient saw his primary care doctor upon returning home and was started on levofloxacin and promethazine. The upper respiratory infection quickly began to improve; however, within a day the patient's vision began to blur and then became fully double. Medications were stopped the next day. On exam, the patient had bilateral mild abduction deficits in the left eye more than the right eye. There was an esotropia of 16 prism diopters in primary gaze that was worse 20 prism diopters in left gaze and 8 prism diopters in right gaze. The patient underwent MRI of the brain with and without gadolinium and MRA of the brain and neck with gadolinium that were all normal. Laboratory tests showed a normal TSH, Lyme, Folate, and Vitamin B-12, and negative acetylcholine receptor antibodies. A trial of pyridostigmine was given without improvement. Steroids were then given with quick resolution.

Conclusions, including unique features of the case:
This case illustrates an association between fluoroquinolones and diplopia. Imaging, lab work, and pyridostigmine trial pointed away from other causes of diplopia. Quick resolution with oral steroid treatment points towards an inflammatory component of the likely extraocular muscle tendonitis. Fraundfelder et al found 171 cases reported in a database search. Two individual cases were reported with unilateral lateral rectus deficit. Our case may be the first report case of bilateral lateral rectus tendonitis.

References: 1. Fraunfelder FW, Fraunfelder FT. Diplopia and Fluoroquinolones. Opthalmology. 116(9): 1814-1817. 2009. 2. Touray M, Ando V, Samutelela E, Zuber J. Binocular Diplopia: A Possible Adverse Effect of Fluoroquinolone Therapy. Case Reports In Ophthalmological Medicine. 2020(1). 2020.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Opsoclonus-Myoclonus Syndrome Secondary To West-Nile Virus Infection In A 24 Year Old Female With Medial Cerebellar Atrophy

Abdulaziz Al Abdulghani [1], Melissa Bucheli [2], Nathaniel Pasmanter [2], Carly Garvin [2], Luke Barrick [2], Rachelle Srinivas [2], Michael Flink [2], Mitchell Biggs [2], Harrison Nabors [2], David Kaufman [2]

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Introduction:
Opsoclonus-myoclonus syndrome (OMS) is a rare neurological disorder characterized by a combination of opsoclonus, myoclonus, and ataxia. Etiology is paraneoplastic in most cases with an identified cause. Herein, we present a case of a 24-year-old Caucasian female who presented with acute onset opsoclonus-myoclonus syndrome, with the etiology ultimately identified as parainfectious due to West Nile virus infection.

Description of Cases:
She presented with acute onset oscillopsia and difficulty ambulating. Her history was notable for self-reported longstanding clumsiness and prior "dizzy" episodes. Her neurological exam showed evidence of opsoclonus and myoclonus of all 4 extremities. Serum studies were largely non-contributory in terms of autoimmune/paraneoplastic workup. Pertinent imaging completed included MRI brain, cervical spine, thoracic spine with and without contrast, and transvaginal ovarian US, which pertinently showed medial cerebellar atrophy. Initial CSF studies showed an opening pressure of 36cm H2O, protein 77, TNC 148 with neutrophilic predominance (82%), after which she was started on ceftriaxone, vancomycin, and acyclovir and IVMP due to a high suspicion of an infection and immune-related condition. Her CSF studies eventually revealed positive West Nile virus (WNV) IgM and IgG. Her symptoms significantly improved by the time of discharge approximately three weeks after her initial presentation (including a stay at IPR).

Conclusions, including unique features of the case:
OMS secondary to WNV is a rare occurrence. Interesting features about this case include the discovery of medial cerebellar atrophy that was corroborated by years of "clumsiness" and isolated episodes of "dizziness," for which the etiology is to be determined. Given the near complete recovery with immunomodulatory and antiviral treatment, this case also emphasizes the need for extensive testing in patients to check for potentially treatable causes of OMS. Further studies are needed to determine the underlying pathophysiology, prognosis, and best management plan of WNV associated OMS.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Trochlear Schwannomas In The Absence Of Systemic Neurofibromatosis: A Case Series

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Introduction:
Trochlear nerve schwannomas are rare, particularly in the absence of neurofibromatosis type 2. These tumors of the fourth cranial nerve can cause diplopia, as well as headache and other compressive effects with larger tumors. Currently, there is limited information regarding the diagnosis, clinical course, treatment outcomes, and prognosis of these tumors. This case series aims to contribute to the existing knowledge by discussing the clinical presentation, imaging characteristics, treatment approach, and outcomes of four patients diagnosed with trochlear nerve schwannomas.

Description of Cases:
We present 4 patients who presented with isolated trochlear nerve palsy to our Neuro-Ophthalmology clinic between May 2022 and September 2024. Each of these patients were found to have trochlear schwannoma corresponding to a symptomatic ipsilateral trochlear nerve palsy in the absence of neurofibromatosis type 2. Our series of patients had a mean age of presentation of 53 years, with 3 out of 4 being men. All of our patients presented with binocular diplopia and had lesions of .8 cm or less in maximal dimension. One patient was treated with gamma knife radiosurgery (patient 1), while the other three (patients 2, 3, and 4) were followed with serial imaging. One patient (patient 3) had spontaneous resolution of symptoms with no recurrence. The remaining patients (patients 1, 2, and 4) have had stable diplopia managed with head positioning, though patient 4 was recently referred for strabismus surgery.

Conclusions, including unique features of the case:
We present 4 cases of isolated trochlear nerve palsies with radiographic evidence of trochlear nerve schwannomas. This is a rare cause of trochlear nerve palsy and resultant binocular diplopia that involves inter-disciplinary management and may require surgical intervention. Clinicians should be aware that sporadic trochlear nerve schwannomas may occur outside of the context of neurofibromatosis.

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Keywords: Tumors, Neuroimaging, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None

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Progressive Ophthalmic Findings of an Intracranial Lesion

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Introduction:
Ophthalmic findings can be diagnostic tools for intracranial lesions and markers for improvement and progression. We report on a patient whose progressive ophthalmic findings guided her systemic treatment for an intracranial lesion.

Description of Cases:
A 55-year-old woman with a history of breast cancer presented with binocular diplopia, vertigo, and headache. She had a vertical gaze deficit and convergence retraction nystagmus with attempted supraduction and infraduction suspicious for a dorsal midbrain lesion. MRI showed a ring-enhancing lesion in the right lower thalamus and upper midbrain adjacent to the third ventricle with associated T2/FLAIR signal hyperintensity. Serum testing for HIV, tuberculosis, and syphilis, as well as a lumbar puncture and CT scan of her chest, abdomen, and pelvis were all negative. MR spectroscopy suggested a metastatic lesion. Sterotactic radiosurgery and systemic chemotherapy with capecitabine were initiated for presumed CNS metastasis of breast cancer with resulting improvement of motility and convergence retraction nystagmus . On follow up four months later , however, she had a dilated, non-reactive right pupil ; MRI at that time showed enlargement of the lesion involving the posterior limb of the internal capsule, thalamus, midbrain, and superior and middle cerebellar peduncles. She started oral steroids in response to these changes, which were thought to be associated with radiation treatment. Shortly after, she developed a right adduction deficit and complete right eyelid ptosis consistent with a right third nerve palsy with continued interval increase in mass size.

Conclusions, including unique features of the case:
This patient with a ring enhancing brain mass showed ophthalmic findings that progressed as the mass enlarged. Her presentation with Parinaud's syndrome suggested involvement of the dorsal midbrain. Despite treatment, the mass gradually impacted the oculomotor nerve fasciculus, causing a non-reactive right pupil and progressively worsening ptosis and motility deficits. Improvement and subsequent progression of her intracranial lesion were identified using her ophthalmic exam.

References: None provided.

Keywords: Tumors, Neuroimaging, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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IgG4 Related Hypertrophic Pachymeningitis in a Child

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Introduction:
Hypertrophic pachymeningitis (HP) is a rare inflammatory disorder marked by thickening of the cranial and spinal dura mater, stemming from idiopathic or secondary causes, including autoimmune diseases. While primarily reported in adults, HP has been documented in only 16 children. HP secondary to IgG4-related disease (IgG4-RD) is also rare, with around 80 cases reported in recent literature. None of the cases of IgG4 related HP were reported in children. We present a case of a 9-year-old girl with HP and biopsy results suggesting an IgG4-related process.

Description of Cases:
The patient presented to the emergency department with double vision and limited left eye movement, which began five days earlier and progressed rapidly. She reported no eye pain or visual deficits and had no recent trauma or systemic symptoms. Her medical history included Bell's palsy four months prior, attributed to stress, which resolved with steroids. Examination revealed normal visual acuity and intraocular pressures in both eyes, significant left eye ptosis, and complete ophthalmoplegia. Contrast-enhanced MRI Brain and Orbits showed thickening and enhancement of the dura mater in the left middle cranial fossa, extending to the cavernous sinus and tentorium. Infectious and autoimmune serologies, as well as CSF analysis, returned negative results. A dura biopsy showed lymphohistiocytic infiltrate consistent with a non-neoplastic inflammatory process, with rare IgG4-positive cells, raising the suspicion of IgG4-related pachymeningitis. Serum IgG4 subclasses were normal. Following treatment with intravenous methylprednisolone, her symptoms improved, and she was discharged on an oral prednisone taper.

Conclusions, including unique features of the case:
This case illustrates the possibility of IgG4-RD as a potential cause of HP and represents the first documented instance of HP due to IgG4-RD in a child.

References: Woo PYM, Ng BCF, Wong JHM, Ng OKS, Chan TSK, Kwok NF, Chan KY. The protean manifestations of central nervous system IgG4-related hypertrophic pachymeningitis: a report of two cases. Chin Neurosurg J. 7(1):13. 2021.

Keywords: Ocular motility, Pediatric neuro-ophthalmology, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Downbeat Nystagmus and Causes of Diplopia in SCA27B: A Newly Described, Novel yet Common, Entity with Unique Neuro-Ophthalmologic Presentations

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[1] New York University Grossman School of Medicine, [2] Johns Hopkins Unversity School of Medicine, [3] Johns Hopkins University School of Medicine, [4] New York University, UCLA, [5] Johns Hopkins University, [6] New York University, [7] Johns Hopkins Hospital

Introduction:
Spinocerebellar ataxia type 27B (SCA27B) due to GAA trinucleotide repeats in the fibroblast growth factor 14 (FGF14) gene, newly discovered in 2022, is emerging as a common cause of late-onset ataxia, as well as neuro-ophthalmologic presentations. We aim to familiarize the neuro-ophthalmologist with this new diagnosis and to delineate the causes of diplopia, which have not yet been described.

Description of Cases:
Retrospective analysis of 12 patients [mean age at symptom onset 64 (range 44-73) years] with genetically confirmed SCA27B. Seven patients had episodic or persistent oscillopsia or diplopia at symptom onset, neurologically isolated for several years in 3. Eight of 11 treated patients experienced improvement in oscillopsia and/or imbalance on 4-aminopyridine. All patients had downbeat nystagmus detectable on exam, though it was clinically obvious in only 3. Diplopia was present in 9 patients: vertical due to skew deviation (static or alternating on lateral gaze) (n=6) and/or horizontal due to vergence dysfunction (n=8), including convergence insufficiency (n=4) and divergence insufficiency with cerebellar esotropia (n=3). One patient had saccadic slowing, confirmed with oculography.

Conclusions, including unique features of the case:
SCA27B is a newly discovered diagnosis that is evolving as a common cause of late-onset episodic or slowly progressive ataxia and idiopathic downbeat nystagmus. Patients often present with oscillopsia or diplopia, including unique features such as hours-long discrete episodes, and exam features can be subtle; thus, it is important that neuro-ophthalmologists become familiar with this condition, particularly given its unique responsivity to 4-aminopyridine.

References: None provided.

Keywords: Genetic disease

Financial Disclosures: The authors had no disclosures.

Grant Support: No grant support, but I am using this space to send a note to the abstract committee. SCA27B - though named as 'just another SCA' was recently discovered and is a VERY common cause of late-onset imbalance and idiopathic downbeat. It has been highlighted at every meeting over the last year in Neurology - Movement Disorders - Neurovestibular - etc. and is certain to show up in neuro-ophthalmology clinics with downbeat nystagmus and even episodic diplopia. Given the need of neuro-ophthalmologists to become familiar with this, we would like to request strong consideration for platform presentation. Thank you.

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Ocular Neuromyotonia After Peribulbar Block

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Introduction:
Ocular neuromyotonia is historically associated with patients with a history of cranial radiation, nerve compression of vascular or meningeal origin, and autoimmune disorders. While vertical strabismus incited by a peribulbar or retrobulbar block is well-known, there are no reports implicating peribulbar local anesthesia as a cause of ocular neuromyotonia.

Description of Cases:
A man in his 60s developed an intermittent, variable left hypotropia with symptomatic diplopia shortly following nasal pterygium surgery in the left eye. He presented with complaints of intermittent diplopia that have been stable for 1 year since the surgery. He was orthotropic for most of the day, but a variable left hypotropia of 25Δ could be provoked with prolonged downgaze. There was no history of radiation or other trauma. MRI of the brain and orbit with gadolinium was unremarkable. The patient was diagnosed with suspected ocular neuromyotonia secondary to the peribulbar block and temporarily managed with Fresnel prisms. A trial of oral carbamazepine partially improved his symptoms. He ultimately underwent a left inferior rectus recession with near complete resolution of his symptoms.

Conclusions, including unique features of the case:
This case represents a unique characterization of ocular neuromyotonia occurring in the context of peribulbar local anesthesia. We postulate that the needle and/or local anesthetic injured the nerve fibers innervating the inferior rectus muscle to produce the manifestations of ocular neuromyotonia and intermittent vertical strabismus. Aside from the highly characteristic ocular motility exam features, this hypothesis is further supported by the patient's response to carbamazepine. Additionally, recession of the involved muscle led to resolution of paroxysms, suggesting that weakening the neuromyotonic muscle effectively ameliorates tonic contracture. Distinguishing whether vertical strabismus following a peribulbar block has a neuromyotonic component is important because nonsurgical, pharmacologic treatment may be effective and surgical dosing may be different for these patients.

References: 1. Bodi TB, Klaehn LD, Kramer AM, et al. Ocular Neuromyotonia: Clinical features, Diagnosis and Outcomes. Am J Ophthalmol. 2024;0(0). doi:10.1016/j.ajo.2024.02.003 2. Capó H, Roth E, Johnson T, Muñoz M, Siatkowski RM. Vertical Strabismus after Cataract Surgery. Ophthalmology. 1996;103(6):918-921. doi:10.1016/S0161-6420(96)30587-3 3. Kim JA, Velez FG, Pineles SL. Strabismus Surgery in Patients With Ocular Neuromyotonia: Potential Unmasking of the Condition and Effective Management Tool. J Neuroophthalmol. 2016;36(3):259. doi:10.1097/WNO.0000000000000371

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

Financial Disclosures: Jia Jia Zhang; Michael Nguyen; Eric Gaier: Luminopia Inc. (advisor, equity, patent), Stoke Therapeutics Inc (consultant), Neurofieldz Inc (consultant)

Grant Support: None.

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Take a HINT[S] (exam): Posterior circulation stroke misdiagnosed as migraine

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[1] *University of Vermont Medical Center*

Introduction:
The HINTS exam is a highly sensitive and specific test for identifying central causes of vertigo, particularly when performed by trained neurologists and neuro-ophthalmologists. Here we report a case of posterior circulation stroke that was repeatedly misdiagnosed as migraine.

Description of Cases:
A 36 year old female with a history of chronic migraine and recent URI who presented with 10 days of posterior headache, dizziness, and blurry vision. CT and MRI brain were unremarkable. She was ultimately diagnosed with migraine and dehydration. She was treated with IV fluids and a migraine cocktail and discharged home. Over the next 5 days, the patient had 5 additional ED visits for these symptoms. During her 3rd ED visit, she had a lumbar puncture with CSF analysis notable for a nucleated cell count of 7. She was diagnosed with aseptic meningitis and again discharged home. Neurology was consulted during the patient's 4th ED visit. Her examination was notable for "left nystagmus", right-sided dysmetria on finger-to-nose testing, and an unsteady gait. Diagnostic impression was migraine with possible superimposed aseptic meningitis. During the patient's 6th ED visit, she became unresponsive and apneic, requiring intubation for respiratory support. CTA head/neck revealed bilateral vertebral artery dissections, extensive infarction of the bilateral cerebellar hemispheres, obstructive hydrocephalus, and herniation. She was taken emergently to the OR for suboccipital decompressive craniotomy. She survived and ultimately discharged from rehab with minimal deficits.

Conclusions, including unique features of the case:
We conclude that our patient would have had a very different course and outcome if they had received a careful HINTS examination as part of their initial work-up. The purpose of our case review is to raise awareness about the usefulness of the HINTS exam for differentiating between peripheral and central causes of dizziness and encourage front-line providers to look at the eyes as an indicator of what is happening in the brain.

References: None provided.

Keywords: Stroke, Nystagmus

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Vertigo on the Hunt: Downbeat Nystagmus During Angiography in Bow Hunter's Syndrome

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Introduction:
Bow Hunter's syndrome is transient vertebrobasilar hypoperfusion occurring when the vertebral artery is mechanically compressed by surrounding bony or ligamentous structures on turning the head. It was originally described after a bow hunter developed lateral medullary syndrome after archery practice. The process is explained by the presence of one hypoplastic or severely stenotic vertebral artery and one dominant vertebral artery that becomes occluded on head rotation.

Description of Cases:
A 68-year-old man presented with 3 years of vertigo that occurred on turning his head to the right. Video-oculography (VOG) with removal of fixation showed downbeat nystagmus (DBN) that was triggered by right head turn with reproduction of symptoms. To further investigate, dynamic digital subtraction angiography was performed with simultaneous VOG recording. These procedures demonstrated a hypoplastic right vertebral artery and significant stenosis of the dominant left vertebral artery during rightward head rotation, with DBN emerging at the exact moment vertigo occurred, providing a clear correlation between vertebral artery compression and the patient's symptoms. The cause of Bow Hunter's syndrome was a C1 arcuate foramen, a congenital bony abnormality also known as a ponticulus posticus, present in ~16% of the population. A congenital hypoplasia of his posterior communicating arteries bilaterally suggested that his entire posterior circulation was dependent on the dominant left vertebral artery for its blood supply. He was managed surgically with vertebral artery decompression with C1 laminectomy and C1-C3 fusion with subsequent resolution of symptoms.

Conclusions, including unique features of the case:
Here we present the first demonstration of simultaneous VOG recording during angiography in a patient with Bow Hunter's Syndrome. DBN can be the only initial reproducible evidence of posterior fossa ischemia brought on by rotational vertebral artery compression, supporting the need for accurate diagnosis.

References: 1. Sorensen BF. Bow hunter's stroke. Neurosurgery. 1978;2(3):259-261. doi:10.1227/00006123-197805000-00013 2. Simpkin CT, Davis KE, Davis BS, Vosko AM, Jorgensen ME. Bow hunter's syndrome in a patient with vertebral artery atresia, an arcuate foramen, and unilateral deafness: a case report. Radiol Case Rep. 2017;12(3):597-601. doi:10.1016/j.radcr.2017.04.001 3. Elliott RE, Tanweer O. The Prevalence of the Ponticulus Posticus (Arcuate Foramen) and Its Importance in the Goel-Harms Procedure: Meta-Analysis and Review of the Literature. World Neurosurg. 2014;82(1):e335-e343. doi:10.1016/j.wneu.2013.09.014

Keywords: Vascular disorders, Neuroimaging, Ocular manifestations of vestibular disorders, Nystagmus

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Late-onset AGRN-associated Congenital Myasthenic Syndromes Presenting With Diplopia

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[1] *Eye and ENT Hospital, Fudan University*

Introduction:
Ocular manifestations of Congenital myasthenic syndrome (CMS) can be identified in some patients, which may have a potential relationship with the gene pattern.

Description of Cases:
Here we described a patient with AGRN mutation-associated CMS who had diplopia as the initial symptom in his adulthood and performed a literature review. A 39-year-old Chinese male had persistent double vision for 2 years. Examinations revealed facial weakness, mild limitations of abduction, and horizontal nystagmus on lateral gazes without ptosis. Whole exon sequencing showed compound heterozygous missense mutations in AGRN gene. He was diagnosed as late-onset AGRN-associated congenital myasthenic syndrome (CMS).

Conclusions, including unique features of the case:
Our study points out that some CMS patients with certain genotypes present ocular symptoms majorly consisting of ptosis and ophthalmoplegia. Notably, ocular symptoms can occur late in adulthood and without other accompanying symptoms in some patients. It raises our awareness of the differential diagnosis of these hidden patients since they are likely to be misdiagnosed as myasthenia gravis or chronic progressive external ophthalmoplegia, as the patients can also present ptosis and ophthalmoplegia.

References: None provided.

Keywords: Adult strabismus with a focus on diplopia, Ocular motility, Myasthenia, Genetic disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

135
Occult Saccadomania

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Introduction:
Opsoclonus-myoclonus syndrome (OMS) is a rare, (~1/1,000,000 incidence) saccadic dyskinesia usually driven by infectious, toxic-metabolic or paraneoplastic processes. It is hallmarked by omnidirectional, high-frequency, variable amplitude, conjugate saccades without intersaccadic delay alongside axial/appendicular myoclonus. Probable pathogenesis includes dorsal vermis dysfunction disinhibiting the fastigial nucleus and horizontal/vertical burst neuron instability. Treatment focuses on managing the underlying cause with aggressive immunosuppression to minimise chronic relapsing sequelae.

Description of Cases:
A 17-year-old man developed subacute oscillopsia, headaches and increased falls. He described persistent circular motion exacerbated by stress, subtly improved laying supine and when adopting a 'chin-down, eyes-up' posture. No definitive constitutional symptoms, however, may have a preceding mild viral prodrome. Family members additionally noted insomnia, irritability and emotional incontinence atypical for him. Several weeks later he developed progressive face, neck and upper-limb myoclonus. History is notable for CRB1 retinal dystrophy (confirmed on whole genome sequencing) supported by fundoscopic/OCT findings (OU 6/18; outer plexiform layer thickening, posterior pole ellipsoid line irregularity). He has morbid obesity at 136 kg with severe steatosis. No regular drug use. Birth history is unremarkable, reaching normal developmental milestones. Parents are first cousins (once removed). Examination confirmed (micro)-opsoclonus, neck and limb myoclonus triggered by auditory/tactile stimuli and gait ataxia with no other long-tract signs. Despite satisfying Mitchell and Pike OMS rating scale criteria, widespread investigations were unfruitful, with no metabolic, oncologic or infective cause found (normal catecholamines, serum/CSF infective and paraneoplastic antibody panel, MRI neuroaxis/whole body and MIBG scan). IV corticosteroids initially yielded a transient improvement in balance, however, repeated corticosteroid/IVIg treatments were not beneficial, and consequently, rituximab will be commenced.

Conclusions, including unique features of the case:
Extensive investigations found no definite aetiology despite fulfilling OMS criteria, with a working diagnosis of a postviral/autoimmune phenomenon. Around 50% of cases are associated with negative investigations and warrant careful long-term follow-up.

References: Leigh, R. J. and Zee, D. S. (2015) The Neurology of Eye Movements. 5th ed. New York, NY: Oxford University Press Oh, S. Y., Kim, J. S., & Dieterich, M. (2019). Update on opsoclonus–myoclonus syndrome in adults. _Journal of Neurology_, 266, 1541–1548. Rossor, T., Yeh, E. A., Khakoo, Y., Angelini, P., Hemingway, C., Irani, S. R., Schleiermacher, G., Santosh, P., Lotze, T., Dale, R. C., Deiva, K., Hero, B., Klein, A., de Alarcon, P., Gorman, M. P., Mitchell, W. G., & Lim, M. (2022). Diagnosis and management of opsoclonus-myoclonus-ataxia syndrome in children: An international perspective. _Neurology Neuroimmunology Neuroinflammation_, 9(3), e1153.

Keywords: Ocular motility, Neuro-ophth & infectious disease (eg, AIDS, prion), Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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A case of thalamic lesion casing vertical one and a half syndrome

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Introduction:
Vertical one-and-a-half syndrome is a very rare clinical syndrome, usually due to a meso-diencephalon lesion leading to a posterior commissure (PC) lesion, which results in damage to the cross fibres reaching the nucleus accumbens. The damage was central to vertical movements in both eyes.

Description of Cases:
A 23-year-old woman with double vision and tremors in both eyes for 3 months after a traumatic injury. She had cerebral hemorrhage after head trauma. Neuro ophthalmologic consultation for inability to read Section. Neuro-ophthalmologic examination: best-corrected visual acuity was 0.8 in both eyes, and bilateral pupils were equal in size and rounded, with sensitive light reflexes and no relative pupillary afferent disorder (RAPD). I Head tilted to the right; no eyelid ptosis. The first eye position was mildly exotropic in the left eye, with basically normal inward and outward movements in both eyes; binocular upgaze was impaired, accompanied by mild convergent regressive nystagmus; right eye downgaze was normal, accompanied by downward jumping nystagmus; and left eye downgaze was insufficient. Cranial CT showed left thalamic hemorrhage into bilateral lateral ventricles. Diagnostic considerations: vertical one and a half syndrome due to thalamic hemorrhage; nystagmus. The patient was advised to continue rehabilitation and nutritional neurological treatment. Strabismus evaluation was performed after 6 months of illness.

Conclusions, including unique features of the case:
It is assumed that the fibres of the interneuromedullary nucleus (riMLF) located on the anastomosing side of the medial longitudinal fasciculus (MLF) cross the posterior commissure to perform binocular upward gaze, while binocular downward gaze is innervated by the ipsilateral side without the need for PC crossings. Therefore, the involvement of midbrain-mesencephalic lesions resulting in damage to the riMFL and PC nuclei can lead to a vertical one-and-a-half syndrome. In this paper, we report a case of oculomotor impairment in a young woman with thalamic haemorrhage due to traumatic brain injury.

References: 1.Côté E, Micieli JA. Vertical One-and-a-Half Syndrome Due to Metastatic Spindle Cell Carcinoma of the Lung. Can J Neurol Sci. 2020;47(5):685-686. 2.Biousse V, Newman NJ. Neuro-Ophthalmology illustrated. 1st Edition. Diplopia. New York: Thieme Medical Publishers Inc, 2009, 382-397.

Keywords: Nystagmus, Vascular disorders, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Iatrogenic CCF's: A Case of Bilateral CCF's Spawned by Tamoxifen Therapy

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Introduction:
Carotid-cavernous fistula (CCF) is an aberrant vascular connection - characterized based on angiographic architecture as direct versus indirect - between the carotid arterial system and cavernous sinus veins. Bilateral concurrent CCF's represent 1-2% of CCF's; of these, spontaneous variants are exceedingly rare with 35 documented cases and only one manifesting with unilateral symptoms as presented here [1]. Etiologies of indirect CCF's include hypertension, Ehlers-Danlos, fibromuscular dysplasia, carotid dissection, and venous thrombosis [2]. We propose a novel etiology of bilateral CCF's in the form of estrogen-modulating tamoxifen.

Description of Cases:
A 47-year-old female on tamoxifen for stage 1 breast cancer diagnosed 12 months prior, presented with two weeks of progressive conjunctival erythema, periorbital edema, and horizontal binocular diplopia, accompanied by headache and pulsatile tinnitus. Examination revealed intact visual acuity, ophthalmoparesis OS with IOP 22 mmHg. CT/CTA revealed a dilated left superior ophthalmic vein (SOV) and left-sided CCF, while MRI's noted left-sided proptosis, slightly dilated optic nerve sheath, and orbital apex congestion. Four-vessel angiography identified bilateral CCF's with multiple feeder vessels from branches of ICA and ECA, but drainage primarily into the left SOV. In spite of multiple attempts at embolization via arterial, venous, and eyelid approaches, her CCF's persisted and symptoms worsened. Emergent transfer to a tertiary center yielded eventual complete embolization and significant improvement of her disfigurement and symptoms, with only trace abduction deficit on follow up.

Conclusions, including unique features of the case:
Observational studies have noted a relationship between tamoxifen and dural arteriovenous fistulas (dAVF) with proposed pathogenesis including induction of a hypercoagulable state due to decreased antithrombin III and proteins C and S, and pro-angiogenic state of endothelial cells due to increased circulating estrogen [3][4]. We highlight a new patient population in which to have a high degree of suspicion: indirect bilateral CCF's, indolent and oft mistaken for inflammatory processes, can cause debilitating symptoms if left untreated.

References: 1. Gasparian SA, Chalam KV. Successful repair of spontaneous indirect bilateral carotid-cavernous fistula with coil embolization. J Surg Case Rep. 2021 Apr 22;2021(4):rjab140. doi: 10.1093/jscr/rjab140. PMID: 33927873; PMCID: PMC8062127. 2. Henderson AD, Miller NR. Carotid-cavernous fistula: current concepts in aetiology, investigation, and management. Eye (Lond). 2018 Feb;32(2):164-172. doi: 10.1038/eye.2017.240. Epub 2017 Nov 3. PMID: 29099499; PMCID: PMC5811734. 3. Robert T, Blanc R, Valsecchi D, Botta D, Ciccio G, Smajda S, Redjem H, Chaalala C, Piotin M. Tamoxifen treatment and occurrence of dural arteriovenous fistulas: An observational study on a series of patients presenting tamoxifen history and diagnosis of DAVf. J Neurol Sci. 2018 Feb 15;385:115-118. doi: 10.1016/j.jns.2017.12.026. Epub 2017 Dec 23. PMID: 29406888. 4. Hwang SK. A case of dural arteriovenous fistula of superior sagittal sinus after tamoxifen treatment for breast cancer. J Korean Neurosurg Soc. 2015 Mar;57(3):204-7. doi: 10.3340/jkns.2015.57.3.204. Epub 2015 Mar 20. PMID: 25810861; PMCID: PMC4373050.

Keywords: Vascular disorders, Orbit/ocular pathology, Chemotherapy and radiation injury, Interventional neuroradiology, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Lamotrigine Induced Downbeat Nystagmus and Oculogyric Crisis: A Case Report

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Introduction:
Lamotrigine (LTG) is a commonly used anticonvulsant with a generally favorable safety profile. However, it can cause a range of neuro-ophthalmic adverse effects. This case highlights LTG as a rare but important cause of progressive ocular motor abnormalities, including oculogyric crisis, downbeat nystagmus, and dysmetria.

Description of Cases:
A 52-year-old woman with epilepsy, intellectual disability, and migraine, taking LTG 300mg twice daily and brivaracetam 100mg twice daily, presented with oculogyric crisis, encephalopathy, nausea, vomiting, and breakthrough seizure. Her symptoms progressed slowly over nearly 10 months, initially manifesting as worsening balance and dizziness attributed to subclinical seizures, later diagnosed as vestibular migraine. One month prior to admission, she developed downbeat nystagmus and dysmetria, prompting an inpatient evaluation. Extensive workup, including MRI, lumbar puncture, and autoimmune panels, was unremarkable. LTG toxicity was suspected and the dose was promptly reduced, with full discontinuation upon her level resulting as elevated to 31.2 ug/mL. The persistent upgaze resolved within a day of lowering dose, though downbeat nystagmus and diplopia persisted for 3-4 days. Symptoms fully resolved over a week.

Conclusions, including unique features of the case:
Oculogyric crises and downbeat nystagmus are rare but recognized complications of lamotrigine toxicity, though the mechanisms are not fully understood. Lamotrigine primarily inhibits voltage-gated sodium channels, but its modulation of neurotransmitter release may lead to cerebellar dysfunction and abnormal ocular motility. Less commonly, it may induce a hypodopaminergic state and dose-dependent oculogyric crises. This case underscores the importance of considering medication toxicity in the differential diagnosis of progressive ocular motor abnormalities, even when other explanations are present. The gradual progression of symptoms over nearly a year emphasizes the need for ongoing vigilance and reconsideration of the diagnosis as new signs and symptoms emerge.

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Keywords: Ocular motility, Nystagmus, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Progressive Internuclear Ophthalmoplegia Secondary To Hypertrophic Olivary Degeneration Of To Be Determined Etiology

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Introduction:
Hypertrophic Olivary Degeneration (HOD) is rare. It is characterized by degeneration of inferior olivary nuclei resulting from a lesion to the Guillain-Mollaret triangle. Possible manifestations include oculomotor disturbances, palatal tremor, and ataxia. We documented a slowly progressive ocular motility defect with videography for over a year, initially starting as a partial bilateral INO that has progressed in a stepwise fashion to currently involving infraduction OU along with other neurologic deficits. The patient was found to have bilateral hypertrophic olivary degeneration on imaging. We speculate on a logical etiology for HOD.

Description of Cases:
60-year-old male presented with oscillopsia and abnormal balance. He has a history of chronic alcohol use and concussions. Examination initially demonstrated ataxia, square-wave jerks and a subtle bilateral INO. Other than a borderline positive ANA, the remainder of the autoimmune, nutritional, rheumatologic, and paraneoplastic panel were negative. Workup also included nutritional deficiency, heavy metal profile, infectious panel, ganglioside panel, and SCA genetic panel. The search for a neoplasm was unremarkable. CSF was normal. MRI brain demonstrated T2/FLAIR hyperintensity of the inferior olivary nuclei bilaterally with no other remarkable abnormalities. Upon subsequent visits over a year, the patient exhibited worsening ophthalmoplegia eventually progressing to weakness in infraduction OU, flaccid dysarthria, and mild oropharyngeal dysphagia as shown by VFSS; supraduction remains less involved, and the neck is supple.

Conclusions, including unique features of the case:
Isolated HOD is a rare imaging finding. The current etiology is idiopathic as in the case described above. However, given the stepwise clinical progression of this disorder, now documented by serial videography in this case, it appears the etiology logically falls into a cell-by-cell like propagation within the Guillain-Mollaret triangle. This type of progression would fit into a model currently being proposed for tauopathies leading to other neuro-degenerative diseases. Further testing with more extensive genetic testing and PET scan is pending.

References: None provided.

Keywords: Ocular motility, Paraneoplastic syndromes

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Centripetal Nystagmus: Why is it so rare and does it have diagnostic value?

Isabel Torres [1], Daniel Gold [2]

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Introduction:
Centripetal nystagmus (CN) manifests as a slow drift towards eccentric gaze and quick return to primary eye position (PEP)(1,2,3). We discuss CN through the lens of patients with Creutzfeldt-Jakob disease (CJD) and anti-glutamic-acid-decarboxylase-65 (GAD65) antibodies.

Description of Cases:
Case 1: A 68-year-old woman presented with 2 years of progressive imbalance. Examination demonstrated square wave jerks, saccadic smooth pursuit, and downbeat nystagmus (DBN). Gaze-evoked nystagmus (GEN) was present but transitioned to CN after 5-10 seconds. Serum and cerebrospinal fluid (CSF) analysis were positive for anti-GAD65. Case 2: A 65-year-old woman presented with weeks of progressive gait imbalance and vertigo. Examination revealed apogeotropic positional nystagmus, dysmetric saccades, saccadic smooth pursuit, DBN and limb ataxia. GEN was present but transitioned to CN after 5-10 seconds. MRI showed T2-weighted/FLAIR thalamic hyperintensities. Positive CSF RT-QuIC and elevated 14-3-3 protein confirmed CJD.

Conclusions, including unique features of the case:
The neural integrators (NI) encode eye position commands based on eye velocity signals (e.g., saccades) to maintain eccentric fixation. GEN results from impaired NI, although compensatory mechanisms often minimize GEN with sustained lateral gaze. This adaptation is also reflected as a reversal of nystagmus when the patient returns to the PEP, referred to as rebound nystagmus (RN) (4,5). CN (rare) and RN (common) probably exist on a spectrum, with both resulting from a shift in the eye position bias to minimize GEN.(6,7). Regarding the localizing or etiologic implications of CN, Patient 2 had a rapid onset and severe cerebellar ataxia. Here, perhaps adaptation 'overshot' the perceived NI impairment, causing a spontaneous reversal (i.e., a periodic alternating nystagmus-like mechanism). Patient 1 did not have a rapid onset, so other possible mechanisms include antibody-mediated predilection for specific cell groups – e.g., severe NI impairment and/or overactive (disinhibited) adaptation. When GEN is observed, prolonged lateral gaze may uncover CN, which is reported in patients with CJD and antibody-mediated cerebellopathy.

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Keywords: Nystagmus, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Downbeat Nystagmus (DBN) as a Sign of Myoclonic Status Epilepticus in a Patient With Anoxic Brain Injury

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Introduction:
Epileptiform nystagmus, typically horizontal jerk, may occur in the setting of epileptiform cortical activity. Nystagmus is rarely seen in coma. We report a comatose patient with downbeat nystagmus (DBN) and epileptiform discharges; DBN resolved upon onset of pharmacologic burst suppression.

Description of Cases:
A 59-year-old man was evaluated for unresponsiveness following cardiac arrest. Examination revealed fixed, dilated, unreactive pupils with absent vestibulo-ocular reflexes (VOR) and weak corneal reflexes. Within 24 hours, he developed myoclonic status epilepticus on EEG, accompanied by jaw contraction and eyelid myoclonus. He was treated with continuous intravenous midazolam, leading to cessation of the myoclonus. However, EEG continued to exhibit generalized periodic epileptiform discharges (GPEDs) with polyspike morphology. Repeat examination revealed DBN characterized as 1-2 hz in frequency with runs of 4-5 hz and variable amplitude in primary gaze. The question arose as to whether the nystagmus could be correlated with ongoing GPEDs as an extension of myoclonic status epilepticus. Aggressive intravenous antiepileptic management was continued, and DBN resolved with titration of midazolam to burst suppression pattern on EEG.

Conclusions, including unique features of the case:
Review of the literature revealed a report of six patients with DBN following periods of sustained upgaze following cardiac arrest. One patient had concomitant myoclonus.1 The proposed mechanism was severe anoxic injury with loss of cerebellar inhibition of the vertical VOR. Our patient was not observed to have sustained upgaze prior to DBN onset. Our patient's clinical picture is similar to those described in a report of vertical ocular oscillations and myoclonus simultaneous with abnormal spike discharges on EEG after anoxic brain injury.2 Such findings portend a poor prognosis. The mechanism for DBN in these settings may include impaired cerebellar inhibition of the VOR, or may relate to bilateral cortical dysfunction in the face of brainstem injury; this may, in turn, lead to vertical eye movements.3

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Keywords: Nystagmus, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Presentation of Eight-And-A-Half Syndrome with Contralateral Hemiparesis Due to a Pontine Hemorrhage

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Introduction:
Eight-and-a-half syndrome is a phenomenon involving a one-and-a-half syndrome consisting of a conjugate horizontal gaze palsy with an ipsilateral internuclear ophthalmoplegia, along with an ipsilateral cranial nerve seven palsy. It occurs due to a lesion, often vascular or inflammatory in nature, involving the median longitudinal fasciculus, paramedian pontine reticular formation, and the facial nerve fascicle.

Description of Cases:
A 66-year-old woman with no known past medical history presented to the emergency department as a stroke alert after waking up with a severe headache and vision loss. Upon arrival, the patient was obtunded with left-sided weakness, dysarthria, left-gaze preference, and dysconjugate gaze. Computed tomography angiogram of the head revealed a right pontine intracerebral hemorrhage with subarachnoid and intraventricular extension, without any related vascular lesion. The patient's hospital course was complicated by external ventricular drain placement, respiratory failure, and hypertension. Her mental status gradually improved to allow for more detailed examination. Over time, the patient developed injection and discharge of her right eye, with inability to fully approximate her right eye. Exam was consistent with an exposure keratopathy with a corneal epithelial defect and neurotrophic cornea of the right eye. In addition to right upper and lower facial weakness, the patient demonstrated a sustained left nystagmus on left gaze, a right conjugate gaze palsy with inability to abduct the right eye, and limited ability to adduct the left eye, consistent with eight-and-a-half syndrome. She was treated with antibiotic eye drops, and a lid weight was added to aid in right eye closure.

Conclusions, including unique features of the case:
Illustrated here is a case of eight-and-a-half syndrome with contralateral hemiparesis due to a hypertensive pontine hemorrhage. Prompt recognition of this phenomenon by carefully testing eye movements not only identifies the precise localization of a lesion, but also helps avoid complications related to associated lower motor neuron facial weakness.

References: None provided.

Keywords: Ocular motility, Stroke

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Windmill nystagmus in blindness

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Introduction:
Windmill nystagmus (WN) manifests as a clock-like spontaneously direction-changing nystagmus. Similarly, periodic alternating nystagmus (PAN) changes direction predictably over time, but stays horizontal whereas WN involves both horizontal and vertical planes. (1,2)

Description of Cases:
A 60-year-old woman presented with visual hallucations due to the Charles Bonnet syndrome. She was diagnosed in early childhood with a retinal degeneration (specific diagnosis unclear and records unavailable), and had no light perception vision for decades. Examination (using a proprioceptive target such as her thumb) demonstrated normal saccades, smooth pursuit, gaze-holding and vestibulo-ocular reflex, as well as the presence of WN (VIDEO), which was characterized by the following: right-beating nystagmus, then right and up-beating, then up-beating, then up and left-beating, then left-beating, then left and down-beating, then down-beating, then right and down-beating, and finally back to right-beating.

Conclusions, including unique features of the case:
Windmill nystagmus is a rare condition that is thought to be explained by an impaired interaction between the visual and vestibular systems, although the exact mechanism is not yet known. Most of the cases have been described in patients with profound visual impairment, but it has also been described in patients with cerebellar dysfunction without visual loss (2,3). One theory is that the neural integrators – which normally require afferent feedback – become less stable in the absence of error signals in the form of visual feedback (1). However, it is a rare finding and severe vision loss is not essential, so there is likely to be another susceptible substrate (i.e., another 'hit' such as impairment of the cerebellar flocculus, a structure that depends on visual and vestibular inputs) to explain its presence.

References: 1. Variants of windmill nystagmus. J Neurol (2016) 263:1375–1381 DOI 10.1007/s00415-016-8152-x 2. Pearls & Oy-sters: Windmill nystagmus in paraneoplastic cerebellar degeneration. Neurology® 2018;91:e1831-e1833. doi:10.1212/WNL.0000000000006477 3. Windmill nystagmus in a patient with subacute visual loss. Volume 265, pages 2737–2739, (2018)

Keywords: Nystagmus

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Artificial Intelligence and Machine Learning in Neuro-Ophthalmology

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Introduction:
This literature review covers the topic of artificial intelligence (AI) and machine learning (ML) in neuro-ophthalmology. AI/ML methodologies, including deep learning (in conjunction with interpretability techniques) and broader machine learning (in conjunction with published, novel protocols regarding papilledema detection), in the context of optic nerve pathologies are presented. The interplay of machine learning and clinical application in the context of fundus photography and optic nerve evaluation/pathologies are discussed, including the implications for physician training and practice. This review will inform the audience on the growing relevance of AI/ML in neuro-ophthalmology and provide examples of works/use cases.

Description of Cases:
This review first provides an overview of the concept of AI/ML in neuro-ophthalmology, informing the audience on the neuro-ophthalmology-specific applications of AI/ML including a foundational outline of developments as well as clinical context. The review then provides a survey of notable works/applications of AI/ML in neuro-ophthalmology. An outline of explainability/interpretability analysis (also known as explainable AI, or XAI) is presented, providing the audience with an understanding of how the inner workings/"thinking" of black-box models can be elucidated for clinical correlation between ML and clinical practice in neuro-ophthalmology. A use case for illustration and commentary on the future of AI/ML in neuro-ophthalmology is presented in conclusion.

Conclusions, including unique features of the case:
The field of neuro-ophthalmology is one that is ripe for the application of AI/ML and has exciting new possibilities in the future. Whether due to conventional ML with textual data or advanced deep learning with the bountiful imaging data in the field bolstered by XAI, neuro-ophthalmology (much like medicine at large) will be inseparable from AI/ML as efforts toward innovation continue in the years ahead. As neuro-ophthalmologists continue in practice seeking to integrate and utilize AI/ML, a broad and substantial grasp of the fundamentals and status of AI/ML and the field is warranted.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Sarcoidosis-Related Myogenic Blepharoptosis with Direct Levator Palpebrae Superioris Involvement

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Introduction:
There are several mechanisms by which sarcoidosis can cause blepharoptosis, including Horner syndrome, lacrimal gland enlargement, myasthenia gravis (MG) or MG-like syndromes, direct cranial nerve or nucleus involvement, and ischemic neuropathy in the setting of a neurosarcoidosis vascular lesion. No cases of sarcoidosis-related blepharoptosis secondary to biopsy-confirmed direct levator palpebrae superioris (LPS) involvement have been reported.

Description of Cases:
A 43 year-old male with hypertension and hyperlipidemia presented with four months of progressive right blepharoptosis as shown in Figure 1 and two months of dry cough. Exam was significant for palpebral fissure of 5 mm OD and 9 mm OS, nearly absent levator function OD, and no anisocoria. Work up included unremarkable ice test, leukemia/lymphoma panel, P/Q-type Ca channel Ab, AChR Ab, MuSK Ab, C-ANCA, P-ANCA, ACE, ESR, CRP, hepatitis serologies. Muramidase and LFTs were elevated. CT chest showed hilar adenopathy. MRI orbits showed bilateral lacrimal gland enlargement with asymmetric enhancement as well as right LPS enhancement as shown in Figure 2. Lacrimal gland biopsy showed localized granulomatous inflammation and numerous giant cells as shown in Figure 3. The cough improved with prednisone and methotrexate, but the blepharoptosis required a frontalis sling. On sling revision, orbital biopsies revealed multinucleated giant cells within the LPS and connective tissue, orbital septum tissue, and orbital/preaponeurotic fat as shown in Figure 4.

Conclusions, including unique features of the case:
Sarcoidosis-related blepharoptosis is a well-known phenomenon, typically associated with Horner syndrome or lacrimal gland enlargement. Subclinical lacrimal gland enlargement may suggest a diagnosis of sarcoidosis. We report a rare case of sarcoidosis-related myogenic blepharoptosis due to direct LPS involvement. The diagnosis was made via lacrimal gland biopsy, even in the absence of clinical dacryoadenitis, and confirmed with orbital biopsies showing multinucleated giant cells in the LPS.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Therapeutic Management of Oculomotor Nerve Palsy Ptosis and Mydriasis with Topical Oxymetazoline and Pilocarpine

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Introduction:
Oculomotor nerve palsy with ptosis and mydriatic anisocoria presents significant clinical challenges. Ptosis restricts superior visual fields and can limit binocular fusion, while mydriasis can cause photophobia and glare. Surgical options for ptosis carry risks like over or under-correction and exposure keratitis, highlighting the need for non-surgical alternatives (1). FDA-approved oxymetazoline 0.1% eyedrops show promise for blepharoptosis, and compounded pilocarpine 0.125% has the potential to address mydriasis (2,3) with minimal side effects. While randomized controlled trials and limited case reports demonstrate the safety and efficacy of oxymetazoline (4,5), its use in oculomotor ptosis and the role of pilocarpine in third nerve palsy mydriasis remain undocumented. We present four patients with partial oculomotor palsy treated symptomatically with these eyedrops, potentially filling a therapeutic gap.

Description of Cases:
Four adult patients (mean age 48.5 years, range 26-64 years), presented with residual, incomplete ptosis (marginal reflex distance, MRD, ranging from 0 to 2 mm) and mydriatic (range 6-7 mm) non-reactive pupils, due to acquired oculomotor nerve palsy. Etiologies included head trauma, meningioma resection, subarachnoid hemorrhage, and intracranial arterial aneurysm. Topical 0.1% oxymetazoline and 0.125% pilocarpine once daily were initiated in the involved eye. While specific MRDs and pupil sizes post-treatment were not able to be recorded, before-and-after photographs revealed notable improvements in lid position and pupil size, and symptomatic differences subjectively reported by each patient were recorded. Each patient demonstrated improvement to normalization of lid position and reduced anisocoria, photophobia, and glare, with a duration of effect lasting hours.

Conclusions, including unique features of the case:
This case series uniquely pioneers the documentation of symptomatic benefits from ophthalmic oxymetazoline 0.1% and pilocarpine 0.125% for incomplete ptosis and anisocoria in oculomotor nerve palsies. It paves the way for further research to determine optimal dosing frequency, evaluate long-term functional outcomes and quality of life, and assess safety across diverse demographics.

References: 1. Eva C, Jun L, Cathleen S, Meredith F, Malena A, Sean M, et al. Comparison of Revision Rates of Anterior- and Posterior-Approach Ptosis Surgery: A Retrospective Review of 1519 Cases. Ophthalmic Plast Reconstr Surg. 2018 Jun 2;34(3). 2. Osmotica Pharmaceuticals plc Receives FDA Approval for UpneeqTM (oxymetazoline hydrochloride ophthalmic solution), 0.1% for Acquired Blepharoptosis (Droopy Eyelid) in Adults | BioSpace. Available from: https://www.biospace.com/article/releases/osmotica-pharmaceuticals-plc-receives-fda-approval-for-upneeq-oxymetazoline-hydrochloride-ophthalmic-solution-0-1-percent-for-acquired-blepharoptosis-droopy-eyelid-in-adults/ 3. Hatim B, Jonathan A. Adie's tonic pupil presenting with unilateral photophobia successfully treated with dilute pilocarpine. BMJ Case Rep. 2020 Jan 2;13(1). 4. Jason B, David M, Robert SM, Michael K, Shane K, Shane F, et al. Rapid and Sustained Eyelid Elevation in Acquired Blepharoptosis with Oxymetazoline 0.1%: Randomized Phase 3 Trial Results. Clin Ophthalmol. 2021; 15:2743–51. 5. David W, Michael K, Shane F, Robert SM, Jason B, Shane K, et al. Safety of Once-Daily Oxymetazoline HCl Ophthalmic Solution, 0.1% in Patients with Acquired Blepharoptosis: Results from Four Randomized, Double-Masked Clinical Trials. Clin Ophthalmol. 2021; 15:4035–48.

Keywords: Pupil, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Acute Bilateral Compressive Optic Neuropathy Secondary to Fibrous Dysplasia of Skull Base in Adult

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Introduction:
Fibrous dysplasia (FD) is a disease of primarily children and adolescents that involves replacement of normal bone by immature bone and osteoid in a cellular fibrous matrix. The authors present a unique case of rapid onset bilateral compressive optic neuropathy secondary to FD with good visual recovery after urgent bilateral optic nerve decompression.

Description of Cases:
A 30-year-old male with history of diabetes presented with sudden blurriness of central vision bilaterally which increased in size until vision was light perception five days after symptom onset in both eyes. He reported ten days of associated waxing and waning retro-orbital pain which was exacerbated by extraocular movements. Patient was found to have minimally reactive pupils and fundus examination showed hyperemia and mild disc edema in both eyes. CT head and MRI orbit showed bilateral expansile hyperostosis in the planum sphenoidale, extending into anterior cranial fossa and the optic canals bilaterally. CT venogram was unremarkable. Lumbar puncture demonstrated normal opening pressure and CSF studies. After a trial of IV solumedrol for 5 days with minimal improvement in vision, patient underwent optic nerve decompression. Biopsy was positive for FD. NMO and MOG testing resulted negative. The final diagnosis was acute bilateral vision loss from compressive optic neuropathy secondary to FD. VA improved to count fingers 1 week post-operatively, 20/400 both eyes at 1 month post-operatively, and to 20/30 right eye and 20/40 left eye at 7 months post-operatively. Generalized pallor of both optic nerves occurred despite the improvement in central acuity. Color vision remained severely diminished.

Conclusions, including unique features of the case:
1. Fibrous dysplasia is a treatable cause of vision loss in children and adolescents if timely diagnosis and optic nerve decompression is done. 2. Our case is rare with bilateral acute vision loss from fibrous dysplasia which mimicked the presentation of optic neuritis.

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Keywords: Optic neuropathy, Orbit/ocular pathology, Skull base

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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The Necessity Of Biopsy In Differentiating Between Spheno-orbital Meningioma And Orbital Diffuse Large B-Cell Lymphoma

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Introduction:
Both the spheno-orbital subtype of meningiomas and orbital diffuse large B-cell lymphoma are rare neoplasms that can present in the orbital region. Importantly, while spheno-orbital meningiomas (SOMs) are typically slow-growing and benign, orbital lymphomas are aggressive and associated with high-mortality, making differentiation between the two paramount. Here, we present a case that strongly resembled a spheno-orbital meningioma on imaging, but upon further investigation with biopsy, was determined to be an orbital diffuse large B-cell lymphoma (DLBCL).

Description of Cases:
A 73-year-old female presented with retro-orbital pressure-like pain, abrupt onset ptosis OS and binocular oblique diplopia. Her past ocular history included glaucoma. On exam, the patient was 20/20 OU with full color plates OU, and pressures of 10 mmHg OD and 13 mmHg OS. Review of MRI orbits revealed enhancement at the superior periphery of the left orbit with extension to the lateral rectus muscle and involvement of the dura of the planum sphenoidale and extension into the region of the ethmoid plate. Based on imaging, spheno-orbital meningioma was the leading consideration for diagnosis with lymphoma or other neoplastic disorders included in the diagnosis. Following biopsy of the left ethmoid sinus, the patient was diagnosed with diffuse large B-cell lymphoma.

Conclusions, including unique features of the case:
Our case represents a key decision point for distinguishing between two uncommon diagnoses. The difference in diagnosis is key for treatment options. The first-line treatment for a spheno-orbital meningioma is surgical resection, whereas for orbital diffuse large B-cell lymphoma, it is chemotherapy. Additionally, mortality for orbital DLBCL is relatively high at 63% due to its aggressive nature, while the mortality rate for SOM after resection is only 6%. This underscores the importance of biopsy for ocular neoplasms identified on imaging, as the decision for a nasal biopsy rather than craniotomy was essential in this case.

References: None provided.

Keywords: Orbit/ocular pathology, Tumors, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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A Battle of Wills: A Resilient CCF in a Noncompliant Patient

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Introduction:

Carotid-cavernous fistula (CCF) is an abnormal connection between the arteries and veins within the cavernous sinus. CCF's are classified as either direct – with involvement of the internal carotid artery (ICA) – or indirect, involving ICA meningeal branches or the external carotid artery. Direct CCFs typically arise from trauma and generate a high-flow system, causing the classic triad of pulsatile exophthalmos, chemosis, and orbital bruit.[1] Swift diagnosis and emergent intervention are required; left untreated, direct CCF's can lead to intraparenchymal or subarachnoid hemorrhage, fatal epistaxis, rapidly progressive proptosis, ophthalmoparesis, and blindness.[2]

Description of Cases:

A 54-year-old male with recently incurred gunshot head wound presented with 10 days of progressive left eye bulging and pain. Left eye examination revealed ophthalmoplegia with chemosis, edema, proptosis, diminished visual acuity, and intraocular pressure of 27 mmHg (18 mmHg OD). Computed tomography angiography (CTA) and 4-vessel digital subtraction angiography (DSA) identified a direct Type A carotid-cavernous fistula. His coil embolization obtained near-complete CCF occlusion; repeat embolization was planned to ensure complete occlusion, however the patient left against medical advice (AMA). He returned within 2 weeks for worsening symptoms, requiring embolization of the superior ophthalmic vein (SOV) and placement of an Evolve flow diverter within the cavernous ICA. Despite progressing proptosis, he threatened to leave AMA. DSA again revealed a patent CCF with robustly filling SOV, prompting a third embolization. Ultimately, the CCF was occluded via Onyx embolization of the fistula and SOV by neurosurgery's direct eyelid SOV approach. On outpatient visit, he had significant improvement in symptoms, partial return of his vision, and improving disfiguration.

Conclusions, including unique features of the case:

Although transarterial endovascular embolization has a 93.93% obliteration rate,[3][4] CCF intervention remains complex and here required multiple advanced procedures while battling the whims of a noncompliant patient. This highlights the importance of a multidisciplinary approach and tailored management to prevent permanent vision loss.

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Keywords: Orbit/ocular pathology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Dangerous Giant Cell Arteritis Mimicker - Mucormycosis

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Introduction:
Mucormycosis is a rare but devastating fungal infection affecting patients with immunosuppression. Central retinal artery occlusion (CRAO) is a rare manifestation of rhino-orbital-cerebral mucormycosis (ROCM). We present a unique case of ROCM with isolated CRAO as the initial ocular presentation with elevated inflammatory markers mimicking giant cell arteritis (GCA). This case highlights the dangers of steroid use in the setting of unrecognized infection.

Description of Cases:
A 70-year-old man on immunosuppression for myelodysplastic syndrome presented with new-onset right-sided headache, jaw pain and sudden vision loss in the right eye. He had a history of steroid-induced diabetes and was on opportunistic infection prophylaxis including voriconazole. A COVID-test at admission was positive. His examination was notable for no light perception vision in the affected eye, and a cherry-red spot indicative of CRAO. ESR was 75, CT showed mild inflammatory changes in the ethmoid sinuses and stroke workup including brain MRI was negative. High-dose steroids were started, and temporal artery biopsy for suspected GCA was postponed at the family's request for further discussion. Six days later, the patient developed increasing pain, right eye proptosis and complete ophthalmoplegia. Repeat brain MRI showed infiltrative inflammatory changes of the orbit associated with necrosis and sinus biopsy showed invasive mucormycosis. Despite aggressive antifungal treatment, the infection progressed rapidly, and the patient ultimately succumbed to the infection.

Conclusions, including unique features of the case:
Occult systemic infections can closely mimic GCA in the early stages particularly in patients with vision compromised conditions, complicating diagnosis and treatment. This case emphasizes the importance of thorough evaluation before initiating corticosteroid therapy in suspected GCA cases, especially in immunocompromised patients. Concomitant antimicrobial coverage along with corticosteroid treatment in selective patients should be considered. The rarity of ROCM presenting with isolated CRAO in the early-stage mimicking GCA due to elevated inflammatory markers makes this case particularly notable and highlights an important diagnostic challenge.

References: None provided.

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Orbit/ocular pathology, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Orbit, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Bilateral Optic Disc Edema and Orbital Inflammation in a Child with Trisomy 21 and B-ALL Following CAR-T Cell Therapy

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Introduction:
Chimeric antigen receptor (CAR) T cells targeting CD-19 are approved for treatment of relapsed B-cell acute lymphoblastic leukemia (B-ALL). CAR T cell therapy has been associated with systemic inflammation, but ocular inflammation is rare. We report a case of a child with B-ALL who developed orbital and ocular inflammation after CAR T cell therapy.

Description of Cases:
A 12-year-old girl with Trisomy 21 and relapsed B-ALL underwent CAR T cell therapy after undergoing a lumbar puncture that was negative for leukemic cells. 5 days starting this therapy, she presented with right eye redness, swelling, fever, and headache. On ophthalmology examination, visual acuity was 20/50 in both eyes without a relative afferent pupillary defect (RAPD). She had right eye injection, proptosis, and limitation to abduction with right esotropia. Dilated fundus examination demonstrated bilateral optic disc edema and right eye serous retinal detachment. MRI brain and orbits showed right orbital inflammation and normal optic nerves, except for a small area of restricted diffusion in the left optic nerve head. Differential diagnoses included leukemic optic nerve infiltration, CAR T cell-mediated inflammation, and infection. She was started on broad-spectrum antibiotics, fluconazole, and acyclovir without improvement. Repeat lumbar puncture showed no malignant cells. Subsequently, bilateral subtenon's triamcinolone injections and aqueous humor biopsies were performed. She was also started on dexamethasone and symptoms improved. Cytology was negative, and cell-free DNA analysis showed no chromosomal alterations indicative of leukemic cells. This led to the decision to defer radiation therapy.

Conclusions, including unique features of the case:
This case demonstrates that B-ALL and CAR T cell therapy can be associated with orbital and intraocular inflammation with optic disc edema. Both CAR T cell-related inflammation and leukemic infiltration can cause optic disc swelling, and aqueous humor biopsy to assess for leukemic cells and cell-free DNA may assist in management decisions.

References: None provided.

Keywords: Pediatric neuro-ophthalmology, Orbit

Financial Disclosures: Anis Hilal; Jesse Berry: Aqueous humor cell free DNA for diagnostic and Prognostic evaluation of Ophthalmic Disease Pending 17/045,435 filed October 5, 2020 SLW 2771.008US1 (Berry, Xu, Hicks); no funds have been generated from this patent; Melinda Chang

Grant Support: None.

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Pediatric Fulminant Idiopathic Intracranial Hypertension Characteristics and Management

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Introduction:
Fulminant idiopathic intracranial hypertension (FIIH) is associated with rapid worsening of visual function. There are no guidelines for treatment of FIIH in children, but due to the significant risk of permanent vision loss, early surgical intervention is often recommended. This study aims to review the presentation and treatment of pediatric FIIH at a single tertiary care children's hospital.

Description of Cases:
Five patients diagnosed with FIIH at a large children's hospital were identified between 01/01/2021-09/16/2024. Retrospective chart review included demographics, opening pressure, medical/surgical interventions, other neurologic/ophthalmic findings, and presenting/final visual function. Included patients ranged in age from 10 to 16 years old and were all female. The opening pressure was ≥ 48 cm H2O in all cases. Presenting acuity was 20/200 or worse in the better eye in 4 patients (80%), and all patients had severe bilateral visual field constriction. Abduction deficits were noted at the time of presentation in 40% of cases. All patients underwent CSF shunting procedures (4 ventriculoperitoneal, 1 lumboperitoneal) with subsequent optic nerve sheath fenestration in 3 patients (60%). Visual acuity recovered to at least 20/40 in the better seeing eye in all cases following treatment, but visual field constriction persisted.

Conclusions, including unique features of the case:
FIIH is an aggressive form of vision loss in children that requires urgent surgical intervention to minimize permanent visual deficits. Our experience describes the presenting characteristics and outcomes of FIIH in children and emphasizes the need for larger studies to elucidate optimal management algorithms.

References: None provided.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Pediatric neuro-ophthalmology, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Cryptic Suprasellar Germinoma Presenting as Autoimmune Hypophysitis in a Pediatric Patient

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Introduction:
Pituitary stalk lesions (PSLs) are difficult to diagnose due to overlapping clinical and radiologic features of the differential pathologies. Such conditions can often cause endocrine and visual issues. Accurate diagnosis is crucial. We report a 9-year-old girl misdiagnosed with idiopathic hypophysitis, later confirmed as a suprasellar germinoma after her vison worsened.

Description of Cases:
A 9-year-old female with a history of autoimmune hypophysitis presented with progressive visual loss over the course of several months. She also had developed adrenal insufficiency, diabetes insipidus, growth hormone deficiency, and hypothyroidism. Her initial MRI showed pituitary stalk thickening (PST) with normal pituitary function except for diabetes insipidus. A follow-up MRI, taken at the time of presentation, revealed increased thickening and mild optic chiasm impingement. Cerebrospinal fluid (CSF) was negative for malignancy markers including alpha-feto-protein and hCG. A biopsy showed no signs of granulomas, abnormal histiocytes, or atypical lymphoid cells. LCH, Rosai-Dorfman disease, IgG4-related disease, lymphoma, and GCT were ruled out at this time. Based on these findings, the patient was diagnosed with idiopathic hypophysitis and started on corticosteroid therapy. Despite treatment, her visual function continued to deteriorate. A subsequent MRI revealed enlargement of the hypothalamic mass with optic nerve and chiasmal extension, suggesting a neoplasm. A second biopsy confirmed germinoma. After treatment, the mass reduced in size; however, the patient developed bilateral optic atrophy with minimal visual recovery and field defects.

Conclusions, including unique features of the case:
This case highlights the importance of considering suprasellar germinoma in pediatric PSLs, even when initial biopsies suggest hypophysitis. Overlapping clinical features can delay diagnosis and increase the risk of complications such as irreversible visual loss from optic atrophy. Clinicians should remain vigilant for progressive symptoms and atypical imaging unresponsive to standard therapies, as early diagnosis is crucial to prevent irreversible outcomes.

References: None provided.

Keywords: Tumors, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Is That Nerve Swollen? A Systematic Literature Review and Our Proposed Paediatric Pathway

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Introduction:
There has been an increase in referrals to paediatric hospitals for suspected optic nerve swelling. Frequently, such patients are asymptomatic. Given possible life threatening associations with papilledema these referrals require urgent review, causing parental stress /concern and burdening of our clinics. We conducted a systematic review of the available literature, which yielded 382 returns, subsequently refined by two reviewers. Filtering for studies focused on paediatric pathways for patients that were otherwise well prior to referral. A secondary review for articles related to possible ophthalmological investigations /assessment of the optic nerve identified 36 papers.

Description of Cases:
5 studies met our primary criteria, totalling 720 patients. Assessment of fundal images is not sufficient, expert reviewers had high sensitivity but low specificity. Raised intracranial pressure symptoms were most useful in identifying true papilledema whereas, headache alone was a common nonspecific symptom. Two studies reported true papilledema rates of 5% and 6% respectively in patients with/without symptoms. Another study reported true disc swelling at 16%, this included referrals from paediatric specialists /ophthalmologists and all causes of disc swelling. OCT RNFL was significantly higher in true disc swelling and a lack of temporal change supported a diagnosis of anomalous disc appearance over pathology.

Conclusions, including unique features of the case:
This review supports that the majority of these patients require no neuroimaging nor invasive lumbar puncture/FFA. Our pathway advises both general emergency departments and ophthalmology staff of whether urgent inpatient investigation is needed versus urgent clinic review for low-risk patients. Neuroimaging prior to ophthalmic review is discouraged for children without neurological symptoms/ red flags. Our ophthalmology pathway includes nerve function tests and multiple imaging modalities, with review by experienced clinicians in urgent virtual clinics resulting in; discharge, short interval repeat virtual review, or urgent tertiary hospital referral. This review suggests we will reduce admissions, protect in-hospital clinics and avoid unwarranted scans/ invasive investigations.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Neuromyelitis Optica Spectrum Disorder in a Young Patient with Shwachman-Diamond Syndrome.

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Introduction:
Shwachman-Diamond syndrome (SDS) is a rare inherited bone marrow failure syndrome characterized by neutropenia, exocrine pancreatic insufficiency, and skeletal abnormalities. Neurocognitive, dermatologic, and retinal changes may also be found in certain phenotypes. Neuromyelitis optica spectrum disorders (NMOSD), is an inflammatory, antibody-mediated, immunologic disease of the central nervous system that causes demyelination of the optic nerve and spinal cord.

Description of Cases:
A 13-year-old girl with a recent diagnosis of pancreatic exocrine insufficiency and a complex medical history of neutropenia, thrombocytopenia, and scoliosis that is now known to be associated with SDS our patient by a homozygous pathogenic mutation in SBDS). During that time, the patient also experienced multiple 30-minute episodes of hiccups, nausea, vomiting, constipation, difficulty urinating, and two episodes of visual disturbance. Pt was admitted in November 2022 for weakness and gait instability and was subsequently found to have multiple spinal cord lesions and mild enhancement in the optic nerves. AQP4 antibodies were present consistent with seropositive NMO. Laboratory tests also revealed multiple auto-antibodies without a specific rheumatologic condition. Pt had notable improvement in symptoms after the use of steroids/PLEX.

Conclusions, including unique features of the case:
There have been previous reports of patients with SDS that developed inflammatory eye conditions. However, to our knowledge this is the first case of an SDS patient that presented with NMOSD. It's unclear that the constellation of symptoms can be explained by a unifying rheumatologic diagnosis in the light of multiple positive autoantibodies (ANA+,RF+,SSA+,SSB+Smith+). Autoimmunity is not a common diagnosis associated with SDS. Treatment of inflammatory manifestations in patients with SDS may be complicated by potential myelosuppressive toxicities. Although these types of studies cannot establish a direct relationship between these two conditions, in our patient most symptoms occurred during the same time, making diagnosis difficult. Further research is needed to better understand the potential link between inflammatory disorders and SDS.

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Keywords: Pediatric neuro-ophthalmology, Optic neuritis, Genetic disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Clinical Presentation of Homozygous Pathogenic Mutations in the CLN3 Gene in a 9-Year-Old Caucasian Male

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Introduction:
Juvenile-onset neuronal ceroid lipofuscinosis (CLN3 disease) is a rare genetic disorder characterized by progressive neurological degeneration and retinopathy. Accurate diagnosis can be confirmed through genetic testing and should be considered in children presenting with vision loss, developmental delay, and a positive family history.

Description of Cases:
A 9-year-old male presented for evaluation of esotropia and amblyopia, with unexplained vision loss that was not corrected with glasses. According to his parents, the vision loss had been ongoing for several years, with the child frequently bumping into objects due to poor vision. He also experienced issues with color vision and photosensitivity. Additional developmental concerns included a history of speech delay and limb asymmetry, for which he received early intervention services. His ancestry was German and Native American. A significant family history of retinal dystrophy was noted, including the patient's maternal grandfather, great-great aunt, and grandfather's sisters. His best corrected visual acuity was 10/300 right, 10/125 left eye. He was noted to have moderate hyperopia and moderate astigmatism. There was no ocular misalignment or nystagmus. His fundus exam noted maculopathy OU, mild peripheral RPE mottling, FAF noted bull's eye maculopathy OU. Given his clinical findings and family history, saliva testing through Invitae revealed homozygous pathogenic mutations in the CLN3 gene (exon 8,9 deletion). This confirmed a diagnosis of CLN3 disease (juvenile neuronal ceroid lipofuscinosis). The patient was referred to pediatric neurology and provided information on potential clinical trials for further management of CLN3 disease.

Conclusions, including unique features of the case:
Juvenile-onset neuronal ceroid lipofuscinosis (CLN3 disease) is an autosomal recessive neurodegenerative disorder characterized by progressive neurological decline and visual deterioration. Genetic testing should be strongly considered in all children presenting with progressive vision loss, especially when accompanied by a positive family history of retinal dystrophy or developmental delays, as early diagnosis is critical for management and access to emerging therapies.

References: None provided.

Keywords: Genetic disease, Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Unveiling A TNF-Receptor Associated Factor 7 Mutation Resulting In Optic Nerve Sheath Meningiomas Through A Pediatric Case

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Introduction:
Optic nerve sheath meningiomas (ONSMs) are rare benign tumors of the anterior visual pathway, comprising 2% of all orbital tumors. TNF-receptor associated factor 7 (TRAF7) regulates important and fundamental biological processes but mutations can lead to intracranial meningiomas (including ONSM) and other congenital malformations. We report a pediatric case who lost vision due to bilateral ONSMs and was found to have a TRAF7 mutation with a history of other syndromic associations.

Description of Cases:
A 14-year old female initially presented with bilateral diminishing vision, increasingly frequent headaches, and outward eye deviation. Medical history included congenital abnormalities such as cardiac defects, brachydactyly of hands, syndactyly of the right foot, epicanthal fold, and speech delay. Previous fluorescence in situ hybridization was inconclusive. Right eye vision was hand motion (HM) with left eye at 20/25-3. Neuroimaging and ancillary testing warranted right eye optic nerve sheath fenestration and optic nerve biopsy, which revealed WHO Grade 1 ONSM. Two years later she presented with decreasing vision in the left eye and underwent optic nerve decompression and biopsy of dura and epidural tissue that revealed a WHO grade 1 meningioma. Neurofibromatosis type 2 testing was negative, but sequencing of the meningioma demonstrated a recurrent missense mutation within TRAF7.

Conclusions, including unique features of the case:
Other cases reporting TRAF7 mutations displayed similar congenital abnormalities and findings on neuroimaging. Because of the connection between TRAF7 mutations and intracranial meningiomas, genetic testing may be helpful in cases of multiple meningiomas and those with syndromic associations. Radiation therapy is generally considered the preferred therapy for symptomatic ONSM; however, pediatric population studies suggest that surgical prevention be the primary treatment for children with ONSM secondary to increased malignant potential relative to adult ONSM.

References: None provided.

Keywords: Genetic disease, Neuroimaging

Financial Disclosures: Michael Miltich; Ximena Infante; Paul Clifford; Luciana Garcia; Elizabeth Colvin; Mohamed Khodeiry; Byron Lam: Research Support: National Eye Institute, United States Department of Defense, Foundation Fighting Blindness, Atsena Therapeutics, Beacon Therapeutics, Endogena Therapeutics, Nanoscope Therapeutics, Ocugen Inc., PYC Therapeutics, Sparingvision, Spark Therapeutics, Splicebio, Stoke Therapeutics; Consulting: BlueRock Therapeutics, Johnson & Johnson, Splicebio, Spulbio; Maja Kostic

Grant Support: None.

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Benign Path to Blindness

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Introduction:
An 11-year-old boy presented with progressive vision loss and optic disc edema. Imaging revealed bilateral optic canal narrowing and irregular skull base trabecular patterns. Genetic testing identified a mosaic DNMT3A mutation linked to Tatton-Brown-Rahman Syndrome (TBRS), although the patient lacked hallmark TBRS features. This case underscores the diagnostic challenges and management dilemmas of rare genetic mutations with atypical presentations.

Description of Cases:
Initially, the patient reported black dots in the left eye, progressing to hand motion vision. Examination showed optic disc edema, light perception vision in the left eye, and a relative afferent pupillary defect. Re-evaluation of imaging revealed bilateral optic canal narrowing and skull base sclerosis. Management included left optic canal decompression and prednisone, yielding some improvement. Symptom recurrence, including pulsatile tinnitus, right eye pain, and elevated intracranial pressure, was managed with acetazolamide. In two years, he developed right-sided hearing loss and worsening right eye vision requiring additional decompressive surgeries. Bone biopsies were normal, but genetic testing confirmed the DNMT3A c.2644C>T (p.Arg882Cys) pathogenic variant, indicating mosaicism. Unlike typical TBRS, the patient had no overgrowth, intellectual disability, or distinct facial features. Hematologic evaluation ruled out acute myeloid leukemia (AML). Despite interventions, vision stabilized at 20/70 in the right eye and counting fingers in the left, with resolution of optic disc edema.

Conclusions, including unique features of the case:
This case highlights presumed DNMT3A missense mutation mosaicism causing localized skull base overgrowth and cranial nerve compression, distinct from classic TBRS. Challenges included confirming mosaicism in bone tissue and timing of decompression. Notably, this isolated presentation expands the spectrum of DNMT3A mutations, as only one prior case involved DNMT3A mosaicism without systemic TBRS features or AML.

References: None provided.

Keywords: Pediatric neuro-ophthalmology, Genetic disease, Skull base, Optic neuropathy, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Nutritional (vitamin A) deficiency, hyperostosis, and compressive optic neuropathy in a young man with autism

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Introduction:

Children with ASD and restrictive diets should be monitored and supplemented for nutritional deficiencies. Vitamin A-deficient diets in animals can lead to abnormal bone growth, and similarly in humans [1-6]. Our case features diffuse skull thickening, resulting in compressive optic neuropathy from severe vitamin A deficiency among other nutritional deficiencies.

Description of Cases:

A 15-year-old male with autism, agenesis of the corpus callosum, colpocephaly, and a restrictive diet primarily of fries had progressive vision and hearing loss. He was HM OD and LP OS, pupils were sluggish with no rAPD, and the oculomotor system was normal. External exam demonstrated bilateral proptosis, and slit lamp revealed subepithelial corneal infiltrates and faint corneal opacities. Fundus exam revealed marked optic atrophy OU and small white outer retinal flecks in the periphery OU. Labs were notable for anemia, hypocalcemia, hyperparathyroidism, and deficiencies in vitamin D, zinc, and copper. His vitamin A level, at the lower end of normal, and the xerophthalmic fundus findings suggest he had prolonged vitamin A deficiency recently reversed with supplementation during an outside hospitalization [7]. CT demonstrated diffuse osseous thickening of the skull base and calvarium, diploic space filled with fat, and narrowing of optic canals and internal auditory canals. He underwent bilateral optic canal decompression but remained HM OU. Deficiencies in vitamin B12, zinc, copper, and thiamine may have contributed, but vitamin A deficiency can manifest as retinopathy and compressive optic neuropathy.

Conclusions, including unique features of the case:

Our case highlights the triad of nutritional (vitamin A) deficiency, hyperostosis, and compressive optic neuropathy in a young man with autism. When caring for children with restrictive diets, ophthalmologists should be aware vitamin and mineral deficiencies may manifest as compressive optic neuropathy due to bone thickening and narrowing of the optic canals. Prior multivitamin supplementation can make it more challenging to recognize this clinical triad.

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Keywords: Optic neuropathy, Pediatric neuro-ophthalmology, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None

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Case Report: Pineal Capillary Hemangioma Causing Obstructive Hydrocephalus Resulting In Vertical Diplopia And Papilledema In A Pediatric Patient

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Introduction:
Pineal masses are a heterogeneous group of neoplasms and often present with neuro-ophthalmologic findings secondary to obstructive hydrocephalus or dorsal midbrain syndrome. They are most often primary pineal parenchymal tumors, but also include germ cell tumors, neuroepithelial tumors and papillary tumors of the pineal region. Cavernous and capillary hemangiomas are well defined vascular hamartomas of the central nervous system and are most often identified in the cerebral hemispheres, basal ganglia and brainstem, however not typically present in the pineal region.We present the first case of a pineal capillary hemangioma in a pediatric patient.

Description of Cases:
We report a case of a 7-year-old boy with rapid onset of binocular vertical diplopia, positional tinnitus, right-sided hearing loss, hypoesthesia of the right face, and intermittent headache. His visual acuity was 20/25 in the right eye and 20/30 in the left. His exam showed bilateral 4th nerve palsies and bilateral disc edema. MRI brain demonstrated obstructive hydrocephalus with transependymal flow due to a homogeneously-enhancing, lobulated 2-cm pineal mass. The patient underwent ventriculoperitoneal shunting and excisional biopsy, which showed histopathologically-confirmed capillary hemangioma. Two months after surgical resection and shunting, the patient had near-complete resolution of all neurological signs and symptoms, with the exception of a mild vertical strabismus. His visual acuity improved to 20/20 in each eye and visual field testing was full.

Conclusions, including unique features of the case:
Pineal masses are typically benign but can present with a variety of neuro-ophthalmologic findings including tectal compression, dorsal midbrain syndrome, and obstructive hydrocephalus. Vascular lesions of the pineal region are extremely rare, and when present may raise concern for genetic syndromes. It may be important for clinicians to consider these lesions in pediatric pineal tumors and obtain imaging to better delineate the vascular anatomy in such cases.

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Keywords: Pediatric neuro-ophthalmology, Neuroimaging, Tumors, Vascular disorders

Financial Disclosures: Siavash Assar; Emily Eng; Kristina Lin; Michael Trainer; Peter Sun; Alyssa Reddy; Arie Perry; Joshua Byers; Vijay Latchuman; Winson Ho; Marc Levin: Unrelated financial compensation as: consultant, Jazz Pharmaceuticals; consultant, Vanda Pharmaceuticals; royalties, University of California; Rabih Hage; Nailyn Rasool

Grant Support: None.

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Presumed Graft-Versus-Host-Disease (GVHD) of the Extraocular Muscles in a Teenager with Leukemia and Systemic GVHD

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Introduction:
Extraocular muscle (EOM) enlargement may be caused by infectious, inflammatory, neoplastic, and vascular etiologies. We report a case of acquired EOM enlargement resulting in diplopia in a teenager with a history of leukemia status post bone marrow transplant (BMT) complicated by systemic graft-versus-host disease (GVHD), with histology suggestive of GVHD involving the EOMs.

Description of Cases:
A 15-year-old boy with a history of hypothyroidism and B-cell acute lymphoblastic leukemia (B-ALL) s/p BMT and GVHD developed acute onset of left eye “swelling” and diplopia. Visual acuity was 20/25 in both eyes. He had mild proptosis and limitation to adduction, abduction, and depression in the left eye, with an exotropia of 40 PD and left hypertropia of 2 PD. The remainder of the ocular examination was normal. There was concern for an orbital process, such as thyroid eye disease or leukemic infiltration, or myasthenia gravis, and he underwent MRI that demonstrated diffuse enlargement and restricted diffusion of the left medial, left lateral, right medial, and right inferior rectus muscles. He was euthyroid and cerebrospinal fluid cytology was negative. He underwent biopsy of the left lateral and right inferior rectus muscles with simultaneous recession. Histologic analysis showed no acute inflammation or neoplastic process; patchy myocyte atrophy was suggestive of GVHD myopathy. He had previously experienced hepatic, gastrointestinal, and cutaneous GVHD, for which he was currently on cyclosporine. Postoperatively, the patient was orthotropic with resolution of diplopia and improved proptosis. Follow-up MRI scan is pending.

Conclusions, including unique features of the case:
GVHD myopathy is rare and associated with myocyte atrophy on pathology. To our knowledge, GVHD myopathy limited to the EOMs has not previously been reported. Given the clinical context and absence of histological findings consistent with thyroid eye disease or other active inflammatory process, we believe this patient developed diplopia and ophthalmoplegia due to GVHD myopathy involving the EOMs.

References: Pestronk A. Chronic Graft Versus Host Myopathies: Noninflammatory, Multi-Tissue Pathology With Glycosylation Disorders. J Neuropathol Exp Neurol. 2020 Jan 1;79(1):102-112.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Combined Marcus Gunn Jaw Winking Synkinesis and Monocular Elevation Deficiency: A Case Report and Literature Review

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Introduction:
Marcus–Gunn Jaw Winking synkinesis (MGJWS) is a condition characterized by congenital ptosis that improves with stimulation of the ipsilateral pterygoid muscles due to misrouted nerve signals. While it can occur as an isolated abnormality, studies have reported a strong association with other ocular conditions such as amblyopia, refractive errors, and strabismus. Among these, monocular elevation deficiency (MED) – a type of strabismus characterized by inability to elevate the eye in both abducted and adducted positions – is most associated with MGJWS.

Description of Cases:
We present a 14-year-old male with refractive amblyopia, congenital ptosis, MGJWS, and MED in the left eye. Slit lamp examination showed a palpebral fissure height of 8 mm in the right eye and 3 mm in the left, with a marginal reflex distance 1 (MRD1) of +3 mm in the right eye and -2 mm in the left. Due to good levator function of 12-13 mm in the left eye, he underwent levator advancement surgery, followed by frontalis sling surgery for further ptosis correction. Postoperatively, ptosis improved to an MRD1 of 0 mm, extraocular movements were full, and the MGJWS became unnoticeable.

Conclusions, including unique features of the case:
Although the mechanism underlying the co-incidence of MGJWS and MED - especially in cases of severe ptosis - remains uncertain, studies suggest shared pathogenesis within congenital cranial dysinnervation disorders. Aberrant innervation of the levator palpebrae superioris and superior rectus muscles from the oculomotor nerve leads to congenital ptosis and MED, respectively. This miswiring may also induce MGJWS due to proximity of the oculomotor and trigeminal nuclei during development. Co-incidence of MGJWS with MED in cases of severe ptosis, as seen in this case, likely relates to the degree of dysinnervation whereby greater dysinnervation increases the chance of this aberrant connection forming. Further research is needed to improve management strategies and minimize patients' visual, cosmetic, and surgical burdens.

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Keywords: Pediatric neuro-ophthalmology, Ocular motility, Orbit, Orbit/ocular pathology, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Exploring the Hidden Autoimmunity Link in Ross Syndrome

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Introduction:

Ross syndrome (RS) is a rare progressive autonomic disorder characterized by a triad of tonic pupil, areflexia, and segmental anhidrosis or hypohidrosis. Etiology of RS has been associated with autoimmune disorders such as Sjogren syndrome and general ANA positivity. An overlap with Holmes-Adie syndrome is known, which has been linked to various autoimmune disorders, including celiac disease and autoimmune hepatitis. Latent Autoimmune Diabetes in Adults (LADA) represents a distinct subtype of diabetes marked by autoimmune destruction of insulin-producing beta cells within the pancreas. To date, no established association has been reported between RS and LADA.

Description of Cases:

A 51-year-old female was referred to the neuro-ophthalmology clinic due to new onset anisocoria. She denies preceding viral prodrome or trauma. Pertinent past medical history included LADA, Sjogren's syndrome, and ITP. She reported chronic inability to sweat and areflexia since childhood. She denies any rashes or areas of hyper/hypopigmentation. Examination revealed preserved visual acuity and visual fields bilaterally. There was no RAPD. Motility was full bilaterally. Anisocoria was more prominent in the light with a dilated poorly reactive left pupil with light-near dissociation. No sectoral palsy or vermiform movements were appreciated. Application of dilute pilocarpine led to left pupillary constriction confirming a diagnosis of Adie's tonic pupil. Motor and sensory examination were unrevealing. Deep tendon reflexes were absent throughout. Neuroimaging was unremarkable and laboratory testing was notable for positive ANA; GAD65 antibodies were negative. Given her autoimmune history and associated ophthalmic, neurologic, and dermatologic conditions a diagnosis of RS was established and close rheumatology follow-up is planned.

Conclusions, including unique features of the case:

Although Adie's tonic pupil is considered benign and idiopathic, it may be indicative of underlying autoimmune conditions. The authors aim to enhance awareness of the established link between autoimmune diseases and RS while also investigating its potential connections to other conditions, including LADA.

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Keywords: Pupil, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Tonic Pupil as the Initial Manifestation of anti-Hu Associated Paraneoplastic Neurological Syndrome in a Patient with Neuroendocrine Carcinoma of the Bladder

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Introduction:
Primary neuroendocrine carcinomas of the urinary bladder are extremely rare. Neurologic paraneoplastic syndrome (PNS) associated with neuroendocrine tumors is not typical. Association of anti-Hu antibody development and neuroendocrine cancer has been found in very few cases. Tonic pupil is mostly idiopathic, however it can develop as PNS. Its association with PNS caused by neuroendocrine carcinoma of the bladder has not been reported.

Description of Cases:
73-year-old male with a history of smoking, abdominal aortic aneurysm, pulmonary embolism and grade 3, poorly differentiated neuroendocrine carcinoma of the bladder with pulmonary metastases presented with left eye mydriasis. His bladder carcinoma was diagnosed 4 years prior, underwent treatment with neoadjuvant chemotherapy, cystoprostatectomy and later on with carboplatine/etiposide. Ophthalmological examination revealed tonic pupil of the left eye and interpreted it idiopathic. About two weeks later the patient developed weakness of the left leg which over a few weeks progressed to paralysis, paresis of the right leg and right hand. Chemotherapy was discontinued. MRI of the brain and spinal cord was negative, CT thorax and abdomen showed regress of the pulmonary metastases. EMG/neurography and clinical examination showed isolated motor neuropathy. Liquor analysis showed oligoclonal IgG bands, serum was positive for anti-Hu antibodies supporting the diagnosis of paraneoplastic motor neuropathy. IVIG was initiated which terminated the progression but did not cause regress of the paresis. The chemotherapy was resumed with positive effect on metastases until the patient passed away 1,5 years later in the burdens of severe pneumonia.

Conclusions, including unique features of the case:
Here we present for the first time tonic pupil as the initial manifestation of PNS in a patient with neuroendocrine carcinoma of the urinary bladder. Consideration of tonic pupil as a manifestation of PNS could result in earlier recognition and treatment of a more severe form of PNS.

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Keywords: Pupil, Paraneoplastic syndromes

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Hyperhidrosis With Associated Pupillary Lag: Questionable Horner's Syndrome

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Introduction:
A 36-year-old male underwent surgery to remove thyroid cancer eccentric to the right in 2019. In 2022, he complained of sweating on one side of his face while eating spicy foods, a smaller right pupil compared to the left, and slight right eyelid drooping. The hyperhidrosis was isolated to the right side of his face, the rest of his body was not involved.

Description of Cases:
Through EOG (electrooculography) testing, the patient's eyes were exposed to bright light followed by ambient lighting. During the test, the patient's right pupil was significantly smaller. The left pupil was round and regularly reactive and demonstrated a normal dilation speed. In neither of the eyes was there obvious ptosis. A classic sweat lab with iodine and corn starch was performed in the clinic to demonstrate the areas of the face that produce hyperhidrosis while eating a spicy pizza. After 5 minutes, there was a clear difference between the right and left side of the face for hyperhidrosis. The right side had turned dark purple and the left remained white from starch powder.

Conclusions, including unique features of the case:
The unique features of this case include the lag in pupil dilation in the right eye, which is typical of Horner's Syndrome. Hyperhidrosis is present rather than anhidrosis, this has been previously reported. It is plausible that these clinical findings are the beginning stages of Horner's Syndrome. Sympathetic fibers designated to innervate sweat cells travel up the external carotid artery whereas fibers sustaining the pupil and lid travel around the internal carotid. Bifurcation of these fibers off the common carotid is located within the tumor site. It is plausible given the three-year delay in onset that there may be fiber entrapment from scar tissue.

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Keywords: Pupil

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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The Intermittently Outstanding Pupil: A Case of Isolated Unilateral Episodic Mydriasis from Oculomotor Schwannoma

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[1] *Mayo Clinic*

Introduction:
Schwannomas of the oculomotor nerve are uncommon. They typically present with progressive oculomotor nerve deficits but can also present with transient or recurring diplopia and mimic recurrent painful ophthalmoplegic neuropathy. The pathophysiology is not clearly understood, but proposed mechanisms include fluctuation of tumor-associated edema, remyelination, and hemodynamic changes. We report a case of episodic unilateral mydriasis without ophthalmoplegia in the context of an oculomotor nerve schwannoma, which has not been previously described.

Description of Cases:
A 29-year-old man with a decade-long history of migraines presented to neuro-ophthalmology clinic with episodic right mydriasis with associated blurry vision but without diplopia. These episodes were intermittent, usually lasting a few hours and occurring several times in a week, but some weeks there would be no episodes of mydriasis. Six months earlier, he developed acute-onset right-sided headache with vomiting, as well as right ptosis and a dilated minimally-reactive right pupil, which resolved after three days. Magnetic resonance imaging (MRI) and magnetic resonance angiography of the brain showed an irregular enhancing cystic mass in the prepontine cistern suggestive of a schwannoma of the right third cranial nerve. At the time of the neuro-ophthalmology clinic visit, he reported no more headaches nor ptosis. He denied any double vision, though he continued to have episodes of right mydriasis. On examination, his pupils responded briskly to light without anisocoria. His motility was full and there was no ocular misalignment. Repeat MRI six months following initial imaging demonstrated a slight decrease in size of the schwannoma and collapse of some of the central cysts. To date, he reports ongoing intermittent episodes of mydriasis, without associated ptosis or diplopia.

Conclusions, including unique features of the case:
Schwannomas of the oculomotor nerve may present with isolated episodic mydriasis without ophthalmoplegia. This presentation may be misattributed to idiopathic episodic mydriasis without neuroimaging.

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Keywords: Pupil, Trauma, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Covert Oculosympathetic Denervation In Adie Pupil Exposed With Apraclonidine

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Introduction:
Pupil size is regulated by the subtle balance between the parasympathetic and sympathetic nervous systems. While the neuroanatomical basis for autonomic control of the pupil is thought to be established, emerging evidence has suggested that autonomic dysfunction may affect both parasympathetic and sympathetic nervous systems concurrently. We present the unique case of a 63-year-old woman with classic Adie pupil, where inadvertent administration of apraclonidine instead of dilute pilocarpine resulted in a pupillary response seen in Horner syndrome. This not only exposed a covert oculosympathetic denervation but also prompts inquiry into whether concomitant sympathetic denervation in Adie pupil is more common than previously understood.

Description of Cases:
A 63-year-old woman with classic left Adie tonic pupil underwent neuro-ophthalmological assessment and pharmacological drop testing. Apraclonidine was accidentally instilled instead of dilute pilocarpine. Initial examination disclosed classic features of a small (“little old”) Adie pupil. However, inadvertent instillation of apraclonidine resulted in an unexpected and marked dilation of the previously small Adie pupil, suggesting concomitant underlying sympathetic denervation of the iris. There was no change in either eyelid. Follow-up testing with dilute pilocarpine was performed correctly one week later and confirmed Adie pupil.

Conclusions, including unique features of the case:
Covert oculosympathetic denervation was detected in a patient with Adie pupil after the accidental use of apraclonidine. While ciliary ganglion inflammation is believed to produce Adie pupil via injury to parasympathetic neurons, we theorize that spill-over of this inflammation may also damage the non-synapsing sympathetic fibers in the ciliary ganglion, resulting in sympathetic denervation of the iris, but not the eyelid. Because this phenomenon was only detected serendipitously, this finding may be more common than previously thought. Further research, including prospective testing of Adie pupil patients with apraclonidine, may be helpful in better understanding the true prevalence and potential clinical significance of these findings.

References: None provided.

Keywords: Pupil

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

What's New – Literature Review [2.00 CME]

Moderators: Julie Falardeau, MD & Marc Dinkin, MD

Introduction, *Julie Falardeau, MD & Marc Dinkin, MD*
What's New in Retina? *Amani Fawzi, MD*
What's New in Neuro-Vascular Neurology? *John Paddock, MD*
What's New in Eye Pain? A Cornea Perspective, *Anat Galor, MD, MSPH*
What's New in Neuro-Immunology? *Fiona Costello, MD, FRCPC*

This session will highlight recent findings from key articles focusing on retinal disorders, corneal neuropathic pain, neuro-vascular disorders, and neuro-immunology. By reviewing and discussing the latest knowledge/research, we aim to enhance clinical practice in neuro-ophthalmology.

Upon completion of this session, participants should be able to:
(1) Review new concepts related to selected retinal diseases, including advancements in imaging modalities.
(2) Discuss new insights into corneal neuropathic pain, including its mechanisms, diagnosis, and management strategies.
(3) Identify best practices for diagnosing and managing neuro-vascular disorders.
(4) Discuss diagnostic criteria, biomarkers, and emerging therapies related to neuro-immunology.

WHAT'S NEW IN RETINA?

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LEARNING OBJECTIVES

- To review new imaging findings in macular disease with neuro-ophthalmology relevance
- To discuss the relevant evidence for new imaging signs
- To discuss the utility of overlooked imaging tools such as near infrared imaging
- To understand the imaging findings of "white dot syndromes" that overlap with neuro-ophthalmologic diagnoses

CME QUESTIONS

1. Near infrared reflectance is useful for detecting
    A. Acute macular neuroretinopathy
    B. Choroidal nevus
    C. Choroidal neurofibromatosis lesions
    D. Geographic atrophy
    E. All of the above

2. Retinal ischemic perivascular lesions (RIPL) are associated with all the following except
    A. Inner retinal fibrous lesions associated with folding
    B. Best seen in cross sectional OCT
    C. Perivascular location of ischemic lesions
    D. Residual lesions of acute infarcts of the middle retina
    E. Related to PAMM

3. Retinal lesions in multiple evanescent white dot syndrome are best seen on
    A. En face OCT
    B. Early frames of indocyanine green angiography
    C. Color photography
    D. Fluorescein angiography

KEYWORDS

1. Retinal ischemic perivascular lesions (RIPL)
2. Paracentral acute middle maculopathy (PAMM)
3. Multiple evanescent white dot syndrome (MEWDS)
4. Near infrared reflectance
5. En face OCT

HIGHLIGHTS

Retinal imaging tools, including multimodal imaging, have revealed new signs of retinal ischemia, and improved the ability to study patients with "unexplained symptoms." Additionally, these tools have allowed the enigmatic "white dot syndromes" to be better understood and classified, and have shed new light on their pathogenesis. This review will highlight recent developments focusing on newly identified "lesions" and their neuro-ophthalmologic relevance. We will review the utility of near infrared reflectance imaging, especially for detecting choroidal neurofibromatosis. We will also review retinal ischemic lesions such as paracentral acute middle maculopathy (PAMM) and retinal ischemic perivascular lesions (RIPL), and their implications for the risk of systemic cardiovascular disease.

CME ANSWERS

1. E
2. A
3. A

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4. Bakhoum, Christine Y., et al. "Retinal ischemic perivascular lesions are associated with stroke in individuals with atrial fibrillation." *Journal of the American Heart Association* 13.17 (2024): e035079.

WHAT'S NEW IN NEURO-VASCULAR NEUROLOGY?

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LEARNING OBJECTIVES

1. Compare risks and benefits of tenecteplase vs alteplase for acute ischemic stroke treatment
2. Appraise patient risk factors that may guide treatment with antiplatelet vs anticoagulation in cervical artery dissection.
3. Summarize current state of treatment for CRAO and systemic barriers to implementation.

CME QUESTIONS

1. All of the following are potential benefits of tenecteplase compared to alteplase except:
   A. Treatment as a single bolus without IV infusion
   B. Potential expansion of treatment window past 4.5 hours
   C. Lower rate of observed disability at 90 days
   D. Shorter half-life
   E. Higher fibrin specificity

2. Which of the following outcomes are associated with anticoagulation use in cervical artery dissection:
   A. Higher risk of major bleeding
   B. Lower risk of ischemic stroke
   C. Lower number needed to treat.
   D. Protection against and dissolution of thrombus
   E. All of the above

3. Which of the following is not true regarding treatment of CRAO:
   A. Retrospective studies show the efficacy of thrombolytics up to 6 hours after symptom onset.
   B. Thrombolytic therapy led to an average visual improvement of 2 Snellen line equivalents.
   C. 75% of patients have delayed presentation after monocular vision loss.
   D. 33% of patients with CRAO initially present to outpatient ophthalmology or optometry offices
   E. Non-mydriatic fundus photography and OCT have the potential to increase access to care.

KEYWORDS
1. Tenecteplase
2. Acute ischemic stroke
3. Cervical artery dissection
4. Central Retinal Artery Occlusion

HIGHLIGHTS

Review of Tenecteplase vs Alteplase for Treatment of Ischemic Stroke

Acute ischemic stroke (AIS) is a common neurological emergency with major mortality and morbidity. While treatable with pharmacological thrombolysis and/or endovascular interventions such as mechanical thrombectomy, treatment is often precluded by delayed patient presentation beyond narrow time intervals. Treatments also carry the risk of hemorrhagic complications like intracerebral hemorrhage that lead to poorer prognosis. While mechanical thrombectomy (MT) is not as widely available, thrombolysis with recombinant tissue plasminogen activator (r-tPA, alteplase) is frequently used and has been the standard of care for decades. Alteplase was initially approved by the Food and Drug Administration for treatment of AIS within 3 hours of stroke symptom onset, but this was expanded to 4.5 hours in 2008. Recently, a bioengineered version of r-tPA called tenecteplase (TNK) has emerged as a treatment for AIS based on several potential pharmacologic and practical advantages including longer half-life (20-25 minutes TNK vs 5 min r-tPA), decreased binding to plasminogen activator inhibition-1 by 80x, and a 15x higher fibrin specificity.

Based on growing evidence, the American Heart Association now recommends TNK as an alternative to r-tPA in patients with AIS who have minor strokes or who are thrombectomy candidates. However, dosing, utility outside the 4.5-hour

treatment window, and use in conjunction with imaging findings for wake-up strokes are yet to be determined. Limitations include lack of current FDA approval for AIS and a potentially higher risk of hemorrhagic conversion. The 2024 TRACE-III trial found that in patients with large vessel occlusions with viable ischemic penumbrae treated with TNK up to 24 hours, there was less disability than standard medical care but no change in 90-day survival and a higher risk of early intracranial hemorrhage. [1] TEMPO-2, also published in 2024, found patients with minor ischemic stroke treated with tenecteplase versus non-thrombolytic standard of care received no benefit and possible harm, suggesting tenecteplase should not be routinely used for minor ischemic stroke with small vascular occlusions. [2]

Cervical Artery Dissection Treatment Paradigms

Cervical artery dissection (CAD) is a common cause of stroke in young adults with multiple environmental and genetic contributors. CAD can lead to AIS, transient ischemic attacks (TIA), amaurosis fugax, or central or branch retinal artery occlusions (CRAO and BRAO). Approximately 15-25% of AIS in young adults are due to CAD, which has an incidence up to 3.0 per 100,000 per year. Intramural hematomas cause vessel dilation and trigger nervi vasorum, leading to head and neck pain, cranial and cervical neuropathies, and Horner's syndrome. Diagnosis may be delayed in those without AIS or TIA, and around 6% are asymptomatic and found incidentally. CT angiogram is superior to MR angiogram for identification of intimal flaps, high-grade stenosis, and pseudo-aneurysmal changes. Digital subtraction angiography remains the gold standard if other testing is inconclusive.

Stroke Prevention

The Stroke Prevention in Cervical Artery Dissection (STOP-CAD) study found that in patients with spontaneous dissections, anticoagulation was associated with lower risk of ischemic stroke, but a higher risk of major bleeding by 180 days compared with antiplatelet therapy. This suggests that anticoagulation may be preferred in those with higher AIS risk (significant luminal thrombus or high-grade stenosis) and lower bleeding risk, while antiplatelet therapy may be preferred in patients with lower stroke risk or higher bleeding risk. The authors suggest transitioning patients from anticoagulation to antiplatelet therapy 180 days when AIS risk is highest to balance risk of bleeding and benefits of stroke prevention, and treatment choice should be individualized for each patient's risks. STOP-CAD also showed that treatment with intravenous thrombolysis improved 90-day functional independence without increasing the risk of intracranial hemorrhage. [3]

Central Retinal Artery Occlusion Treatments and Hurdles to Implementation

Central retinal artery occlusion (CRAO) is a form of AIS that causes retinal infarction, typically causing severe vision loss, with only 17% recovering functional vision. In the absence of proven therapies, thrombolytic therapies streptokinase and urokinase have been attempted since the 1960s. A 2015 metanalysis demonstrated improved visual acuity after urokinase, streptokinase, or r-tPA within 4.5 hours of vision loss and showed a detrimental effect of traditional therapies such as anterior chamber paracentesis and ocular massage on visual acuity. A 2020 retrospective study demonstrated recovery of >2 lines of Snellen visual acuity with tPA up to 4.5 hours after onset as compared with natural history. [4] The AHA published a scientific statement suggesting thrombolysis as a reasonable treatment for CRAO. European trials including 1) THEIA (French interventional study comparing r-tPA to placebo), 2) TenCRAO (Norwegian prospective study evaluating TNK to aspirin), 3) REVISION (German prospective study evaluating r-tPA vs placebo) should provide valuable prospective thrombolytic data. Retrospective analysis shows statistically significant improvement in vision after hyperbaric oxygen therapy, with most benefit achieved with earlier treatment (within 9 hours of symptom onset). [5]

Delayed presentation remains an important barrier to treatment of CRAO. In a 2024 study, 75% of patients presented outside the 4.5-hour window, and 33% presented to an outpatient ophthalmologist or optometrist, allowing a more accurate diagnosis, but delaying the possibility of IV thrombolytic therapy. Recent work suggested that incorporation of non-mydriatic fundus photography and OCT can identify CRAO remotely and even identify inner retinal ischemic changes in hyperacute cases that lack visible funduscopic changes.

CME ANSWERS

1. D
2. E
3. A

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NEUROPATHIC PAIN- THE CORNEA PERSPECTIVE

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LEARNING OBJECTIVES

1. Highlight common sources of nociceptive ocular pain that present to the cornea specialist and discuss when to suspect neuropathic/nociplastic sources of ocular pain
2. Identify interactions at the level of the cornea (immune/neuro) that can lead to chronic ocular pain
3. Discuss the management of neuropathic/nociplastic ocular pain from the perspective of a cornea specialist.

CME QUESTIONS

1. What is an important clinical test to differentiate between nociceptive/peripheral neuropathic vs central/ non-ocular sources of pain?
   A. In vivo confocal microscopy
   B. Blink rate
   C. Schirmer test
   D. Anesthetic challenge

2. What patient reported symptom, in an otherwise healthy eye, has been most intricately linked to central nervous system abnormalities?
   A. Alternating periocular numbness
   B. Monocular diplopia
   C. Sensitivity to light
   D. Visual snow

3. What nociceptive cell type is thought to encode a cooling effect when stimulated?
   A. ASIC
   B. RUNX1
   C. TrkA
   D. TRPM8

KEYWORDS
1. Ocular pain
2. Dry eye/Sjögren's disease
3. Immune cell/neuron interaction
4. Neuropathic/nociplastic pain
5. Corneal nociception

HIGHLIGHTS
This lecture will review neuropathic/nociplastic ocular pain (NOP) presentations, assessments, and treatments from the perspective of a cornea specialist, supported by recent studies on the topic. In addition, we will discuss important basic science papers that investigated corneal neurobiology, including molecular mechanisms behind unpleasant ocular sensations that are now being studied as potential disease targets.

SUMMARY
The eye is an organ that should not be felt. Yet, many individuals report feeling their eyes, using terms such as "dryness," "irritation," "aching," and "tenderness," to name a few descriptors. As corneal specialists, the feeling of "dryness" led to a closer examination of the ocular surface, with a focus on inadequate tear production and epithelial disruption as a cause of symptoms. However, when these metrics proved insensitive to identify the cause of symptoms in many patients, cornea specialists expanded their search to examine other aspects of tear health, including tear instability (i.e., tear break up time)

and Meibomian gland disease (e.g., dropout, meibum quality) as potential symptom contributors. Yet, the addition of these metrics did not improve our ability to explain symptom report across a large subset of patients. In fact, several studies highlighted a disconnect between ocular surface symptom report and observed signs of disease. Why is that? The answer likely lays in pain report being a central phenomenon. It may start with peripheral inputs-based noxious stimuli in the environment and the activation of innate and adaptive immune responses on the ocular surface. Ultimately, however, peripheral signals are processed and interpreted by the central nervous system (CNS), whose output is the final form of symptom report. This complex interaction highlights the need for cornea specialists and neuro-ophthalmologists to cooperate and collaboratively investigate mechanisms of ocular surface pain that can be translated into improved diagnostic and therapeutic algorithms. This lecture will review ocular pain from the perspective of a cornea specialist, reviewing both basic science and clinical studies on the topic. It will discuss sources of nociceptive pain (e.g., ocular surface inflammation, decreased tear production) that need to be examined and addressed and discuss clues to the presence of a neuropathic/nociplastic component to pain (e.g., pain characteristics, symptoms out of proportion to observed signs). Finally, an update on the management of NOP will be reviewed coupling therapeutic algorithms to exam findings.

This includes:

- topical neuromodulatory strategies such as autologous blood products for those with a suspected peripheral neuropathic component to pain
- oral therapies such as α2δ ligands, tricyclic antidepressants, serotonin–norepinephrine reuptake inhibitors, low dose naltrexone
- adjuvant therapies such as botulinum toxin, transcutaneous electrical stimulation therapy, and cognitive behavioral therapy in those with a presumed central component to pain

CME ANSWERS

1. D
2. C
3. D

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WHAT'S NEW IN NEURO-IMMUNOLOGY?
The Revised McDonald Criteria for MS: What Does the Neuro-Ophthalmologist Need to Know?

Fiona Costello, MD, FRCPC
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LEARNING OBJECTIVES

1. To review the significance of the optic nerve in the topography of multiple sclerosis (MS) diagnosis
2. To highlight the role of visual "biomarkers" in the diagnosis of MS
3. To discuss challenges the revised McDonald criteria may introduce to neuro-ophthalmic practice, and describe how neuro-ophthalmologists may contribute to the multi-disciplinary care of people living with MS (pwMS)

CME QUESTIONS

1. How will including the optic nerve in the topography of MS diagnosis impact patient care?

2. Which of the following findings is NOT key to identifying optic nerve involvement in a person with MS?
   A. inter-eye differences in macular ganglion layer measures on OCT
   B. abnormal peripapillary retinal nerve fiber layer values on OCT
   C. prolongation of p100 latencies on VEP
   D. longitudinally extensive intrinsic optic nerve lesion on MRI

3. Name 3 major changes anticipated in the revised McDonald criteria for MS diagnosis.

KEYWORDS

1. Optic Nerve
2. Optical Coherence Tomography (OCT)
3. Magnetic Resonance Imaging (MRI)
4. Visual Evoked Potentials (VEPs)
5. Radiologically Isolated Syndrome (RIS)

HIGHLIGHTS

The new "McDonald" criteria for MS diagnosis will include several key changes relevant to neuro-ophthalmic practice. For the first time, the optic nerve will be included in the topography of MS diagnosis. Moreover, several "biomarkers" of structural integrity and function in the visual system will be part of the diagnostic "toolbox" for MS including: optical coherence tomography (OCT) (abnormal or inter-eye differences in macular ganglion layer measures and peripapillary retinal nerve fiber layer values), visual evoked potentials (VEPs) (significant inter-eye asymmetry or prolongation of p100 latencies), and orbital magnetic resonance imaging (MRI) findings (one or more short segment intrinsic optic nerve lesions). Inherent to accurate MS diagnosis is that no better explanation(s) account for the OCT, VEP, or MRI findings. Therein lies a challenge, since reviewing OCT findings, for example, may be unfamiliar to many clinicians involved in MS care. Thus, there may be a need for neuro-ophthalmologists to interpret OCT results, identify poor quality scans, recognize artefacts, and highlight cases of potential misdiagnosis in individuals being evaluated for MS.

Other anticipated changes to the McDonald criteria that will impact neuro-ophthalmic practice are the addition of new MRI features (central vein sign [CVS] and paramagnetic rim lesions) and fluid markers (myelin oligodendrocyte glycoprotein IgG [MOG IgG] and cerebrospinal fluid measures of kappa free light chains) serving as inclusion or exclusion criteria for MS diagnosis. Finally, individuals presenting with what was previously labelled radiologically isolated syndrome (RIS) may be diagnosed with MS in the absence of clinical events.

SUMMARY

This presentation will address specific aspects of the revised McDonald Criteria that will impact neuro-ophthalmic practice. The role of visual outcome measures, the significance of including the optic nerve in the topography of MS, and potential pitfalls that may lead to misdiagnosis will be discussed.

CME ANSWERS

1. Individuals presenting with optic neuritis may be diagnosed with MS and qualify for disease modifying therapy at earlier points in their clinical course.
2. D
3. Inclusion of the optic nerve as an anatomical compartment used for MS diagnosis; adopting novel imaging and fluid markers to render MS diagnosis (OCT, central retinal vein sign, paramagnetic rim lesions, MOG IgG, kappa light chains); and diagnosing MS in cases previously labelled as "RIS".

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Scientific Platform Session I – Monday, March 17th [2.0 CME]

Moderators: Stacy Pineles, MD & Samuel Spiegel, MD

10:00 am – 10:15 am	**Demographic, Clinical and Imaging Characteristics of Newly Diagnosed Optic Pathway Gliomas Associated with NF1: Results from the International Multicenter NF1-OPG Natural History Study,** *Robert Avery, DO*
10:15 am – 10:30 am	**Lack of Clinically Significant Ocular Toxicity in Children Treated with Mitogen-activated Protein Kinase Kinase Inhibitors,** *Connor Dallas*
10:30 am – 10:45 am	**FALCON: A Prospective Natural History Study in Patients with Optic Atrophy 1-Associated Autosomal Dominant Optic Atrophy,** *Raghu Mudumbai, MD*
10:45 am – 11:00 am	**Artificial Intelligence Can Differentiate Causes of Optic Disc Edema Using Unsegmented OCTs***, David Szanto, MD (nominee for best abstract by a student)*
11:00 am – 11:15 am	**Flavoprotein Fluorescence Imaging As a Novel Method To Quantify Disease Burden In Optic Disc Drusen,** *Rishita Pujari, MD*
11:15 am – 11:30 am	**Time-Driven Activity-Based Costing of Outpatient STAT vs. ED Neuroimaging for Optic Disc Edema,** *Florian H. Guillot, MD*
11:30 am – 11:45 am	**Non-Mydriatic Ocular Fundus Imaging on Consecutive Patients Presenting to a General Emergency Department (ED) with Vision Complaints,** *Jessica McHenry, MD (nominee for best abstract by a student)*
11:45 am – 12:00 pm	**Long-Term Outcomes of Bilateral Injection of Lenadogene Nolparvovec Gene Therapy for Leber Hereditary Optic Neuropathy***, Nancy Newman, MD (Late Breaking)*

Scientific Platform Session I – March 17th, 2025

Demographic, Clinical and Imaging Characteristics of Newly Diagnosed Optic Pathway Gliomas Associated with NF1: Results from the International Multicenter NF1-OPG Natural History Study

Robert Avery [1], Robert Listernick [2], Peter de Blank [3], Grant Liu [1], Rosalie Ferner [4], David Gutmann [5], Janice Zeid [6], Nicole Ullrich [7], Gena Heidary [7], Miriam Bornhorst [2], Steven Stasheff [8], Tena Rosser [9], Mark Borchert [10], Simone Arden-Holmes [11], Trent Hummel [3], William Motley III[12], Kevin Bielamowicz [13], Paul Phillips [14], Eric Bouffet [15], Arun Reginald [16], David Wolf [17], Jason Peragallo [18], David Van Mater [19], Mays A El-Dairi [20], Aimee Sato [21], Kristina Tarczy-Hornoch [22], Laura Klesse [23], Nick Hogan [24], Nicholas Foreman [25], Emily McCourt [25], Milan Ranka [26], Cynthia Campen [27], Shannon Beres [27], Christopher Moertel [28], Raymond Areaux Jr.[29], Duncan Stearns [30], Henry O'Halloran [31], Julius Oatts [32], Alyssa Reddy [33], Michael Brodsky [34], Sean Donahue [35], Gary Cutter [36], Michael Fisher [1]

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Introduction:
Treatment and clinical management decisions for children with NF1-OPGs remain challenging as most existing data are retrospective and have not included standardized visual outcomes. In this study, we prospectively enrolled newly diagnosed NF1-OPGs and performed standardized neuro-oncology and ophthalmology assessments in order to develop evidence-based guidelines for monitoring and treatment.

Methods:
Children with NF1-OPG on MRI who were evaluated by both a study ophthalmologist and neuro-oncologist/NF1 expert within 1 month of radiologic diagnosis were eligible for enrollment. All subjects attempted quantitative visual acuity using Teller acuity cards (TAC) as well as ATS-HOTV testing. The neuro-oncologist/NF1 expert provided reasons for obtaining the MRI as well as initiating treatment, if applicable. Descriptive statistics calculated the success rate of acquiring TAC and reasons to obtain the MRI.

Results:
Two-hundred fifty subjects from 22 institutions were enrolled and had at least one visit beyond baseline (Median age 3.1 years, range 0.1–16.8; 53% female). TAC was successfully acquired in both eyes (N=195, 78%) and at least one eye in (N=206, 82%). ATS-HOTV was successfully acquired in both eyes (N=97, 39%) and at least one eye in (N=98, 39%). The two most common reasons to obtain an MRI were screening due to a diagnosis of NF1 (N=99, 39%) and ophthalmologic concern (N=81, 32%). At enrollment, continued observation occurred in a majority of subjects (N=221, 88%) while treatment with chemotherapy was initiated in only 11% (N=29). Twenty-nine (11%) subjects initially observed transitioned to treatment after enrollment (range: 2.5–25 months) thus far.

Conclusions:
We present a prospective multicenter study of children with newly diagnosed NF1-OPGs. The ability to acquire quantitative visual acuity was higher than anticipated. The frequency of NF1-OPGs requiring treatment is lower than previously reported. Regression models of clinical and MRI features that prompted immediate treatment with chemotherapy versus observation will be discussed.

References: None provided.

Abstract Type: Pediatric Neuro-Ophthalmology

Keywords: Tumors, Pediatric neuro-ophthalmology, Genetic disease

Financial Disclosures: Robert Avery: No; Robert Listernick: No; Peter de Blank: No; Grant Liu: No; Rosalie Ferner: No; David Gutmann: No; Janice Zeid: No; Nicole Ullrich: No; Gena Heidary: No; Miriam Bornhorst: No; Steven Stasheff: No; Tena Rosser: No; Mark Borchert: No; Simone Arden-Holmes: No; Trent Hummel: No; William Motley: No; Kevin Bielamowicz: No; Paul Phillips: No; Eric Bouffet: Advisory Board, Alexion, Novartis, Servier; Arun Reginald: No; David Wolf: No; Jason Peragallo: No; David Van Mater: No; Mays A El-Dairi: Not applicable to the abstract; Aimee Sato: No; Kristina Tarczy-Hornoch: No; Laura Klesse: No; Nick Hogan: No; Nicholas Foreman: No; Emily McCourt: No; Milan Ranka: No; Cynthia Campen: No; Shannon Beres: No; Christopher Moertel: Shareholder and Consultant, OX2 Therapeutics Consultant, Alexion Pharmaceuticals Consultant, Springworks Therapeutics; Raymond Areaux: No; Duncan Stearns: No; Henry O'Halloran: No; Julius Oatts: No; Alyssa Reddy: No; Michael Brodsky: No; Sean Donahue: No; Gary Cutter: No; Michael Fisher: No

Grant Support: Children's Tumor Foundation, Gilbert Family Foundation, US Department of Defense

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Lack of Clinically Significant Ocular Toxicity in Children Treated with Mitogen-activated Protein Kinase Kinase Inhibitors

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Introduction:
Mitogen-activated protein kinase kinase inhibitors (MEKi) are commonly used to treat oncologic conditions in children, yet the risk of ophthalmic toxicity is not well understood−especially beyond neurofibromatosis type 1 (NF1) plexiform neurofibromas. We investigated the incidence of ophthalmic toxicity from MEKi in children participating in a clinical trial or in standard clinical practice.

Methods:
Children (≤18yo) initiating MEKi who underwent an ophthalmic exam before and during therapy were eligible for inclusion and curated from two cohorts at different institutions. Cohort 1 (C1): Phase 1/2 clinical trial of selumetinib for NF1 plexiform neurofibromas. Cohort 2 (C2): any MEKi as part of a clinical trial or standard clinical practice. Multivariable logistic regression models evaluated the impact of clinical variables on the presence of ocular toxicity.

Results:
C1 (N=48, 41.6% female; median age 11.1 years) and C2 (N=101, 51% female; 8.4 years) were monitored for a median of 5.4 and 2.2 years respectively. In C2, monotherapy with selumetinib (N=46, 46%) or trametinib (N=35, 35%) were the most common followed by combination therapy of trametinib and the B-Raf inhibitor dabrafenib (N=18, 18%). Eleven (23%) asymptomatic C1 participants had OCTs demonstrating outer retinal layer separation−all resolved. One asymptomatic C2 participant with an ocular contraindication to this drug class stopped MEKi because of outer retinal layer separation visualized on OCT without sequelae. Age, medical condition, type and duration of MEKi were not associated with the development of long-term ocular toxicity, retinal thinning or vision loss ($P > 0.05$).

Conclusions:
Despite increasing use of MEKi in children, no long-term ocular toxicity or visual morbidity have been observed. The frequency and utility of ophthalmic surveillance exams for children taking MEKi in clinical trials and clinical care may need to be reconsidered.

References: None provided.

Abstract Type: Pediatric Neuro-Ophthalmology

Keywords: Chemotherapy and radiation injury, Pediatric neuro-ophthalmology, Genetic disease

Financial Disclosures: The authors had no disclosures.

Grant Support: Richard Shafritz Endowed Chair in Pediatric Ophthalmology Research

Contact Information: Robert Avery, Averyr@chop.edu

FALCON: A Prospective Natural History Study in Patients with Optic Atrophy 1-Associated Autosomal Dominant Optic Atrophy

Raghu Mudumbai [1], Byron Lam [2], Yaping Joyce Liao [3], Marcela Votruba [4], Steven Gross [5], Kelly Saluti [5], Barry Ticho [5], Yue Wang [5], Patrick Yu-Wai-Man [6], Marc Bouffard [7], Julie Falardeau [8], Michael Larsen [9], Chiara La Morgia [10], Piero Barboni [11]

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Introduction:
Autosomal dominant optic atrophy (ADOA) is the most common inherited optic neuropathy, with a global prevalence of 1:30,000. Up to 90% of ADOA cases are linked to pathogenic variants of the OPA1 gene, which lead to mitochondrial dysfunction, retinal ganglion cell death, and irreversible vision loss often beginning before age 10.

Methods:
FALCON is a 24-month multicenter natural history study aiming to elucidate functional and anatomical changes in ADOA over time and inform the development of future interventional trials. Across 10 sites in the U.S. and Europe, patients aged 8–60 years with genetically confirmed ADOA and heterozygous OPA1 variants were enrolled. Assessments include best-corrected visual acuity (BCVA), high-contrast visual acuity (HCVA, 100%), low-contrast visual acuity (LCVA, 25%, 5%, 2.5%), retinal nerve fiber layer (RNFL) thickness, ganglion cell layer/inner plexiform layer (GCL/IPL) thickness, and Humphrey 10-2 automated perimetry. Pattern electroretinogram (PERG) parameters and photopic negative response (PhNR) were assessed at selected sites. As flavoprotein fluorescence (FPF) is correlated with oxidative stress, retinal FPF was assessed at baseline (OcuMet Beacon™, OcuSciences Inc., Ann Arbor, MI).

Results:
Forty-eight patients were enrolled; 47 completed the baseline and at least one post-baseline visit. At baseline, mean (SD) age was 28.1 (14.1) years. Mean BCVA was 56.6 (16.9) Early Treatment Diabetic Retinopathy Study (ETDRS) letters. At Month 12, patients with baseline BCVA < 0.3 logMAR (n=9) demonstrated a decline in LCVA (-5.1 [9.3] ETDRS letters). No patients demonstrated improvement in BCVA. At Month 12, there was no significant change in HCVA, RNFL thickness, GCL/IPL thickness, perimetry, PERG parameters, or PhNR. Baseline FPF correlated with older age, worse BCVA, and lower RNFL thickness (all $p < 0.05$, n=19).

Conclusions:
Minimal structural and functional changes demonstrate the slowly progressing nature of ADOA. The trend towards worse LCVA at 12 months suggests that LCVA may be a more sensitive outcome measure than HCVA.

References: None provided.

Abstract Type: Pediatric Neuro-Ophthalmology

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

Financial Disclosures: Raghu Mudumbai: Clinical Trial Support: Stoke Therapeutics, Viridian Therapeutics, Nicox;

Byron Lam: Research Support: National Eye Institute, United States Department of Defense, Foundation Fighting Blindness, Atsena Therapeutics, Beacon Therapeutics, Endogena Therapeutics, Nanoscope Therapeutics, Ocugen Inc., PYC Therapeutics, Sparingvision, Spark Therapeutics, Splicebio, Stoke Therapeutics; Consulting: BlueRock Therapeutics, Johnson & Johnson, Splicebio, Spulbio; Yaping Joyce Liao: Consulting: Stoke Therapeutics; Marcela Votruba: Research support: Fight for Sight UK; Consulting: Transine Therapeutics, Chiesi Pharmaceuticals, Stoke Therapeutics; Speaker honoraria and/or financial support: Stoke Therapeutics, Chiesi Pharmaceuticals; Steven Gross: Employee: Stoke Therapeutics; Kelly Saluti: Employee: Stoke Therapeutics; Barry Ticho: Employee: Stoke Therapeutics; Yue Wang: Employee: Stoke Therapeutics; Patrick Yu-Wai-Man: Consulting: GenSight Biologics, Stoke Therapeutics, Transine Therapeutics; Speaker honoraria and/or financial support: GenSight Biologics, Santhera Pharmaceuticals; Marc Bouffard: No; Julie Falardeau: Clinical trial support: Stoke Therapeutics; Michael Larsen: Clinical trial support: Stoke Therapeutics; Consulting: Novo Nordisk, Bayer, Roche, Janssen (now Johnson & Johnson Innovative Medicine), Novartis, Stoke Therapeutics; Chiara La Morgia: Chiara La Morgia is a consultant for Chiesi Farmaceutici, Gensight Biologics, Regulatory PharmaNet and Thenewway srl. She received speaker honoraria and/or financial support for meetings from Santhera Pharmaceuticals, Chiesi Farmaceutici, Gensight Biologics, Regulatory PharmaNet, Thenewway srl, First Class srl and Biologix.; Piero Barboni: Omikron pharma, Gensight biologic, Chiesi pharma

Grant Support: None.

Contact Information: None provided.

Artificial Intelligence Can Differentiate Causes of Optic Disc Edema Using Unsegmented OCTs

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Introduction:
AI has been used to differentiate papilledema from healthy eyes and optic disc elevation using fundus photos. We hypothesized that a deep learning approach using the full 3D OCT volume, without retinal layer segmentation, could reliably differentiate NAION, papilledema and healthy eyes.

Methods:
We utilized 3441 raw Cirrus SD-OCT 200x1024x200 ONH volume scans from 1181 eyes, consisting of scans from healthy eyes (1655), eyes with IIH with a Frisén grade ≥ 1 (1138), and eyes with acute NAION (648). We developed three models for analysis - 1) the entire OCT volume, 2) the peripapillary retina (PPR) alone, where we applied a cylindrical mask over the optic nerve head (ONH) to exclude it and focus solely on the PPR, and 3) the ONH alone, where the cylindrical mask was used to isolate the ONH and exclude the PPR. We fine-tuned a ResNet3D model and evaluated its performance using 5-fold cross-validation and evaluated model performance with accuracy, AUC-ROC, precision, recall, F1 scores, and confusion matrices.

Results:
Using the entire OCT volume, our model classified the three conditions over all folds with an accuracy of 96.1% and a weighted ROC-AUC of 0.9958. The precision, recall, and F1 scores of each class for every model ranged from 0.89 to 0.98. The PPR model attained an accuracy of 94.9% with a weighted AUC-ROC of 0.9941. The ONH alone model attained an accuracy of 94.3% with a weighted AUC-ROC of 0.9911.

Conclusions:
Our findings demonstrate that this AI OCT model, without retinal layer segmentation, using the entire volume scan including both the optic nerve head and peripapillary retina is a robust diagnostic tool for differentiating IIH, NAION and normal eyes. AI of unsegmented OCT demonstrates potential for automated approaches to assist in the diagnosis of acquired optic disc swelling when access to neuro-ophthalmologists is limited.

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Abstract Type: Clinical Trials

Keywords: Optic neuropathy, Neuroimaging

Financial Disclosures: David Szanto: No; Jui-Kai Wang: No; Brian Woods: No; Mona Garvin: No; Randy Kardon: No; Mark Kupersmith: Consultant for QRK207 trial

Grant Support: The New York Eye and Ear Infirmary Foundation, New York, N.Y.; NEI EY032522; Research to Prevent Blindness, Inc., New York, NY unrestricted grant to the Department of Ophthalmology; Shulman Family NAION Fund at Icahn School of Medicine at Mount Sinai

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Flavoprotein Fluorescence Imaging As a Novel Method To Quantify Disease Burden In Optic Disc Drusen

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Introduction:
Optic disc drusen (ODD) are calcified, autofluorescent deposits on the optic disc, which are common causes of pseudopapilledema and a leading risk factor in young-onset optic nerve stroke.1-3 Although easily visualized on autofluorescence imaging or enhanced depth imaging optical coherence tomography (EDI-OCT), these only allow qualitative measures of disease burden. In this study, we use flavoprotein fluorescence (FPF) imaging, a noninvasive imaging modality to detect endogenous autofluorescence signal to quantify ODD severity.

Methods:
We prospectively recruited 94 patients with ODD (157 eyes) and 36 healthy controls (48 eyes) for multimodal assessments, including static perimetry, optical coherence tomography (OCT), disc and macular FPF imaging (OcuMet Beacon). Data was analyzed using custom Python scripts, statistical analysis was performed using Mann-Whitney U, ANOVA and Spearman correlation tests.

Results:
Quantification of ODD eyes revealed significantly increased optic disc FPF ($p < 0.001$) but not macular FPF compared with healthy controls. Age-based analyses revealed relatively stable disc FPF in controls and significantly elevated disc FPF in ODD eyes across 2nd-8th decades of life. FPF was also measurable in eyes with buried ODD. Spearman correlation showed a strong negative correlation between disc FPF and peripapillary retinal nerve fiber layer thickness (r=-0.78) and moderate negative correlation with macular ganglion cell complex thickness (r=-0.64). Further comparison showed significantly higher disc FPF in ODD eyes without visual field loss and highest in those with visual field loss as compared to controls. Power analyses to estimate sample sizes for a study comparing ODD ±visual field loss with a power of 0.8 , alpha of 0.05 with 1:1 ratio revealed that this can be achieved with sample sizes of 8 per group, which is about 1/3 that needed for static perimetry.

Conclusions:
Flavoprotein fluorescence imaging is an easy way to quantify disease burden and is a promising functional surrogate clinical trial endpoint for ODD.

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Abstract Type: Clinical afferent disease

Keywords: Optic neuropathy, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Neuroimaging

Financial Disclosures: Rishita Pujari: No; Miaomiao Yu: No; Jamie Zhang: No; Ping Zhu: No; Collin Rich: I am an employee and shareholder of OcuSciences, Inc.; Sangeethabalasri Pugazhendhi: No; Lorraine Almeda: No; Shannon Beres: No; Yaping Joyce Liao: Consulting: Stoke Therapeutics

Grant Support: None.

Contact Information: Rishita Pujari, rpujari@stanford.edu

Time-Driven Activity-Based Costing of Outpatient STAT vs. ED Neuroimaging for Optic Disc Edema

Florian Guillot [1], Divya Manikandan [2], James Davis [3], Michael Carper [1], Andrew Carey [4], Rohini Nadgir [2], Amanda Henderson [4]

[1] Wilmer Eye Institute, Johns Hopkins University School of Medicine, [2] Johns Hopkins University School of Medicine, [3] Nassau University Medical Center, [4] Wilmer Eye Institute, Johns Hopkins School of Medicine

Introduction:
Patients with optic disc edema are frequently referred to the emergency department (ED) for urgent neuroimaging, contributing to high costs, overcrowding, and extended wait times. Our team piloted an outpatient STAT MRI pathway, demonstrating that urgent neuroimaging can often be safely performed within 48 hours without compromising outcomes in patients with optic disc edema. We conducted a time-driven activity-based cost analysis to assess the financial impact of this STAT pathway compared to ED-based neuroimaging.

Methods:
We retrospectively reviewed patients who underwent neuroimaging for optic disc edema at a quaternary academic center from 2018 to 2024. Collaborating with radiology and ED faculty, we developed process maps outlining ED and outpatient neuroimaging steps. Key resources including personnel, equipment, and space were identified. Capacity cost rates ($/hour) were estimated using internal financial data, equipment vendor estimates, and regional salary data. Time metrics were obtained from medical records or estimated by staff to quantify resource utilization time. Costs were compared using Wilcoxon rank sum tests.

Results:
129 patients were included: 33 (25.6%) imaged in the ED before protocol implementation (ED-Pre), 37 (28.7%) through the outpatient STAT pathway, and 59 (45.7%) in the ED after protocol implementation (ED-Post). The STAT pathway was cost-effective compared with ED imaging (median [IQR] cost per patient: $298.5 [279.6-333.7] for STAT vs. $407.4 [361.3-442.3] for ED-Post, $p < 0.001$). The combined STAT and ED-Post period showed a cost reduction compared to ED-Pre ($361.5 [300.6-424.7] vs. $373.3 [351.2-414.8], respectively). Overall, the STAT pathway saved an average cost of $109 (27%) per patient, totaling $4,033 in savings for those bypassing the ED.

Conclusions:
Outpatient STAT MRI significantly reduces costs associated with neuroimaging for optic disc edema and is a strong alternative to the typical ED-based imaging.

References: Gibbons AB, Huang P, Sklar M, Kim P, Henderson AD. Evaluation of a STAT MRI Protocol for Emergent Ophthalmology Patients. J Neuro-Ophthalmol Off J North Am Neuro-Ophthalmol Soc. December 5, 2023. Yun BJ, Prabhakar AM, Warsh J, et al. Time-Driven Activity-Based Costing in Emergency Medicine. Ann Emerg Med. 67(6):765-772, 2016. da Silva Etges APB, Cruz LN, Notti RK, et al. An 8-step framework for implementing time-driven activity-based costing in healthcare studies. Eur J Health Econ. 20(8):1133-1145, 2019.

Abstract Type: Clinical afferent disease, Quality Improvement

Keywords: Neuroimaging, Optic neuritis, High intracranial pressure/headache, Pseudotumor cerebri

Financial Disclosures: Florian Guillot: No; Divya Manikandan: No; James Davis: No; Michael Carper: No; Andrew Carey: None related to this submission: Horizon Therapeutics/Amgen, Bristol-Myers-Squibb, Springer publishing.; Rohini Nadgir: No; Amanda Henderson: None related to this submission: Horizon Therapeutics/Amgen.

Grant Support: None.

Contact Information: Florian Guillot, fguillo1@jh.edu

Non-Mydriatic Ocular Fundus Imaging on Consecutive Patients Presenting to a General Emergency Department (ED) with Vision Complaints

Jessica McHenry [1], Mung Yan Lin [1], Andrew Pendley [1], George Alencastro [1], Kevin Yan [1], Nithya Shanmugam [1], Stuart Duffield [1], Daniel Adamkiewicz [1], Duyen Vo [1], Jordan Prosky [1], Matthew Keadey [1], David Wright [1], Andrew Fischer [1], Michael Dattilo [2], Nancy Newman [3], Valérie Biousse [1]

[1] Emory University School of Medicine, [2] Emory University Department of Medicine, [3] Emory University School of Medicine, Atlanta GA

Introduction:
ED visits for vision complaints are common, especially in medically-underserved areas where access to eye-care providers may be limited. However, ophthalmologists are rarely available in EDs, resulting in costly/often-unnecessary transfers to centers with ophthalmic coverage. Implementation of non-mydriatic color fundus photographs with OCT (NMFP-OCT) in general EDs has the potential to facilitate on-site ophthalmologic diagnoses and opens the door to tele-ophthalmology for remote triage/rapid treatment. Our goal was to evaluate which ocular complaints/pathology would benefit most from NMFP-OCT in a general ED.

Methods:
Quality improvement project, prospective over 16 consecutive days/nights. NMFP-OCT OU [table-top Maestro2/Topcon-Japan: color photographs, posterior pole (45-degree view including optic discs/macula/vascular arcades)] and OCT nerve/macula were ordered for all patients presenting to our ED with any vision complaint. Demographic information, final diagnosis and NMFP-OCT findings were collected.

Results:
Of 1838 ED visits over 16 days/nights, 185 (10.1%) patients had vision complaints; 162 underwent NMFP-OCT in the ED. 82/162 patients (50.6%) also had an in-person ED examination by an ophthalmologist. NMFP-OCT was ordered for vision loss [51 (31.5%)]; other visual changes [13 (8.0%)]; papilledema/papilledema rule-out [60 (37.0%)]; painless red eye [7 (4.3%)]; eye/orbital pain [28 (17.3%)]; diplopia [3 (1.9%)]. 99/162 (61.1%) had relevant findings on NMFP-OCT; 31/162 (19.1%) had non-relevant incidental findings. NMFP-OCT was most useful in patients with posterior segment pathology [45 (27.8%)] and neurologic disorders [72 (44.4%)], by either demonstrating pathology (such as acute retinal ischemia [5 (3.1%)], optic disc edema [14 (8.6%)], retinal detachment/vitreous hemorrhage [3 (1.9%)], posterior uveitis/retinitis/vasculitis [3 (1.9%)], retinopathy/maculopathy [9 (5.6%)]), or by ruling out papilledema [52 (32.1%)].

Conclusions:
Given that 10% of all ED visits were for vision complaints, having NMFP-OCT obtained in the ED in these patients allows for rapid/reliable diagnosis of ocular emergencies mostly involving the posterior segment, including acute retinal arterial ischemia and papilledema/rule-out papilledema, thereby facilitating remote triage and treatment.

References: None provided.

Abstract Type: Quality Improvement

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Neuroimaging, Miscellaneous

Financial Disclosures: Jessica McHenry: No; Mung Yan Lin: No; Andrew Pendley: No; George Alencastro: No; Kevin Yan: No; Nithya Shanmugam: No; Stuart Duffield: No; Daniel Adamkiewicz: No; Duyen Vo: No; Jordan Prosky: No; Matthew Keadey: No; David Wright: No; Andrew Fischer: No; Michael Dattilo: No; Nancy Newman: Consultant for GenSight, Chiesi, Neurophth (all involved with the treatment of Leber hereditary optic neuropathy. Research support as PI to my institution from GenSight for clinical trials.; Valérie Biousse: Consultant for Topcon which commercializes fundus cameras. The current research is completely independent from Topcon and is not funded by the company.

Grant Support: None. **Contact Information:** Jessica McHenry, Jessica.mchenry@emory.edu

Long-Term Outcomes of Bilateral Injection of Lenadogene Nolparvovec Gene Therapy for Leber Hereditary Optic Neuropathy

Nancy Newman [1], Patrick Yu-Wai-Man [2], Prem Subramanian [3], Sarah Thornton [4], An-Guor Wang [5], Sean Donahue [6], Bart Leroy [7], Valerio Carelli [8], Valérie Biousse [9], Catherine Vignal-Clermont [10], Alfredo Sadun [11], Robert Sergott [4], Gema Rebolleda Fernandez [12], Bart Chwalisz [13], Rudrani Banik [14], Magali Taiel [15], José-Alain Sahel [16]

[1] Emory University School of Medicine, Atlanta GA, [2] John van Geest Centre for Brain Repair and MRC Mitochondrial Biology Unit, Department of Clinical Neurosciences, University of Cambridge, Cambridge, United Kingdom; Cambridge Eye Unit, Addenbrooke's Hospital, Cambridge University Hospitals, Cambridge, United Kingdom; Moorfields Eye Hospital NHS Foundation Trust, London, United Kingdom; Institute of Ophthalmology, University College London, London, United Kingdom., [3] UCHealth Sue Anschutz-Rodgers Eye Center, [4] Departments of Neurology and Ophthalmology, Wills Eye Hospital and Thomas Jefferson University, [5] Taipei Veterans General Hospital, [6] Vanderbilt Medical Center, [7] Department of Ophthalmology Ghent University Hospital, [8] IRCCS Istituto delle Scienze Neurologiche di Bologna, [9] Emory University School of Medicine, [10] Department of Neuro Ophthalmology and Emergencies, Rothschild Foundation Hospital, [11] UCLA Doheny Eye Institute, [12] University of Alcala, [13] Massachusetts General Hospital, [14] Icahn School of Medicine at Mount Sinai, [15] GenSight Biologics, [16] Sorbonne Université, INSERM, CNRS, Institut de la Vision

Introduction:
Lenadogene nolparvovec (LN) is an AAV2-based gene therapy for patients with Leber hereditary optic neuropathy (LHON) carrying the m.11778G>A MT-ND4 mutation. REFLECT (NCT03293524) is a clinical study designed to evaluate the efficacy and safety of bilateral injection of LN gene therapy in patients with MT-ND4 LHON.

Methods:
This is a randomized, double-masked, placebo-controlled phase 3 study. The first-affected eye received LN gene therapy; the other eye was randomly injected with LN or placebo. REFLECT interim data at 4 years after LN administration are presented.

Results:
Forty-eight patients were treated bilaterally and 50 unilaterally. The mean (standard deviation [SD]) improvement in best-corrected visual acuity (BCVA) from nadir to 4 years was -0.40 (0.32) (+20 ETDRS letters) and -0.34 (0.31) (+17 ETDRS letters) LogMAR in the first and second-affected eyes of bilaterally treated patients, and -0.38 (0.41) (+19 letters) and -0.27 (0.32) (+14 letters) LogMAR in the first and second-affected eyes of unilaterally treated patients. Clinically relevant recovery from nadir at 4 years was observed in 75.0% of bilaterally treated patients and 56.0% of unilaterally treated patients. An improvement of at least 0.3 LogMAR (+15 letters) from nadir was achieved in 72.9% of patients receiving a bilateral LN injection versus 62.0% of patients receiving a unilateral LN injection. Overall, LN safety was favorable, with no difference in the incidence of adverse events between bilaterally and unilaterally treated patients.

Conclusions:
The persistence of the LN effect and the favorable safety profile were confirmed 4 years after treatment. Bilateral administration of LN provided additional benefit compared with unilateral administration of LN. The final results at 5 years should confirm the long-term benefit/risk ratio of LN gene therapy.

References: None provided.

Abstract Type: Clinical Trials

Keywords: Optic neuropathy, Genetic disease

Financial Disclosures: Nancy Newman: Consultant for GenSight, Chiesi, Neurophth (all involved with the treatment of Leber hereditary optic neuropathy. Research support as PI to my institution from GenSight for clinical trials.; Patrick Yu-Wai-Man: Consulting: GenSight Biologics, Stoke Therapeutics, Transine Therapeutics; Speaker honoraria and/or financial support: GenSight Biologics, Santhera Pharmaceuticals; Prem Subramanian: P.S.S. is a consultant for GenSight Biologics, Horizon Therapeutics, Invex Therapeutics, Viridian Therapeutics, and Kriya Therapeutics, and has received research support from Santhera Pharmaceuticals, GenSight Biologics, and Horizon Therapeutics; and is a medical legal consultant.; Sarah Thornton: No; An-Guor Wang: No; Sean Donahue: No; Bart Leroy: B.P.L. is a consultant for GenSight Biologics and has received research support from GenSight Biologics.; Valerio Carelli: VC is a consultant for GenSight Biologics, Chiesi, Stoke, and Pretzel.; Valérie Biousse: Consultant for Topcon which commercializes fundus cameras. The current research is completely independent from Topcon and is not funded by the company.; Catherine Vignal-Clermont: Catherine Vignal-Clermont is a consultant for GenSight Biologics and has received research support from Santhera Pharmaceuticals.; Alfredo Sadun: No; Robert Sergott: Robert C. Sergott is a consultant for GenSight Biologics.; Gema Rebolleda Fernandez: No; Bart Chwalisz: No; Rudrani Banik: Omni Actives Health Technologies: Lecture Fees/Speakers Bureau Rupa Health: Lecture Fees/Speakers Bureau Optomed USA, Inc.: Consultant/Advisor, Lecture Fees/Speakers Bureau GenSight Biologics: Research Support Viridian Therapeutics: Research Support; Magali Taiel: MT is an employee of GenSight Biologics.; José-Alain Sahel: JAS is a consultant/contractor for Avista Therapeutics and Tenpoint; has financial interests (stock/stock options) in GenSight Biologics, Sparing Vision, Prophesee, Chronolife, Tilak Healthcare, VegaVect, Inc., Avista, Tenpoint, SharpEye, Celanese and Netramind; is owner/co-owner/founder/co-founder for Gensight Biologics, Sparing Vision, Avista, Tenpoint, Prophesee, Chronolife, Tilak Healthcare, SharpEye, Celanese, Vegavect and Netramind; participates in scientific advisory board for Gilbert Foundation, Foundation Fighting Blindness, Institute of Ophthalmology Basel and Senses Institute Lausanne; is an observer at Gensight Biologics, SparingVision, Avista and Vegavect; is President of Fondation Voir et Entendre (Paris) and StreetLab (Paris); has patent for allotopic expression, rod-derived cone viability factor and related patents; is a recipient for patent royalties and GenSight Biologics.

Grant Support: GenSight Biologics

Contact Information: None provided.

Scientific Platform Session II – Monday, March 17th [2.0 CME]

Moderators: Valerie Biousse, MD & Ali Hamedani, MD, MHS

3:00 pm – 3:15 pm	**THRIVE and THRIVE-2 Phase 3 Trials: Efficacy and Safety at 15 Weeks of Veligrotug (VRDN-001), a Full Antagonist Antibody to IGF-1R, in Thyroid Eye Disease (TED),** *Kimberly P. Cockerham, MD*
3:15 pm – 3:30 pm	**Phase 3 Myasthenia Gravis Inebilizumab Trial (MINT): Efficacy and Safety Results in Patients with Generalized MG***, Richard J. Nowak, MD*
3:30 pm – 3:45 pm	**Prevalence and Clinical Features of Spinocerebellar Ataxia 27B in Patients with Idiopathic Downbeat Nystagmus at a Tertiary Care Center,** *Leigh A. Rettenmaier, MD (nominee for best abstract by a fellow in training)*
3:45 pm – 4:00 pm	**Characteristics of Eye Movement Disorders in Adult-Onset Autoimmune and Paraneoplastic Neurological Syndromes,** *Natthapon Rattanathamsakul, MD*
4:00 pm – 4:15 pm	**Advancing Otolith Function Assessment: Integrating Artificial Intelligence with VideoOculography (VOG) for Enhanced Vestibular Diagnosis,** *Krishna N. Mukunda, MD*
4:15 pm – 4:30 pm	**Non-Invasive Identification of Alzheimer's Disease Through Ocular Analysis Utilizing Raman Spectroscopic Data Analysis,** *Nitza Goldenberg-Cohen, MD*
4:30 pm – 4:45 pm	**In Vivo Transfer of Glial Mitochondria to Retinal Neurons***, Sidney Gospe III, MD, PhD*
4:45 pm – 5:00 pm	**Retinal Input to Macaque Superior Colliculus Derives from Branching Axons Projecting to the Lateral Geniculate Nucleus***, Jonathan C. Horton, MD, PhD*

Scientific Platform Session II – March 17th, 2025

THRIVE and THRIVE-2 Phase 3 Trials: Efficacy and Safety at 15 Weeks of Veligrotug (VRDN-001), a Full Antagonist Antibody to IGF-1R, in Thyroid Eye Disease

Kimberly Cockerham [1], Rosa Tang [2], John Mandeville [3], Mohammad Al Khudari [4], Steven Leibowitz [5], Daniel Lemor [6], Amy Patel Jain [7], Roger Turbin [8], Andrea Kossler [9], Michael Yen [10], Raghu Mudumbai [11], Navdeep Nijhawan [12], Sandy Zhang-Nunes [13], Will Conroy [14], Abhijit Narvekar [15], Tom Ciulla [14], Jody Abrams [16]

[1] Sharp Neuroscience Institute, [2] Neuro-Eye Clinical Trials, Inc., Houston, TX, USA, [3] Ophthalmic Consultants of Boston, [4] Vision Medical Research (M1 Health Site), [5] Stein Eye Institute, UCLA, [6] Advancing Research International, LLC, [7] Cedars Sinai Medical Center, Department of Ophthalmology, [8] Rutgers NJMS Newark, [9] Stanford University, Department of Ophthalmology at Byers Eye Institute, [10] Baylor College of Medicine, [11] Department of Ophthalmology, University of Washington, [12] Oshawa Clinic, [13] Keck School of Medicine of USC Roski Eye Institute, [14] Viridian Therapeutics, Inc., [15] Viridian Therapeutics, [16] Sarasota Retina Institute

Introduction:
Previously presented efficacy and safety data from the ongoing phase 3 THRIVE (NCT05176639) RCT in active TED showed treatment with the humanized monoclonal antibody veligrotug (veli) led to rapid onset of treatment effect and statistically significant improvements in proptosis, clinical activity, and diplopia at 15 weeks. Here we focus on new results from the THRIVE-2 (NCT06021054) RCT of veli in chronic TED.

Methods:
In THRIVE-2, 188 adults with moderate-to-severe chronic TED (onset >15 months and any clinical activity score [CAS]) were randomized to 5 IV infusions Q3W of 10 mg/kg veli or placebo. Efficacy outcomes and treatment-emergent AEs (TEAEs) were assessed through 15 weeks (primary timepoint).

Results:
188 patients received veli (n=125) or placebo (n=63). Baseline values for veli vs placebo were balanced, including CAS ≥3 in 57% vs 52% and diplopia in 52% vs 59%. At 15 weeks, veli vs placebo proptosis responder rate (PRR; ≥2-mm reduction vs baseline by Hertel exophthalmometry) was 56% vs 8% ($p< 0.0001$), with a mean reduction of 2.34 mm vs 0.46 mm ($p< 0.0001$). In patients reporting diplopia on the Gorman subjective diplopia scale at baseline, improvement was reported in 56% vs 25% (p=0.0006) and complete resolution in 32% vs 14% (p=0.0152). Exploratory analyses were nominally significant for treatment effect as early as 3 weeks in overall population and for achievement of CAS 0/1 at 15 weeks in patients with CAS ≥3 at baseline (54% vs 24%; p=0.0060). Most TEAEs were mild; most common was muscle spasms (36% vs 6%). Hearing impairment TEAEs occurred in 13% vs 3% and serious TEAEs in 2% vs 3% (1 treatment-related/group).

Conclusions:
Veli was generally well tolerated and led to statistically significant improvements in all primary and secondary endpoints in both active and chronic TED RCTs. With a 5-dose treatment regimen, rapid onset, and effect on diplopia, veli may represent a promising new treatment for active and chronic TED. Follow-up through 52 weeks is ongoing.

References: None provided.

Abstract Type: Clinical Trials

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

Financial Disclosures: Kimberly Cockerham: I am a Principal Investigator and consultant for Viridian, Amgen, Genentech, Immunovant, Lassen, Tourmaline and ArgenX.; Rosa Tang: R. Tang is a consultant for Viridian, Alexion, Valenza, and Acelyrin, an investigator for Horizon (now Amgen), Viridian, Novartis, Immunovant, Vasaragen, Sling

Therapeutics, Lassen, Roche, ArgenX, Tourmaline Bio and a speaker for Serono journal club. Her institution received funds from Horizon (now Amgen) to perform this trial on site.; John Mandeville: Research investigator for Viridian Therapeutics, Inc.; Mohammad Al Khudari: Dr Al Khudari is a research investigator for Viridian Therapeutics, Inc.; Steven Leibowitz: I am a Principal Investigator and Advisory Board Member for Viridian Therapeutics, Inc., a Research Investigator for Lassen Therapeutics, LLC, and I served on speaker's bureau at Amgen.; Daniel Lemor: Research investigator for Viridian Therapeutics, Inc.; Amy Patel Jain: Dr Amy Patel Jain is a research investigator for Viridian Therapeutics, Inc. and serves on the speakers bureau for Amgen.; Roger Turbin: Research investigator for Viridian Therapeutics, Inc. I am currently receiving research support to my institution and advisory board status, past travel support, and own a small equity position below federal approved thresholds. My conflicts have all been thoroughly declared and approved by my institution.; Andrea Kossler: Research investigator for Viridian Therapeutics, Inc., Consultant for Viridian Therapeutics, Inc. Consultant/contracted research Amgen/Horizon Therapeutics Contracted research Sling Research/consultant lassen, consultant, Immunovant, Genentech, Argenx, Acelyrin; Michael Yen: I am a Clinical trial investigator for Viridian Therapeutics, Amgen, Lassen Therapeutics, and a Consultant for Viridian Therapeutics, Sling Therapeutics.; Raghu Mudumbai: Clinical Trial Support: Stoke Therapeutics, Viridian Therapeutics, Nicox; Navdeep Nijhawan: Navdeep Nijhawan is a Research investigator for Viridian Therapeutics, Inc; Sandy Zhang-Nunes: Sandy Zhang-Nunes is a Research Investigator for Amgen, consultant/advisor for Amgen, consultant/advisor for Tarsus.; Will Conroy: Research investigator for Viridian Therapeutics, Inc; advisory board member for Viridian Therapeutics, Inc and Horizon Therapeutics; consultant for Viridian Therapeutics, Inc and Horizon Therapeutics; speaker for Horizon Therapeutics.; Abhijit Narvekar: Abhijit Narvekar is an employee of Viridian Therapeutics, Inc.; Tom Ciulla: Thomas Ciulla is an employee of Viridian Therapeutics, Inc.; Jody Abrams: Jody Abrams is a research investigator and serves on the advisory board for Viridian Therapeutics, Inc., and is a speaker for and serves on the advisory board for Amgen.

Grant Support: None.

Contact Information: Kimberly Cockerham, cockerhammd@gmail.com

Phase 3 Myasthenia Gravis Inebilizumab Trial (MINT): Efficacy and Safety Results in Patients with Generalized MG

Richard J. Nowak [1], Kimiaki Utsugisawa [2], Michael Benatar [3], Emma Ciafaloni [4], M. Isabel Leite [5], John Vissing [6], Fengming Tang [7], Yanping Wu [7], Mikhail Rojavin [7], Sue Cheng [7], James F. Howard Jr. [8]

[1] Yale School of Medicine, [2] Hanamaki General Hospital, [3] University of Miami Miller School of Medicine, [4] University of Rochester, [5] University of Oxford, [6] University of Copenhagen, [7] Amgen Inc., [8] Department of Neurology, The University of North Carolina

Introduction:
Autoimmune gMG, a disorder of postsynaptic neuromuscular transmission, characterized by production of antibodies against acetylcholine receptor (AChR+), muscle-specific kinase (MuSK+), and less frequently against other proteins, and where autoreactive B-cells are pivotal in upstream pathogenesis. We investigated the efficacy and safety of inebilizumab, a monoclonal antibody targeting CD19+ B-cells, in generalized myasthenia gravis (gMG).

Methods:
MINT, a phase 3 clinical study (NCT04524273) was conducted in adult gMG patients and included a protocol-required steroid taper. The complete randomized control period (RCP) was 52-weeks (AChR+ population) and 26-weeks (MuSK+ population). Participants were randomized (1:1) to 300 mg of intravenous inebilizumab or placebo, administered on RCP Day-1 and Day-15 and at Week-26 (AChR+ only). The primary endpoint was the change from baseline in MG-ADL score at Week-26 in the combined population. Key secondary endpoints included change in QMG score from baseline to Week-26 in the combined population, and changes from baseline to Week-26 in MG-ADL and QMG-scores in the AChR+ and MuSK+ populations separately.

Results:
Total of 238 patients were randomized: inebilizumab 119 (95 AChR+, 24 MuSK+), placebo 119 (95 AChR+, 24 MuSK+). The primary endpoint was achieved demonstrating a clinically meaningful improvement in MG-ADL score change in the inebilizumab group (-4.2) as compared to placebo (-2.2) at Week-26 [difference, -1.9; 95% CI: -2.9, -1.0;$p< 0.001$]. Key secondary endpoint for the combined population demonstrated greater improvement in the QMG score in the inebilizumab group (-4.8) as compared to placebo (-2.3) at Week-26 [difference, -2.5; 95% CI: -3.8, -1.2; $p< 0.001$]. Adverse events occurred in 80.7% inebilizumab and 73.1% placebo-treated participants. Serious adverse events occurred in 8.4% inebilizumab and 13.4% placebo-treated participants.

Conclusions:
This study provides evidence that inebilizumab is effective and safe for patients with AChR+ or MuSK+ gMG. Targeting an upstream immunopathogenic mechanism may be an effective tool in reducing disease severity and steroid burden.

References: None provided.

Abstract Type: Clinical Trials

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

Financial Disclosures: Richard J. Nowak: R.J. Nowak receives research support from the National Institutes of Health, Genentech, Inc., Alexion Pharmaceuticals, Inc., argenx, Annexon Biosciences, Inc., Ra Pharmaceuticals, Inc. (now UCB S.A.), the Myasthenia Gravis Foundation of America, Inc., Momenta Pharmaceuticals, Inc. (now Janssen), Immunovant, Inc., Grifols, S.A., and Viela Bio, Inc. (Horizon Therapeutics, now Amgen Inc.). Served as a consultant and advisor for Alexion Pharmaceuticals, Inc., argenx, Cabaletta Bio, Inc., Cour Pharmaceuticals, Ra Pharmaceuticals, Inc. (now UCB S.A.), Immunovant, Inc., Momenta Pharmaceuticals, Inc. (now Janssen), and Viela Bio, Inc. (Horizon Therapeutics, now Amgen Inc.).; Kimiaki Utsugisawa: K. Utsugisawa served as a paid consultant

for UCB Pharma, argenx, Janssen Pharma, Viela Bio (Horizon Therapeutics, now Amgen Inc.), Chugai Pharma, Hanall BioPharma, Merck and Mitsubishi Tanabe Pharma, and has received speaker honoraria from Argenx, Alexion Pharmaceuticals, UCB Pharma and the Japan Blood Products Organization.; Michael Benatar: M. Benatar receives research support from Immunovant & Alexion. Served as a consultant to Alexion, Cartesian, Canopy, CorEvitas, Horizon Therapeutics (now Amgen Inc.), Immunovant, Sanoi, Takeda, and UCB.; Emma Ciafaloni: E. Ciafaloni received compensation for serving on advisory boards and/or as a consultant for Alexion, argenx, Biogen, Amicus, Pfizer, Italfarmaco, Sarepta, Janssen, NS Pharma, and Roche.; M. Isabel Leite: M.I. Leite funded by the NHS (Myasthenia and Related Disorders Service and National Specialised Commissioning Group for Neuromyelitis Optica, UK) and by the University of Oxford, UK. She has been awarded research grants from the UK association for patients with myasthenia (Myaware), Muscular Dystrophy UK and the University of Oxford. She has received speaker honoraria or travel grants from Biogen, Novartis, UCB Pharma, and the Guthy-Jackson Charitable Foundation. She serves on scientific or educational advisory boards for UCB Pharma, argenx, and Horizon Therapeutics (now Amgen Inc.).; John Vissing: J. Vissing advisor on advisory boards for Regeneron, UCB Pharma, argenx, Alexion Pharmaceuticals, Horizon Therapeutics (now Amgen Inc.), Dianthus Therapeutics, Janssen, and Roche.; Fengming Tang: F. Tang is an employee of and stockholder in Amgen Inc.; Yanping Wu: Y. Wu is an employee of and stockholder in Amgen Inc.; Mikhail Rojavin: M. Rojavin is an employee of and stockholder in Amgen Inc.; Sue Cheng: S. Cheng is an employee of and stockholder in Amgen Inc.; James F. Howard Jr.: JFH has received research support (paid to his institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, NMD Pharma, PCORI, and UCB Pharma; honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, Amgen, argenx, Biohaven, Ltd., Biologix Pharma, CheckRare CME, Curie.bio, F. Hoffmann-LaRoche Ltd, Medscape CME, Merck EMB Serono, Novartis Pharma, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, TG Therapeutics, UCB Pharma, and Zai Labs; nonfinancial support from Alexion AstraZeneca Rare Disease, argenx, Biohaven Ltd., Cartesian Therapeutics, Toleranzia AB, UCB Pharma. and Zai Labs.

Grant Support: None.

Contact Information: None provided.

Prevalence and Clinical Features of Spinocerebellar Ataxia 27B in Patients with Idiopathic Downbeat Nystagmus at a Tertiary Care Center

Leigh Rettenmaier [1], Jinyun Helen Chen [2], Jason MacMore [3], Anoopum Gupta [2], Christopher Stephen [2], David Pellerin [4], Bernard Brais [4], Sashank Prasad [1], Jeremy Schmahmann [2]

[1] University of Pennsylvania, Perelman School of Medicine, [2] Massachusetts General Hospital, Department of Neurology, Harvard Medical School, [3] Massachusetts General Hospital, [4] Montreal Neurological Hospital and Institute, Department of Neurology and Neurosurgery, McGill University

Introduction:
The etiology of downbeat nystagmus (DBN) remains unknown in a significant proportion of patients despite thorough diagnostic investigation. Spinocerebellar ataxia 27B (SCA27B), resulting from >250 intronic GAA repeat expansions in the FGF14 gene, is a recently described cause of late-onset cerebellar ataxia associated with DBN. The prevalence of this mutation in patients with DBN, its clinical spectrum, and the pathogenic threshold of GAA repeats has yet to be fully characterized.

Methods:
We screened the Ataxia Center registry (n=3,182) for patients with idiopathic DBN with or without cerebellar ataxia who remained undiagnosed despite comprehensive evaluation. Participants were consented and screened for FGF14 GAA repeat expansion by long-range PCR and bidirectional repeat-primed PCR.

Results:
Of 47 genetically undiagnosed DBN patients, genetic testing was completed on 33. Pathogenic FGF14-GAA expansions (>250 repeats) were found in 21/33 (64%). In isolated DBN, 9/14 (64%) had a pathogenic repeat expansion, 1 had an intermediate expansion (200-249 copies), and 4 had normal alleles. In DBN and ataxia, 12/19 (63%) had a pathogenic expansion, 1 had an intermediate expansion, and 6 had normal alleles. Aminopyridine was administered to 30/33 patients. Of those with follow-up data, 16/23 (70%) experienced subjective improvement . Positive treatment response occurred in 10/12 (83%) patients with pathogenic expansions and 55% (6/11) with normal alleles. No significant differences were found between patients with pathogenic FGF14-GAA expansions and those with normal alleles in terms of symptom onset, severity, or family history.

Conclusions:
FGF14-GAA repeat expansions are a common cause of DBN, found in 64% of genetically undiagnosed DBN cases in this study. Larger cohorts are needed to further define its epidemiology and pathogenic threshold. Genetic testing for FGF14-GAA repeat expansions should be considered in idiopathic DBN. Aminopyridine may offer therapeutic benefit, warranting further study in clinical trials.

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Abstract Type: Clinical afferent disease

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Characteristics of Eye Movement Disorders in Adult-Onset Autoimmune and Paraneoplastic Neurological Syndromes

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Introduction:
Paraneoplastic neurological syndromes (PNS) are immune-mediated remote effects of systemic cancer affecting the nervous system. Advancement in antibody detection has raised awareness of these syndromes, yet specific studies addressing the eye movement abnormalities in these disorders remain limited.

Methods:
We conducted a retrospective review of medical records for adult patients consecutively seen in our center, between September 2023 and August 2024. We included those diagnosed with autoimmune/paraneoplastic neurological syndromes having positive neuronal antibodies, and excluded patients under 18 years of age at onset, isolated sensory neuronopathy, or isolated gastrointestinal dysmotility. We analyzed data regarding presenting features, eye movement abnormalities and cancer detection.

Results:
We identified 204 PNS patients, with a mean age at onset was 55.4±16.6 years (52.9% female). Visual symptoms were reported in 37.3%, including blurred vision (24.0%), diplopia (22.5%), and/or oscillopsia (7.4%). Abnormal eye movement findings were observed in 41.2%. Ophthalmoparesis/strabismus was noted in 18.6%, including hypertropia (6.9%), esotropia (6.3%), exotropia (2.9), gaze deviation (4.4%), lateral rectus palsy (2.5%) and/or vertical supranuclear palsy (2.0%). Pursuits were impaired in 16.2%. Saccade abnormalities included saccadic dysmetria (5.9%), slow velocity (3.9%), and delayed initiation (1.5%). Nineteen percent exhibited nystagmus, with gaze-evoked nystagmus being the most common type (11.8%), followed by downbeat nystagmus (5.9%), and torsional nystagmus (2.0%). Saccadic oscillations comprised square wave jerks (3.9%), opsoclonus (2.5%) and ocular flutter (1.0%). PCA-1 antibodies were associated with nystagmus (87.5%, $p< 0.001$) and impaired pursuits (87.5%, $p=0.005$), whereas anti-LGI-1 antibodies were associated with lower nystagmus rate (8.3%, $p=0.014$). T2 hyperintense lesions were observed in 10% of patients, with no significant difference between those with and without eye movement abnormalities ($p=0.961$).

Conclusions:
Eye movement abnormalities are found in nearly 40% of PNS patients. Specifically, anti-PCA-1 antibodies are notably associated with eye movement disorders, whereas anti-LGI-1 antibodies are likely associated with lower nystagmus rate.

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Abstract Type: Clinical efferent disease

Keywords: Paraneoplastic syndromes, Ocular motility, Nystagmus, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Adult strabismus with a focus on diplopia

Financial Disclosures: Natthapon Rattanathamsakul: No; Deena Tajfirouz: No; Kevin Chodnicki: No; Sean Pittock: Sean J. Pittock has received personal compensation for serving as a consultant for Roche/Genentech, Sage Therapeutics, Arialys and Astellas. He has received personal compensation for serving on scientific advisory boards or data safety monitoring boards for F. Hoffman-LaRoche AG, Genentech, Arialys and UCB. His institution has received compensation for serving as a consultant for Astellas, Alexion, and Viela Bio/MedImmune. All compensation is paid to Mayo Clinic. He has received research support from Alexion, Viela Bio/MedImmune, Roche/Genentech and Adimmune. He has a patent, Patent# 8,889,102 (Application#12-678350, Neuromyelitis Optica Autoantibodies as a Marker for Neoplasia)—issued; a patent, Patent# 9,891,219B2 (Application#12-573942, Methods for Treating Neuromyelitis Optica (NMO) by Administration of Eculizumab to an individual that is Aquaporin-4 (AQP4)-IgG Autoantibody positive)-issued and from which he has received royalties and a patent for GFAP-IgG; Septin-5-IgG; MAP1B-IgG; Kelch-like protein 11; PDE10A pending. He is working as a consultant in the Mayo Clinic Neuroimmunology laboratory clinical service. The Mayo Clinic Neuroimmunology Laboratory commercially offers MOG-IgG testing, but revenue accrued does not contribute to salary, research support, or personal income; Scott D.Z. Eggers: No; Eoin Flanagan: The institution of Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Alexion. Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Genentech. Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Horizon Therapeutics. The institution of Dr. Flanagan has received personal compensation in the range of $10,000-$49,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Roche. Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Speakers Bureau for Pharmacy times. The institution of Dr. Flanagan has received personal compensation in the range of $5,000-$9,999 for serving on a Speakers Bureau for UCB. The institution of Dr. Flanagan has received research support from Viela Bio. The institution of Dr. Flanagan has received research support from UCB. The institution of Dr. Flanagan has received research support from Roche. Dr. Flanagan has received publishing royalties from a publication relating to health care. Dr. Flanagan has a non-compensated relationship as a Member of medical Advisory Board with The MOG Project. Dr. Flanagan has a non-compensated relationship as a Editorial board member with Journal of The Neurologic Sciences. Dr. Flanagan has a non-compensated relationship as a Editorial board member with Neuroimmunology Reports. Dr. Flanagan has a non-compensated relationship as a Editorial Board Member with Neurology, Neuroimmunology Neuroinflammation (N2) Journal.; John Chen: No

Grant Support: None.

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Advancing Otolith Function Assessment: Integrating Artificial Intelligence with Video-Oculography (VOG) for Enhanced Vestibular Diagnosis

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Introduction:
Dizziness affects around 7.4% of adults, presenting diagnostic challenges, particularly in early differentiation of benign (inner ear disease) vs dangerous (stroke) causes. The ability to detect subtle changes in the otolith can provide clues regarding central and peripheral vestibular function. The degree and direction of dynamic ocular torsion obtained using the beside vOCR test is a quantitative measure of vestibular function. Recent advances in deep learning-based dynamic torsional detection may make it possible to automate the vOCR, increasing accessibility to non-expert providers on the frontline.

Methods:
36 participants were enrolled, including 18 healthy controls and 18 with vestibular loss. Each participant underwent the vOCR test, involving 24 tilts consisting of both neck and trunk movements to stimulate otolith function. Torsional waveforms were recorded, and beats of torsion, each consisting of a fast and slow phase, were extracted. Clips of 500ms, containing at least one full beat of torsion, were isolated. Several Machine Learning Models (MLMs) were trained on the extracted waveform features. For image-based analysis, a filtered image was generated by summing the differences between consecutive video frames, creating a visualization that captured the dynamic motion in each clip. A simplified 2D ResNet18 model was then trained on these filtered images.

Results:
The simplified 2D ResNet18 image-based model outperformed the waveform-based MLMs, achieving an AUC of 81.07% on the validation set compared to the top waveform model's AUC of 66.00%.

Conclusions:
This study highlights the effectiveness of artificial intelligence in capturing and classifying subtle torsional movements associated with vestibular function. By leveraging a ResNet18 model, we demonstrate the potential to automate vOCR assessments, facilitating wider access to accurate vestibular diagnostics in clinical settings where specialist expertise may be limited.

References: None provided.

Abstract Type: Clinical afferent disease, Basic Science, Other

Keywords: Vestibular disorders, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Ocular manifestations of vestibular disorders, Ocular motility

Financial Disclosures: Krishna Mukunda: Summer Student Fellowship 2024, Institute for Data Intensive Engineering; Amir Kheradmand: No; Kemar Green: No

Grant Support: Institute for Data Intensive Engineering and Sciences at Johns Hopkins University, Summer Student Fellowship 2024

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Non-Invasive Identification of Alzheimer's Disease Through Ocular Analysis Utilizing Raman Spectroscopic Data Analysis

Nitza Goldenberg-Cohen [1], Basel Obeid [1], Stephen Richard [2], Alex kaufman [1], Alon Zahavi [3], Eran Adato [4], Zeev Zalevsky [5]

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Introduction:
Alzheimer's disease (AD) is characterized by accumulation of amyloid-β (βA) in the brain, which can also be detected in the eye. Here we propose the use of Raman spectroscopy (RS) based novel photonic sensing and analysis to measure in- vivo AD biomarkers in the eye.

Methods:
The behavioral characteristics of 7-months-old transgenic 5XFAD AD mice compared to control mice were assessed using the open field test and Morris water maze, followed by brain MRI, for quantification of AD related features. Concurrently, in-vivo analysis of biomarker accumulation in the tears, lens, and retina was performed using RS. RS light was focused within the semi-transparent media of the lens, significantly enhancing the signal-to-noise ratio, which is critical for detecting chemicals at ultra-low concentrations. Tear samples from AD patients and healthy controls were collected on filter paper from the lower fornix. Lens material extracted during cataract surgery was collected from AD and heathy controls.

Results:
Tear samples from 29 transgenic 5XFAD mice were collected and analyzed. Human lenses were obtained from 20 controls and 9 AD patients (mean age 74.4 and 81.2 years, respectively). Whole lenses were extracted by ECCE (8 and 4, respectively), and 17 via phacoemulsification (12 and 5, respectively). RS, combined with machine learning and AI algorithms, enabled efficient in-vivo detection of biomarkers. A significant increase in βA levels in the lenses of AD patients was detected as compared to controls.

Conclusions:
The preliminary findings from RS analysis of βA in the eye of both humans and transgenic AD mice as compared to controls are promising. The utilization of optical sensing and data analysis allows in-vivo RS usage for early diagnosis and monitoring of AD progression. If proof-of-concept is achieved, this technique could lead to early diagnosis of AD, monitoring disease progression, and assessing responses to experimental treatments.

References: None provided.

Abstract Type: Basic Science

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Neuroimaging, Retina

Financial Disclosures: The authors had no disclosures.

Grant Support: Nanos Pilot Grant Support

Contact Information: None provided.

In Vivo Transfer of Glial Mitochondria to Retinal Neurons

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Introduction:
Mitochondrial dysfunction is a key driver of a number of ophthalmic diseases, including pigmentary retinopathies and heritable optic neuropathies. Currently there are no approved therapies that specifically address mitochondrial dysfunction in ophthalmic diseases. Provision of exogenous mitochondria to affected retinal neurons is one potential therapeutic strategy. In the retina, there have been reports of transfer of damaged mitochondria from photoreceptors and retinal ganglion cells to retinal glia for the purposes of their degradation ('trans-mitophagy'), but the reverse process of transfer of glia-derived mitochondria to retinal neurons has not been described. We assessed for evidence of in vivo glia-to-neuron mitochondrial transfer in mouse retinas.

Methods:
We used the GFAP-Cre mouse line with glia-specific expression of Cre recombinase to drive the expression of fluorescent constructs in Müller glia and astrocytes by excising loxP-STOP-loxP (LSL) cassettes otherwise precluding their translation. The Cre-dependent constructs included an outer mitochondrial membrane-targeted green fluorescent protein (OMM-GFP) and the soluble fluorophore tdTomato. Control experiments employed the iCre75 mouse line with rod photoreceptor-specific Cre expression. Confocal microscopy and immunoelectron microscopy were used to assess for the presence of glia-derived mitochondria within retinal neurons.

Results:
The retinas of GFAP-Cre;LSL-OMM-GFP mice demonstrated robust GFP labeling of mitochondria in Müller glia and astrocytes. In addition, the OMM-GFP construct was found in approximately 4% of photoreceptor inner segments (both rods and cones). The construct was confirmed to localize to photoreceptor mitochondria on immunoelectron microscopy. Conversely, GFAP-Cre;LSL-tdTomato mice did not exhibit significant red fluorescence in photoreceptor inner segments, in stark contrast to the robust red signal identified in iCre75;tdTomato photoreceptors, arguing against leaky Cre recombinase expression in photoreceptors of GFAP-Cre mice. Approximately 1% of retinal ganglion cells in GFAP-Cre;LSL-OMM-GFP mice contained glia-derived OMM-GFP-labeled mitochondria.

Conclusions:
We have uncovered evidence of physiological glia-to-neuron mitochondrial transfer in mammalian retinas, a phenomenon that might be harnessed therapeutically in mitochondrial disorders.

References: None provided.

Abstract Type: Basic Science

Keywords: Genetic disease, Retina

Financial Disclosures: The authors had no disclosures.

Grant Support: Research to Prevent Blindness Career Development Award

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Retinal Input to Macaque Superior Colliculus Derives from Branching Axons Projecting to the Lateral Geniculate Nucleus

Jonathan Horton [1], Yicen Zheng [1], Thomas Gentry [1], Mikayla Dilbeck [1], Daniel Adams [1], john Economides [1]

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Introduction:
Retinal ganglion cells project to both the superior colliculus (SC) and the lateral geniculate nucleus (LGN). The SC governs eye movements while the LGN mediates visual perception. Given this difference in function, it is logical to expect different classes of ganglion cells to supply each structure. To address this issue, a double-label experiment was performed in two macaques.

Methods:
The animals were trained to fixate a target while potential injection sites were scouted in the superior colliculus by recording and stimulating with a tetrode. Once a suitable site was identified, cholera toxin subunit B Alexa -Fluor 488 was injected via an adjacent micropipette. In a subsequent experiment, cholera toxin subunit B - Alexa Fluor 555 was injected into the lateral geniculate nucleus under general anesthesia at matching retinotopic locations. After a brief survival period, retinal flatmounts were prepared, and ganglion cells were surveyed to determine if they were single- or double-labeled.

Results:
The percentage of double-labeled cells varied locally, depending on the relative efficiency of retrograde transport by each tracer and the precision of retinotopic overlap of injection sites in each target nucleus. In counting boxes with extensive overlap, 76-98% of ganglion cells projecting to the superior colliculus were double-labeled. Cells projecting to the superior colliculus constituted 4.0 – 6.7% of the labeled ganglion cell population. In one particularly large retinal zone, there were 5,746 cells labeled only by CTB-AF555, 561cells double-labeled by CTB-AF555 and CTB-AF488, but no cells labeled only by CTB-AF488.

Conclusions:
The direct retinal projection to the primate SC arises from a collateral axonal branch supplied by about 5% of the ganglion cells that project to the LGN. Surprisingly, there exist no ganglion cells that project exclusively to the SC. The next challenge is to determine the function of this shared retinal input to the SC and LGN.

References: None provided.

Abstract Type: Basic Science

Keywords: Retina

Financial Disclosures: The authors had no disclosures.

Grant Support: R01-EY029703 and administrative supplement R01-EY029703-05S1 EY02162 (Vision Core Grant) Unrestricted grant from Research to Prevent Blindness

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Scientific Platform Session III – Tuesday, March 18th [2.0 CME]

Moderators: Michael Gilhooley, MB, PhD, FRCOphth & Paula Grigorian, MD

10:30 am – 10:45 am	**Pocket Steroids for MOGAD Relapses: a Prospective Study**, *John J. Chen, MD, PhD*
10:45 am – 11:00 am	**Prevelence of Multiple Sclerosis, Neuromyelitis Optica, and Myelin Oligodendrocyte Associated Disease in Patients with Optic Neuritis: a United States Large Database Study,** *Alexander S Kwok, MD (nominee for best abstract by a resident)*
11:00 am –11:15 am	**A Phase III Randomized Controlled Trial Of Intravenous Alteplase Initiated Within 4.5 Hours Of Central Retinal Artery Occlusion (CRAO). The THEIA Study**, *Valérie Biousse, MD*
11:15 am – 11:30 am	**Is There a Pharmacogenomic Basis to Ethambutol Optic Neuropathy?**, *Shweta Singhal, MD*
11:30 am – 11:45 am	**Acute Progression of NAION – Minimal Role of Cardiovascular Risk Factors,** *Zoë R. Williams, MD*
11:45 am – 12:00 pm	**Glucocorticoid Induced Adrenal Insufficiency and Elevated Intracranial Pressure: Molecular Mechanisms Underlying CSF Physiology and Rescue Effect,** *Ozair Nissar Sheikh, MD*
12:00 pm – 12:15 pm	**Glymphatic Function in Idiopathic Intracranial Hypertension,** *Marc Bouffard, MD*
12:15 am – 12:30 pm	**Dysregulation of Lipid Metabolism in Idiopathic Intracranial Hypertension,** *Yin Allison Liu, MD*

Scientific Platform Session III – March 18th, 2025

Pocket steroids for MOGAD relapses: a prospective study

John Chen [1], Nanthaya Tisavipat [1], Natthapon Rattanathamsakul [1], Deena Tajfirouz [1], Kevin Chodnicki [1], Eric Eggenberger [2], Marie Di Nome [3], Amrita Vuppala [4], Elias Sotirchos [5], Amanda Henderson [6], Anthony Arnold [7], Laura Bonelli [8], W. Oliver Tobin [9], Sean Pittock [1], Eoin Flanagan [1]

[1] Mayo Clinic, [2] Mayo Clinic, Jacksonville, FL, [3] Mayo Clinic, Arizona, [4] Medical College of Wisconsin, [5] Johns Hopkins, [6] Wilmer Eye Institute, Johns Hopkins School of Medicine, [7] UCLA, [8] University of California Los Angeles, [9] Mayo Clinic College of Medicine and Science

Introduction:
Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a distinct demyelinating disorder with optic neuritis (ON) as a prominent clinical feature. Several retrospective studies have suggested that early steroids may lead to better visual outcomes, but this has not been evaluated prospectively.

Methods:
Between 7/2020 and 10/1/24, MOGAD patients were recruited into a prospective study evaluating the use of hyperacute high dose steroids for relapses in MOGAD. If a patient developed eye pain or vision loss concerning for relapse, they were instructed to self-administer oral (PO) 1250 mg prednisone ideally within 12 hours of symptom onset. During an attack, patients self-monitored visual acuity twice per day with at home near visual acuity cards. Patients were seen within 1 week of symptoms to confirm a true relapse.

Results:
Eighty five MOGAD patients have been enrolled to date with a median age of 39 (range 11-76); 60% were female. Twenty five (29%) were on chronic immunotherapy prior to or started at the time of enrollment. The median follow-up was 2 years (range 0-4 years) with 51 having ≥1 year of follow-up. There was a total of 10 confirmed ON relapses, which all had complete recovery after PO prednisone (median time to treatment < 1 day). There were 10 attacks with eye pain only, which resolved without vision loss after hyperacute PO prednisone treatment. One patient had confirmed mild ON that improved spontaneously without steroids. Four patients were initiated on chronic immunotherapy during the study while 2 had chronic immunotherapy stopped; 32% were on chronic immunotherapy at the last follow-up.

Conclusions:
Hyperacute high dose steroid treatment, “Pocket steroids”, may reduce the risk of developing permanent deficits from MOGAD relapses. This data is promising and supports a future multicenter prospective randomized placebo-controlled clinical trial to confirm these findings.

References: None provided.

Abstract Type: Clinical afferent disease

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

Financial Disclosures: John Chen: No; Nanthaya Tisavipat: No; Natthapon Rattanathamsakul: No; Deena Tajfirouz: No; Kevin Chodnicki: No; Eric Eggenberger: No; Marie Di Nome: No; Amrita Vuppala: No; Elias Sotirchos: No; Amanda Henderson: None related to this submission: Horizon Therapeutics/Amgen.; Anthony Arnold: No; Laura Bonelli: No; W. Oliver Tobin: Dr. Tobin reports receiving research funding from the National institutes of Health, Mayo Clinic Center for Multiple Sclerosis and Autoimmune Neurology and Mallinckrodt Inc. He receives royalties from the publication of “Mayo Clinic Cases in Neuroimmunology” (OUP).; Sean

Pittock: Sean J. Pittock has received personal compensation for serving as a consultant for Roche/Genentech, Sage Therapeutics, Arialys and Astellas. He has received personal compensation for serving on scientific advisory boards or data safety monitoring boards for F. Hoffman-LaRoche AG, Genentech, Arialys and UCB. His institution has received compensation for serving as a consultant for Astellas, Alexion, and Viela Bio/MedImmune. All compensation is paid to Mayo Clinic. He has received research support from Alexion, Viela Bio/MedImmune, Roche/Genentech and Adimmune. He has a patent, Patent# 8,889,102 (Application#12-678350, Neuromyelitis Optica Autoantibodies as a Marker for Neoplasia)—issued; a patent, Patent# 9,891,219B2 (Application#12-573942, Methods for Treating Neuromyelitis Optica (NMO) by Administration of Eculizumab to an individual that is Aquaporin-4 (AQP4)-IgG Autoantibody positive)-issued and from which he has received royalties and a patent for GFAP-IgG; Septin-5-IgG; MAP1B-IgG; Kelch-like protein 11; PDE10A pending. He is working as a consultant in the Mayo Clinic Neuroimmunology laboratory clinical service. The Mayo Clinic Neuroimmunology Laboratory commercially offers MOG-IgG testing, but revenue accrued does not contribute to salary, research support, or personal income; Eoin Flanagan: The institution of Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Alexion. Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Genentech. Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Horizon Therapeutics. The institution of Dr. Flanagan has received personal compensation in the range of $10,000-$49,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Roche. Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Speakers Bureau for Pharmacy times. The institution of Dr. Flanagan has received personal compensation in the range of $5,000-$9,999 for serving on a Speakers Bureau for UCB. The institution of Dr. Flanagan has received research support from Viela Bio. The institution of Dr. Flanagan has received research support from UCB. The institution of Dr. Flanagan has received research support from Roche. Dr. Flanagan has received publishing royalties from a publication relating to health care. Dr. Flanagan has a non-compensated relationship as a Member of medical Advisory Board with The MOG Project. Dr. Flanagan has a non-compensated relationship as a Editorial board member with Journal of The Neurologic Sciences. Dr. Flanagan has a non-compensated relationship as a Editorial board member with Neuroimmunology Reports. Dr. Flanagan has a non-compensated relationship as a Editorial Board Member with Neurology, Neuroimmunology Neuroinflammation (N2) Journal.

Grant Support: NIH (R01NS113828)

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Prevelence of Multiple Sclerosis, Neuromyelitis Optica, and Myelin Oligodendrocyte Associated Disease in Patients with Optic Neuritis: a United States Large Database Study

Alexander Kwok [1], Muhammad Chauhan [1], Omar Solyman [1], Abdelrahman Elhusseiny [1], Paul Phillips [1], Joseph Chacko [1]

[1] *University of Arkansas for Medical Sciences*

Introduction:
Data on the prevalence of multiple sclerosis (MS), neuromyelitis optica (NMO), and myelin oligodendrocyte glycoprotein-associated disease (MOGAD) among patients with optic neuritis (ON) is limited. Previous epidemiological studies in the U.S. focused on specific counties or cities, often lacking comprehensive racial/ethnic breakdowns and insights into ON etiology. This study aims to establish the prevalence of MS, NMO, and MOGAD among ON patients in the U.S. over the last decade.

Methods:
This was a retrospective epidemiologic study utilizing a large U.S. federated platform of EHRs. Patients were identified by ICD-10 and LINOIC codes. Patients with ON were identified using codes for unspecified optic neuritis, retrobulbar neuritis, and other optic neuritis, excluding optic papillitis, nutritional optic neuropathy, and toxic optic neuropathies. NMO cases were identified using diagnostic codes and/or a positive Aquaporin 4 water channel IgG antibody LOINC code. MOG cases were identified using diagnostic codes and/or a positive MOG-antibody LOINC code. Prevalences and odds ratios were calculated using the number of baseline patients in each population of interest.

Results:
We found an overall increasing trend for MOGAD, NMO, and MS-related ON diagnoses across the study period. In 2023, the prevalence rates per 1,000 patients for MS, NMO, and MOGAD among ON patients were 297.9, 43.7, and 12.9, respectively. White females (387.0), black females (339.8), and Hispanic females (336.9) had the highest prevalence rates of MS. Hispanic females (92.8), Black females (87.3), and Asian females (83.3) had the highest prevalence rates of NMO. Asian females (26.3), Hispanic females (25.8), and Asian males (22.6) had the highest prevalence rates of MOGAD. Relative to white females in 2023, Hispanic females had higher odds of NMO (OR: 2.5) and MOGAD (OR: 1.9) diagnoses, respectively.

Conclusions:
This is the first study to utilize nationwide data to establish the prevalence of MS, NMO, and MOGAD associated ON by race/ethnicity.

References: None provided.

Abstract Type: Other

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

A Phase III Randomized Controlled Trial Of Intravenous Alteplase Initiated Within 4.5 Hours Of Central Retinal Artery Occlusion (CRAO). The THEIA Study.

Valérie Biousse [1], Benoit Guillon [2], Cecile Preterre [2], Michael Obadia [3], Isabelle Mourand [4], Marie Gaudron [5], Denis Sablot [6], Gaelle Godeneche [7], Guillaume Marc [8], Gilles Rodier [9], Cedric Urbanczyk [10], Sarah Evain [11], Evelyne Massardier [12], Marion Boulanger [13], Lionel Calviere [14], Sebastien Marcel [15], Laura Mechtouff [16], Thomas Ronziere [17], Aurelie Gaultier [18], Pierre Lebranchu [19], For The THEIA Study Investigators [1]

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Introduction:
Although open label studies and meta-analyses have suggested that early revascularization of the retina with intravenous thrombolysis within 4.5 hours of vision loss is associated with improved visual recovery in acute central retinal artery occlusion (CRAO), there is currently no level 1 evidence to support this treatment. Three randomized clinical trials are ongoing in Europe (France, Germany and Norway), and we will present the results of the French THEIA study, which is the first RCT to assess intravenous alteplase in CRAO patients within 4.5 hours of onset of vision loss.

Methods:
THEIA (THrombolysis in patients with acutE Central retinal Artery occlusion) is a phase-III, multicenter, randomised, single-blind, double-dummy study assessing the efficacy and safety of intravenous-alteplase versus aspirin in acute CRAO. Patients ≥18 yo, with acute CRAO and severe vision loss (best-corrected visual acuity (BCVA) worse than < 1/20 [< 20/400 or > 1.3 Log.MAR]) and no contraindication to [intravenous-alteplase with placebo aspirin] or [oral aspirin with intravenous-saline] were randomized in a 1:1 ratio to receive intravenous-alteplase 0.9 mg/kg over 1hr (10% bolus) or aspirin (300 m) within 4.5 hours of vision loss onset. The primary outcome was improvement of BCVA of 15 letters (0.3 Log.Mar VA) or more on the ETDRS-VA chart (increase of ≥3 lines) between baseline and 30-days. Main secondary outcomes were safety (especially intracranial/other hemorrhages), functional recovery defined by VA ≤log-Mar 0.5 (able to read with affected eye), quality of life (Rankin score and NEI-VFQ-25). ClinicalTrials.gov: NCT03197194.

Results:
70 patients were randomized [mean age 70.2±9 (47-89); 36% women]. Patients were treated within 270min of vision loss onset. There was no safety warning from the DSMB. Lock database occurred in June 2024 and analysis of the data is ongoing.

Conclusions:
The final results of the THEIA study will be available in March 2025 for presentation at the NANOS meeting.

References: None provided.

Abstract Type: Clinical afferent disease

Keywords: Vascular disorders, Stroke

Financial Disclosures: Valérie Biousse: Consultant for Topcon which commercializes fundus cameras. The current research is completely independent from Topcon and is not funded by the company.; Benoit Guillon: No; Cecile Preterre: No; Michael Obadia: No; Isabelle Mourand: No; Marie Gaudron: No; Denis Sablot: No; Gaelle Godeneche: No; Guillaume Marc: No; Gilles Rodier: No; Cedric Urbanczyk: No; Sarah Evain: No; Evelyne Massardier: No; Marion Boulanger: No; Lionel Calviere: No; Sebastien Marcel: No; Laura Mechtouff: No; Thomas Ronziere: No; Aurelie Gaultier: No; Pierre Lebranchu: No; For The THEIA Study Investigators: No

Grant Support: None.

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Is There a Pharmacogenomic Basis to Ethambutol Optic Neuropathy?

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Introduction:
WHO reports 10 million new cases of Tuberculosis (TB) every year of whom 6-8% develop ethambutol related optic neuropathy (EON). This has increased further with recent escalation in the dose and duration of ethambutol treatment to address multidrug resistant TB. Patients also develop EON despite receiving recommended doses EMB. Although there are reports of EON with pre-existing mitochondrial genetic defects; genetic risk factors for development of EON remain unknown.

Methods:
Patients with confirmed EON were recruited from three neuro-ophthalmology clinics at a tertiary eye hospital. Clinical data (visual acuity/ colour vision/ visual fields/ optic nerve OCT thickness, renal function, drug dose and BMI) was collected along with a blood sample for genetic testing. A genome wide association study (GWAS) using a global screening array was performed to identify small nucleotide polymorphisms (SNPs) that might predispose to EON. The results were compared with age and ethnicity matched historical control population data.

Results:
This is an interim report of the early results from our discovery cohort. A total of 56 EON cases and 1068 controls were included. Genetic ancestry matching was confirmed by principle component analysis. Charting observed against expected p-values of the detected SNPs showed a small subset of extremely significant p values suggesting true genetic association with risk of EON. The most significant association was seen on chromosome 6 mapping to HLA locus with odds ratio of 3.127 (CI 2.094- 4.668) and p value of 5.3 -9

Conclusions:
Early results from our first of its kind GWAS of EON are highly suggestive of a genetic predisposition to EON. However this data needs further validation and is limited by the mixed nature of the control cohort. We are currently recruiting additional EON cases which will be compared specifically against drug treated controls to validate and establish the true significance of these findings.

References: None provided.

Abstract Type: Clinical afferent disease, Basic Science

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Acute Progression of NAION – Minimal Role of Cardiovascular Risk Factors

Zoë Williams [1], Rachelle Morgenstern [2], Asala Erekat [2], David Szanto [2], Michael Wall [3], Neil Miller [4], Leonard Levin [5], Brian Woods [6], Mark Kupersmith [2]

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Introduction:
The frequency and reasons for progressive vision loss due to NAION are unknown. Few prospective NAION reports describe acute progressive BCVA and/or visual field (VF) loss. 1,2 Our aim is to report the true frequency and risk factors for acute NAION progression to identify modifiable features to reduce vision worsening.

Methods:
We analyzed 599 study eyes with acute NAION (of 729 prospectively enrolled in QUARK 207 trial) with separate screening and day 1 (mean 2.5-day interval) evaluations for progression (defined at day 1: loss of ≥10 letter BCVA or worsening by ≥ 4 dB average total deviation [TD]). We evaluated systemic and ophthalmic features associated with progression. In the placebo group, we also report subacute worsening from Day 1 to Month-2.

Results:
Acute worsening vision after presentation occurred in 45/597 eyes (7.5%) for BCVA and 47/599 eyes (7.8%) for TD. BCVA worsened an average of 21 ± 12.2 letters (4 lines) and TD worsened by 6.56 ± 2.31 dB. Worsening was not correlated with duration of vision loss, age, sex, race, BMI, hypertension, diabetes, vital signs, or labs. BCVA worsened more frequently in participants with sleep apnea (p=0.02) or prior fellow eye NAION (p=0.002). In setting of fellow eye prior NAION, 13.7% had ≥10 letter BCVA loss from screening to day 1 versus 5.4% without prior NAION (p=0.0002). Screening ophthalmic evaluation features were not associated with progression for either BCVA or TD. Participants with worse VFs had more hyperlipidemia (p=0.002). In the sham group, 6/16 (37.5%) had worse BCVA at 8 days and 2/15 (13.3%) had worse average TD at Month-2.

Conclusions:
Worsening of vision in NAION occurs acutely. The results do not support cardiovascular risk factors as important hazard features for NAION progression The only consistent factor associated with progression for both BCVA and VF loss was fellow eye NAION before screening.

References: 1. The Ischemic Optic Neuropathy Decompression Trial Research Group. Optic nerve decompression surgery for nonarteritic anterior ischemic optic neuropathy (NAION) is not effective and may be harmful. JAMA, 273, 625-632, 1995. 2. Bialer OY, Stiebel-Kalish H. Clinical characteristics of progressive nonarteritic anterior ischemic optic neuropathy. Int J Ophthalmol. 14(4), 517-522, 2021.

Abstract Type: Clinical afferent disease, Clinical Trials

Keywords: Optic neuropathy

Financial Disclosures: Zoë Williams: I was a site principal investigator for the QRK207 trial; Rachelle Morgenstern: No; Asala Erekat: No; David Szanto: No; Michael Wall: No; Neil Miller: Study director for QRK207 Receive royalties from Elsevier and Wolters Kluwer; Leonard Levin: Annexon: C; Dompe: C; Eyevensys: C; GENENTECH: C; Gilbert Family Foundation: C; Janssen Pharmaceuticals, Inc.: C; Neuroptika: C; Perfuse: C; Prilenia: C; Roche Pharmaceuticals: C; Santen, Inc.: C; UNITY: C; Wisconsin Alumni Research Foundation: P.

Consultant for QRK207 trial; Brian Woods: No; Mark Kupersmith: Consultant for QRK207 trial

Grant Support: Unrestricted Departmental Grant from Research to Prevent Blindness

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Glucocorticoid induced adrenal insufficiency and Elevated intracranial pressure: Molecular mechanisms underlying CSF physiology and Rescue effect.

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Introduction:
Mechanisms underlying elevated intracranial pressure (ICP) in idiopathic intracranial hypertension (IIH) are poorly understood. We previously demonstrated that adrenal insufficiency (AI) secondary to exogenous steroids may manifest in a quasi-IIH manner with elevated ICP and papilledema in a mouse model. Using this model, we sought to study the molecular mechanisms of the CSF physiology that contribute to elevated ICP and can respond to a rescue effect.

Methods:
In our AI model, adult C57 BL/6J mice were administered Dexamethasone (Dex) in 2 groups a) Treatment group, received Dex 1mg/kg orally for 8 weeks. b) Withdrawal group given Dex 1mg/kg orally for 8 weeks and withdrawn for a week. The third Control group received no treatment. At the end of withdrawal week, ICP (via intraventricular catheterization) and OCT were measured, and choroid plexus tissue harvest done in all groups for transcriptomic analysis. A subset in Dex group was given, after 8 weeks, hydrocortisone (5mg/kg) intraperitoneally, daily for a week, and then ICP and OCT recorded at the end of one week.

Results:
Bulk RNA-Sequence from the choroid plexi comparing all three groups identified 303 differentially expressed genes. 225 immune response genes were downregulated and corrected on withdrawal. 18 cellular structure and protein homeostasis genes were downregulated and not withdrawal corrected. 36 cytoskeletal dynamics genes got upregulated, withdrawal corrected, and 24 cell differentiation genes were upregulated not corrected on withdrawal. ICP and OCT findings were comparable in controls and the DEX group(4-6mmHg). ICP was elevated (10mmHg) in the withdrawal group with OCT findings showing papilledema with increased RNFL layer thickness (by 19 microns). In the rescue group the ICP was not raised (4-5mmHg).

Conclusions:
Our study demonstrates that steroid withdrawal induces raised ICP, seemingly mediated by genes involved in cytoskeletal dynamics and amino acid transporters and is rescued by administration of physiological steroids.

References: None provided.

Abstract Type: Basic Science

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Glymphatic Function in Idiopathic Intracranial Hypertension

Marc Bouffard [1], Mahsa Alborzi Avanaki [2], Donnella Comeau [2], Jeremy Ford [3], Narjes Jaafar [2], Alexander Brook [2], Bardia Abbasi [2], Nurhan Torun [2], David Alsop [2], Katherine Reinshagen [4], Yu-Ming Chang [2]

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Introduction:
Recently-published work correlated MRI-derived ALPS-indices, which putatively reflect glymphatic function, with duration of disease in idiopathic intracranial hypertension (IIH). ALPS-indices were also higher in patients with chronically present, untreated IIH than in recent-onset, untreated IIH (< 6 months) or healthy controls1. Whether aberrant glymphatic function represents the mechanism of IIH or a homeostatic response to it remains unclear. Ongoing work aims to 1) compare ALPS-indices between previously unstudied IIH populations (cured and treated IIH) and previously described groups (untreated IIH and controls) and 2) to establish a receiver-operating-characteristic (ROC) curve to assess the diagnostic utility of ALPS-indices.

Methods:
We imaged IIH patients (per modified Dandy criteria) and healthy controls aged 18-55 years using a GE Signa Premier XT 3T MRI scanner. ALPS-indices were derived as previously described1. Kruskal-Wallis testing with a Tukey-Kramer procedure for pairwise comparison was used to compare ALPS-indices between groups. ROC curves were used to assess diagnostic performance in distinguishing IIH groups from controls.

Results:
We enrolled 4 participants with acute untreated IIH, 6 with chronic untreated IIH, 7 with treated IIH, 7 with cured IIH, and 17 controls. ALPS-indices were lower in acute untreated vs. chronic untreated ($p< 0.001$) and cured IIH ($p=0.01$), higher in chronic untreated IIH vs. controls ($p=0.03$), and higher (but not significantly) in chronic untreated IIH vs. treated IIH ($p=0.39$) with similar numerical values between treated IIH and controls ($p=0.9$). ROC curves revealed an area-under-the-curve of 0.94 (CI 0.72-1) for chronic IIH vs. controls and 0.93 (CI 0.58-0.1) for acute IIH vs. controls.

Conclusions:
ROC analyses suggest that ALPS-indices may be a valid IIH biomarker and a practice-changing diagnostic aid. Sample size enlargement, serial intra-individual imaging, and correlation between duration of treatment/cure and ALPS-index will clarify whether ALPS-indices normalize with IIH's treatment or cure, offering potential mechanistic insights into the disease's pathophysiology.

References: Bouffard, M.A., Avanaki, M.A., Ford, J.N., Jaafar, N., Brook, A., et al. MRI Indices of Glymphatic Function Correlate With Disease Duration in Idiopathic Intracranial Hypertension. Journal of Neuro-Ophthalmology 2024; doi: 10.1097/WNO.0000000000002259.

Abstract Type: Clinical afferent disease, Basic Science

Keywords: Pseudotumor cerebri, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: This work was supported by a grant from the Neurology Department at the Beth Israel Deaconess Medical Center.

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Dysregulation of Lipid Metabolism in Idiopathic Intracranial Hypertension

Yin Liu [1], ANASTASIA KRAJNOVIC [1], JooYeon Jung [2], Christopher Brydges [2], Oliver Fiehn [2], Shana McCormack [3], Heather Collins [4], Mark Kupersmith [5], Michael Wall [6], Grant Liu [3]

[1] University of California, Davis, [2] Univeristy of California, Davis, [3] Children's Hospital of Philadelphia, [4] Perelman School of Medicine at the University of Philadelphia, [5] Icahn School of Medicine at Mount Sinai, [6] University of Iowa

Introduction:
The association between idiopathic intracranial hypertension (IIH) and obesity is well established. Recent studies suggest a link between hormonal imbalances and IIH, however, the evidence is weak, and specific causes remain unknown. In this study, we conducted a cross-sectional analysis to evaluate metabolomic changes in IIH patients using specimens from the Idiopathic Intracranial Hypertension Treatment Trial (IIHTT).

Methods:
Blood specimens were collected and metabolomic profiles were analyzed from 165 patients at diagnosis and 157 controls. Demographic features, including age, sex, race, body mass index (BMI), and eye examination findings, were recorded. Control subject inclusion criteria included age between 18 and 60, sex, BMI>30, and race/ethnicity. Samples were not standardized for fasting status or time of day. Independent-sample t-tests were used for analysis.

Results:
We found 55 significantly altered compounds in patients compared to controls at diagnosis, with 31 upregulated and 24 downregulated. The most upregulated compounds were Allantoin (1.6-fold, p< 0.001 95% CI[0.953,1.039]) and Arg-Pro (1.6-fold, p< 0.001 95% CI[0.953,1.039]) The most downregulated compounds were Ornithine (0.7-fold, p=0.001 95% CI[0.953,1.039]) and 3-methylxanthine (0.7-fold, p=0.018 95% CI[0.953,1.039]) Among the upregulated compounds, 14 of 31 were lipids (14 fatty acyls, 1 carbohydrate, 4 organic acids). In the downregulated compounds, 14 of 24 were organic acids (0 fatty acyls, 0 carbohydrates, 14 organic acids). The most impactful pathways altered in patients compared to controls included Valine, Leucine, and Isoleucine degradation and biosynthesis, Cysteine and Methionine metabolism, Tyrosine metabolism, Fatty Acid biosynthesis, and Linoleic Acid metabolism.

Conclusions:
Our study reveals significant metabolomic alterations in patients with IIH, characterized by the upregulation of lipids and downregulation of organic acids. These findings suggest metabolic dysregulation that may be linked to mitochondrial dysfunction and oxidative stress, providing insights into the pathophysiology of IIH and potential therapeutic targets for management. Our findings are similar to studies done by the Sinclair group.

References: None provided.

Abstract Type: Basic Science

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

Financial Disclosures: Yin Liu: No; ANASTASIA KRAJNOVIC: No; JooYeon Jung: No; Christopher Brydges: No; Oliver Fiehn: No; Shana McCormack: No; Heather Collins: No; Mark Kupersmith: Consultant for QRK207 trial; Michael Wall: No; Grant Liu: No

Grant Support: None.

Contact Information: None provided.

Analytical Studies Poster Reception – March 17, 2025 (Monday)

Poster #	Submission Title	Author	Category
170	Novel Instrument for Clinical Evaluations of Active Extraocular Muscle Tension	Hyunjin Shin (he/him/his)	Biomechanics
171	Vestibular rotation cancellation perception by vision in patients with increased visual dependency	Konrad Weber	Biomechanics
172	Investigating differences in the early visual response to a moving visual field in patients with visual dependency	Vergil V. Mavrodiev (he/him/his)	Biomechanics
173	Automated Retinal Vascular Fractal Analysis Can Distinguish Presymptomatic Alzheimer's Disease	Oana Dumitrascu	Cognition, Mood & Neuro-degenerative Disease
174	Visual symptoms correlated with visual function in a cohort of patients with Optic Disc Drusen	Marius B.. Maartensson (he/him/his)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
175	Applying an Alternate Threshold of Clinically Relevant Visual Acuity Change When Assessing the Natural History of Leber Hereditary Optic Neuropathy	Neringa Jurkute	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
176	New Onset Non-arteritic Ischemic Optic Neuropathy In Confirmed COVID-19 infections: A Retrospective Study	Nadine Abdeljabbar	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)

177	Clinical Relevance of Plasma Limitrin Level in Patients with MOG-IgG-Positive Optic Neuritis	Bo Young Chun	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
178	Comparing Scotoma Characteristics in Leber Hereditary Optic Neuropathy Versus Toxic-Nutritional Optic Neuropathy	Altug Ay (he/him/his)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
179	Assessing the Treatment Effect of Idebenone in Leber Hereditary Optic Neuropathy Using an Alternate Threshold of Clinically Relevant Visual Acuity Change	Marcela Votruba	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
180	The Effects Of Optic Nerve Head Disc Area on Visual Acuity, Retinal Nerve Fiber Layer, and Visual Field In Leber's Hereditary Optic Neuropathy	Danielle A. Gauthier (she/her/hers)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
181	Visual Outcomes Of First Affected Eye Vs. Second In Leber's Hereditary Optic Neuropathy Patients	Maryam Golmohammadi (she/her/hers)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
182	The correlation between HLA class II variants and patients diagnosed with Ethambutol-induced Optic Neuropathy (EtON)	Prabhjit Kaur (she/her/hers)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
183	Increased Toxic Lipids as Biomarker of Non-arteritic Anterior Ischemic Optic Neuropathy	Anas Alkhabaz	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
184	Metabolic Therapeutic Using Niacinamide As Possible Treatment For Nonarteritic Anterior Ischemic Optic Neuropathy	Yaping Joyce Liao (she/her/hers)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
185	Trends in the Utilization of Thrombolytics in Central Retinal	Akosman Sinan	Disorders of the Anterior Visual

	Artery Occlusion in the United States		Pathway (Retina, Optic Nerve, and Chiasm)
186	Efficacy of Lenadogene Nolparvovec Gene Therapy Versus Idebenone: Two Matched Adjusted Indirect Comparisons	Patrick Yu-Wai-Man	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
187	Efficacy of Hyperbaric Oxygen Therapy for Retinal Artery Occlusion: A 20-Year Retrospective Analysis	Nitsan Duvdevan-Strier (she/her/hers)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
188	Prognostic Factor of Favorable Visual Outcome in Pediatric Optic Neuritis	Sunita Sawangsribanterng (she/her/hers)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
189	Pain Features in Acute Demyelinating Optic Neuritis	Phoebe Hu (she/her/hers)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
190	Clinical and Demographic Insights into MOG-Associated Optic Neuritis: A Comprehensive Study from Alberta, Canada	Abdullah Al-Ani (he/him/his)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
191	Expression of Yeast NDI1 as a Neuroprotective Approach to Retinal Ganglion Cell Mitochondrial Deficiency in a Mouse Model of Leber's Hereditary Optic Neuropathy.	Gregory McElroy (he/him/his)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
192	Compressive optic neuropathy due to paraophthalmic artery aneurysms: Patient characteristics and neuro-ophthalmic outcomes after endovascular treatment	Gabriele Berman	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
193	Effect of Acetazolamide Use for Disc Edema after Intracranial Mass Resection	Kim Firn	Disorders of the Anterior Visual Pathway (Retina,

			Optic Nerve, and Chiasm)
194	Etiology of Optic Disc Edema: A Retrospective Cohort Study from a Tertiary Care Facility	Isabella C. Gomez Gonzalez (she/her/hers)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
195	Association Between GLP-1 Inhibitor Use and Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION) in Diabetic Patients: A Retrospective Study	Logan Allee (she/her/hers)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
196	Attrition of Retinal Ganglion Cell Complex Following Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION): A Disparity in the Structure: Function Relationship	Drenushe Krasniqi	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
197	Neuroretinal Degeneration in Leber Hereditary Optic Neuropathy Continues During the First 5 Years After Onset Without Affecting Visual Recovery Under Treatment with Idebenone	Berthold Pemp	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
198	Retrospective Clinical Analysis of Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION) in Patients Using Semaglutide	Ari August (she/her/hers)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
199	The Risk of Age-related Macular Degeneration in Multiple Sclerosis Optic Neuritis	Kannan J. Freyaldenhoven (he/him/his)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
200	Correlation Between Visual Field Index Measurements and Mean Deviation in Compressive Optic Neuropathy and Primary Open Angle Glaucoma	Setu Mehta (she/her/hers)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
201	Traumatic Optic Neuropathy: Comparison of Clinical Factors	Grant L. Howell (he/him/his)	Disorders of the Anterior Visual Pathway (Retina,

	and Visual Outcomes in Patients With Orbital Wall Fractures		Optic Nerve, and Chiasm)
202	The Impact of Obstructive Sleep Apnea Syndrome on Visual Functions in Patients with Optic Disc Drusen: A Retrospective Cross-Sectional Study	Fannie Nadeau (she/her/hers)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
203	Evaluating Diagnostic Protocols for Central Retinal Artery Occlusion (CRAO): A Retrospective Study	Trevor Lin	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
204	Developing the Mitochondrial Visual Impairment – Inherited Optic Neuropathy Impact Questionnaire (mitoVISION-IQ)	Benson S. Chen	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
205	Spontaneous Visual Recovery in Leber Hereditary Optic Neuropathy: Correlation with Residual Thickness of the Ganglion Cell Complex on OCT	Miguel A. Santiago Cruz (he/him/his)	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
206	Innovative 3D Volumetric Imaging of the Vasculature of the Human Optic Nerve Head: A New Era to Explore Vascular Vulnerability	Joseph Rizzo	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
207	Ophthalmic and Systemic Characteristics of Acute Nonarteritic Anterior Ischemic Optic Neuropathy in the NARROW cohort	Lea Lykkebirk	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
208	Semaglutide and the Risk of NAION: The Unfolding Story	Jimena T. Hathaway	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
209	Predictive Factors of Improved Final Visual Outcome in Patients with Leber Hereditary Optic Neuropathy Treated with Lenadogene Nolparvovec Gene Therapy	Robert Sergott	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)

210	Estimating “equivalent noise” in the visual system among children with neurofibromatosis type 1 and optic pathway gliomas.	Steven F. Stasheff (he/him/his)	Disorders of the Posterior Visual Pathway and Visual Processing
211	Trans-synaptic Retrograde Degeneration Of Retinal Ganglion Cell-Inner Plexiform Layer And Retinal Nerve Fiber Layer With Visual Field Defect After Posterior Cerebral Artery Infarction	BOREE KIM	Disorders of the Posterior Visual Pathway and Visual Processing
212	Face Imagery And Perception in Acquired Prosopagnosia	Jason J S. Barton (private person)	Disorders of the Posterior Visual Pathway and Visual Processing
214	Changes in Outcome Measures in Posterior Cortical Atrophy: A Pilot Study for TRAC-PCA	Victoria S. Pelak (she/her/hers)	Disorders of the Posterior Visual Pathway and Visual Processing
215	Optimizing The Screening And Early Evaluation Of Papilledema And Idiopathic Intracranial Hypertension In A Tertiary Care Hospital	Michael P. Gemmell (he/him/his)	Idiopathic Intracranial Hypertension (IIH)
216	Investigating The Correlation Between COVID-19 and Idiopathic Intracranial Hypertension: A Retrospective Cohort Study	Donia Shawn (she/her/hers)	Idiopathic Intracranial Hypertension (IIH)
217	Risk of Idiopathic Intracranial Hypertension With Hormonal Contraceptives, A TriNetX Analysis	Yusuf Ahmed	Idiopathic Intracranial Hypertension (IIH)
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221	Risk Factors for Post-Dural Puncture Headaches in Idiopathic Intracranial Hypertension	Kayla Kendall	Idiopathic Intracranial Hypertension (IIH)
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237	Neuro-ophthalmic Findings of Visual Snow Syndrome in East Asia	Hyunjin Shin (he/him/his)	Miscellaneous
238	Identifying the Association between Clinical Characteristics and Presenting Visual Acuity in Patients with Optic Neuritis: A Case-Control Study	Natalie Chen (she/her/hers)	Miscellaneous
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242	Diffusion Weighted MRI of Optic Nerves in Idiopathic Intracranial Hypertension – A Population-Based Study.	Nathan J. Arboleda (he/him/his)	Neuro-Imaging
243	Quantifying Time Savings of STAT Outpatient Neuroimaging versus ED Neuroimaging for Patients with Optic Disc Swelling	Divya Manikandan (she/her/hers)	Neuro-Imaging
244	Relation of Optical Coherence Tomography (OCT) Measures to Volumetric MRI in Pediatric-Onset Multiple Sclerosis (POMS)	Scott Grossman	Neuro-Imaging
245	Interrater Reliability of Optical Coherence Tomography Parameters in Acute Nonarteritic Anterior Ischemic Optic Neuropathy	Sedra Al Yousef (she/her/hers)	Neuro-Imaging
246	AI-Assisted Diagnosis and Grading of Papilledema from Fundus Photographs: A Comparative Study of Neuro-Ophthalmologists and ChatGPT	David N. Younessi	Neuro-Imaging
247	Ophthalmic Manifestations and Management of Cerebral Venous Thrombosis	Tony Chae (he/him/his)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
248	Lesion Location Along the Optic Nerve: Clinical and Radiographic Correlations in Myelin Oligodendrocyte Glycoprotein Antibody Disease	Amna M. Ali (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases

249	The Presence of Vitritis on Multimodal Imaging in Patients with Syphilitic Optic Neuropathy	Marko Oydanich	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
250	Optic nerve sheath meningiomas: a retrospective cohort study comparing outcomes in treated versus observed patients	Chi-Wei Tien (he/him/his)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
252	Adherence to Biologic Therapies Among Patients with Neuromyelitis Optica Spectrum Disorder (NMOSD) in the United States	Kristina R. Patterson	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
253	Meningococcal Infection With Eculizumab Or Ravulizumab In Patients With Generalized Myasthenia Gravis Or Neuromyelitis Optica Spectrum Disorder: An Analysis Of United States Clinical Practice	Shirali Pandya	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
254	Neuro-Ophthalmic Manifestations of Pachymeningitis	Reeda Bou Said	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
255	Epidemiology of Double Vision and Falls in Spinocerebellar Ataxia	Klyve Otinkorang (he/him/his)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
256	Time to Vaccination after Rituximab Discontinuation in Patients with Anti–Aquaporin–4 Antibody–Positive Neuromyelitis Optica Spectrum Disorder: A Post-hoc Analysis of the CHAMPION-NMOSD Trial	Jeffrey Bennett	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
257	Incidence of Relapses After Meningococcal Vaccination In Clinical Trials And Real-World Evidence Of Eculizumab And Ravulizumab In Anti-Aquaporin-4 Antibody-Positive	Sami Fam	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases

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258	Persistent Visual Field Defects Despite Excellent Visual Acuity Recovery in Optic Neuritis Associated with Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease	Aviv Fineberg (he/him/his)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
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260	Visual Pathway Structure and Function in Pediatric-Onset Multiple Sclerosis (POMS): Are Social Determinants of Health (SDOH) Related?	Ruben Jauregui (he/him/his)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
261	Optic Atrophy Predominant WFS1 Disorder – A Case-Control Study	Nicholas R. Levergood	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
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263	Dynamic optic nerve MRI changes in acute optic neuritis in MOG antibody-associated disease	Stephanie B. Syc-Mazurek	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
264	Association of Ocular Cranial Nerve Palsies and Risk of Future Strokes – A Systematic Review and Meta-Analysis	Reuben Chao Ming Foo (he/him/his)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
265	Genetic Associations of Non-Arteritic Anterior Ischemic Optic Neuropathy	Ryung Lee	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
266	Characterizing the Use of Remote Interpretation of	Jessica Trinh (she/her/hers)	Neuro-Ophthalmic Disorders of

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268	Isolated third cranial nerve palsy: Etiologies, demographic data, and clinical characteristics of 207 subjects	Paramat Khamlert (he/him/his)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
269	Phase 1 Healthy Volunteer Results Show Potential for Subcutaneous Administration of VRDN-003, a Half-life Extended Full Antagonist Monoclonal Antibody to IGF-1R, for Thyroid Eye Disease	Raghu Mudumbai (he/him/his)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
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271	Optic Atrophy in Wolfram Syndrome: Prevalence and Use as a Diagnostic Indicator	Bradley McNeely (he/him/his)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
272	Autonomic Symptoms Differentiate Lambert–Eaton Myasthenic Syndrome from Myasthenia Gravis among Patients with Certain Ocular Signs	Andrew Lee	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
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274	Differentiating Myasthenia Gravis and Cranial Nerve Palsies through Saccadic Eye Movement Analysis: A	Sun-Young Oh	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases

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277	Evaluating Microperimetry in Multiple Sclerosis: A Cross-Sectional Study of Disease Stages Compared to Healthy Controls	Heather E.. Moss (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
278	Impact Of Visual Snow Syndrome On Daily Life	Khadijah Farooqui (she/her/hers)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
279	Plasma calprotectin: A Blood Biomarker for Identifying Giant Cell Arteritis	Michael Stormly Hansen	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
280	Associations Between Eye Pain, Vision Loss, and Imaging Findings in Myelin Oligodendrocyte Glycoprotein Antibody Disease	Bohan Kim (he/him/his)	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
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308	Ophthalmologic Cranial Nerve Palsies and COVID-19 Infection: A Retrospective Analysis	Amal Hamed (she/her/hers)	Ocular Motility Disorders and Nystagmus
309	Risk of Oculomotor and Trochlear Nerve Palsies Following Covid-19 Vaccination	Muhammad Chauhan (he/him/his)	Ocular Motility Disorders and Nystagmus
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317	Relations Between Retinal Microstructure, Microvasculature and Microcirculation in Patients with Parkinson's Disease	Potyra R. Rosa (she/her/hers)	Ocular-Imaging
318	Non-Mydriatic Ocular Fundus Imaging On Consecutive Headache Patients In An Emergency Department (ED)	Kevin Y. Yan	Ocular-Imaging
319	Retinal Microstructural Changes in Aging Rhesus Macaques	Marco Antonio. Olivares Ordoñez	Ocular-Imaging
320	In Vivo Two-Photon Microscopy in Thy1-GcAMP Transgenic Rats Demonstrates that Electric Field Stimulation Directly Modulates Retinal Ganglion Cells	Nicholas A. Householder (he/him/his)	Ocular-Imaging
321	Features of intraretinal and subretinal fluid in non-arteritic anterior ischemic optic neuropathy	Jim Xie	Ocular-Imaging
322	Non-Mydriatic Ocular Fundus Imaging on Consecutive Neurologic and Neurosurgical Patients in an Emergency Department (ED)	Stuart J. Duffield (he/him/his)	Ocular-Imaging
323	Non-Mydriatic Ocular Fundus Imaging in a General Emergency Department: Feasibility and Findings	Nithya Shanmugam	Ocular-Imaging
324	The use of prompt engineering in a Vision-Language Model (VLM) for disc swelling identification from fundus photos	Kelvin Zhenghao. Li (he/him/his)	Ocular-Imaging

325	Machine Learning-Based Papilledema Detection Leveraging the Quantification of Optic Disc Margin Clarity	Sarah Jeanne Miller	Ocular-Imaging
326	Visual Field Threshold Changes in Normal Pressure Hydrocephalus Patients With and Without Primary Open-Angle Glaucoma	sepideh jamali dogahe	Ocular-Imaging
327	Differentiating Compressive Optic Neuropathy from Primary Open Angle Glaucoma Using the Macular Naso-Temporal Ratio	Lucy Chen (she/her/hers)	Ocular-Imaging
328	Validating Averaged OCT as a Tool for Identifying Scattering Features in the Retinas of People with MS	Sylvia E. Villarreal Navarro (she/her/hers)	Ocular-Imaging
329	Retinal vascular signs in intracranial atherosclerotic stenosis	Xuxiang Zhang	Ocular-Imaging
330	Comparative Image Quality of Slit Scan vs Xenon Flash Photography in Screening Afferent Visual System Pathologies	Megan K. Piraino (she/her/hers)	Ocular-Imaging
331	Rapid Automatized Naming and Retinal Neurodegeneration in Multiple Sclerosis and Neuro-Myelitis Optica Spectrum Disorder	Christina Marini	Ocular-Imaging
332	Lower retinal arteriolar and venular fractal dimension are associated with higher risk of incident dementia - The UK Biobank (n=65,727)	Frank van der Heide	Ocular-Imaging
333	The Relationship of Optical Coherence Tomography with Visual Outcomes in Children with Sellar Tumors	Michael T. Curley (he/him/his)	Ocular-Imaging
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335	Extraocular Muscle Enlargement in Graves' Orbitopathy: A Systematic Review and Meta-Analysis	Chris Zajner	Orbital and Eyelid Disorders
336	Retrospective Study of Orbital Tumors in the Modern Era	Swetha Sathi	Orbital and Eyelid Disorders
337	LX-101, a Novel Payload-bearing Insulin-like Growth Factor-1 Receptor Targeted Therapy, Inhibits Thyroid Eye Disease Inflammation	Collynn F.. Woeller	Orbital and Eyelid Disorders
338	Teprotumumab Efficacy and Safety in an Open-label (OL) Extension in Patients with Chronic Thyroid Eye Disease (TED)	Prem S.. Subramanian	Orbital and Eyelid Disorders
339	Systemic Effects of Teprotumumab Treatment on Thyroid Function in Patients with Thyroid Eye Disease: A Retrospective Study	Rafaella C. Penteado (she/her/hers)	Orbital and Eyelid Disorders
340	Impact of Insurance Coverage on Healthcare Access and Coordination for Patients with Thyroid Eye Disease	Shaili S. Davuluru (she/her/hers)	Orbital and Eyelid Disorders
341	Interleukin-6 Receptor Signaling Inhibition With Satralizumab in Thyroid Eye Disease: Phase 3 SatraGO-1 and SatraGO-2 Trial Design	Madhura Tamhankar	Orbital and Eyelid Disorders
343	Preliminary Safety, Efficacy, and Quality of Life Outcomes of Subcutaneous Lonigutamab (Anti–IGF-1R) from a Phase 1/2 Study of Thyroid Eye Disease (TED)	Shoaib Ugradar	Orbital and Eyelid Disorders
344	Smartphone-based artificial intelligence system for measurement of ptosis and other oculofacial measurements	Etienne Bénard-Séguin	Orbital and Eyelid Disorders
345	Evaluation of Topological Data Analysis in Detecting Papilledema Using Oral	Florin Grigorian (he/him/his)	Pediatric Neuro-Ophthalmology

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347	Impact of Neonatal Hyperbilirubinemia on Optic Nerve Parameters in Children: A Cross-sectional Study	Sally Al Hassan	Pediatric Neuro-Ophthalmology
348	The Rates of Retinal Nerve Fiber Layer Change in Children with Optic Disc Drusen	Tais Estrela (she/her/hers)	Pediatric Neuro-Ophthalmology
349	Pediatric Idiopathic Intracranial Hypertension with Venous Sinus Stenosis and Congenital Sinus System Anomalies: Outcomes Following Medical Management	Jose Cijin Puthussery	Pediatric Neuro-Ophthalmology
350	Treatment of increased intracranial pressure secondary to Otitic Hydrocephalus with corticosteroids and factors associated with treatment failure leading to procedural intervention.	Esha Prakash (she/her/hers)	Pediatric Neuro-Ophthalmology
351	Visual Hallucinations, Quality of Life, and Psychological Distress in Visually Impaired Adolescents with Charles Bonnet Syndrome	Alison Martin (she/her/hers)	Pediatric Neuro-Ophthalmology
352	Differences In The Diagnostic Approach Of Medical Trainees To A Case Of Pharmacologic Anisocoria	Thanh-Liem Huynh-Tran (he/him/his)	Pupillary Disorders

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Novel Instrument for Clinical Evaluations of Active Extraocular Muscle Tension

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Introduction:

Strabismus can be caused by abnormal tension of the extraocular muscles (EOMs) attached to the eyeball in superior, inferior, lateral, medial, superior oblique, and inferior oblique positions. Evaluating the tension in each EOM is crucial for surgical planning in strabismus, which is conducted by adjusting the tension on the EOM. The purpose of this study was to develop a compact measuring device to non-invasively evaluate the active EOM tension.

Methods:

The proposed device employed a cottontipped medical swab to transfer the EOM tension connected to the force sensor as a non-invasive medium. The tilting angle of the swab and the force of active EOMtension were wirelessly transferred to a laptop computer for recording and real-time displaying of the measured values.

Results:

The active EOM tensions for the four recti muscles were 101.7 ±15.0 g (mean ± SD) for the lateral rectus; 88.0 ± 15.4 g for the medial rectus; 61.3 ± 6.8 g for the inferior rectus; and 121.3 ± 38.5 g for the superior rectus. These values were higher than the reported values of 45–60 g measured in previous studies. In the previous studies, however, the EOM was detached from the globe and attached to a strain gauge, and, thus, there were no passive elastic forces from ocular connective tissue, resulting in lower values compared with the current study.

Conclusions:

The previous methods were also complex and not suitable for clinical measurement. Thus, the proposed method, which is non-invasive and mimics the conventional force generation test with a cotton-tipped swab, could facilitate the evaluation of active EOM tension, both clinically in paralytic strabismus management and in research into understanding its pathophysiology.

References: None provided.

Keywords: Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Vestibular rotation cancellation perception by vision in patients with increased visual dependency

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Introduction:
Our goal was to investigate differences in patients with visual dependancy compared to healthy controls utilizing perceptual measures of self-movement in situations where visual motion and vestibular signals give conflicting information.

Methods:
Recruitment was conducted at the outpatient clinic of the University Hospital Zurich. Prospective data was collected from 25 healthy individuals as well as 21 subjects with increased visual dependency. Subjects were passively rotated in space and exposed to visual stimulation that conflicted with the actual motion and the motion sensed by the vestibular system. Subjects indicated their perceived direction of self-motion. We measured how long it takes for the perception of self-motion, initially dominated by vestibular signals, to transition into being dominated by visual signals. This was carried out by a rotating chair, moving independently of a patterned drum around the chair. Runs with various conditions were performed - movement of the chair in darkness, movement of the chair and the drum with the same speed with lights on (cancellation trial) as well as movement of the chair and drum in the same direction but with different speeds with lights on (reverse trial).

Results:
In normal movement trials in darkness without visual stimuli, healthy subjects perceived the vestibular rotation for about around 10.9 seconds on average while the duration was 11.2 seconds for subjects with an increased visual dependency. The visual stimuli reduce the duration of perceived rotation to 7.7 and 4 seconds in the cancellation and reversal trials, respectively for healthy subjects, and to 7.7 and 4.3 seconds for individuals with an increased visual dependancy.

Conclusions:
On average, patients with visual dependency did not show greater reliance on visual cues when visual and vestibular self-motion stimuli conflict. We could not measure a quantifiable difference in the perception of movement when putting the vestibular and the visual systems in conflict.

References: None provided.

Keywords: Visual fields, Vestibular disorders, Non-organic visual disorders, Nystagmus, Miscellaneous

Financial Disclosures: Vergil Mavrodiev; Konrad Weber: Konrad Weber has previously acted as a paid consultant for Alexion Pharmaceuticals but declares no non-financial competing interests. Alexion Pharmaceuticals also provided some study equipment (spirometer).; Christopher J Bockisch; Luisa Manca; Fabienne Fierz

Grant Support: None.

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Investigating differences in the early visual response to a moving visual field in patients with visual dependency

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Introduction:
Our goal was to study the discrepancies in the early visual response between patients with visual dependency and healthy controls. We utilized the ocular following responses (OFRs) to moving visual fields as well as the participants' ability to suppress eye movements when instructed. OFRs are quick eye movements that track sudden movements of a textured pattern.

Methods:
The prospective data was collected from 25 healthy subjects and 9 participants with or without vestibular disorders reporting visual dependency. The subjects were seated in front of a projection screen. A field of dots was projected on the screen, including a moving central visual field with four different radii of visual angle or a moving annular visual field with a stationary center. Two sets of instructions were given: the first one allowed the subjects to follow the moving portion of the dots, and the second one instructed them to fixate a flashing cross in the center without allowing their eyes to move with the dots. Using a video eye tracker, the eye velocity was recorded.

Results:
In the healthy group, eye velocities were as follows for the biggest and the smallest radius of a moving visual field - 1.54 ± 0.71°/s (5°) and 2.78 ± 1.42°/s (60°). In the group of subjects with visual dependency, the mean velocities for the same sizes of moving visual fields were as follows: 2.21 ± 1.15°/s and 3.66 ± 1.66°/s.

Conclusions:
Subjects with visual dependency exhibited an enhanced ocular following response velocity and an enhanced response to smaller-sized stimuli compared to healthy controls. When given fixation instructions, they showed a decreased ability to suppress the OFR. The findings may contribute to a better clinical characterization of patients with visual dependency, thus forming the basis for targeted treatment approaches.

References: None provided.

Keywords: Visual fields, Vestibular disorders, Higher visual functions, Non-organic visual disorders, Miscellaneous

Financial Disclosures: Vergil Mavrodiev; Christopher J Bockisch; Konrad Weber: Konrad Weber has previously acted as a paid consultant for Alexion Pharmaceuticals but declares no non-financial competing interests. Alexion Pharmaceuticals also provided some study equipment (spirometer).; Luisa Manca; Fabienne Fierz

Grant Support: None.

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Automated Retinal Vascular Fractal Analysis Can Distinguish Presymptomatic Alzheimer's Disease

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Introduction:
Retinal vasculopathy had been reported across the continuum of neurodegeneration. Retinal color fundus photography coupled with automated retinal vascular analysis offers potential to non-invasively screen for Alzheimer's disease (AD) neurodegeneration. Amyloid positron emission tomography (PET) and apolipoprotein 4 (APOE4) carrier status are known biomarkers of AD risk. Herein, we examined the relationship between retinal vascular fractal dimensions in non-mydriatic color fundus photographs, amyloid-PET and APOE4 carrier status in a cohort of individuals with intact cognition.

Methods:
Our dataset included 91 macula-centered and 39 optic disc-centered images from 96 cognitively intact participants (29% male). 25 (26%) were amyloid-PET positive, defined as amyloid-PET standardized uptake value ratio centiloid cut-off > 20. AutoMorph software automatically determined retinal arteriolar and venular density, tortuosity and width, among other fractal dimensions. To test the effect of amyloid-PET status on the vascular parameters, we used a generalized linear model compensated for age, sex and the interaction between APOE4 carrier and amyloid-PET status. A t-test corrected for age and gender compared amyloid-PET positive and negative subjects for vascular fractal dimensions. We adjusted for multiple comparisons using the False Discovery Rate correction and reported significant P values that were less than 0.05.

Results:
Compared to amyloid-PET negative, cognitively intact amyloid-PET positive cohort had greater mean age (71 vs 66 years, P=0.06), more males (60% vs 35%, P=0.02), more APOE4 carriers (P< 0.001), similar vascular risk factors and significantly lower macular vessel tortuosity density (P=0.019). The amyloid-PET positive status had a significant effect on the retinal artery distance tortuosity (corrected P=8.75E-04, β=13.9, 95% CI [7.75-19.99]) and artery squared curvature tortuosity (corrected P=8.91E-10, β=464, 95% CI [359.10-569.15]).

Conclusions:
Automatically determined retinal vascular fractal dimensions on non-mydriatic color fundus photos predict amyloid-PET burden. Future longitudinal studies should assess the utility of automated quantitative retinal vasculopathy analysis to screen for presymptomatic AD.

References: None provided.

Keywords: Higher visual functions, Retina, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Visual symptoms correlated with visual function in a cohort of patients with Optic Disc Drusen

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Introduction:
Optic disc drusen (ODD) is a degenerative optic neuropathy affecting approximately 2% of the population. This study investigated the correlation between visual symptoms, structural anatomy of the optic nerve head, and visual function in patients with ODD.

Methods:
Patients with ODD, enrolled from November 30, 2017, to February 29, 2024, in a prior study and consenting to future contact, were invited to participate. Participants completed a National Eye Institute Visual Function Questionnaire-25 adapted for ODD (VFQ-25+). Patients had previously undergone OCT scans of the ONH and macula per ODDS Consortium OCT scanning guidelines. Eyes were classified into two groups based on ODD location relative to Bruch's membrane opening: superficial (above) and deep (below). Additionally, all patients underwent a 30-degree automated perimetric visual field examination.

Results:
128 patients (252 eyes) were included. The most frequently reported symptoms were transient visual obscurations (68.7%) and nyctalopia (65.6%) with no significant differences among groups ($p = 0.89$ and $p = 0.68$, respectively). There was no significant difference in VFQ-25+ scores between groups ($p = 0.19$). Correlation analyses revealed a weaker impact of deep ODD on perceived visual function, with peripapillary RNFL volume at -0.06 compared to 0.26 for superficial ODD. Macular GCL volume correlations were also lower for deep ODD (0.17 versus 0.37). Stronger correlations were observed between perimetric mean deviation (MD) and ODD size in superficial ODD (0.74) compared to deep ODD (0.35). The superficial ODD group showed worse MD and significant thinning of peripapillary RNFL, macular GCL, IPL, and INL layers (p-values < 0.001).

Conclusions:
Despite consistent symptom reporting across ODD locations, superficial ODD correlated with greater visual function decline, indicated by worse perimetric MD and significant retinal thinning. However, minimal impact on VFQ-25+ scores suggest these changes may not be readily perceived by patients, indicating a complex interaction between ODD location and visual symptoms.

References: None provided.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Applying an Alternate Threshold of Clinically Relevant Visual Acuity Change When Assessing the Natural History of Leber Hereditary Optic Neuropathy

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Introduction:
The Case Record Survey (CRS-2; NCT02796274) was designed to enhance understanding of the natural history of Leber hereditary optic neuropathy (LHON) in idebenone-naïve patients. In this post-hoc analysis, visual acuity (VA) outcomes were re-assessed using an FDA-recommended benchmark for clinically relevant VA change.

Methods:
Data were extracted from multinational case records of patients aged ≥12 years, with a confirmed m.11778G>A, m.3460G>A or m.14484T>C mitochondrial DNA (mtDNA) mutation, onset of symptoms (OoS) after 1999, and ≥2 VA assessments (VAA) within 5 years of OoS. Baseline (BL) was the first VAA after OoS. Only subacute/dynamic eyes (≤1 year from OoS at BL) were included in the presented analyses. Spontaneous clinically relevant recovery, and worsening (sCRR and sCRW, respectively) were calculated as previously described [1], but using a VA threshold of ±0.3 logMAR rather than ±0.2 logMAR.

Results:
Individual analyses were conducted at 12 (n = 96) and 24 months (n = 44) post-BL (i.e., eyes with VAA at 12±3 and/or 24±3). At 12 months, the rates of sCRR and sCRW using ±0.2 and ±0.3 logMAR thresholds, respectively, were; sCRR: 12.5% (12/96) and 12.5% (12/96); sCRW: 65.8% (50/76) and 65.8% (50/76). At 24 months, the corresponding rates were; sCRR: 27.3% (12/44) and 25.0% (11/44); sCRW: 45.7% (16/35) and 40.0% (14/35). The rate of sCRR/sCRW varied according to the causative mtDNA mutation, with the most favorable outcomes observed for m.14484T>C. Using the ±0.3 logMAR threshold: sCRR was 50.0% (6/12) at 12 months and 66.7% (2/3) at 24 months; sCRW was 33.3% (4/12) at 12 months and 0% (0/3) at 24 months.

Conclusions:
CRS-2 provides important insights into the natural history of LHON and the impact of causative mutations. The analyses presented here highlight a moderate impact on outcomes when using a more stringent threshold for clinically relevant VA change.

References: [1] Yu-Wai-Man P, et al. Therapeutic benefit of idebenone in patients with Leber hereditary optic neuropathy: The LEROS nonrandomized controlled trial, Cell Reports Medicine, 5:101437, 2024.

Keywords: Optic neuropathy, Genetic disease

Financial Disclosures: Neringa Jurkute: NJ received research support from Chiesi Farmaceutici.; Patrick Yu-Wai-Man: Consulting: GenSight Biologics, Stoke Therapeutics, Transine Therapeutics; Speaker honoraria and/or financial support: GenSight Biologics, Santhera Pharmaceuticals; Valerio Carelli: VC is a consultant for GenSight Biologics, Chiesi, Stoke, and Pretzel.; Xavier Llòria: XL is an employee of Chiesi Farmaceutici S.p.A.; Magda Joana Silva: MJS received honoraria or consultation fees from Chiesi and Santhera Pharmaceuticals.; Thomas Klopstock: Thomas Klopstock received research support and/or personal compensation for presentations and/or consulting from GenSight Biologics and Chiesi Farmaceutici.

Grant Support: The Case Record Survey (CRS-2) was funded by Santhera Pharmaceuticals

Contact Information: None provided.

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New Onset Non-arteritic Ischemic Optic Neuropathy In Confirmed COVID-19 infections: A Retrospective Study

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Introduction:
Non-arteritic ischemic optic neuropathy (NAION) results from compromised blood flow to the optic nerve, causing acute, painless vision loss, primarily in older adults. While neuro-ophthalmologic complications linked to COVID-19 are documented, post-COVID NAION cases remain underreported. This study examines the potential connection between COVID-19 infection and NAION onset.

Methods:
This retrospective cohort study analyzed the demographics, comorbidities, and clinical data of post-COVID NAION patients from an IRB-approved University of Missouri database. A linear regression analysis was conducted to explore the relationship between COVID-19 diagnosis timing and NAION onset. We report the average time to diagnosis and common risk factors, including smoking, hypertension, and diabetes, across 9 cases.

Results:
Nine post-COVID NAION patients were included. The average age at diagnosis was 60.8 years, with 77.8% (n=7) female and 22.2% (n=2) male. Comorbidities included smoking (33.3%), diabetes (33.3%), and hypertension (44.4%). Only 2 patients had pre-COVID ophthalmologic evaluations. The average time from COVID-19 diagnosis to NAION onset was 306 days (range: 49–735 days), and linear regression indicated a positive association between longer time intervals and increased likelihood of NAION.

Conclusions:
While our data do not establish a direct causal link between COVID-19 and NAION, the significant time interval between infection and NAION onset suggests that COVID-19 may act as a precipitating factor for ischemic optic neuropathy. The persistent inflammatory response following COVID-19 infection could lead to delayed vascular changes in the optic nerve. The linear regression analysis further supports the notion that the onset of NAION may be influenced by the time elapsed since infection. Future studies with larger cohorts, detailed imaging, and longitudinal follow-up are essential to further explore this relationship and better understand the risk factors contributing to post-COVID neuro-ophthalmologic complications.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Clinical Relevance of Plasma Limitrin Level in Patients with MOG-IgG-Positive Optic Neuritis

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Introduction:
To evaluate the plasma concentration of limitrin and elucidate its clinical relevance in patients with myelin oligodendrocyte glycoprotein (MOG)-immunoglobulin G (IgG)-positive optic neuritis (ON).

Methods:
We conducted a prospective case-control study involving 33 patients diagnosed with ON (12 MOG-IgG-positive and 21 MOG-IgG-negative) and 30 healthy controls. Plasma limitrin and MOG-IgG levels were measured using enzyme-linked immunosorbent assay and a cell-based assay, respectively. The correlation between plasma limitrin levels and MOG-IgG titers in patients with ON was analyzed. Receiver operating characteristic (ROC) curve analysis was performed to assess the diagnostic potential of plasma limitrin.

Results:
Patients with MOG-IgG-positive ON demonstrated significantly higher mean plasma limitrin levels (2.76 ng/mL) compared to both healthy controls (0.74 ng/mL) and patients with MOG-IgG-negative ON (1.43 ng/mL) ($p < 0.001$). A significant positive correlation was observed between plasma limitrin and MOG-IgG levels in ON patients ($r = 0.55$, $p = 0.001$). ROC analysis revealed that a plasma limitrin level of 1.22 ng/mL could predict MOG-IgG positivity with 100% sensitivity and 52.4% specificity (Area Under the Curve = 0.806, $p < 0.001$).

Conclusions:
Plasma limitrin levels were significantly elevated in MOG-IgG-positive ON and correlated with MOG-IgG titers. These findings suggest that limitrin may play a role in the pathogenesis of MOG-IgG-positive ON and could serve as a potential biomarker for disease diagnosis. Further research is warranted to validate these results in larger cohorts and explore the specific mechanisms linking limitrin to MOG-IgG-associated diseases.

References: None provided.

Keywords: Optic neuritis, Demeylinating disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Comparing Scotoma Characteristics in Leber Hereditary Optic Neuropathy Versus Toxic-Nutritional Optic Neuropathy

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Introduction:
Leber hereditary optic neuropathy (LHON) and toxic-nutritional optic neuropathies (TNON) primarily affect optic nerve fibers in the papillomacular bundle, leading to central visual loss. LHON is an inherited mitochondrial disease, whereas TNON occurs secondary to exposure to toxins or nutritional deficiencies. We aim to compare scotoma characteristics to help differentiate LHON and TNON.

Methods:
Patients were retrospectively identified from a single quaternary referral center using ICD-10 codes for LHON and TNON. Inclusion criteria required formal visual fields and appropriate history and laboratory testing to confirm diagnosis. Primary outcomes were pattern of visual field loss (central scotoma vs. other), and central scotoma size measured in degrees along the horizontal meridian. Patterns were analyzed using mixed effect logistic regression, and scotoma size via a linear mixed effect model, with diagnosis as the primary exposure of interest, after controlling for age, sex, race and smoking status.

Results:
53 patients were included (30 LHON, 9 nutritional optic neuropathy, 9 toxic optic neuropathy and 5 mixed TNON). Of these, 38 (71.7%) were male, and mean age at time of vision loss was 36.6 ± 17.1 years. The mean horizontal scotoma diameter was 27.6 ± 16.2 degrees in LHON versus 13.6 ± 10.2 degrees in non-LHON patients. Controlling for other variables, LHON patients were 2.18 times more likely than non-LHON patients to have central scotoma, although this was not statistically significant. Scotoma size was on average 12.67 degrees higher in LHON than non-LHON patients (p=0.022).

Conclusions:
Compared with TNON patients, patients with LHON tend to have central scotomas as opposed to other patterns on automated perimetry. They were also found to have significantly larger scotomas compared with TNON patients. These results highlight the severity of central vision loss in LHON and can help further differentiate between the two conditions, especially in the absence of other genetic or clinical markers.

References: None provided.

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

Financial Disclosures: Altug Ay; Florian Guillot; Yan Wang; Ximin Li; Amanda Henderson: None related to this submission: Horizon Therapeutics/Amgen.; Andrew Carey: None related to this submission: Horizon Therapeutics/Amgen, Bristol-Myers-Squibb, Springer publishing.

Grant Support: None.

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Assessing the Treatment Effect of Idebenone in Leber Hereditary Optic Neuropathy Using an Alternate Threshold of Clinically Relevant Visual Acuity Change

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Introduction:
In LEROS, a Phase IV, open-label, natural-history (NH) controlled study (NCT02774005), with a 2-year follow-up, idebenone improved visual acuity (VA) outcomes for patients with Leber hereditary optic neuropathy[1], although response varied by disease phase and mitochondrial DNA (mtDNA) mutation. In this post-hoc analysis, VA outcomes were re-assessed using an FDA-recommended threshold for clinically relevant VA change.

Methods:
Clinically relevant benefit (CRB), recovery (CRR), and worsening (CRW) were assessed in idebenone-treated and matched NH eyes at 12 months, as previously described[1]; however, clinically relevant VA change was defined as ±0.3, rather than ±0.2 logMAR. Eyes were stratified by time since onset at baseline; subacute/dynamic (≤1 year) and chronic (>1 year), and by mtDNA mutation; m.11778G>A, m.3460G>A, m.14484T>C.

Results:
Similar trends in VA outcome by disease phase were observed compared to previous analyses[1]. In the subacute/dynamic phase, idebenone-treated eyes exhibited a significantly higher CRB rate (36.6% [52/142] vs 20.7% [40/193], p=0.039, OR 1.75), and significantly lower CRW rate (23.1% [27/117] vs 53.1% [69/130], p< 0.001, OR 0.31), compared to matched NH eyes. CRR was observed in 26.1% (37/142) of idebenone-treated eyes vs 17.6% (34/193) of matched NH eyes (p=0.538, OR 1.20). In the chronic phase, idebenone-treated eyes exhibited a significantly higher CRB (46.2% [66/143] vs 36.6% [56/153], p=0.031, OR 1.71) and CRR rate (26.6% [38/143] vs 16.3% [25/153], p=0.016, OR 2.03), and a significantly lower CRW rate (3.1% [3/96] vs 12.4% [11/89], p=0.010, OR 0.20) compared to matched NH eyes. Assessing outcomes by mutation, similar trends were observed as in previous analyses[1], although the magnitude of difference in CRR/CRW (treated vs NH) was different in some cases.

Conclusions:
This re-assessment of LEROS data using the FDA's stricter threshold for clinically relevant VA change demonstrates that idebenone improves outcomes in many cases; however, treatment effect can vary dependent on disease phase and mtDNA mutation.

References: Yu-Wai-Man P, et al. Therapeutic benefit of idebenone in patients with Leber hereditary optic neuropathy: The LEROS nonrandomized controlled trial, Cell Reports Medicine, 5:101437, 2024.

Keywords: Optic neuropathy, Genetic disease

Financial Disclosures: Marcela Votruba: MV received honoraria or consultation fees from Santhera Pharmaceuticals, Chiesi Farmaceutici S.p.A, GenSight Biologics, and Stoke Therapeutics.; Patrick Yu-Wai-Man: Consulting: GenSight Biologics, Stoke Therapeutics, Transine Therapeutics; Speaker honoraria and/or financial support: GenSight Biologics, Santhera Pharmaceuticals; Valerio Carelli: VC is a consultant for GenSight Biologics, Chiesi, Stoke, and Pretzel.; Xavier Llòria: XL is an employee of Chiesi Farmaceutici S.p.A.; Magda Joana Silva: MJS received honoraria or consultation fees from Chiesi and Santhera Pharmaceuticals.; Thomas Klopstock: Thomas Klopstock received research support and/or personal compensation for presentations and/or consulting from GenSight Biologics and Chiesi Farmaceutici.

Grant Support: The LEROS study was funded by Santhera Pharmaceuticals.
Contact Information: None provided.

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The Effects Of Optic Nerve Head Disc Area on Visual Acuity, Retinal Nerve Fiber Layer, and Visual Field In Leber's Hereditary Optic Neuropathy

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Introduction:
Leber's Hereditary Optic Neuropathy (LHON) is characterized by deficits in functional visual acuity (VA), retinal nerve fiber layer (RNFL), and visual field (VF). This study evaluates the impact of optic nerve head disc area on treatment response to idebenone over 12 months, comparing results to a matched cohort of carriers.

Methods:
We retrospectively analyzed LHON patients with onset ≥ 12 months prior aged 5 to 77 years. All three primary mutations (m.3460G>A/MT-ND1, m.11778G>A/MT-ND4, m.14484T>C/MT-ND6) were included. Patients received idebenone (300 mg TID) for ≥ 12 months, with VA and RNFL measured in 62 patients and VF in 46. Primary outcome measures—VA (LogMAR), VF (mean dB), and RNFL average (μm)—were compared to matched LHON carriers (N=19) in comparison to disc area. Statistical analyses included residual plots, linear models, and paired t-tests using R software ($p < 0.05$).

Results:
VA outcomes for idebenone-treated patients showed significant improvement, indicated by a negative linear regression for disc area (p=0.005, t=-2.831). RNFL outcomes were also significant with a positive regression (p=0.01, t=2.523), suggesting that larger disc areas correlate with better visual recovery. In contrast, VF outcomes did not reach significance (p=0.2, t=1.335).

Conclusions:
A larger optic nerve disc area was associated with improved recovery in VA and better RNFL preservation compared to smaller discs. A larger disc may preserve more fibers from damage and inflammation, while a smaller disc may indicate mechanical crowding, leading to increased damage to adjacent fibers. These findings underscore the importance of the disc area in managing LHON and suggest potential pathways for treatment optimization.

References: 1. Carelli V, d'Adamo P, Valentino ML, et al. Parsing the differences in affected with LHON: genetic versus environmental triggers of disease conversion, Brain: a journal of neurology, Vol. 139 (Pt 3), 2016. 2. Carelli, V., Ross-Cisneros, F. N., & Sadun, A. A. Mitochondrial dysfunction as a cause of optic neuropathies. Progress in retinal and eye research, Vol. 23(1), 53–89, 2004. 3. Borrelli E, Bandello F, Boon CJF, et al. Mitochondrial retinopathies and optic neuropathies: The impact of retinal imaging on modern understanding of pathogenesis, diagnosis, and management, Prog Retin Eye Res, Vol. 101, 2024. 4. Barboni P, Savini G, Valentino ML, et al. Leber's hereditary optic neuropathy with childhood onset. Invest Ophthalmol Vis Sci., Vol.47(12), 5303–5309, 2006

Keywords: Visual fields, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Optic nerve trauma and treatment, Neuroimaging, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Visual Outcomes Of First Affected Eye Vs. Second In Leber's Hereditary Optic Neuropathy Patients

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Introduction:
Leber's Hereditary Optic Neuropathy (LHON) is a mitochondrial optic neuropathy characterized by bilateral vision loss with asymmetrical onset. While both eyes experience significant deterioration, uncertainty remains regarding the relative severity of visual outcomes between them. This study aimed to assess differences in visual acuity (VA), visual field (VF), and optical coherence tomography (OCT) measurements between the first and second affected eyes in LHON patients.

Methods:
We retrospectively analyzed 114 eyes from 57 patients diagnosed with LHON between 2009 and 2024. Patients received idebenone (N=49) for ≥12 months. The cohort included 11 females and 46 males, with three primary mutations (m.3460G>A/MT-ND1, m.11778G>A/MT-ND4, m.14484T>C/MT-ND6). Primary outcome measures included VA (LogMAR), VF (mean dB), and retinal nerve fiber layer (RNFL) thickness on OCT, comparing the first to the second affected eye. Statistical analyses included paired t-tests, with significance set at $p < 0.05$, using R software.

Results:
A significant difference in final VF was observed between the first and second affected eyes. The first affected eye had a mean VF of -16.30 ± 10.85, while the second affected eye was -18.37 ± 9.8 ($t = 2.48$, $p = 0.016$). No significant differences were observed in VA (first eye: 1.29 ± 0.65; second eye: 1.20 ± 0.76, $t = 1.03$, $p = 0.30$) or OCT RNFL average (first eye: 62.49 ± 15.23; second eye: 63.09 ± 15.79, $t = -0.64$, $p = 0.52$). Among mutation carriers, 14.28% were female with the 11778 mutations, while males had the following distributions: m.3460 (10.20%), m.11778 (67.34%), and m.14484 (8.16%).

Conclusions:
Our data indicated significantly worse VF in the second affected eye, possibly reflecting the decreased efficacy of idebenone when given sooner. Further research is needed to explore these underlying factors and develop individualized treatment strategies for managing bilateral LHON.

References: 1. Carelli, V., Ross-Cisneros, F. N., & Sadun, A. A. Mitochondrial dysfunction as a cause of optic neuropathies. Progress in retinal and eye research, Vol. 23(1), 53–89, 2004. 2. Borrelli E, Bandello F, Boon CJF, et al. Mitochondrial retinopathies and optic neuropathies: The impact of retinal imaging on modern understanding of pathogenesis, diagnosis, and management, Prog Retin Eye Res, Vol. 101, 2024. 3. Carelli V, d'Adamo P, Valentino ML, et al. Parsing the differences in affected with LHON: genetic versus environmental triggers of disease conversion, Brain: a journal of neurology, Vol. 139 (Pt 3), 2016.

Keywords: Optic neuropathy, Visual fields, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease, Optic nerve trauma and treatment, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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The correlation between HLA class II variants and patients diagnosed with Ethambutol-induced Optic Neuropathy (EtON)

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Introduction:
Ethambutol (EMB) -induced Optic neuropathy (EtON) is a known adverse effect but its exact etiopathogenesis is still unknown. Recent NTEP guidelines allow the prolonged use of EMB increasing the cumulative drug exposure and hence the risk of EtON. To ensure that the duration and dosage of this drug are convenient and safe, it is prudent to identify population at risk. We aimed to assess the association of HLA Class II alleles in patients with EtON.

Methods:
Prospective observational case-control study carried on 100 patients with EtON and 190 patients on ATT without visual complaints. Clinical, neuro-ophthalmological, serum and CSF investigations were carried out. All possible risk factors of EtON were noted. 5 ml of blood sample was stored in EDTA Vial at -20 C. DNA was isolated using Qiagen Mini kit which was further processed for HLA Typing using PCR-SSP method.

Results:
Median age of the patients was 47 (18-73) years. Median duration of EMB intake was 6 (2-23) months in cases and 6 (6-9) months in controls. Majority of the patients had pulmonary tuberculosis (TB). Median dosage of EMB was 18.83 (10.5-36.53) mg/kg/day. Among those with EtON, 80% experienced severe vision loss, and 59% had complete loss of the visual field. Allele frequency of HLA-DQB1*05:01 was significantly high in cases than controls ($p = < 0.0001$). Similarly, allele frequency of HLA-DQB1*03:01 ($p=0.03$); HLA-DRB1*03:01 ($p=0.04$) and HLA-DRB1*12:01 ($p = 0.03$) was higher in cases than controls. HLA-DQB1*05:01 was found to be significantly associated with low cumulative dose (< 150 grams) on univariate analysis.

Conclusions:
This is the first study highlighting the association of EtON with HLA Class II alleles and providing an insight into the role of HLA alleles in understanding the etiopathogenesis. Identifying population at risk is prudent in order to decide surveillance strategies specifically related to dose and duration of EMB.

References: None provided.

Keywords: Optic neuropathy, Optic neuritis, Retina, Visual fields, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Increased Toxic Lipids as Biomarker of Non-arteritic Anterior Ischemic Optic Neuropathy

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Introduction:
Non-arteritic anterior ischemic optic neuropathy (NAION) is the most common acute optic neuropathy in adults ≥ 50 years, leading to irreversible vision loss. Key risk factors for NAION include aging, cardiometabolic and vascular diseases, sleep apnea, and disc-at-risk. However, we do not understand how these risk factors lead to disease. Additionally, there is currently no effective treatment – a critical unmet need. Hence, we aimed to identify novel disease biomarkers and therapeutic targets for NAION.

Methods:
We prospectively recruited 51 NAION patients (median age 64Y, 72% male) and 14 healthy controls (median age 41, 43% male) and collected fasting blood, which was immediately processed and stored. We extracted plasma lipids for an LC/MS-based validated targeted lipidomic analysis. Statistically relevant lipids were identified based on p-value< 0.05 and a fold change ≥2 and further analyzed.

Results:
We quantified 719 plasma lipids in 51 NAION and 14 controls. Principal component analysis showed clear separation of NAION and control groups. Of these, 54 lipids were significantly altered in the NAION group (50 increased, 4 decreased), including 4 ceramides, 4 cholesteryl esters, 19 diacylglycerols, 2 phosphatidylcholines, 8 phosphatidylethanolamines, 2 sphingomyelins, and 15 triacylglycerols. Increased ceramides have been implicated in initiating oxidative stress-induced apoptotic cell death in retinal ganglion cells(1), photoreceptors, and is associated with cardiometabolic diseases,(2) and cerebral small vessel disease.(3-5) Alterations in 8 docosahexaenoic acid(22:6)-containing lipids, essential compounds for a healthy retina, were also observed.

Conclusions:
There was significant upregulation of toxic lipids in NAION compared with healthy controls – a novel biomarker of disease and clue to the pathogenesis of NAION. Studies of lipidomics in NAION may lead to better understanding of disease pathogenesis, and modulation of lipids may be a particularly important therapeutic approach. In fact, treatment to rapidly modulate systemic lipids has already been proposed for NAION.(6)

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

Financial Disclosures: Anas Alkhabaz; Karanvir Kaushal; Rishita Pujari; Jamie Zhang; Ping Zhu; Mengying Fu; Shannon Beres; Yuqin Dai; Yaping Joyce Liao: Consulting: Stoke Therapeutics

Grant Support: None.

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Metabolic Therapeutic Using Niacinamide As Possible Treatment For Nonarteritic Anterior Ischemic Optic Neuropathy

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Introduction:
Axonal health is dependent on nicotinamide adenine dinucleotide (NAD+)[1], and niacinamide (NAM), a NAD+ precursor, is robustly neuroprotective in animal studies[2,3] and currently in clinical trials for glaucoma[4,5]. We asked whether NAM treatment impacts outcome in nonarteritic anterior ischemic optic neuropathy (NAION).

Methods:
We induced photochemical thrombosis model of NAION, treated mice for 5-weeks with oral NAM 550 mg/kg/day (~3000 mg/day in humans), and assessed visual function. We also performed retrospective analysis of NAION patients with visual acuity 20/40 or worse treated with NAM 3000 mg/day within 3-months of onset and follow-up up to 1-year. We analyzed high-contrast visual acuity outcomes in NAION+NAM group (22 eyes, 21 patients, median age 68Y, 70% male) and NAION-no-NAM group (12 eyes, 11 patients, median age 69Y, 62% male).

Results:
In mouse model of NAION, the NAM-treated group exhibited significant improvement of vision, including optokinetic responses and pattern electroretinogram P1-N2 amplitudes at 1 and 5 weeks relative to vehicle-treated group ($p=0.0043$, $p=0.0022$, $p=0.001$, $p=0.036$, respectively). In human study, we fitted a linear mixed-effects model to analyze the effect of treatment on visual acuity over time, with age and gender as covariates. The model indicates a significant interaction between time since onset and treatment group in predicting LogMAR trajectories ($p = 0.0078$). Negative interaction estimate (-0.0018) means that the NAM-treated group shows a steeper decrease in LogMAR, reflecting greater improvement over time in the NAION+NAM group. As more time passes, there was increasing disparity in visual improvement between the two groups. Age also had significant association ($p = 0.0025$), with older participants experiencing greater visual impairment, while gender did not affect visual acuity.

Conclusions:
Oral NAM treatment is associated with improved visual outcome in animal model of NAION and in patients with NAION. The efficacy of NAM in NAION should be evaluated in a randomized clinical trial.

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Keywords: Optic neuropathy

Financial Disclosures: Yaping Joyce Liao: Consulting: Stoke Therapeutics; Rishita Pujari; Shweta Modgil; Jamie Zhang; Yulan Ren; Min Young Kim; Miaomiao Yu; Ping Zhu; M. Ali Shariati; Heather Moss; Shannon Beres; Liping Liu

Grant Support: None.

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Trends in the Utilization of Thrombolytics in Central Retinal Artery Occlusion in the United States

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Introduction:
Several studies have suggested that thrombolytics may be effective for central retinal artery occlusion (CRAO). In 2019, the AAO released Preferred Practice Patterns recommending immediate referral of CRAO presentations for acute intervention and workup. While there are no randomized clinical trials of thrombolytics for CRAO, thrombolysis can be considered for CRAO if given within 4.5-6 hours according to the American Heart Association Scientific Statement. This study investigates trends in thrombolytics utilization and practice patterns in the United States (US) in recent years.

Methods:
A retrospective cross-sectional study of patients (≥18 years old) admitted with a primary diagnosis of CRAO (ICD-10: H34.1) in the US was conducted utilizing the National Inpatient Sample and National Emergency Department Sample from 2016 through 2021. Patient sociodemographics, geographic trends, hospital characteristics, inpatient length of stay, total charge incurred, and thrombolytics utilization rates were analyzed.

Results:
A total of 5,659 patients with CRAO were identified, of which 270 (4.8%) received thrombolysis. The number of cases treated with thrombolysis increased over the study period, with a notable stepwise jump from 2016-2018 (98 cases) to 2019-2021 (172 cases). In hospitalized patients, thrombolysis utilization was highest in the South (34.8%) and Midwest (26.8%), and lower in the Northeast (20.9%) and West (17.5%). On multivariate analysis, male sex was significantly less associated with thrombolysis administration (OR: 0.59; $p< 0.05$). Intracerebral hemorrhage (ICD-10: I61) occurred in 8 cases (0.15%) in the non-thrombolysis group versus 4 cases (1.47%) in the thrombolysis group ($p< 0.01$). The average length of hospital stay was 2.72 days, which did not differ across treatment cohorts. However, patients receiving thrombolysis had higher total charges compared to the non-thrombolysis cohort ($89,186 versus $38,882; $p< 0.001$).

Conclusions:
While only a small percentage of CRAO's receive thrombolysis, this study highlights an increase in thrombolytics use in recent years with notable variability across US geographies.

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Keywords: Retina, Stroke, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: Virginia Lions Eye Institute Foundation Research Grant

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Efficacy of Lenadogene Nolparvovec Gene Therapy Versus Idebenone: Two Matched Adjusted Indirect Comparisons

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Introduction:
Lenadogene nolparvovec is an intravitreal gene therapy (LNGT) for LHON patients carrying the m.11778G>A MT-ND4 mutation.

Methods:
To estimate the relative treatment effects of LNGT vs. idebenone, we performed two matched adjusted indirect comparisons (MAICs) between LNGT results from the REFLECT study (individual patient level) and idebenone results from the LEROS or EAP study (aggregated data). Matching covariates included age at disease onset, gender, baseline best-corrected visual acuity (BCVA), and time from vision loss to treatment. The outcomes of interest were clinically relevant recovery (CRR) from nadir at 24 months, time to initial CRR in responders, and change from baseline of BCVA at 24 months.

Results:
For the MAIC REFLECT bilateral vs. LEROS, the effective sample size (ESS) was 77.08. A higher CRR at 24 months was observed with LNGT compared to idebenone: 60.4% vs. 35.4%; odds ratio (OR): 2.78, 95% CI [1.53; 5.06]; P=0.001. No statistically significant difference was observed between LNGT and idebenone regarding time to initial CRR and delta change from baseline BCVA at 24 months. All sensitivity analyses were consistent with the main analysis. For the MAIC REFLECT bilateral vs. EAP study, there was a low overlap of the two populations related to a difference in the time from vision loss to treatment (8.4 [3.4] vs. 4.3 [2.7] months; P < 0.001). After matching, the ESS was 10.48, with 16 patients in the LNGT group, making interpretation of the results difficult. When removing the time from vision loss covariate in the sensitivity analysis, the weighted difference in CRR was 76.7% for LNGT vs. 39.0% for idebenone (OR: 5.16 [2.14; 12.46]; P < 0.001).

Conclusions:
The two MAICs comparing data from the REFLECT bilateral population with those from the LEROS or EAP study demonstrated a higher recovery rate at 24 months with LNGT compared with idebenone.

References: None provided.

Keywords: Optic neuropathy, Genetic disease

Financial Disclosures: Patrick Yu-Wai-Man: Consulting: GenSight Biologics, Stoke Therapeutics, Transine Therapeutics; Speaker honoraria and/or financial support: GenSight Biologics, Santhera Pharmaceuticals; Nancy Newman: Consultant for GenSight, Chiesi, Neurophth (all involved with the treatment of Leber hereditary optic neuropathy. Research support as PI to my institution from GenSight for clinical trials.; Valerio Carelli: VC is a consultant for GenSight Biologics, Chiesi, Stoke, and Pretzel.; Valérie Biousse: Consultant for Topcon which commercializes fundus cameras. The current research is completely independent from Topcon and is not funded by the company.; Adeline Pierache; François Montestruc: FM is the CEO of eXYSTAT and is consultant for AbbVie, Arcagy, ARTIC, Biocodex, Bioprojet, Carely, CEVA, Cureety, Eurofins, Geneuro, GenSight Biologics, IFM, Imcheck, Mapreg, Orphelia, Ose immunotherapeutics, Pfizer, PTC and Takeda.; Magali Taiel: MT is an employee of GenSight Biologics.; José-Alain Sahel: JAS is a consultant/contractor for Avista Therapeutics and Tenpoint; has financial interests (stock/stock options) in GenSight Biologics, Sparing Vision, Prophesee, Chronolife, Tilak Healthcare, VegaVect, Inc., Avista, Tenpoint, SharpEye, Celanese and Netramind; is owner/co-owner/founder/co-founder for Gensight Biologics, Sparing Vision, Avista, Tenpoint, Prophesee, Chronolife, Tilak Healthcare, SharpEye, Celanese, Vegavect and Netramind; participates in scientific advisory board for Gilbert Foundation, Foundation Fighting Blindness, Institute of Ophthalmology Basel and Senses Institute Lausanne; is an observer at Gensight Biologics, SparingVision, Avista and Vegavect; is President of Fondation Voir et Entendre (Paris) and StreetLab (Paris); has patent for allotopic expression, rod-derived cone viability factor and related patents; is a recipient for patent royalties and GenSight Biologics.

Grant Support: None.

Contact Information: None provided.

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Efficacy of Hyperbaric Oxygen Therapy for Retinal Artery Occlusion: A 20-Year Retrospective Analysis

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Introduction:
Retinal artery occlusions (RAO), including central (CRAO) and branch (BRAO) occlusions, are medical emergencies with serious ocular and systemic implications, requiring prompt diagnosis and intervention.1,2. Without treatment, less than 20% of patients regain functional vision in the affected eye.3. Several treatment options have been proposed for CRAO, including intra-arterial thrombolysis 4, systemic thrombolysis, lowering of intraocular pressure and hyperbaric oxygen therapy. However, there is no consensus on the most effective approach 1,2. Studies suggest that HBOT may enhance oxygen delivery to ischemic tissues, potentially mitigating retinal damage in CRAO and BRAO 5,6,7. Nevertheless, its effectiveness remains debated, warranting further research. This study aims to evaluate the efficacy of HBOT in managing CRAO and BRAO over a period of more than twenty years.

Methods:
A retrospective cohort study. The medical records of all patients diagnosed with non-atretic retinal artery occlusion and treated with HBOT at a tertiary center between January 1st, 2001, and May 1st, 2023 were analyzed.

Results:
Of 267 patients, preliminary data from the first 70 (mean age 63) is presented. Diagnoses included 61 CRAO, 8 BRAO, and 1 cilioretinal artery occlusion. Best corrected visual acuity (BCVA) improved from 2.16 ± 0.73 LogMAR to 1.41 ± 1.06 LogMAR after HBOT ($Z=-5.095$, $p< 0.001$, large effect size $r=0.61$). Eighty-two percent were treated within 12 hours. Thirty-two percent of patients achieved VA ≥ 0.3 LogMAR (20/40), and 54% improved by ≥ 3 vision lines. Older age correlated with less improvement ($r=0.269$, $p=0.025$). No significant correlation was found between gender, cherry red spot, or presence of relative afferent pupillary defect and treatment response. No serious adverse events were reported.

Conclusions:
HBOT is a safe and effective treatment option for acute CRAO and BRAO.

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Keywords: Stroke, Retina, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Prognostic Factor of Favorable Visual Outcome in Pediatric Optic Neuritis

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Introduction:
Data regarding prognostic factors of visual outcome in Thai pediatric optic neuritis (ON) patients is scarce. Therefore, we aimed to identify prognostic factors of favorable visual outcome in Thai pediatric ON subjects.

Methods:
Thirty-one pediatric subjects with the first-ever ON attack were included. Demographic data, etiologies, clinical and magnetic resonance imaging characteristics, acute treatment, and visual outcome of ON were retrospectively reviewed. Only one eye of each subject was included in the statistical analysis. Therefore, subjects who presented with bilateral ON, only the eyes with worse visual acuity (VA) at nadir were included. A favorable visual outcome was defined as VA at recovery better than or equal to 20/40.

Results:
The mean age at onset was 10.76 (standard deviation (SD): 2.47) years and 21 subjects (67.7%) were female. The most common etiology of ON was idiopathic (10 subjects, 32.2%), followed by both neuromyelitis optica spectrum disorder (7 subjects, 22.6%) and myelin oligodendrocyte glycoprotein antibody-associated disease (7 subjects, 22.6%). The mean VA at nadir was 2.07 (SD: 0.95) logarithm of the minimum angle of resolution (logMAR). Twenty-three subjects (74.2%) had bilateral ON at presentation. All subjects were treated with intravenous methylprednisolone (IVMP) with the median time from initial symptoms onset to IVMP treatment of 5 (interquartile range (IQR): 1, 10) days. The median VA at recovery was 0.1 (IQR: 0.0, 0.5) logMAR. Twenty-one subjects (67.7%) achieved a favorable visual outcome. Time from initial symptoms onset to IVMP treatment of less than 14 days was the only significant factor associated with favorable visual outcome (odds ratio 10.19, 95% confidence interval: 1.27-81.83, p = 0.029).

Conclusions:
The time from initial symptoms onset to IVMP treatment of less than 14 days was the significant prognostic factor of favorable visual outcome in Thai pediatric ON subjects.

References: None provided.

Keywords: Optic neuritis, Pediatric neuro-ophthalmology, Demeylinating disease, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Pain Features in Acute Demyelinating Optic Neuritis

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Introduction:
Ocular pain is a hallmark of acute optic neuritis (ON). However, pain is variably perceived and found to be worse among women and minoritized groups. We aimed to understand the impact of gender and race on pain in ON and secondarily explore the presence of chronic ocular pain.

Methods:
This is a secondary analysis of pre-existing data from the Optic Neuritis Treatment Trial (ONTT) and subsequent 15-year Longitudinal Optic Neuritis Study (LONS). Associations between baseline pain, and demographic and clinical features (e.g., optic disc edema) were assessed using univariate logistic regression for dichotomous variables, two tailed t-tests for continuous variables, and Chi-square for categorical variables. The prevalence of chronic ocular pain leading up to the end of the LONS was assessed using descriptive statistics of responses to two ocular pain questions collected in the NEI-VFQ.

Results:
Among the 455 patients enrolled in the ONTT (2 excluded for compressive optic neuropathy), men had lower odds of ocular pain compared to women (OR 0.48, 95% CI 0.24, 0.98) and significantly less severe pain (P = 0.006). No differences in the presence of pain were observed between White, Black, or other minoritized racial participants. However, when pain was present, it was significantly more severe among Black and other minoritized participants (P = 0.049). The prevalence of chronic ocular pain causing impairment in daily activities at least some of the time was 10.9% and 13.6% at 10 and 15 years respectively.

Conclusions:
Similar to other acute pain conditions, pain severity is worse among women and non-minoritized racial groups. However, the presence of chronic ocular pain is similar to other eye conditions. Future studies should investigate how social determinants of health may impact pain perception, the influence of acute pain, and pain perception on ON quality of life and response to treatment.

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Keywords: Optic neuritis, Demeylinating disease, Orbit/ocular pathology, Orbit, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Clinical and Demographic Insights into MOG-Associated Optic Neuritis: A Comprehensive Study from Alberta, Canada

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Introduction:
Myelin Oligodendrocyte Glycoprotein (MOG)-associated Optic Neuritis (ON) is an antibody-mediated demyelinating disease of the central nervous system. Unlike other demyelinating disorders, such as Multiple Sclerosis and neuromyelitis optica spectrum disorder, MOG-ON differs in clinical presentation, treatment, and prognosis. This study investigates the demographics, clinical features, and treatment of patients with MOG-ON in Alberta, focusing on patients who tested positive for MOG-IgG at Alberta's centralized testing facility.

Methods:
This retrospective study investigated all the patients who underwent MOG-IgG cell-based assays in Alberta, conducted by MitogenDx through Alberta Precision Labs, from July 2017 to July 2023. The medical records for all patients with a positive MOG-IgG titer were reviewed. Collected data included demographics, initial symptoms, diagnostic investigations, primary diagnosis, treatment, and final visual acuity. Patients without confirmed diagnoses were excluded.

Results:
Of 3996 tested patients over 6 years, 208 were MOG-IgG positive (positivity rate: 5.4%). Of these, 82 were diagnosed with MOG-ON, with 51 (62.2%) females and 31 (37.8%) males, and follow-up time ranging from 3 to 219 months (mean: 42.7). Based on antibody titers, 34 (42.0%) were highly positive, 20 (24.7%) moderately positive, 21 (25.9%) weakly positive, and 6 (7.4%) initially negative before seroconverting. Ages of presentations ranged from 7.3 to 85.2 years (mean: 34.4). Ocular pain was reported in 78.1%, 41.3% had bilateral ON, and 81.4% displayed a relative afferent pupillary defect. Disease was monophasic in 51.2% and relapsing in 48.8%, with 71.8% treated with pulse steroids on initial presentation. Baseline visual acuity range was variable, with 46.6% of patients presenting with 20/200 or worse. Final visual acuity improved, with 79.5% achieving 20/40 or better.

Conclusions:
This is the first comprehensive analysis of MOG-ON in a Canadian province. The data provide guidance for clinical practice and help prioritize ON investigations. Further analysis will evaluate treatment effectiveness and identify prognostic factors influencing visual outcomes.

References: None provided.

Keywords: Optic neuritis, Optic neuropathy, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Expression of Yeast NDI1 as a Neuroprotective Approach to Retinal Ganglion Cell Mitochondrial Deficiency in a Mouse Model of Leber's Hereditary Optic Neuropathy.

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Introduction:
Leber Hereditary Optic Neuropathy (LHON) is an inherited disorder of mitochondrial complex I (NADH dehydrogenase) that causes retinal ganglion cell (RGC) death and profound vision loss. In yeast there is an alternative NADH dehydrogenase, NDI1, that can bypass mammalian complex I in the mitochondrial electron transport chain. We hypothesized that expression of yeast NDI1 would rescue RGC degeneration in a mouse model with RGC-specific complex I deficiency.

Methods:
We employed Cre-Lox-mediated recombination to express yeast NDI1 and to delete the key mitochondrial complex I subunit NDUFS4 in a cell-specific manner. Using the vesicular glutamate transporter Vglut2 as a Cre driver, we achieved NDI1 expression and NDUFS4 deletion within RGCs of Vglut2-Cre;ndufs4loxP/loxP;Ndi1loxP-stop-loxP mice. The mice and control littermates lacking one or more of the genetic modifications (n≥5 animals per genotype) were allowed to age to postnatal day 60 (P60) and P90, at which point retinal and optic nerve tissue was harvested. Surviving RGC somas were quantified in retinal flat mounts labeled for RBPMS1, and axons were counted on optic nerve cross sections stained with methylene blue.

Results:
Consistent with our previous data, Vglut2-Cre;ndufs4loxP/loxP mice lost approximately one-third of RGCs by P60 and >50% by P90. Those mice expressing NDI1 in the NDUFS4-deficient RGCs exhibited complete rescue of RGCs at both time points, and only modest morphological abnormalities were observed in the RGC axons at P90.

Conclusions:
Our findings suggest that yeast NDI1 can substitute for dysfunctional mammalian complex I to prevent RGC degeneration. The observation of RGC neuroprotection by NDI1 in our model of severe complex I deficiency supports the concept that NDI1 expression may serve as a mutation-independent therapeutic strategy for restoring complex I function and reducing RGC death in LHON, a condition resulting from mutations in a variety of complex I subunits.

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Keywords: Genetic disease, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Compressive optic neuropathy due to paraophthalmic artery aneurysms: Patient characteristics and neuro-ophthalmic outcomes after endovascular treatment

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Introduction:
There is paucity of neuro-ophthalmological data to inform on visual prognosis in patients with compressive optic neuropathy from paraophthalmic artery aneurysms. One study suggested no visual improvement in compressive optic neuropathy following treatment (mostly microsurgical clipping). A cohort of patients without compressive optic neuropathy treated with endovascular flow diversion was shown to have good long-term ophthalmic outcome.

Methods:
Retrospective cohort study of patients presenting with compressive optic neuropathy due to paraophthalmic artery aneurysm who underwent endovascular treatment in 2012-2023 at one tertiary centre. Patient demographics, aneurysm characteristics, treatment modality, best corrected visual acuity, pRNFL and GCL volume (Heidelberg Spectralis) was collected.

Results:
A total of 16 patients with 17 aneurysms and median follow-up 35 months (range 0-151) met inclusion criteria. Median age was 58 (38-78), 93% were women (15/16), and 56% had a smoking history. Aneurysm median size was 17 mm (8-33 mm). Majority presented more than 6 months after symptoms onset (9/17), 29% (5/17) at 1-6 months, and 18% (3/17) within 1 month. Treatment methods were most frequently flow diversion and coils (9/17), flow diversion alone (6/17) and coils (2/17). Of the 24% eyes that had significant vision improvement after endovascular procedure and available OCT data, average pRNFL at presentation was 89 microns and average GCL volume was 0.74 mm3.

Conclusions:
A subset of patients with compressive optic neuropathy had visual improvement after endovascular procedure highlighting the value of multidisciplinary team approach. Further studies are warranted to explore utility of OCT for structure function correlation in pre and post procedure assessment.

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Keywords: Interventional neuroradiology, Optic neuropathy, Vascular disorders, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Effect of Acetazolamide Use for Disc Edema after Intracranial Mass Resection

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Introduction:
Acetazolamide is commonly used to treat residual optic disc edema after intracranial mass resection, but there is no data to support this practice.

Methods:
This is a single-institution retrospective study of patients treated with acetazolamide for residual optic disc edema after intracranial mass resection from 2016 to 2023. Data collected included demographic information, mass pathology, and optic nerve data. Data was analyzed using SPSS version 29.0.2.0 (IBM SPSS Statistics for MacIntosh. Armonk, NY: IBM Corp, 2019).

Results:
48 eyes were included. Median age was 35 years (14-47). 70.8% were female. 45.8% were Hispanic, 29.2% were white. 33.3% were noted to have optic atrophy at the time of acetazolamide initiation. 10.8% had grade 1, 16.2% had grade 2, 24.3% had grade 3, 37.8% had grade 4, and 10.8% had grade 5 optic disc edema. Ophthalmology ordered acetazolamide in 62.5% of patients, with the rest ordered by neurosurgery (29.2%) and neurology (8.3%). Masses included meningioma/shwannoma (37.5%), astrocytoma/low grade glioma (16.7%), metastasis (12.5%), and pituitary mass/craniopharyngioma (12.5%). Mass locations included sellar/pituitary (29.2%), frontal/anterior fossa (29.2%), temporal/middle fossa (16.7%), cerebellopontine angle/posterior fossa (8.3%), parietal/occipital (8.3%), and intraventricular/pineal region (8.3%). 35% had optic nerve or chiasm compression. 50% had subtotal resection. 25% had hydrocephalus requiring a shunt. There was a median decrease in NFL thickness of 38.5 ($p< 0.001$), a median decrease in GCL thickness of 1.7 ($p=0.002$), and no change in HVF ($p=0.131$) between measurement 1 and 2.

Conclusions:
This is the first study to evaluate the effect of acetazolamide in this patient population. There was a statistically significant decrease in NFL thickness as well as a small decrease in GCL thickness. There was not a statistically significant difference in HVF with acetazolamide treatment. More analyses should be performed comparing outcomes for patients with residual optic disc edema after intracranial mass resection with and without acetazolamide treatment.

References: None provided.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Etiology of Optic Disc Edema: A Retrospective Cohort Study from a Tertiary Care Facility

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Introduction:
The differential diagnosis for optic disc edema is broad, with treatment implications varying based on the underlying cause. The etiology may be ischemic, autoimmune, infectious, compressive, or elevated intracranial pressure. However, a standardized work-up for initial onset of optic neuropathies and disc swelling remains unclear. This study reports relative incidences of presenting etiologies of optic disc edema at a tertiary care center in the U.S. to contribute to the future development of an effective, cost-efficient clinical workflow.

Methods:
This descriptive retrospective cohort study included 206 patients with optic disc edema from 2015 to 2020. We investigated demographic characteristics, vital signs, neurological findings, past medical history, objective eye exam findings, serologies, lumbar puncture analyses, and neuroimaging results. Final diagnoses were made by neuro-ophthalmologists.

Results:
The cohort included 144 females and 72 males, aged 17 to 94 years, with a median age of 37.5 years. Idiopathic intracranial hypertension (IIH) was the most common etiology (106 cases, 49.07%), with an average age of 33 and BMI of 38.62. In comparison, other etiologies had an average age of 52 and BMI of 30.76. Non-arteritic ischemic optic neuropathy (NAION) accounted for 39 cases (18.06%), while 23 patients (10.65%) were diagnosed with demyelinating diseases, including multiple sclerosis, MOG-positive optic neuritis, and neuromyelitis optica. Less common diagnoses included Lyme papillitis (5.09%), giant cell arteritis (4.17%), neurosarcoidosis (3.24%), infectious optic neuropathy (1.85%), mass lesions (0.93%), and neuroretinitis (0.93%). Thirteen patients presented with multiple factors contributing to optic disc edema.

Conclusions:
IIH and NAION were the predominant causes of optic disc edema. These findings illustrate the broad distribution of presenting etiologies of optic neuropathy and underscore the need for a systematic approach to diagnosing and managing optic disc edema.

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Keywords: Optic neuropathy, High intracranial pressure/headache, Pseudotumor cerebri, Demeylinating disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Association Between GLP-1 Inhibitor Use and Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION) in Diabetic Patients: A Retrospective Study

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Introduction:
Glucagon-like peptide-1 (GLP-1) inhibitors have gained popularity for their benefits in managing type 2 diabetes and reducing cardiovascular risks. However, concerns have emerged regarding their potential association with adverse ocular events, particularly non-arteritic anterior ischemic optic neuropathy (NAION). This study aims to investigate whether GLP-1 inhibitor use is associated with an increased incidence of NAION in diabetic patients.

Methods:
A retrospective cohort study was conducted using data from diabetic patients diagnosed with NAION at our institution. We compared the proportion of GLP-1 inhibitor users among diabetic NAION patients to the national proportion of GLP-1 users in the diabetic population (19.4%). Statistical analyses included a one-sample z-test for proportions to assess whether GLP-1 use in the study population differed significantly from the national average.

Results:
Among the 50 patients with NAION included in the study, 9 were identified as diabetics (%). Among diabetic patients with NAION, 44% (n=4) were identified as GLP-1 inhibitor users. This proportion was significantly higher than the national average of 19.4% ($p < 0.01$). However, the calculated z-score was 1.90, indicating there was not a statistically significant difference between the sample and the population estimate ($p=0.057$).

Conclusions:
Our findings did not demonstrate a significant association between GLP-1 inhibitor use and the occurrence of NAION in diabetic patients. Further research is needed to confirm these findings in larger, prospective studies. Given the widespread use of GLP-1 inhibitors for diabetes management, clinicians should be aware of this potential risk and monitor patients accordingly.

References: None provided.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Attrition of Retinal Ganglion Cell Complex Following Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION): A Disparity in the Structure: Function Relationship

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Introduction:
Non-arteritic anterior ischemic optic neuropathy (NAION) causes blindness due to loss of retinal ganglion cells (RGCs), which can be demonstrated by optical coherence tomography (OCT) within two weeks of the event. This study examined attrition of RGCs following an attack of NAION and how such attrition correlates with visual function.

Methods:
This study followed 24 patients after NAION with sequential measurements of central acuity, testing with automated visual fields (for which we captured the mean deviation score), and measurement of the thickness of the retinal ganglion cell complex (GCC) and retinal nerve fiber layer (RNFL) with the Cirrus OCT machine. Each OCT was reviewed to ensure acceptable technical performance. Structure: function relationships were examined by comparing visual parameters with GCC and RNFL thickness over time, applying t-tests from initial to 3-month post-NAION exams.

Results:
There was a 13.4% reduction in GCC thickness from initial exam to the plateau, which was reached ≈3 months post NAION. A paired t-test of GCC thickness showed a statistically significant decline between the first value compared to the plateaued value ($t=4.74$, $p=0.0002$). The mean deviation values did not statistically differ (paired t-test) from the first exam post-NAION to the GCC plateau.

Conclusions:
Our findings reveal an attrition of GCC thickness over 2-3 months following NAION, other than for a single patient who had a mild attack of NAION and whose GCC thickness dropped only slightly within the first two months. In all but one patient, this attrition of GCC occurred without a significant decline in vision. The attrition of RGCs suggests that sub-populations of these cells can be metabolically compromised and visually dysfunctional but nonetheless survive for several months. If true, our findings also would suggest there might be a greater window of opportunity to rescue RGCs that have been injured by NAION.

References: None provided.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Neuroretinal Degeneration in Leber Hereditary Optic Neuropathy Continues During the First 5 Years After Onset Without Affecting Visual Recovery Under Treatment with Idebenone

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Introduction:
Leber hereditary optic neuropathy (LHON) results in bilateral optic atrophy and permanently reduced visual acuity (VA) in a majority of patients. Visual recovery can occur after the subacute/dynamic phase, and can be stimulated by treatment with idebenone. However, time and magnitude of recovery are variable. We assessed the long-term course of optic nerve degeneration in LHON and potential relationships with changes in visual acuity (VA) during treatment.

Methods:
30 eyes of 15 patients with genetically confirmed LHON were retrospectively analyzed. Parapapillary retinal nerve fiber layer thickness (RNFLT) and ganglion cell complex thickness (GCCT), the combined three innermost macular layers, were measured every six months using OCT. All patients received treatment with idebenone. VA was monitored using ETDRS charts.

Results:
RNFLT and GCCT declined sharply during the first two years after LHON onset, but showed further loss until a median of 54 (range: 36-60) and 36 (18-54) months, respectively. Semi-annual decrease of mean RNFLT and GCCT was statistically significant until month 60 and 36, respectively. In contrast, VA began to increase after a median of 12 (5-30) months from LHON onset. Duration of RNFLT loss correlated with age ($r=0.54$, $p=0.002$), but not with timing of visual recovery or treatment. Best VA after the nadir correlated with nadir VA ($r=0.82$, $p< 0.001$), final RNFLT ($r=-0.61$, $p< 0.001$) and GCCT ($r=-0.44$, $p=0.01$), and inversely with time to clinically relevant recovery ($r=0.87$, $p< 0.001$) and age ($r=0.53$, $p=0.003$).

Conclusions:
The results indicate that neuronal loss in LHON continues well into the chronic phase after the VA nadir has passed. This long-term degeneration does not appear to affect the time course of visual recovery in patients treated with idebenone. Visual outcome is negatively influenced by the magnitude of subacute visual loss and the final extent of neurodegeneration, and positively relates to earlier recovery during treatment and younger age.

References: Yu-Wai-Man, Carelli, Newman, Silva, Linden et al. Therapeutic benefit of idebenone in patients with Leber hereditary optic neuropathy: The LEROS nonrandomized controlled trial. Cell Reports Medicine. 5(3):101437, 2024.

Keywords: Optic neuropathy, Genetic disease, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

Financial Disclosures: Berthold Pemp: honoraria for lectures and consulting from Chiesi; Christoph Stapf; Martin Michl; Karl Kircher; Andreas Reitner

Grant Support: None.

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Retrospective Clinical Analysis of Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION) in Patients Using Semaglutide

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Introduction:
Semaglutide use has been linked to an increased risk of Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION), independent of medical comorbidities. However, the clinical characteristics and progression of NAION in semaglutide users remain poorly understood. This study aims to fill that gap by reviewing the clinical presentation and outcomes of patients diagnosed with NAION while using semaglutide.

Methods:
At a tertiary referral center, a retrospective chart review of patients on semaglutide diagnosed with NAION (independently confirmed by two neuro-ophthalmologists) was performed. Preliminary data is presented; additional case review and statistical analyses are ongoing.

Results:
Eight eyes from eight patients were included. Six patients were men, and the average age was 61.5 years (SD 7.0). All patients had body mass index > 25 and hypertension. All patients started semaglutide less than one year before initial NAION onset (mean 6.3, SD 4.7 months). All patients were on antihypertensive medications (mean 1.9, SD 1.0). Average number of anti-diabetic medications was 3.2 (SD 1.3). Seven patients experienced weight loss ≥ 5% of total body weight in the month prior to NAION onset. Four patients had at least one hypotensive blood pressure measurement a week prior to NAION onset. All patients had a cup to disc ratio ≤ 0.15 in the fellow eye. Six patients were treated with steroids and three patients discontinued semaglutide following NAION. Average follow up time was 4 months (SD 2), and only one patient had significant improvement in visual field defects following NAION.

Conclusions:
All patients with NAION while taking semaglutide had other risk factors known to be associated with increased risk of NAION. Rapid weight loss on semaglutide may lead to greater fluctuations in blood pressure, which may predispose susceptible patients to increased NAION risk. Patients experiencing NAION on semaglutide rarely experienced improvement of symptoms with either steroid treatment and/or semaglutide discontinuation.

References: None provided.

Keywords: Optic neuropathy, Vascular disorders, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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The Risk of Age-related Macular Degeneration in Multiple Sclerosis Optic Neuritis

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Introduction:
Multiple sclerosis (MS) is an inflammatory demyelinating condition that frequently affects the optic nerve causing optic neuritis (ON). Age-related macular degeneration (AMD) is a distinct ocular condition that similarly involves inflammation in its pathophysiology. The purpose of this study is to explore the associations between ON and the risk of developing AMD among MS patients.

Methods:
A retrospective cohort study was conducted using the TriNetX platform, a federated database containing de-identified health records from several large health care organizations globally. Patients ≥ 18 with MS were identified by ICD-10 code and divided into two cohorts: those with and without a history of ON. Patients were matched by age, sex, race, ethnicity, tobacco use, and the presence of essential hypertension, type II diabetes mellitus, and hyperlipidemia. Primary outcomes measured were new diagnosis of exudative AMD, nonexudative AMD, and unspecified macular degeneration. Risk of new onset AMD was determined using cox proportional hazards regression; hazard ratios (HR) and 95% confidence intervals (CI) were reported.

Results:
A total of 26,511 MS patients with an ON history and 26,511 MS patients without an ON history were included in this study. Patients with an ON history had a higher risk of developing AMD than patients without (HR: 2.40 [CI: 1.88-3.06]). Risk of nonexudative AMD (HR: 2.70 [CI: 1.87-3.90]) was greater than that of exudative AMD (HR: 2.09 [CI: 1.18-3.69]). Subgroup analyses demonstrated an increased risk of developing AMD among ON patients aged 50-64 (HR: 2.12 [CI: 1.22-3.68]) and ≥ 65 (HR: 2.21 [CI: 1.62-3.01]). Elevated hazard ratios were observed in both females (HR: 2.14 [CI: 1.64-2.80]) and males (HR: 2.30 [CI: 1.26-4.20]) with an ON history.

Conclusions:
Patients with MS and an ON history demonstrated an increased risk of developing AMD compared to their non-ON counterparts, highlighting the importance of appropriate follow up to prevent long-term ocular comorbidities.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Correlation Between Visual Field Index Measurements and Mean Deviation in Compressive Optic Neuropathy and Primary Open Angle Glaucoma

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Introduction:
The visual field index (VFI) is a relatively newer perimetric index originally developed to estimate the rate of progression in glaucoma. Although primary open-angle glaucoma (POAG) and compressive optic neuropathy (CON) can present with similar clinical features, the use of VFI in CON remains largely unexplored. We aim to investigate the suitability of VFI in CON and POAG by comparing it with mean deviation (MD).

Methods:
We performed a retrospective review of patients with POAG and CON who presented at an academic quaternary care center from 1/1/2013 to 6/31/2023. POAG was defined using the United Kingdom Glaucoma Treatment Study (UKGTS) criteria, excluding those with cranial mass lesions. CON was defined by UKGTS visual field criteria, inter-eye asymmetry in retinal nerve fiber layer or mGCIPL, or intra-eye asymmetry in mGCIPL. Humphrey SITA protocol size 3 visual fields were used. Linear regression analysis was performed to evaluate the correlation between VFI and MD in both conditions.

Results:
A total of 305 CON and 410 POAG eyes were included. The CON cohort had a mean MD of -7.9 ± 7.9dB and mean VFI of 77.8 ± 24.1%. The POAG cohort had a mean MD of -8.7 ± 7.7dB and mean VFI of 76.9 ± 25%. The linear regression model showed a strong correlation between VFI and MD in both conditions, with R2=0.95 in CON and 0.92 for POAG. For each decibel increase in MD, VFI increased by 3.25% ($p< 0.001$) in CON and 3.10% ($p< 0.001$) in POAG. In CON, VFI corresponding to an MD of -6 dB and -10 dB were 83.9% and 70.8%, respectively. In POAG, these MD values corresponded to a VFI of 84.4% and 72.0%, respectively.

Conclusions:
VFI demonstrated a very strong correlation to MD in both CON and POAG. These results support the novel use of VFI to monitor CON.

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

Financial Disclosures: Setu Mehta; Lucy Chen; Florian Guillot; James Davis; Altug Ay; Amanda Henderson: None related to this submission: Horizon Therapeutics/Amgen.; Andrew Carey: None related to this submission: Horizon Therapeutics/Amgen, Bristol-Myers-Squibb, Springer publishing.

Grant Support: None.

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Traumatic Optic Neuropathy: Comparison of Clinical Factors and Visual Outcomes in Patients With Orbital Wall Fractures

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Introduction:
Traumatic optic neuropathy (TON) can be a blinding condition and pathophysiologic understanding is lacking. TON commonly occurs in setting of orbital wall fractures (OWF), but how OWF relates to TON is not well understood. We aim to identify risk factors for and visual outcomes of TON in patients with OWF.

Methods:
In this single-institution retrospective cohort study, patients with orbital wall fractures from 2014 to 2017 were reviewed. Patients less than 18 years of age, history of prior OWF, ophthalmic surgery, ocular injury, or who were not evaluated by ophthalmology at time of diagnosis were excluded. Data collected at presentation and follow up included: age, sex, mechanism, visual acuity, pupillary response, intraocular pressure, extraocular motility, confrontation visual fields, anterior and posterior segment exams, and number and laterality of bones fractured. TON patients were compared with age-matched controls to assess relationships between bone involvement, mechanism of injury, and visual outcomes.

Results:
535 patients with OWF met inclusion criteria. Of those, 33 (6.1%) patients were diagnosed with TON at initial evaluation, of which, 16 had follow-up. Mean follow-up for TON patients was 7.97 months (standard deviation [SD] 12.45) and there was no difference in follow-up time (p=0.540) and number of visits (p=0.46) compared to controls. Incidence of direct and indirect TON were 41% and 59%, respectively. TON patients had worse visual acuity at presentation and follow-up compared to controls (p=0.016 and p=0.005, respectively). No relationship was found between TON and bone fractured, total number of bones involved (p=0.822), or mechanism of injury.

Conclusions:
Traumatic optic neuropathy and orbital wall fracture often coincide. Prior evidence has suggested that specific mechanisms of injury, such as lateral wall and roof fractures, are higher risk for developing TON, but we did not identify any similar relationships. Future studies are needed to assess TON risk factors.

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Keywords: Optic nerve trauma and treatment, Orbit/ocular pathology

Financial Disclosures: Grant Howell; Preston Luong; Raghu Mudumbai: Clinical Trial Support: Stoke Therapeutics, Viridian Therapeutics, Nicox

Grant Support: None.

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The Impact of Obstructive Sleep Apnea Syndrome on Visual Functions in Patients with Optic Disc Drusen: A Retrospective Cross-Sectional Study

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Introduction:
Obstructive sleep apnea (OSA) has been associated with adverse visual outcomes in optic neuropathies. Optic disc drusen (ODD), calcified deposits in the anterior optic nerve, can lead to severe visual field defects and contrast sensitivity reduction. The interaction between OSA and ODD and its potential impact on visual function remains underexplored.

Methods:
Chart reviews were carried out to identify clinical characteristics, sleep study results, and visual parameters of patients with confirmed diagnoses of both ODD and OSA. These patients were compared to a control group diagnosed with ODD only. Records were excluded if they contained insufficient information, or if patients had another optic neuropathy.

Results:
180 patients with ODD+OSA were identified, and 32 patient records (61 eyes) contained sufficient information to be included in our analysis. 34 patients (67 eyes) with ODD only were selected as controls. Females represented 62.5% of the ODD+OSA group and 68.75% of controls ($p>.05$). Bilateral ODD was observed in 87.5% of the ODD+OSA and 90.6% of the controls ($p>.05$). Functional (HVF Mean Deviation) and structural (RNFL and GCC thickness) ophthalmic parameters were similar between the two groups. In addition, a sub-analysis of the ODD patients with only moderate-to-severe OSA revealed no worse outcomes compared to the control group ($p>.05$).

Conclusions:
There is no statistically significant difference in functional and structural ophthalmic parameters between ODD+OSA and ODD-only cohorts, even after excluding mild OSA cases.

References: None provided.

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

Financial Disclosures: Fannie Nadeau; Anas Alkhabaz; Yaping Joyce Liao: Consulting: Stoke Therapeutics

Grant Support: None.

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Evaluating Diagnostic Protocols for Central Retinal Artery Occlusion (CRAO): A Retrospective Study

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Introduction:
Central Retinal Artery Occlusion (CRAO) is an ischemic stroke that necessitates immediate hospitalization. The American Heart Association and the American Academy of Ophthalmology emphasize the need to treat CRAO as a medical emergency, advocating for urgent stroke workups to identify cardiovascular causes and reduce the risk of future strokes. However, no standardized systemic workup protocol has been established for CRAO management. This study aims to evaluate whether CRAO patients at a tertiary academic medical center receive an adequate stroke workup and determine the impact on patient outcomes.

Methods:
A retrospective chart review was conducted for patients diagnosed with CRAO between May 2008 and May 2023. The study followed whether patients underwent angiography, ESR, CRP, clotting studies, EKG, echocardiogram, and CBC upon admission. Visual acuity before and after the CRAO event and length of stay was recorded. Ophthalmology outpatients with follow-ups were assessed for completion of OCT and fluorescein angiography. Statistical analysis included Mann-Whitney tests, Spearman's correlation, and Pearson's chi-square.

Results:
Of the 89 patients reviewed, 39.8% had all recommended procedures completed. Only 18.2% of ophthalmology outpatients had both OCT and fluorescein angiography. No significant differences were observed in length of stay ($p=0.394$), cerebrovascular accident recurrence ($p=0.705$), or vision outcomes ($p > 0.403$) between patients who adhered to all protocols and those who did not. Additionally, no significant correlation was observed between the proportion of the protocol followed and length of stay ($p=0.216$), cerebrovascular accident recurrence ($p=0.634$), or vision outcomes ($p>0.466$). There were not enough mortalities to assess differences in mortality rates between groups.

Conclusions:
The findings suggest that a comprehensive protocol for CRAO workup does not significantly impact length of stay, cerebrovascular accident recurrence, or visual outcomes. Given the lack of association, future studies should explore alternative approaches to CRAO management and investigate other potential factors affecting patient outcomes.

References: None provided.

Keywords: Stroke, Vascular disorders, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Developing the Mitochondrial Visual Impairment – Inherited Optic Neuropathy Impact Questionnaire (mitoVISION-IQ)

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Introduction:
Assessing the impact of vision loss on quality of life is an important outcome measure in clinical studies of inherited optic neuropathies (IONs), including dominant optic atrophy (DOA) and Leber hereditary optic neuropathy (LHON). The purpose of this study was to develop and evaluate a patient-reported outcome measure (PROM) for assessing the impact of visual impairment in people with IONs.

Methods:
A total of 195 individuals affected by DOA or LHON participated in the development of mitoVISION-IQ across three phases. Concept elicitation interviews were conducted to characterise the impact of IONs and to generate an item set (phase one), which were then refined through a series of cognitive debriefing interviews (phase two). The draft mitoVISION-IQ was piloted with an international cohort of 167 affected individuals (100 with DOA and 67 with LHON) and evaluated by Rasch analysis (phase three).

Results:
The impact of IONs was determined to affect three core domains, with 63 items generated (34 "physical health", 17 "mental health", 12 "social health"). A total of 29 items (14 physical health, 8 mental health, 7 social health) were retained after phase two. In phase three, the draft mitoVISION-IQ was deemed to be of high value and low burden by study participants. Rasch analysis informed the creation of three separate unidimensional scales for assessing the impact of IONs on "visual functioning" (10 items), "social functioning" (7 items), and "mental wellbeing" (7 items). Visual acuity of the better seeing eye correlated moderately with scores on the visual functioning (Pearson r = –0.45, P<.001) and social functioning (–0.39, P<.001) scales, but not with mental wellbeing (–0.057, P=.58).

Conclusions:
The impact of visual impairment on visual functioning, social functioning, and mental wellbeing can be assessed using the mitoVISION-IQ, a conceptually grounded and psychometrically valid PROM developed with people affected by IONs.

References: None provided.

Keywords: Genetic disease, Optic neuropathy, Miscellaneous

Financial Disclosures: Benson Chen; Chloe Seikus; James Ferguson; Sander Dikhoff; Stephanie Archer; Mike Horton; Valerija Tadić; Patrick Yu-Wai-Man: Consulting: GenSight Biologics, Stoke Therapeutics, Transine Therapeutics; Speaker honoraria and/or financial support: GenSight Biologics, Santhera Pharmaceuticals

Grant Support: UK National Institute of Health Research (NIHR) Award (NIHR301696)

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Spontaneous Visual Recovery in Leber Hereditary Optic Neuropathy: Correlation with Residual Thickness of the Ganglion Cell Complex on OCT

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Introduction:
Leber Hereditary Optic Neuropathy (LHON) is a mitochondrial disorder that causes acute bilateral blindness due to an optic neuropathy associated with specific mitochondrial DNA mutations. There is potential for spontaneous visual recovery, which occurs with varying frequency depending upon the specific mitochondrial mutation. The potential for spontaneous recovery has not previously been considered with respect to the degree of residual thickness of the retinal ganglion cell complex (GCC).

Methods:
We conducted a retrospective chart review of patients with LHON who experienced blindness followed by spontaneous recovery of vision. OCT data were examined to assess GCC thickness months after the onset of blindness. We also collected demographic information, details of clinical presentation, and type of genetic mutation.

Results:
We identified 32 patients (81% males) with near-complete spontaneous visual recovery from LHON. The mean age at presentation was 28.5 years (range: 8-71 years), and the mean recovery time was 5.62 years (SD: 4.46 years). At their last follow-up visit, patients achieved an average final visual acuity of 0.23 logmar; the mean GCC thickness for these patients was 58.37 microns. The 11778 mutation accounted for 47% of the cases of visual recovery, while 28% were associated with the 14484 mutation and 12.5% were associated with the 3460 mutation; four cases (12.5%) had secondary mitochondrial mutations.

Conclusions:
Patients with LHON-induced blindness can experience significant visual recovery despite significant depletion of the GCC, which defies a straightforward structure: function correlation. Our results suggest that the thickness of the GCC cannot be used to anticipate which patients might recover vision

References: None provided.

Keywords: Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Innovative 3D Volumetric Imaging of the Vasculature of the Human Optic Nerve Head: A New Era to Explore Vascular Vulnerability

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Introduction:
The human optic nerve head (hONH) is a common site of damage that causes blindness. The pathologies that cause the two most common forms of optic nerve blindness - glaucoma and non-arteritic anterior ischemic optic neuropathy (NAION) - are not known, but disordered blood flow is believed to be consequential. Our study employed advanced imaging techniques to create volumetric topographical maps of human orbital and optic nerve vasculature, which has remained poorly understood due to limitations in traditional imaging methods.

Methods:
We have produced 4D volumetric renderings of human orbital blood vessels, including branches of posterior ciliary arteries that supply the meninges and internal elements of the hONH. Our processes include injecting the ophthalmic arteries with a fluorescent dye in fresh cadaveric tissue, then removing the entire orbit en bloc, fixing and then "clearing" the tissue to enable imaging with light sheet fluorescence microscopy.

Results:
We have retrieved 11 human orbits which were used to develop our methods. Our last three specimens yielded confluent imaging of arteries extending from the origin of the ophthalmic artery to the ONH, including lumina 5-10 microns in diameter. The anatomical data is fully digitized and with applied software has yielded 4D videos of human orbital vessels (which will be shown).

Conclusions:
Our work establishes a foundational dataset that fills a significant gap in knowledge, as no previous research has provided 3D or 4D volumetric imaging of human orbital blood vessels. Our anatomical datasets are also enabling development of a patient-specific, parameterizable blood flow model to study vulnerabilities in blood flow that may be caused by aging and mechanical forces and which may predispose to NAION and possibly some forms of blindness. Future directions include applying advanced techniques such as Immuno-SABER to probe cellular and molecular mechanisms contributing to the health and disease of the hONH.

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Keywords: Orbit, Optic neuropathy, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Ophthalmic and Systemic Characteristics of Acute Nonarteritic Anterior Ischemic Optic Neuropathy in the NARROW cohort

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Introduction:
Nonarteritic anterior ischemic optic neuropathy (NAION) causes sudden, irreversible vision loss. Although NAION is a prevalent and debilitating eye disease, its pathophysiology remains poorly understood, and conflicting evidence about the role of cardiovascular risk factors exists. Retrospective studies have documented that optic disc drusen (ODD) is an anatomical risk factor in young NAION patients. This study describes the baseline demographic, ophthalmologic, and systemic characteristics of NAION patients in the NARROW (Nonarteritic anterior ischemic optic neuropathy risk factors: New perspectives) cohort.

Methods:
This prospective cohort study included acute NAION of all ages from 14 sites in 8 countries. Demographic, clinical, and ophthalmologic data were collected. Comorbidities were documented via patient interviews and medical records. ODD was diagnosed based on enhanced depth imaging optical coherence tomography (EDI-OCT) scan of the optic nerve head following ODDS (Optic Disc Drusen Studies) Consortium guidelines. Numeric variables are represented as median (IQR) and categorical as %.

Results:
We enrolled 156 patients, aged 63 (56-71), 55% male. Bilateral involvement occurred in 15% due to either bilateral NAION during the study period or a previously affected contralateral eye. Study eye BCVA was 79 (55-85) letters, and perimetric mean deviation was -14 (-18-(-8)). The prevalence of cardiovascular risk factors were: Diabetes mellitus 20%, arterial hypertension 52%, dyslipidemia 54%, and tobacco smoking 11%. We found ODD on EDI-OCT in 14% of patients, while in 9% of patients, we couldn't confidently confirm or rule out ODD. Patients with ODD were younger (55 (50-64) vs. 63 (57-71), P = 0.03) and had a lower prevalence of dyslipidemia (25% vs. 59%, P =0.005).

Conclusions:
At least 14% of patients had ODD, and they were younger with lower prevalence of dyslipidemia compared to patients without ODD. The cohort overall had similar demographic, ophthalmologic, and systemic characteristics as described in previous studies.

References: None provided.

Keywords: Optic neuropathy, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Vascular disorders

Financial Disclosures: Lea Lykkebirk: I have received research grant for my PhD: - Fight for Sight - Denmark - Synoptikfonden - VELUX Foundation; Anastasiia Skliarova; Bardia Abbasi; Lulu Bursztyn; Masoud Aghsaei Fard; Clare Fraser; Jesse Gale; Neringa Jurkute: NJ received research support from Chiesi Farmaceutici.; Bradley Katz; Yaping Joyce Liao: Consulting: Stoke Therapeutics; Line Petersen; Suganiah Ragunathan; Marie-Bénédicte Rougier; Prem Subramanian: P. S. Subramanian is a consultant for Gensight, Amgen (formerly Horizon) and Viridian. His institution received funds from Horizon (now Amgen) to perform the trial on site.; Sasikala Thineshkumar; Steffen Hamann

Grant Support: Research grants from: Fight for Sight - Denmark Synoptikfonden VELUX Foundation

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Semaglutide and the Risk of NAION: The Unfolding Story

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Introduction:
In 2024 we asserted relatively high hazard ratios for developing NAION in patients with type 2 diabetes (T2D) or overweight/obesity (O/O) who were prescribed semaglutide. This report presents new biomarker data on our cohorts and summarizes research from others that provide further insight into the association between semaglutide and NAION.

Methods:
A sub-analysis of our original cohorts was performed. Medical charts identified with the ICD-10 code for "ischemic optic neuropathy" were manually reviewed to confirm the diagnosis of NAION. Propensity matching (considering age, sex, hypertension, T2D, obstructive sleep apnea, obesity, hyperlipidemia, and others) compared the incidence of NAION in patients prescribed semaglutide versus non–GLP-1 RA medications. For NAION cases, data outside our healthcare system was obtained on cup-to-disc ratios, HbA1c levels, and BMIs. A mixed-effects model was used. Recent reports from other groups on this topic were reviewed.

Results:
In T2D NAION patients, the semaglutide group had higher BMIs (p=< 0.01), but neither group (i.e. semaglutide or non-GLP-1 RA treated) had significant BMI change from shortly before to shortly after NAION (p=0.66). HbA1c levels decreased (p=0.03) but without significant differences between groups (p=0.67). Cup-to-disc ratios showed no significant differences between groups (p=0.08). In O/O NAION patients, there was no significant BMI difference between groups (p=0.76), and pre- vs. post-NAION BMI did not change significantly (p=0.81). HgbA1c levels (p=0.84) and cup-to-disc ratios (p=0.46) did not significantly differ between groups. Results from other groups, each using different methodologies, have both supported and refuted our original findings.

Conclusions:
The lack of significant differences in the studied biomarkers suggests these factors are not key contributors to the NAION risk. Outcomes of studies performed by others are dependent upon methods to detect NAION.

References: None provided.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Predictive Factors of Improved Final Visual Outcome in Patients with Leber Hereditary Optic Neuropathy Treated with Lenadogene Nolparvovec Gene Therapy

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Introduction:
We aimed to identify predictive factors of improved final best-corrected visual acuity (BCVA) in patients with Leber hereditary optic neuropathy (LHON) due to m.11778G>A MT-ND4 mutation who received lenadogene nolparvovec gene therapy.

Methods:
The following covariates were individually evaluated as possible factors associated with final BCVA: age, gender, timing of treatment, baseline BCVA value and baseline optical coherence tomography (OCT) parameters. Univariate analyses were performed from three phase 3 studies (RESCUE, REVERSE and REFLECT), using BCVA at 1.5 years post-treatment as the dependent variable. In RESCUE and REVERSE, ND4-LHON patients received an injection of gene therapy in one eye and a sham injection in the other. In REFLECT, the first-affected eye received gene therapy, while the other eye was randomly injected with gene therapy or placebo.

Results:
In 113 eyes treated at least 6 months after disease onset, the covariates statistically significantly associated with an improvement in final BCVA were thicker OCT measurements at baseline: ganglion cell layer (GCL) temporal outer segment, GCL superior outer segment, GCL nasal outer segment, and GCL inferior outer segment at ETDRS analysis, and retinal nerve fiber layer (RNFL) inferior quadrant, RNFL nasal quadrant and RNFL superior quadrant ($p< 0.05$). The greatest effects [95% confidence interval] were observed for the thickness of the superior and temporal outer GCL segments at baseline (-0.28 [-0.41; -0.16] and -0.26 [-0.38; -0.13] LogMAR, respectively; both $p< 0.001$). A better baseline BCVA was associated with a better final BCVA (-0.09 [-0.11; -0.08] LogMAR; $p< 0.0001$).

Conclusions:
Better baseline BCVA value and increased baseline OCT thickness of GCL and RNFL were predictive of the improved BCVA 1.5 years after treatment in patients with MT-ND4 LHON who received lenadogene nolparvovec at least 6 months after disease onset.

References: None provided.

Keywords: Optic neuropathy, Genetic disease

Financial Disclosures: Robert Sergott: Robert C. Sergott is a consultant for GenSight Biologics.; Nancy Newman: Consultant for GenSight, Chiesi, Neurophth (all involved with the treatment of Leber hereditary optic neuropathy. Research support as PI to my institution from GenSight for clinical trials.; Valérie Biousse: Consultant for Topcon which commercializes fundus cameras. The current research is completely independent from Topcon and is not funded by the company.; Patrick Yu-Wai-Man: Consulting: GenSight Biologics, Stoke Therapeutics, Transine Therapeutics; Speaker honoraria and/or financial support: GenSight Biologics, Santhera Pharmaceuticals; Valerio Carelli: VC is a consultant for GenSight Biologics, Chiesi, Stoke, and Pretzel.; Catherine Vignal-Clermont: Catherine Vignal-Clermont is a consultant for GenSight Biologics and has received research support from Santhera Pharmaceuticals.; Constant Josse; Magali Taiel: MT is an employee of GenSight Biologics.; José-Alain Sahel: JAS is a consultant/contractor for Avista Therapeutics and Tenpoint; has financial interests (stock/stock options) in GenSight Biologics, Sparing Vision, Prophesee, Chronolife, Tilak Healthcare, VegaVect, Inc., Avista, Tenpoint, SharpEye, Celanese and Netramind; is owner/co-owner/founder/co-founder for Gensight Biologics, Sparing Vision, Avista, Tenpoint, Prophesee, Chronolife, Tilak Healthcare, SharpEye, Celanese, Vegavect and Netramind; participates in scientific advisory board for Gilbert Foundation, Foundation Fighting Blindness, Institute of Ophthalmology Basel and Senses Institute Lausanne; is an observer at Gensight Biologics, SparingVision, Avista and Vegavect; is President of Fondation Voir et Entendre (Paris) and StreetLab (Paris); has patent for allotopic expression, rod-derived cone viability factor and related patents; is a recipient for patent royalties and GenSight Biologics.; Piero Barboni: Omikron pharma, Gensight biologic, Chiesi pharma

Grant Support: None.

Contact Information: None provided.

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Estimating "equivalent noise" in the visual system among children with neurofibromatosis type 1 and optic pathway gliomas.

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Introduction:
There is a perpetual challenge to estimate the risk of vision loss for individual children with neurofibromatosis type 1 (NF1) and optic pathway gliomas (OPGs) and judge whether/how to treat these OPGs. Inspired by our findings in an experimental mouse model and aiming to better inform such decisions, we implemented a variant of visual acuity testing in a pilot cohort, to estimate visual system "background noise" that degrades vision.

Methods:
During routine neuro-ophthalmologic examination, we asked NF1-OPG patients and controls to read a publicly available Dual Contrast Acuity Chart with added "noise" on one side (1), until failing to identify correctly any of the letters on the side without noise. We analyzed each patient's effective acuity for each side of the chart according to published methods, estimating visual processing "equivalent noise" for each subject. Those with greater intrinsic "noise" detect small letters at a similar contrast level with or without added chart noise. Statistical comparisons were made with Wilcoxon-Mann-Whitney tests.

Results:
We successfully tested 24 patients (44 eyes; 10 female (42%)/14 male (58%), ages 6-½ to 30 years), revealing reliable differences in acuity estimated from the standard and "added noise" sides of the chart in 41/44 (93%) eyes. All 20 patients (100%) in whom estimates could be made for both eyes had a measurable difference in the contribution of equivalent noise between the two eyes.

Conclusions:
This pilot study demonstrates the feasibility of estimating "equivalent noise" in visual processing (1,2) to identify disparities in vision among children with NF1 at risk for visual loss due to OPGs. Novel advantages of this approach include 1) its basis in detecting an aspect of visual dysfunction recently identified in an animal model; 2) easy incorporation into clinical evaluations; and 3) potential adaptation for the NF1 infants and toddlers at highest risk for vision loss.

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Keywords: Pediatric neuro-ophthalmology, Genetic disease, Higher visual functions, Tumors, Chemotherapy and radiation injury

Financial Disclosures: The authors had no disclosures.

Grant Support: Gilbert Family Foundation & Neurofibromatosis Institute

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Trans-synaptic Retrograde Degeneration Of Retinal Ganglion Cell-Inner Plexiform Layer And Retinal Nerve Fiber Layer With Visual Field Defect After Posterior Cerebral Artery Infarction

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Introduction:
Trans-synaptic retrograde degeneration (TRD), previously thought to occur only after prenatal injury to the visual pathway, has been shown in recent studies to follow postnatal damage, such as unilateral occipital injury, leading to retinal nerve fiber layer (RNFL) thinning in the adult human visual pathway. The aim of this study was to investigate the changes of Retinal Nerve Fiber Layer (RNFL) thickness and Ganglion Cell-Inner Plexiform Layer (GCL-IPL) thickness in Posterior Cerebral Artery (PCA) infarction patients with visual field defects.

Methods:
A retrospective analysis was conducted on patients presenting visual field defects after PCA infarction. Data included gender, age, diagnosis date, visual field results, and optical coherence tomography (OCT) results. This longitudinal study compared GCL-IPL and RNFL thickness and further analyzed the points of thinning progression. Paired T-test was performed to assess progression between baseline and final.

Results:
A total of 22 patients were analyzed. The average age at diagnosis was 59 years (range: 24-85), and 13 (59%) were male. The average follow-up duration was 48.7 months (95% CI: 44.5-53, SD: 47.6). 9 patients (41%) progressed GCL-IPL thinning, and 7 patients (32%) progressed RNFL thinning. The mean duration of initial progression was 12.1 months (SD 7.64) in GCL-IPL thinning and 15.9 months (SD 13.5) in RNFL thinning. 6 patients progressed thinning in the temporal region of the ipsilateral eye corresponding to the brain lesion, which subsequently progressed to the nasal region of the contralateral eye.

Conclusions:
Thinning of GCL-IPL and RNFL occurs in some patients after PCA infarction. Thinning progresses in the temporal region of the ipsilateral eye corresponding to the brain lesion and eventually progresses to the nasal region of the contralateral eye. These retinal changes are consistent with TRD, indicating that damage to the CNS leads to retrograde neuronal loss.

References: None provided.

Keywords: Stroke, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Face Imagery And Perception in Acquired Prosopagnosia

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Introduction:
Models of face perception and the face-processing network suggest that acquired prosopagnosia may not be a single disorder but a family of variants differing in mechanism. We proposed in 2008 that tests of perception and face imagery can probe component processes to support apperceptive, associative, and amnestic distinctions. However, validating this proposal is hampered by the rarity of this condition.

Methods:
We report data gather over 25 years from 23 patients classified by whether they had damage to the fusiform gyri or anterior temporal lobes, in either hemisphere. Perception was indexed by inverse efficiency for perceiving changes in the facial shape of unfamiliar faces, and facial memories probed by a test of imagery for famous faces.

Results:
Patients with fusiform lesions were impaired in face perception but had no or mild deficits for face imagery. Their apperceptive defect affected not just configuration but also feature size and external contour, especially in the upper face, and more so when they had to attend to multiple facial regions. An amnestic profile, with severely impaired imagery and minimally affected perception, was seen in two patients, one with right and one with bilateral anterior temporal damage. Four patients had an apperceptive/amnestic combination, all with bilateral occipitotemporal and right anterior temporal damage. Right anterior temporal damage alone often caused only mild imagery deficits: along with their relatively intact face perception, these subjects came closest to meeting proposed exclusionary criteria for an associative variant, i.e., relative preservation of both imagery and perception.

Conclusions:
These results confirmed a link between apperceptive prosopagnosia and occipitotemporal lesions. The key component for creating a severe amnestic deficit for faces was damage to the right anterior temporal lobe, though often this was not sufficient and required additional damage to other regions.

References: None provided.

Keywords: Higher visual functions, Neuroimaging, Stroke, Trauma, Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: JB was supported by Canada Research Chairs 950-202111, 950-228984, and 950-232752, and the Marianne Koerner Chair In Brain Diseases. This work was supported by NIMH grant 1R01 MH069898 and CIHR grants MOP-77615, MOP-85004, and MOP-102567

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Changes in Outcome Measures in Posterior Cortical Atrophy: A Pilot Study for TRAC-PCA

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Introduction:
Posterior Cortical Atrophy (PCA) is a rare, atypical syndrome of Alzheimer's disease (AD) marked by early cortical visual dysfunction. The rarity of the presentation, the predominance of visual dysfunction, and the lack of longitudinal data have impeded AD clinical trial participation for people with PCA. In preparation for TRAC-PCA, a clinical trial readiness study, this investigation assessed 1) standard AD and PCA-specific outcome measures and 2) the Rapid Eye Clinic Screening Battery for Visual Cortical Dysfunction (VisCorD) over 6 months in people with PCA.

Methods:
Patients meeting the 2017 'Pure-PCA' criteria were prospectively enrolled and evaluated with cognitive, functional, and patient-reported outcome measures at baseline and 6-months. Descriptive statistics, a linear mixed model, and Pearson correlation were used to analyze outcomes.

Results:
Thirteen participants were enrolled, with one withdrawn after failing the 10-point Cognitive Screen test. Participants were 75% female, with a median age of 72 years (IQR 13), median baseline MMSE score of 21 (IQR 7), and a median symptom duration of 5.9 years (IQR 5.3). Declines in all outcome measures were noted, with significant changes noted for two: the Clinical Dementia Rating – Sum of Boxes ($p = 0.03$) and the Addenbrooke's Cognitive Examination III or ACE-III ($p = 0.02$). Significant results were not mediated by age or symptom duration. Baseline scores for ACE-III and MMSE were correlated ($p = 0.005$), but ACE-III was more sensitive to decline. The VisCorD was abnormal for all participants.

Conclusions:
This pilot investigation, the first of its kind, supports standard AD and PCA-specific outcome measures for tracking PCA progression. Further validation of the VisCorD as a screening tool is indicated. The results inform the design of the TRAC-PCA study, a 12-month longitudinal study to advance clinical trial readiness for PCA.

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

Financial Disclosures: Victoria Pelak: John and Joanne Hare Fund to Accelerate PCA Research; Asher Mahmood: John and Joanne Hare Fund to Accelerate PCA Research; Lily Noteboom: John and Joanne Hare Fund to Accelerate PCA Research; Allison McKendrick; Brianne Bettcher

Grant Support: John and Joanne Hare Fund for Accelerating PCA Research

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Optimizing The Screening And Early Evaluation Of Papilledema And Idiopathic Intracranial Hypertension In A Tertiary Care Hospital

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Introduction:
Patients presenting to the Emergency department (ED) with concerns of papilledema are subject to over testing, leading to ineffective resource use and increased burden on consultations. Recent studies emphasize improving standardized evaluations for emergencies, such as papilledema. This study aimed to reduce disposition times, increase consult efficiency, and optimize the management of papilledema in the ED through a novel standardized approach.

Methods:
We conducted a retrospective chart review of 240 patients at a tertiary care hospital who presented to the ED with confirmed optic disc edema between 2016-2024. We compared resource utilization between patients managed before and after a change in the approach algorithm for new papilledema evaluations in the ED. The algorithm excludes cases without confirmed optic disc edema, focuses on ruling out secondary causes of papilledema, and guides Neurology and Ophthalmology consults based on specific clinical findings. Patients over 12 years old with confirmed optic disc edema were included. Data collection covered demographics, consult times, and papilledema evaluation details. Statistical analysis included chi-square/Fisher's exact tests for consultation rates and t-tests for disposition times.

Results:
Preliminary results showed that average post-protocol disposition time was 2hr 34min, a 65.3% reduction from the pre-protocol disposition time average of 7hr 36min. Mean Retinal Nerve Fiber Layer (RNFL) thickness pre-protocol was 211.12 ±22.93, compared to 97.84 ±4.83 post-protocol. Early data shows the average time to consult Ophthalmology or Neurology was reduced by 38.8%. This reflects the effectiveness of a standardized approach in improving patient outcomes and optimizing resource utilization.

Conclusions:
Our new ED algorithm for evaluation of papilledema reduced disposition times and time to consult Ophthalmology or Neurology. This suggests that a standardized approach can lead to more efficient use of resources, earlier intervention, and better patient outcomes. This approach can serve as a model for optimizing care in other institutions looking to implement similar changes.

References: Channa, Zafar, Canner, Haring, Schneider; Epidemiology of Eye-Related Emergency Department Visits, JAMA Ophthalmology, 134(3), 312–319, 2016. Hall, Jeng-Miller, Gardiner, Kim; Utilization trends of an ophthalmology-specific emergency department: the Massachusetts Eye and Ear experience, Digit J Ophthalmol. 26(4), 31-35, 2020.

Keywords: High intracranial pressure/headache, Optic nerve trauma and treatment

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Investigating The Correlation Between COVID-19 and Idiopathic Intracranial Hypertension: A Retrospective Cohort Study

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Introduction:
Numerous studies investigating the complications of COVID-19 infections have shown the virus can infect the nervous system, causing neuroinflammation. Recent studies show the Sars-COVID virus can cross the retina-blood barrier in mouse models. However, little research has investigated correlations between COVID-19 infections and ocular/neuro-ocular pathologies, including rises in idiopathic intracranial hypertension (IIH) since the COVID-19 pandemic. Early detection and management of IIH can prevent ocular complications and vision loss, making it important to investigate predictive methods such as correlations.

Methods:
A retrospective review was conducted on a COVID-19 dataset of 2,795 patients selected if they (1) had undergone ophthalmologic evaluation before and after COVID-19 infection and (2) had physical exam diagnoses of IIH. Data was collected on demographics (age, sex, BMI), comorbidities (smoking, diabetes, hypertension (HTN), hyperlipidemia (HLD), obstructive sleep apnea (OSA)), vaccination status, ophthalmologic findings, ocular exam findings, and time from COVID-19 diagnosis to onset of IIH symptoms. Linear analysis regression was performed to find any correlation between COVID-19 infection and disease diagnosis.

Results:
Thirty-one patients were identified with new-onset IIH post-COVID; 96.8% female, with a mean age of 30.87. The mean BMI was 39.87 kg/m². Comorbidities included 19.4% current smokers, 12.9% former smokers, 12.9% diabetic, 25.8% HTN, 6.5% HLD, and 25.8% OSA. Only 12.9% of the patients were vaccinated. IIH symptom onset occurred 175 days after COVID-19 diagnosis on average. The results showed an R^2 of 0.13.

Conclusions:
While data suggests a weak correlation between the COVID-19 infection and IIH, it is important to continue monitoring for IIH symptoms in patients with COVID-19 infections. This is especially true for patients with predisposing risk factors such as female and high BMI. Early detection and management for these patients is crucial to prevent long term vision loss. More multi-institutional studies are required to fully characterize the relationship.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Risk of Idiopathic Intracranial Hypertension With Hormonal Contraceptives, A TriNetX Analysis

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Introduction:
Hormonal contraceptives may be potential risk factors for idiopathic intracranial hypertension (IIH). This study aims to evaluate the risk of IIH with various hormonal contraceptives.

Methods:
A retrospective cohort study was conducted using the TriNetX database, a global research network with data from 120 million patients. Study cohort included patients using oral contraceptive pills (OCP), medroxyprogesterone acetate, contraceptive patch, levonorgestrel-releasing intra-uterine device (IUD), etonogestrel/ethinyl-estradiol vaginal ring, and contraceptive implants. Control cohort included patients with copper IUD. Exclusion criteria included previous IIH, secondary causes of raised intracranial pressure (ex. venous sinus thrombosis), tetracycline use, lithium use, and more. Propensity score matching (PSM) was used to balance cohorts based on age, body mass index (BMI), and other risk factors. Time-to-event analyses and hazard-ratios (HRs) with 95% confidence intervals (CIs) for development of IIH at 6 and 12-months post-contraceptive initiation were completed.

Results:
After 6-month PSM, cohort sizes were 85,337 for OCP, 80,236 for medroxyprogesterone acetate, 42,463 for contraceptive patch, 71,551 for levonorgestrel-releasing IUD, 61,313 for vaginal ring, and 63,069 for contraceptive implant. At 6 months, OCP users (HR: 2.294, 95% CI: 1.231, 4.275) and contraceptive implant users (HR: 2.084, 95% CI: 1.016, 4.276) had statistically significantly increased risk of IIH development compared to copper IUD users. Statistical significance for risk of IIH compared to control were lost at 1 year. Medroxyprogesterone acetate (HR: 1.4, 95% CI: 0.712, 2.754), contraceptive patch (HR: 1.584, 95% CI: 0.623, 4.023), levonorgestrel-releasing IUD (HR: 0.965, 95% CI: 0.402, 2.319), and vaginal ring (HR: 0.965, 95% CI: 0.402, 2.319) showed no significant difference in risk.

Conclusions:
OCP and contraceptive implants were associated with a significantly increased risk of IIH compared to copper IUDs at 6 months but not at 1 year. Hormonal contraceptives may contribute to IIH development, highlighting the need for further research to elucidate this association.

References: None provided.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Assessing the Risk of Retina Disorders in Idiopathic Intracranial Hypertension within Aggregated Electronic Health Record Data

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Introduction:
Idiopathic intracranial hypertension (IIH) is a condition in which intracranial pressure (ICP) is elevated with no identified underlying cause. Patients with IIH frequently experience vision changes caused by high pressure that compresses the optic nerve. Retinal damage has also been reported that may cause independent deleterious effects on vision, however these studies are limited due to the small size of the patient population. The aim of this study is to assess the risk of retina complications in patients with IIH using TriNetX, a large population platform of electronic health record data.

Methods:
This study used a retrospective cohort design. Inclusion criteria were selected based on ICD-10 codes for benign intracranial hypertension and papilledema. Conditions known to cause elevated ICP were excluded. Propensity score matching was performed for two control cohorts, obesity (any BMI > 30) and migraine. Subjects were matched based on age, demographics, BMI, and comorbidities.

Results:
Propensity score matching generated well-matched cohorts between IIH and obesity controls (n = 14,578) and IIH and migraine controls (n = 14,580). Two outcomes were associated with significantly elevated risk in IIH: retinal vascular occlusion (RR [95%CI]: 2.20 [1.20, 4.05] vs. obesity; 2.54 [1.34, 4.82] vs. migraine) and retinal edema (RR [95% CI]: 1.72 [1.20, 2.45] vs. obesity; 3.18 [2.04, 4.93] vs. migraine). Chorioretinal scar, retinal neovascularization, diabetic retinopathy, and non-exudative AMD were not significantly different between IIH patients and controls.

Conclusions:
Although the optic nerve is the most vulnerable part of the eye in IIH, anecdotal reports suggest that the retina is not always spared. Using a large population platform, we have demonstrated that there is a significantly elevated risk of conditions that arise from damage to the retinal vasculature. The results of this study highlight the need for careful monitoring of the retina in patients with IIH.

References: None provided.

Keywords: High intracranial pressure/headache, Retina

Financial Disclosures: Rebecca Schur: Funding: P30EY025585(BA-A), Research to Prevent Blindness (RPB) Challenge Grant, Cleveland Eye Bank Foundation Grant; Jacqueline Shaia: JKS National Eye Institute: T32 EY024236 (Jacqueline Shaia) P30EY025585(BA-A), Research to Prevent Blindness (RPB) Challenge Grant, Cleveland Eye Bank Foundation Grant honorarium: Impact Education - Regeneron Pharmaceuticals, Inc. RPS reports personal fees from Apellis, Iveric Bio, Eyepoint, Regenxbio, Genentech, Bausch and Lomb, Zeiss, Alcon, and Regeneron, and research grants from Jannsen. KET: Alimera (consultant), Apellis (consultant), Bausch and Lomb (consultant), Eyepoint (consultant), Genentech (consultant, speaker's bureau), Iveric Bio (speaker's bureau), Regeneron (research), Regenxbio (research), Zeiss (research); Priya Shukla: Funding: P30EY025585(BA-A), Research to Prevent Blindness (RPB) Challenge Grant, Cleveland Eye Bank Foundation Grant; David Kaelber; Rishi Singh: RPS reports personal fees from Apellis, Iveric Bio, Eyepoint, Regenxbio, Genentech, Bausch and Lomb, Zeiss, Alcon, and Regeneron, and research grants from Jannsen.; Katherine Talcott: KET: Alimera (consultant), Apellis (consultant), Bausch and Lomb (consultant), Eyepoint (consultant), Genentech (consultant, speaker's bureau), Iveric Bio (speaker's bureau), Regeneron (research), Regenxbio (research), Zeiss (research); Devon Cohen

Grant Support: None.

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Evaluating Quality of Life in Patients with Idiopathic Intracranial Hypertension (IIH) and Fulminant IIH

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Introduction:
Limited research has been conducted on quality of life (QOL) in IIH patients and it has never been reported on the fulminant IIH (FIIH) population. This study aimed to evaluate and compare QOL for IIH and FIIH patients.

Methods:
All IIH and FIIH patients currently aged 18 years or older and seen at a single tertiary care center from June 1st 2012 and September, 2023, were contacted. Patients completed two validated surveys: 36 Item Short Form Health Survey and validated National Eye Institute 25 question survey through a REDCap® link. The following was collected from their EHR: date of IIH diagnosis, last visual field mean deviation value and visual acuity, race/ethnicity, sex, age at diagnosis, current age, and if they had FIIH. Patients were compared to the general population as well as glaucoma patients who completed the same surveys.

Results:
108 patients (95% women) completed the survey, of which 17 had FIIH. Average current age was 36.31 years. Patients who underwent multiple surgeries had significantly impaired vision health as compared to those with one surgery or no surgery ($p < 0.001$), and worse physical limitations compared to others with surgeries or no surgeries ($p = 0.032$). Patients who underwent stenting for IIH had the least physical limitations (mean 70 SD 44.72). Patients with a stent required less support driving (mean 91.67 SD 8.33) compared to shunted patients (mean 62.12 SD 39.85). IIH patients had worse general, vision, social, mental, and emotional health and required more driving assistance than the general population ($p< 0.05$). IIH patients also had worse general health, mental health, and required more driving assistance than glaucoma patients ($p< 0.05$).

Conclusions:
IIH and FIIH patients had overall worse QOL measures than the general population. No significant QOL difference was found between IIH and FIIH patients.

References: None provided.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache

Financial Disclosures: Devon Cohen; Karl Koster; Bernard Pan; Hayden Reed; Katherine Talcott: KET: Alimera (consultant), Apellis (consultant), Bausch and Lomb (consultant), Eyepoint (consultant), Genentech (consultant, speaker's bureau), Iveric Bio (speaker's bureau), Regeneron (research), Regenxbio (research), Zeiss (research); Rishi Singh: RPS reports personal fees from Apellis, Iveric Bio, Eyepoint, Regenxbio, Genentech, Bausch and Lomb, Zeiss, Alcon, and Regeneron, and research grants from Jannsen.; Jacqueline Shaia: JKS National Eye Institute: T32 EY024236 (Jacqueline Shaia) P30EY025585(BA-A), Research to Prevent Blindness (RPB) Challenge Grant, Cleveland Eye Bank Foundation Grant honorarium: Impact Education - Regeneron Pharmaceuticals, Inc. RPS reports personal fees from Apellis, Iveric Bio, Eyepoint, Regenxbio, Genentech, Bausch and Lomb, Zeiss, Alcon, and Regeneron, and research grants from Jannsen. KET: Alimera (consultant), Apellis (consultant), Bausch and Lomb (consultant), Eyepoint (consultant), Genentech (consultant, speaker's bureau), Iveric Bio (speaker's bureau), Regeneron (research), Regenxbio (research), Zeiss (research)

Grant Support: None.

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What Are Patients Asking Online About Idiopathic Intracranial Hypertension (IIH)? An Analysis of the IIH Subreddit.

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Introduction:
Idiopathic Intracranial Hypertension (IIH) is a condition characterized by increased intracranial pressure without secondary causes, often leading to headaches and vision loss from papilledema. IIH predominantly affects obese women of reproductive age, with prevalence rising alongside the global obesity epidemic. For many reasons, patients frequently seek information about their condition and treatment options on social media platforms like Reddit, where anonymity facilitates candid discussions. This study investigates patient concerns and perceptions of IIH based on posts from the r/IIH subreddit that may not be addressed in clinical settings.

Methods:
A mixed-methods study was conducted to analyze 500 posts from the r/IIH subreddit collected in 2023. Posts were categorized based on content, including treatment-related inquiries, emotional tone, and physician relationships. The qualitative analysis focused on identifying key themes such as surgical versus non-surgical treatment preferences, medication and emotional distress.

Results:
The majority of posts were from patients [486 (97%)] with 295 [59%) neutral tone and 189 (38%) negative tone. The most frequently expressed emotions were anxiety [52(20%)], confusion [44(17%)], and fear [40(15%)]. The most frequently posted content was the sharing of symptoms, asking for advice [115(23%) each], medical treatment [91(18%)], and diagnosis [82(16%)]. Of 116 posts regarding diagnostic evaluation, the most of frequent were related to lumbar puncture [62(53%)]. Of 137 medical treatment-related posts, 88 concerned side effects. Of 49 posts for surgical treatment, [14(29%)] were post-operative questions and [10(20%)] were for type of treatment.

Conclusions:
Patients with IIH actively use Reddit to seek advice and share their experiences, with significant emphasis on medical treatment options and emotional distress related to their condition. Understanding patient concerns through social media can aid clinicians in improving patient education, addressing misconceptions, and offering targeted support. Further studies are needed to explore how online platforms like Reddit influence patient decision-making and treatment outcomes.

References: None provided.

Keywords: Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Risk Factors for Post-Dural Puncture Headaches in Idiopathic Intracranial Hypertension

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Introduction:
One of the most common complications of lumbar punctures (LP) are post-dural puncture headaches (PDPH). Very few studies have addressed PDPH in the idiopathic intracranial hypertension (IIH) patient population. We aimed to identify potential risk factors for PDPH in IIH patients, including needle type.

Methods:
In this retrospective chart review at a tertiary health center, we identified 268 patients who underwent LP between 2019 and 2022 and included all patients with IIH based on the modified Dandy criteria. We identified a separate subgroup of IIH patients who underwent LP using atraumatic needles that were introduced at our facility in January 2023. Primary outcomes included the impact of demographic, clinical, and procedural variables on the development of PDPH. Secondary outcomes included severity of PDPH and incidence of therapeutic blood patch.

Results:
A total of 33 out of 84 LP had documented PDPH (39%). There was a strong association between needle type and PDPH, with 81.8% occuring with traumatic needles versus 18.2% with atraumatic needles. PDPH severity was also greater for traumatic needles. Twenty-two patients (81%) with PDPH from the traumatic needle had therapeutic blood patch compared to zero from the atraumatic needle. PDPH were associated with increased opening pressure, but not CSF volume removed. There was no association between PDPH and mean retinal nerve fiber layer thickness (RNFL) as determined by pre-LP OCT. A statistically significant relationship was found between PDPH and history of headaches, but not anxiety, age, BMI, sex, or ethnicity.

Conclusions:
Our results show that larger gauge traumatic needles are associated with a higher incidence of PDPH in IIH patients, similar to the general population. Chronically elevated ICP in IIH patients can modify CNS compliance, leading to high risk for developing PDPH in IIH patients. Utilizing atraumatic needles can significantly improve patient experience and reduce PDPH in this subset of patients.

References: None provided.

Keywords: High intracranial pressure/headache, Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Improvements In Headaches And Pulsatile Tinnitus With Dural Venous Sinus Stenting In Idiopathic Intracranial Hypertension

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Introduction:
Idiopathic intracranial hypertension (IIH) is a condition characterized by elevated intracranial pressure (ICP). The symptoms are a wide spectrum including headaches, tinnitus, blurred vision, or transient visual disturbances. While mainstay treatment has been pharmacological management, literature reveals that there is little correlation between intracranial pressure ICP correction and resolution of subjective symptoms with this treatment modality. This investigation looks at the efficacy of DVSS on symptomatic relief, namely headaches and pulsatile tinnitus.

Methods:
19 patient charts status-post DVSS from April 2020 to September 2023 were reviewed. The presence of headaches, probable migraines, and pulsatile tinnitus were noted at the visit prior to venous stenting. Post-stent placement, patients were asked about the continued presence of these symptoms. The results were stratified into continued presence, worsened, and improvement of symptoms compared to values pre-stent. A correlation coefficient was drawn between lumbar puncture opening pressure (LP OP), a proxy for disease severity, and post-DVSS symptom relief.

Results:
Of 19 patients, 18 patients presented with some sort of headaches varying in severity. Half of the 18 demonstrated migraine-like qualities in conjunction with typical pressure headaches. In addition, 9 patients presented with pulsatile tinnitus. After stent placement, 82.3% of patients with headaches demonstrated improvement or complete resolution of symptoms. 11.1% were stable and 5.5% had worsened headaches. Of the 9 patients with prior pulsatile tinnitus, 7 had complete resolution. LP OP to headache relief had an r of 0.40 indicating a modest correlation.

Conclusions:
DVSS proves to be an effective treatment . The high rate of headache, migraine, and pulsatile tinnitus relief give further credibility to DVSS as a treatment modality for the treatment of IIH.

References: None provided.

Keywords: High intracranial pressure/headache, High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Longitudinal Optical Coherence Tomography Indices in Pediatric Idiopathic Intracranial Hypertension

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Introduction:
The exact timing of the optical coherence tomography (OCT) indices reaching the lowest value (nadir) and the factors that predict the patient's anatomical outcome are not known in the pediatric population. We aimed to determine the timing of nadir value and the factors that affect nadir retinal nerve fiber layer (RNFL) thickness values in the pediatric IIH population.

Methods:
The records of all pediatric IIH patients (Age< 17 years) who were treated in our institution from December 2009 to January 2023 were retrospectively reviewed. The following data were recorded at baseline and at nadir OCT: lumbar puncture opening pressure, body mass index (BMI), visual acuity, visual field mean deviation (MD), OCT RNFL, ganglion cell complex (GCC) values, and management

Results:
Twenty of the 26 patients (77%) were female, the cohort's average age was 12.6±3.4 years, their mean BMI was 25.7±6.5 Kg/m2, the mean menarche age was 11.87±1.1 years. The mean RNFL thickness at presentation was 307.3±125.3 µm. The mean time to nadir was 5.8±2.9 months. The average RNFL and GCC thickness at first nadir OCT appearance were 101.6±16.3µm, and 81.7±6.8 µm, respectively. Longer time to nadir correlated with younger age (r=-0.37 p=0.05). The mean follow-up was 40.7±33.7 months, during which 6 (26.1%) patients sustained a recurrent IIH episode.

Conclusions:
Our results showed that in contrast to adults, pediatric IIH patient’s final anatomical outcome of IIH episodes resulted in RNFL and GCC preservation, and that it was reached after a mean of 5.8±2.9 months, which is shorter than the time to nadir in adults. The time to RNFL nadir and its values correlated with younger age, indicating that pediatric IIH patients have unique characteristics that should be considered during follow-up and treatment of these patients.

References: None provided.

Keywords: Pseudotumor cerebri, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

Grant Support: Arrow Project, Sheba Medical Center, Tel Hashomer, Israel

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Regression Of Papilledema In IIH Does Not Reliably Mirror Intracranial Tension Dynamics Assessed By Standardized A-Scan Echography

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Introduction:
Idiopathic intracranial hypertension (IIH) is an increasingly prevalent disease bearing the risk of visual impairment due to axonal damage in presence of papilledema. Optical coherence tomography (OCT) yields valuable markers for diagnosis and disease monitoring, but its association with intracranial tension is controversially discussed.

Methods:
We analyzed longitudinal data in patients with papilledema from the Vienna Idiopathic Intracranial Hypertension (VIIH) database with definitive IIH according to revised Friedman criteria. Change from baseline in retinal nerve fiber layer (RNFL, SD-OCT) and retrobulbar arachnoid optic nerve sheath diameter (ONSD, standardized A-scan) was compared at three follow-ups. Receiver-operating-characteristics (ROC) analysis of area under the curve (AUC) was calculated for RNFL change predicting normal ONSD (< 5mm).

Results:
We included 44 IIH patients (88.6% female, median age 31 years, median BMI 32kg/m²). Median weeks to follow-ups were 6 (IQR=10.4; n=13), 32.5 (IQR=60.5; n=20), and 66.5 (IQR=89.9, n=18). Mean weight loss was 8.64±13.28%, median highest Acetazolamide dosage 750mg/d. At baseline and three consecutive follow-ups, mean RNFL thickness was 255.36±131.55µm, 149.8±76.14µm (-33.28±30.35%, p< 0.001), 108.3±34.63µm (-47.3±24.81%, p< 0.001), and 99.69±32.29µm (-50.33±25.31%, p< 0.001). Mean worse-eye ONSD was 5.34±0.76mm, 5.02±0.81mm (-11±15.09%, p=0.02), 5.24±0.59mm (2.16±17.98%, p=0.99), and 5.03±0.84mm (-7.74±18.06%, p=0.06), respectively. RNFL/ONSD correlation was -0.01, -0.23, 0.05, 0.22. AUCs (90% CI) of RNFL change for normal ONSD were 0.51, 0.49, and 0.36.

Conclusions:
While RNFL decreased continuously, ONSD reduced significantly only during initial treatment but not later on, which may indicate insufficient long-term control of intracranial pressure in many cases. In addition, RNFLT reduction did not predict normalized ONSD. Our data suggest using OCT RNFLT cautiously when estimating intracranial tension, and to simultaneously apply standardized A-scan echography where available.

References: None provided.

Keywords: High intracranial pressure/headache

Financial Disclosures: Christoph Mitsch; Karl Kircher; Bsteh Gabriel; Krajnc Nik; Macher Stefan; Berthold Pemp: honoraria for lectures and consulting from Chiesi

Grant Support: None.

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Prognostic Indicators of Idiopathic Intracranial Hypertension at a Single Practice Located in a Low-Income Metro Area

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Introduction:
The Idiopathic Intracranial Hypertension Treatment Trial (2014) identified that male gender, high-grade papilledema, and poor best-corrected visual acuity at presentation were important risk factors for treatment failure. Since our practice is located in a large metropolitan area that ranks among the top-ten U.S. cities in both poverty and obesity rates, we aim to identify prognostic indicators of IIH that may be unique to our patient population.

Methods:
In this retrospective study, ICD10 codes G93.2 and H47.11 were used to identify all consecutive IIH patients managed by two neuro-ophthalmologists at a single neuro-ophthalmology practice from January 2023 to April 2024. Medical records queried for age, gender, race, systemic comorbidities, logMAR visual acuity, Frisen grade at presentation, retinal nerve fiber layer (RNFL) global thickness, Humphrey visual field (HVF) mean deviation, and need for surgical intervention. Patients with potentially identifiable secondary causes of elevated intracranial pressure or patients carrying a diagnosis of IIH for greater than five years were excluded.

Results:
A total of 118 patients met inclusion criteria. 90.7% of patients were female and mean patient age was 38 years. 82 patient were African American, 32 patients were Caucasian, and 4 were of other descent. Among comorbid medical conditions, 13% had hypertension, 8% had type 2 diabetes mellitus, and 7% had chronic kidney disease. Although not statistically-significant, men had worse presenting visual acuity and HVF mean deviation than women. There was a statistically significant increase in RNFL global thickness in men compared to women. Patients with chronic kidney disease had significantly worse presenting visual acuity, RNFL, and mean deviation compared to patients with comorbid hypertension alone or neither comorbidity.

Conclusions:
Male patients and those with chronic kidney disease may present with severe forms of IIH with increased risk of treatment failure. As such, these patients require closer monitoring and have lower threshold for surgical intervention.

References: None provided.

Keywords: High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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The diagnostic utility of the absence of radiographic findings of Idiopathic Intracranial Hypertension

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Introduction:
This study aims to investigate the utility of neuro-radiographic evaluation for ruling out idiopathic intracranial hypertension (IIH). Several recognized radiographic signs of IIH include empty sella, flattening of the posterior globes, optic nerve head protrusion, distention of the optic nerve sheaths, cerebellar tonsillar herniation, meningoceles, slit-like ventricles, enlargement of Meckel's cave, and transverse venous sinus stenosis. However, the positive predictive value of these findings is low, as they are often seen in normal patients or in other conditions, resulting in poor specificity. This study will assess the clinical utility of the absence of these findings in suspected IIH cases, focusing on negative predictive value and negative likelihood ratio.

Methods:
This retrospective study, at a Midwestern tertiary care center, will review 300 patients with newly diagnosed IIH (September 2019 to September 2024). Diagnosis is confirmed by lumbar puncture showing an opening pressure of ≥25 cm H2O within 3 months of neuro-imaging, and papilledema. Secondary causes of elevated intracranial pressure will be excluded. Controls will be patients with pseudo-papilledema (lumbar puncture opening pressure < 25 cm H2O and no true optic disc edema). Neuroradiologists will review neuroimaging for the presence or absence of known IIH radiographic features. Data will include lumbar puncture pressures and CSF results.

Results:
A pilot cohort of 7 patients with confirmed IIH has been reviewed. All patients had empty sella, 4 had flattening of the posterior globes, 2 had optic nerve head protrusion, 1 had Meckel's cave enlargement, and 4 had transverse sinus stenosis. The average lumbar puncture pressure was 34.14 cm H2O. Full dataset analysis will follow.

Conclusions:
Pilot results suggest that absent radiographic signs may lower the likelihood of IIH. Full cohort analysis will clarify the diagnostic role of absent neuro-imaging features, potentially improving diagnostic specificity in equivocal cases.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Trends Among Normal-Weight Patients with Pseudotumor Cerebri Syndrome (PTCS)

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Introduction:
Pseudotumor cerebri syndrome (PTCS) is a vision-threatening condition characterized by increased intracranial pressure, headaches, papilledema and normal imaging. The main risk factors for primary PTCS or idiopathic intracranial hypertension (IIH) include obesity, female sex, and being of reproductive age. PTCS can occur with use of medications. We aimed to characterize differences among PTCS patients with and without obesity.

Methods:
This study was approved by the Institutional IRB. We reviewed the records of 898 PTCS patients in a Redcap database from 1999-2024. Records without patient BMI at diagnosis were excluded. We compared age, sex, presenting symptoms, illness duration, symptom recurrence, causes of PTCS, visual acuity grade, Humphrey Visual Field mean deviation, papilledema grade, and treatment between the patient groups.

Results:
Normal-weight PTCS (NW-PTCS) patients made up 11.16% (n=66) of the total cohort and 89% were women. Obese PTCS patients were 92% women. NW-PTCS patients presented at a younger mean age (18.24 vs. 28.79, p=< 0.001) and with diplopia more than patients with obesity (33% vs. 20%, p=0.015). Migraine history was less common among NW-PTCS patients (31% vs. 48%, p=0.010). NW-PTCS individuals had more medication-induced PTCS (33% vs.13%, p=< 0.001). Optic nerve sheath fenestration was not required in normal-weight patients (0% vs. 9.1%, p=0.010). Therapeutic lumbar puncture was less common in the normal-weight group (3% vs. 11%, p=0.042). Normal-weight patients were less likely to have recurrence after symptom resolution (3.4% vs. 14% p=0.006). There were no differences in visual outcomes between the two groups (p>0.05).

Conclusions:
Normal-weight PTCS is uncommon.. We report comparable visual outcomes among our NW-PTCS patients, despite differences in symptoms at presentation. Further research is needed to evaluate risk factors for IIH development among normal-weight individuals.

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Keywords: High intracranial pressure/headache, Visual fields

Financial Disclosures: Samuel Ahanonu; Kathleen Digre; Jacqueline Shaia: JKS National Eye Institute: T32 EY024236 (Jacqueline Shaia) P30EY025585(BA-A), Research to Prevent Blindness (RPB) Challenge Grant, Cleveland Eye Bank Foundation Grant honorarium: Impact Education - Regeneron Pharmaceuticals, Inc. RPS reports personal fees from Apellis, Iveric Bio, Eyepoint, Regenxbio, Genentech, Bausch and Lomb, Zeiss, Alcon, and Regeneron, and research grants from Jannsen. KET: Alimera (consultant), Apellis (consultant), Bausch and Lomb (consultant), Eyepoint (consultant), Genentech (consultant, speaker's bureau), Iveric Bio (speaker's bureau), Regeneron (research), Regenxbio (research), Zeiss (research); Srav Vegunta; Judith Warner

Grant Support: Samuel Ahanonu (medical student) was funded by the T35 grant (5T35EY026511-07) from the National Eye Institute through the summer Medical Student Research Program at the Spencer Fox Eccles School of Medicine at the University of Utah. Drs Digre and Warner are supported by an unrestricted grant from Research to Prevent Blindness; Department of Ophthalmology and Visual Sciences, Moran Eye Center, University of Utah.S

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A Comparison of Clinical and Demographic Profiles in Patients with Malignant versus Non-malignant Pseudotumor Cerebri

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Introduction:
The purpose of this study is to determine differences in the clinical and demographic profiles between patients with malignant (MPTC) versus non-malignant pseudotumor cerebri (PTC). The secondary aim is to determine whether there is an association between clinical and demographic profiles of MPTC and PTC patients and visual outcomes.

Methods:
A retrospective, cross-sectional study including patients treated for PTC or MPTC at large academic centers with follow-up at an affiliated ophthalmology clinic. Inclusion criteria include age 5-75, a diagnosis of PTC per the Modified Dandy Criteria, receiving laboratory evaluation included in the data collection, and at least 2 months of follow up. To date, 69 patients have met the inclusion criteria from two institutions. Demographic data included, but was not limited to age, race, and sex. Clinical data assessed included serum laboratory markers, medical history, comorbid conditions, medications, MRI findings, and ophthalmic examinations.

Results:
Of the 69 patients, 50 (72%) had PTC with a mean age of 26.56 (±10.48) and 19 (28%) had MPTC with a mean age of 26.16 (±8.34). Twenty-nine (42%) are black, 30 (43%) white, and 10 (15%) other. Statistically significant clinical markers ($P< 0.05$) included CSF opening pressure, visual acuity, visual fields, and papilledema grade. The laboratory markers that reached statistical significance were elevated serum glucose, anion gap, and eGFR, while HCO3 and CSF white count trended towards an association with MPTC ($0.05< P< 0.1$). Additionally, histories of hyperthyroidism and headache, and the MRI finding of cerebellar tonsillar ectopia trended towards the development of MPTC ($0.05< P< 0.1$).

Conclusions:
Several factors appear to be associated with the development of MPTC versus NMPTC. This knowledge may be helpful in guiding assessment of high-risk patients for the development of MPTC and management of patients with MPTC or NMPTC. A multi-center study has been established to increase data collection.

References: None provided.

Keywords: High intracranial pressure/headache, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Neuroimaging, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Mental Health Evaluation and Suitability for Cognitive-Behavioural Therapy among patients with Idiopathic Intracranial Hypertension

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Introduction:
High rates of mental health disorders have been reported among patients with IIH. Cognitive-behavioral therapy (CBT) has been suggested as a complementary treatment to help manage anxiety and headache pain in IIH. However, no study has yet formally assessed the mental health of IIH patients through a psychiatric interview, nor evaluated their suitability or interest in CBT.

Methods:
People with IIH were recruited from a tertiary care outpatient neuro-ophthalmology practice. Demographic characteristics were recorded, and self-rated scales were completed for depression (PHQ-9), anxiety (GAD-7), headaches (HIT-6), and disability (WHODAS-12). DSM-5 diagnoses, patient's suitability for CBT (SSCT scale), and potentially meaningful therapy goals were identified through a psychiatric interview.

Results:
Among 14 participants (mean age 34 years, 93% female), 7 (50%) had significant disability (WHODAS score 2-4). 8 (57%) reported substantial or severe impact of headaches (HIT-6 score >56). Self-rated scales suggested high rates of depressive symptoms (mean PHQ-9 9.4±3.1) and anxiety (mean GAD-7 9.2±3.0). Among the 10 participants who underwent psychiatric assessment, high rates of mental disorders caused or worsened by IIH were found, notably 3 cases of anxiety disorders, 3 adjustment disorders, 2 depressive disorders, and 2 post-traumatic stress disorders. 9 (90%) expressed a high level of interest for CBT, and 8 (80%) were deemed suitable for CBT (mean SSCT 36.4±7.0). Anxiety reduction was the preferred and most meaningful therapy goal for 7 (70%) of interviewed participants.

Conclusions:
Our results confirm high rates of mental health comorbidities among patients with IIH. In our pilot study, most were very interested in CBT and were deemed good candidates to benefit from this type of psychotherapy. CBT should therefore be considered in the therapeutic management of IIH patients with psychiatric comorbidities.

References: None provided.

Keywords: High intracranial pressure/headache, Optic neuropathy, Pseudotumor cerebri, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: Funding: NIH P30 026877, unrestricted grant from research to prevent blindness

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Optic Nerve Sheath Enhancement in Patients with a New Diagnosis of Idiopathic Intracranial Hypertension

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Introduction:
Optic nerve sheath enhancement (ONSE) is a radiologic sign commonly associated with a diagnosis of optic perineuritis. However, a recent study has reported this radiologic sign in patients with idiopathic intracranial hypertension (IIH). The presence of ONSE in patients with IIH may lead to optic perineuritis diagnosis in excess. We evaluated the prevalence of ONSE in patients with a new diagnosis of IIH.

Methods:
Retrospective study of consecutive patients who presented to the Emergency Department of our quaternary care center with a suspected intracranial pressure disorder between 6/15/23-7/1/24. Patients who received a new diagnosis of IIH fulfilling the most recent diagnostic criteria and had orbital MRI with fat suppression sequences and contrast use were included. An expert neuroradiologist evaluated the presence of ONSE on all orbital MRIs from the included patients.

Results:
Forty-three patients with a new diagnosis of IIH were included (mean age 31±7 years; 100% women; 70% black, 20 % white, and 8 % other). In 5 of these 43 patients, the presence of ONSE was suggested: 3 pts with probable ONSE vs. blood vessels, 1 pt with possible ONSE vs. blood vessels, and 1 patient with questionable ONSE vs. probable blood vessels. The remaining 38 patients were categorized as normal or no ONSE.

Conclusions:
ONSE is a radiological sign that may occur in approximately 12 % of patients who are newly diagnosed with IIH. However, the distinction between mild ONSE vs. blood vessels surrounding or within the optic nerve sheath is challenging. A localization at the distal infraorbital portion of the optic nerve sheath and a corkscrew appearance are suggestive of a vascular etiology. Being aware of this possible radiologic sign in patients with IIH is important in order to avoid optic perineuritis misdiagnosis, which could lead to unnecessary ancillary tests and/or treatment, increasing the risk of iatrogenesis.

References: None provided.

Keywords: Neuroimaging

Financial Disclosures: Fernando Labella Álvarez; Amit M. Saindane; Nancy Newman: Consultant for GenSight, Chiesi, Neurophth (all involved with the treatment of Leber hereditary optic neuropathy. Research support as PI to my institution from GenSight for clinical trials.; Valérie Biousse: Consultant for Topcon which commercializes fundus cameras. The current research is completely independent from Topcon and is not funded by the company.

Grant Support: None.

Contact Information: None provided.

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Dural Venous Sinus Stenting as a Therapeutic Option for Medication-Refractory Idiopathic Intracranial Hypertension

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Introduction:
Idiopathic intracranial hypertension (IIH) is a condition marked by elevated intracranial pressure without an identifiable cause, leading to a spectrum of clinical symptoms. A subset of patients with IIH demonstrate stenosis in the dural venous sinuses (DVS) indicated by an elevated pressure gradient; in these patients, a stent can be placed to improve flow. This study aims to evaluate the post-operative effects of dural venous sinus stenting (DVSS) on symptoms and acetazolamide (ACZ) dosage in patients with IIH.

Methods:
A retrospective review was conducted on charts of 19 patients who underwent DVSS over the past 6 years. Papilledema was evaluated through fundoscopy and OCT, and symptoms such as headache, migraines, and pulsatile tinnitus were categorized based on resolution, improvement/deterioration, and stability. ACZ doses (in mg/day) were recorded before and after DVSS. The Wilcoxon signed-rank test was employed to analyze the significance of changes in ACZ dosage and papilledema from pre- to post-stenting.

Results:
In a cohort of 19 patients, 17 presented with papilledema prior to stenting, with 88% showing improvement and 52% achieving complete resolution. However, results of Retinal Nerve Fiber Layer (RNFL) showed no statical significance ($p = 0.11$ OD, $p = 0.36$ OS). Of the 19 patients, 18 experienced headaches, with 82% reporting symptom relief, and 44% showing complete resolution after the stent. Among 9 patients with migraines prior to stenting, 55% improved, 44% remained stable, and 11% reported worsening symptomatology. Furthermore, there was a statistically significant difference in ACZ dosage before and after stent placement ($p = 0.0078$).

Conclusions:
This study provides evidence for the efficacy of DVSS as an intervention to enhance the quality of life in individuals with IIH. The findings indicate that DVSS may facilitate a reduction or cessation of ACZ therapy while simultaneously improving clinical symptoms.

References: None provided.

Keywords: High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Correlation of Body mass index (BMI) and spinal tap opening pressure in pediatric Idiopathic Intracranial Hypertension (IIH)

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Introduction:
There has been increased incidence of IIH in the pediatric population over the past decade. The purpose of this study was to gather demographic and clinical data on pediatric IIH patients seen in our neuro-ophthalmology clinic so that we may better elucidate any relationship between BMI and spinal tap opening pressure.

Methods:
This is a retrospective study of pediatric IIH patients with neuroimaging and a documented spinal tap opening pressure seen in our clinic between November 17, 2017, and February 13, 2024. IRB approval was obtained, and data was collected using electronic medical records.

Results:
This study included 50 patients between the ages of 5 and 18. 80% were female and 20% were male. 96% were white, 2% were black, and 2% were mixed race. The clinical symptoms included headache/eye pain in 94%, diplopia in 14%, transient vision loss in 28%, blurry vision in 34%, and pulsatile tinnitus in 36%. The median BMI was 34.2 (17-54.9) and the median opening pressure was 34 cm of water (12-55). Using spearman correlations, the relationship between BMI and diagnostic opening pressure was statistically significant (r value 0.325, p value 0.022). There was no association between age and diagnostic opening pressure (r value -0.219, p value 0.131). There was also no correlation between gender and diagnostic opening pressure.

Conclusions:
From this select number of pediatric patients with diagnosed idiopathic intracranial hypertension, there was compelling evidence for a relationship between diagnostic opening pressure and BMI. However, there was no relationship between age, gender and spinal tap diagnostic opening pressure. Further data with larger sample size should be collected to also explore the differences between prepubertal and post pubertal pediatric patients with IIH.

References: None provided.

Keywords: High intracranial pressure/headache, Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Effects of a "Pseudotumor Board" on the Interdisciplinary Management of Intracranial Hypertension

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Introduction:
Intracranial hypertension is both over- and underdiagnosed and proper evaluation and management often requires multiple specialists. To enhance care for these patients, our institution established a multidisciplinary “pseudotumor board” in 2019, which facilitates case discussions among specialists to improve diagnosis and management. This study assesses the pseudotumor board's impact on patient triage, diagnostic precision, and treatment.

Methods:
This prospective study analyzed pseudotumor board meetings from January 2023 to February 2024. Monthly videoconference sessions included neurology, neuro-ophthalmology, neurosurgery, neuroradiology, and otology (added mid-study), allowing providers from an academic medical center and an affiliated public hospital to discuss complex intracranial hypertension cases. The study collected pre- and post-meeting clinical plans, the content of case discussions, and patient demographic and clinical information.

Results:
A total of 57 patients (age range 14-83) were presented over 14 months. In 21 cases, conference alone was sufficient to steer clinical care. In 20 cases interdisciplinary input and referrals within the group led to changes in management. During the conference, neuro-ophthalmology answered the plurality of clinical questions (33) followed by radiology (17). Modifications to diagnostics, therapeutics, or referrals during conference were more often additive (48 changes) than reductive (17 changes). The referral diagnosis changed in 32/57 patients presented to the conference. Experience during the conference led us to triage outside referrals for IH intervention to neuro-ophthalmology prior to their first neurosurgery visit, avoiding many unnecessary visits. 29 presentations involved discussions between neuro-ophthalmology and headache neurology, prompting us to start a multidisciplinary headache clinic.

Conclusions:
The pseudotumor board improved IH management by enhancing diagnostic accuracy and reducing redundant specialty consultations, though it also led to increased diagnostic testing and referrals. Experience during the meetings led to the formation of a dedicated triage system and a multispecialty clinic, streamlining patient care. This model may be replicable in other institutions with similar caseloads.

References: None provided.

Keywords: High intracranial pressure/headache, Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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A Comparative Evaluation Of Artificial Intelligence Chatbot Responses To Questions Regarding Idiopathic Intracranial Hypertension

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Introduction:
Artificial intelligence (AI) large language models (LLMs) like ChatGPT-4, Copilot, and Gemini are increasingly being explored for patient education and clinical decision support. Idiopathic intracranial hypertension (IIH), a neuro-ophthalmologic condition with serious visual and neurological outcomes, requires accurate, accessible information for both patients and providers. This study evaluates the accuracy and completeness of responses provided by these LLMs to commonly posed IIH-related questions.

Methods:
ChatGPT-4, Google Gemini Advanced, and Bing Copilot Pro were assessed using two sets of questions: 25 questions that patients would potentially ask about IIH (e.g., related to symptoms, treatments, and disease understanding) and 25 questions that healthcare providers would ask neuro-ophthalmologists (e.g., related to clinical management and treatment strategies). Responses were graded by an independent neuro-ophthalmologist as acceptable, incomplete, or unacceptable. Data were analyzed using descriptive statistics and percentage calculations.

Results:
Google Gemini delivered 100% acceptable responses to patient questions and 96% to provider questions, with the highest rate of completeness for patient answers. ChatGPT-4 provided 100% acceptable responses to patient questions and 92% for provider questions. Bing Copilot Pro showed 88% acceptable responses to patient queries and 92% to provider queries but had the most incomplete responses overall (8%). Limitations in responses were more evident in provider questions, particularly for complex or highly specific clinical inquiries.

Conclusions:
Overall, all examined chatbots provided a high rate of acceptable responses, especially to patient questions. Google Gemini demonstrated the highest rate of acceptable and complete responses compared to ChatGPT-4 and Bing Copilot Pro. However, all LLMs exhibited limitations in answering complex provider questions, signaling a need for improvement in clinical applicability. Further advancements in prompt engineering, AI training datasets, and clinical workflow integration will bridge the gap between patient education and real-world clinical decision-making.

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Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Pregnancy and delivery outcomes associated with idiopathic intracranial hypertension in the U.S., 2016-2020

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Introduction:
Idiopathic intracranial hypertension (IIH) affects women of childbearing potential and can occur during pregnancy, but data on pregnancy and delivery outcomes in IIH are lacking.

Methods:
We performed a retrospective cross-sectional analysis of 2016-2020 data from the National Inpatient Sample (NIS), a stratified 20% sample of all hospitalizations in the U.S. Using ICD-10 codes, we identified delivery-related hospitalizations, IIH diagnoses, and outcomes including viability, pre-eclampsia/eclampsia, gestational diabetes, placental abruption, post-partum hemorrhage, preterm labor, premature rupture of membranes, intrauterine growth restriction, fetal death, cesarean delivery and epidural procedure. We compared outcomes for IIH vs. non-IIH pregnancies using logistic regression adjusting for age, race/ethnicity, median income by ZIP, insurance payer, hospital location and characteristics, and obstetric comorbidity index. Because obesity and PCOS are risk factors for both IIH and adverse pregnancy outcomes, we performed sensitivity analyses comparing IIH to a subset of non-IIH pregnancies with obesity or PCOS. Sample weights were applied to account for the complex survey design of NIS.

Results:
There were 24,136,282 delivery-related hospitalizations in the U.S. between 2016-2020. Of 23,996,087 viable deliveries, 7,640 women had IIH. Compared to women without IIH, IIH-related deliveries were associated with an increased risk of pre-eclampsia/eclampsia in both unadjusted (OR 5.21, 95% CI: 4.70-5.77) and adjusted analyses (OR 2.29, 95% CI: 2.00-2.63). Results were similar in our sensitivity analyses using controls with obesity or PCOS. IIH was also associated with gestational diabetes compared to all non-IIH controls (OR 2.39, 95% CI: 2.06-2.77), but not compared to obese (OR 0.92, 95% CI: 0.79-1.07) or PCOS (OR 0.79, 95% CI: 0.67-0.92) controls. IIH was not associated with other pregnancy or delivery outcomes.

Conclusions:
IIH is associated with pre-eclampsia/eclampsia, and associations with gestational diabetes may be explained by underlying risk factors such as obesity or PCOS. IIH was not associated with other complications of delivery.

References: None provided.

Keywords: High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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The frequency and characteristics of prodromal symptoms of visual aura

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Introduction:
Prodrome and visual aura are two phases that precede migraine headache and are thought to originate in the hopothalamus and occipital cortex, respectively. Prodromal symptoms are known to occur in up to 80% of migraine without aura. However, prodromal symptoms in visual aura have not been well studied. The aim of this study was to investigate the prevalence and characteristics of prodromal symptoms preceding visual aura.

Methods:
A total of 100 patients with visual aura were recruited at Nowon Eulji Medical Centre. The diagnoses of visual aura were based on the third edition of the International Classification of Headache Disorders (ICHD-3). We collected information on the clinical characteristics of the prodromes using questionnaires and interviews. When patients had more than one prodrome, we considered the most prominent and frequent symptom as a prodrome.

Results:
A total of 100 patients with visual aura were enrolled. The mean age of the study population was 29.8 years (range, 12 to 66 years), 74% were female. The mean age of onset was 22.0 years. Fourteen patients had two or more auras. These included aphasic aura (n=10), sensory aura (n=8) and brainstem aura (n=2). Thirty-five patients with visual aura had a prodrome. The mean duration of the prodrome was 4.8 hours (IQR 1, 3). The most common prodrome was a sense of impending aura (23.7%), followed by fatigue (n=7, 18.4%) and dull headache (n=4, 10.5%). The presence of photophobia was associated with prodromes in visual aura (OR=4.860, 95% CI=1.934-12.211, p< 0.001).

Conclusions:
Prodromes in visual aura appear to be less frequent and shorter in duration than those in migraine without aura. These results suggest that cortical spreading depression, rather than hypothalamic activation, plays an important role in the initiation of visual aura.

References: None provided.

Keywords: Miscellaneous, Higher visual functions

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Neuro-ophthalmic Findings of Visual Snow Syndrome in East Asia

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Introduction:
The aim of this study was to determine the neuro-ophthalmology and treatment responses in visual snow syndrome (VSS).

Methods:
We retrospectively reviewed the data of patients diagnosed with VSS at a tertiary referral hospital from March 2021 to February 2024. Data on visual and nonvisual symptoms, self-reported events that caused VSS, and medical and psychiatric comorbidities were extracted from medical charts. Neuroimaging findings from MRI and 18F-FDG PET were evaluated, along with treatment responses to pharmacological interventions and filter glasses.

Results:
The sample comprised 27 males and 36 females, with a mean age of 27±11 years (mean±SD) and onset age of 22.4±11 years. Common symptoms included floaters, palinopsia, anxiety, and depression. Fourteen participants attributed VSS onset to specific ophthalmic events (e.g. bright-lights during dilated ophthalmic examinations or refractive surgeries). 18F-FDG PET scans showed hypermetabolism in the visual cortices, with no significant MRI abnormalities. Lamotrigine (18.9%), alprazolam (20%), and filter glasses (32.1%) showed modest efficacy in reducing the intensity of VSS.

Conclusions:
Bright-light ophthalmic examinations and refractive surgery might trigger VSS in susceptible subjects. Functional brain scanning methods such as 18F-FDG PET may be an objective diagnosing tool for VSS. The pharmacological treatment responses for VSS were variable and modest. A multidisciplinary treatment strategy that combines medication and filter glasses and also addresses psychological aspects may improve the quality of life in patients with VSS. East Asian patients with VSS demonstrated similar symptoms, PET scan findings, and response to treatment to reports from Europe and North America.

References: None provided.

Keywords: Ocular motility, Non-organic visual disorders, Optic nerve trauma and treatment

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Identifying the Association between Clinical Characteristics and Presenting Visual Acuity in Patients with Optic Neuritis: A Case-Control Study

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Introduction:
Patients with atypical optic neuritis (ON) may experience vision loss constituting blindness (i.e. visual acuity (VA) logMAR 1.30 or worse).1,2 However, there is limited literature characterizing the diagnostic and clinical features associated with blindness in ON, especially in comparison to typical ON patients. We seek to further analyze this through a case-control study design.

Methods:
All patients with ON seen at two tertiary neuro-ophthalmology practices from 2014 to 2024 were reviewed. Inclusion criteria were clinical diagnosis of ON and presentation within 2 months of symptom onset. 156 patients presenting with a VA≤1.30 were designated as cases and matched by initial visit date to 156 controls presenting with a VA>1.30.

Results:
The mean age of the cases was 39.3±13.2 years, with 67% being women. On average, cases presented 10.8±9.2 days following symptom onset with a VA of 2.2±0.4. The mean age of controls was 37.5±13.6, with 73% being women. On average, controls presented 14±13 days after symptom onset with a VA of 0.3±0.3. A significantly greater proportion of cases had antibody-associated ON (20%, 31/156 vs. 8%, 12/156; p=0.002). Furthermore, cases were more likely to have diffuse visual field (VF) defects (76%, 94/124 vs. 21%, 29/135; p< 0.001). Controls were more likely to present with normal VFs (16%, 22/135 vs. 2%, 2/124; p< 0.001) and altitudinal VF defects (20%, 27/135 vs. 9%, 11/124; p=0.01). There were no differences between peripapillary retinal nerve fiber layer (pRNFL) thickness (p=0.07), ganglion cell analysis (GCA) (p=0.93), or proportion of patients with eye pain (p=0.22), headache (p=0.44), or disc edema (p=0.27).

Conclusions:
Antibody-mediated ON and diffuse VF defects are associated with blindness in ON patients. Although clinical investigations (pRNFL and GCA) are often used to inform diagnosis and management, they may not be reliably used to distinguish between ON patients with or without severe vision loss indicating blindness.

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Keywords: Optic neuritis

Financial Disclosures: The authors had no disclosures.

Grant Support: None

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Real World Management Patterns and Outcomes in Thyroid Eye Disease: A Claims Analysis

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Introduction:
Thyroid eye disease (TED), an autoimmune disorder affecting ~10/10,000 people, is a major extrathyroidal manifestation of Graves' disease (GD).1 Despite recent advances, gaps persist in understanding TED onset, treatment efficacy, the benefits of early intervention, and the role of various healthcare providers (HCPs) in patient care.

Methods:
This retrospective cohort study analyzed Optum claims data of patients newly diagnosed with TED, collected between January 1, 2016, to September 30, 2023. Patients were identified using diagnosis codes and physician notes. Moderate-to-severe (MTS) disease was determined based on the use of TED-specific interventions within 6 months of diagnosis.

Results:
Of the 112,546 patients presenting with GD and TED symptoms, 36,527 were included in the analysis; 7,494 patients were classified as MTS TED cases. Patients with TED were seen by many HCPs from specialists to internal medicine and advanced practitioners. At the index date, patients presented with a variety of TED symptoms including exophthalmos (30%), diplopia (29%), orbit inflammation (25%), and lid retraction (12%). For MTS TED, pharmacological intervention was often chosen over surgery (across all time points); median time to initiation of first pharmacological treatment was 60 days. Most patients with MTS TED (78%) received steroids as first-line therapy, while fewer received immunotherapy (4%). There was a notable preference for oral steroids over IV administration (79.2% vs. 35.9%). For MTS patients receiving immunotherapy (11%), the majority were treated with Teprotumumab (9.4%); 36.1% required second treatment. While 61.5% of steroid users reported no second treatment, this may not account for potential additional steroid courses. Additionally, 6% of patients received teprotumumab immunotherapy as a third treatment after a second steroid therapy.

Conclusions:
Despite multidisciplinary care, symptom persistence and underestimated secondary treatment rates suggest gaps in treatment continuity and symptom resolution. This highlights the variability in TED management and the need for improved treatment strategies.

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Keywords: Graves' disease, Orbit

Financial Disclosures: Nick Yang: Employee of Tourmaline Bio, Inc.; Kristine Erickson: Employee of Tourmaline Bio, Inc.; Cathy Andorfer: Employee of Tourmaline Bio, Inc.; John Walsh: Employee of Tourmaline Bio, Inc.

Grant Support: None.

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Prevalence of MRI findings Believed to be Associated with Papilledema in Children

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Introduction:
Specific brain MRI features (i.e., enlarged optic nerve sheaths, empty sella, cerebellar ectopia, optic nerve head protrusion, flattened sclerae, and sinus venous stenoses) are believed to indicate papilledema. However, their predictive value has not accounted for the background prevalence of these features in children. This study examined the prevalence and diagnostic utility of MRI features in a large random sample of children with and without papilledema.

Methods:
Two thousand randomly selected patients were included if they underwent brain MRI and ophthalmic evaluation within ± 3 months. Patients with genetic or systemic/acquired conditions were excluded. All cases were extracted and classified from the electronic medical record using natural language processing, then manually confirmed. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated.

Results:
MRI features were more prevalent in those with papilledema (N=89/106, 84.0%) than in those without (N=166/1894, 8.8%). Optic nerve head protrusion (PPV=71%, NPV=98%) demonstrated the highest diagnostic accuracy for papilledema. Optic nerve sheath dilation (PPV=60%, NPV=97%), venous stenosis (PPV=62%, NPV=96%) and flat sclera (PPV=61%, NPV=97%) had similar utility. Cerebellar ectopia had a poor PPV (15%) due to high prevalence in the no papilledema group (N=76/1849, 4%). The PPV for papilledema increased with the total number of MRI features: ≥1 (35%), ≥2 (69%), ≥3 (81%), ≥4 (90%), and ≥5 (90%), with modest declines in NPV (range: 99% to 95%).

Conclusions:
While children that manifest papilledema frequently have MRI features suggestive of elevated ICP, the frequency of these findings are prevalent in the general population and poorly predictive of papilledema in isolation.

References: Beier D, Korsbæk JJ, Bsteh G, et al. Magnetic Resonance Imaging Signs of Idiopathic Intracranial Hypertension. JAMA Netw Open. 2024;7(7):e2420138.

Keywords: Pseudotumor cerebri, Pediatric neuro-ophthalmology, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: N/A

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Association of Neuroimaging Optic Nerve Enhancement With Visual Acuity Outcome: A Systematic Review And Meta-Regression Analysis

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Introduction:
To-date, few predictors of final visual outcome after myelin oligodendrocyte glycoprotein (MOG) auto-antibody disease optic neuritis (ON) have been reliably elucidated. While some studies report excellent visual recovery, others suggest poorer visual acuity (VA) prognosis. To address this between-study heterogeneity, we evaluate whether between-study differences in ON neuroimaging regional enhancement features may explain this heterogeneity.

Methods:
PROSPERO (CRD42024580123). Medline and Embase were searched to August 2024. We included any study reporting baseline and final visual outcome with region-specific neuroimaging enhancement along the ON. We report within-study analyses correlating neuroimaging ON findings with visual outcome. Between studies, we conducted a meta-regression of ON segmental and regional inflammation (intraorbital, pre-chiasmal, intra- or post-chiasmal, and longitudinal extension) as a predictor of final visual acuity (VA; LogMAR). Secondarily, we evaluate neuroimaging regional inflammation as a predictor of VA change from baseline.

Results:
We identified 26 reports (n=1197 participants), eleven of which reported VA analyses or data stratified by enhancement region. Despite conflicting reports on the association between final VA and enhancement region, most studies report against this association. Meta-regression across all studies similarly determined that, at the study level, there was no significant association of any ON segment nor region with final or change-from-baseline VA. Risk of bias analysis indicated generally favourable quality across included studies.

Conclusions:
Studies with poorer VA outcome did not significantly differ in the proportion of patients with various ON regional enhancement patterns. Future studies stratifying VA by neuroimaging findings with raw data reported are needed.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Diffusion Weighted MRI of Optic Nerves in Idiopathic Intracranial Hypertension – A Population-Based Study.

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Introduction:
MRI/MRV are necessary components of the diagnostic evaluation of patients with idiopathic intracranial hypertension (IIH). Neuroimaging signs identified in IIH have varying sensitivities and specificities. Optic nerve head DWI (Diffusion-Weighted Imaging) and ADC (Apparent Diffusion Coefficient) sequences obtained during standard MRI are less well-characterized in support of IIH diagnosis. The purpose of this study is to assess the diagnostic utility of optic nerve DWI/ADC and their association with lumbar puncture opening pressure (OP) in IIH.

Methods:
A retrospective chart review of IIH patients and control patients, who had brain MRI for other reasons, was conducted. Demographic, clinical, OP, and DWI/ADC findings were collected and analyzed with student's t-test, Mann-Whitney and Pearson correlation calculations using STATA-17 software. Sensitivity, specificity, positive predictive value (PPV), and likelihood ratios (LR) were calculated. Significance was set at $P< 0.05$. IIH patients with intercurrent ophthalmic or neurologic comorbidities were excluded.

Results:
128 confirmed IIH and 122 control patients were included. IIH patients were younger, more female with higher BMI than control patients ($P< 0.001$). Forty-seven (40.2%) IIH and 16 (13.8%) control MRIs displayed optic nerve DWI/ADC changes. Among IIH patients, the mean(SD) OP was 33.98(10.95) cmH20. DWI/ADC changes had 40.2% sensitivity, 86.2% specificity and PPV of 74.60. Positive LR was 2.91 and negative LR was 0.69 for the diagnosis of IIH. There was significant correlation between DWI/ADC and rising OP in IIH patients ($r=0.184$, $P=0.047$). However, there was no significant association between DWI/ADC and specific patient demographics or BMI.

Conclusions:
Optic nerve head DWI/ADC sequences may be useful adjuvant findings for diagnosing IIH. Combination with established MRI features may strengthen suggestions of IIH. Additionally, the presence of DWI/ADC changes correlated with elevated OP, thus these sequences may be useful in patients unable or unwilling to undergo a lumbar puncture so that appropriate management may proceed without delay.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None

Contact Information: None provided.

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Quantifying Time Savings of STAT Outpatient Neuroimaging versus ED Neuroimaging for Patients with Optic Disc Swelling

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Introduction:
Patients with optic disc swelling are often referred to the Emergency Department (ED) for urgent neuroimaging, which leads to high costs, long wait times, and ED overcrowding (1–3). Often, the goal of ED referral is rapid neuroimaging rather than further management (4). In a pilot study, patients with optic disc swelling deemed stable for outpatient management by a neuro-ophthalmologist received an outpatient MRI within 48 hours (STAT pathway), without inferior outcomes compared with patients evaluated in the ED. Significant charge reductions were found (5). This study examines differences in patient time spent for ED versus STAT neuroimaging for optic nerve swelling.

Methods:
We performed a retrospective chart review of patients who received neuroimaging for optic disc edema from 2020-2024. Of 146 patients, 33 were referred to the ED before implementation of our protocol, 50 used the STAT outpatient pathway, and 63 were referred to the ED post-protocol, based on specialist assessment. Check-in, check-out, and MRI timestamps were obtained from medical records. For ED patients, the total visit time was truncated to a discharge time of 35 minutes post-MRI (as determined by interviews with hospital staff) to limit the impact of additional interventions. T-tests compared ED to STAT.

Results:
The STAT cohort had a shorter average visit length than the post-protocol ED group (1.67 ± 1.16 versus 8.03 ± 5.9 hours, $p < 0.001$) and a shorter wait time from check-in to MRI start (59.2 ± 47.9 minutes vs. 6.6 ± 5.8 hours, $p< 0.001$). STAT was also significantly faster than pre-protocol ED patients, whose average visit length was 5.9 ± 2.5 hours ($p< 0.001$) with a waiting time of 4.6 ± 2.5 hours ($p< 0.001$).

Conclusions:
The use of STAT outpatient neuroimaging significantly saves patient time compared with MRI via the ED.

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Keywords: Neuroimaging, Optic nerve trauma and treatment, Optic neuritis

Financial Disclosures: Divya Manikandan; Florian Guillot; Amanda Henderson: None related to this submission: Horizon Therapeutics/Amgen.

Grant Support: None.

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Relation of Optical Coherence Tomography (OCT) Measures to Volumetric MRI in Pediatric-Onset Multiple Sclerosis (POMS)

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Introduction:
Whole and regional brain tissue volumes and OCT measures have emerged as important structural markers that reflect impairment and disability in MS. How these structural measures of the eye and brain relate to each other is unclear in POMS. Here we aim to examine the relation of optical coherence tomography (OCT) measures to MRI brain volumetrics in patients with pediatric-onset multiple sclerosis (POMS).

Methods:
This was a retrospective cross-sectional study of OCT and MRI measures in a POMS cohort at a single pediatric MS center. MRI measures of brain volume that were performed as part of clinical care include overall lesion and black hole volumes and percentiles (based on age- and sex-related norms) for whole brain (WB), cortical grey matter (CGM), grey matter (GM), hippocampus, and thalamus. Peripapillary retinal nerve fiber layer (RNFL) thickness and macular volumes were recorded from clinical OCT scans.

Results:
Among 72 patients (144 eyes), median age at the time of the volumetric MRI scan was 18.8 (range 10.6-27.7) years, with a median disease duration of 3.7 (0.13-16.7) years. Lower (worse) RNFL thicknesses (median 93.1 microns [53-134]) were associated with reduced volumes of WB ($p< 0.001$), CGM ($p< 0.001$), GM ($p< 0.001$), and thalamus ($p=0.03$, generalized estimating equation [GEE] models). RNFL thinning was also associated with greater lesion ($p=0.009$) and black hole volumes ($p=0.003$). Macular volumes were reduced for eyes associated with lower WB ($p=0.001$) and hippocampal volume ($p=0.006$). On average, 5 micron reductions in RNFL thickness were associated with decreases in whole brain volume by 12 percentile points and with increases in black hole volume by 12 mm3.

Conclusions:
Peripapillary RNFL thinning in POMS may reflect loss in overall brain volume and greater lesion and black hole burden on volumetric MRI. As such, OCT measures represent useful markers of disease status including optic nerve involvement in POMS.

References: None provided.

Keywords: Demeylinating disease, Pediatric neuro-ophthalmology, Neuroimaging, Optic neuropathy, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Interrater Reliability of Optical Coherence Tomography Parameters in Acute Nonarteritic Anterior Ischemic Optic Neuropathy

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Introduction:
Nonarteritic anterior ischemic optic neuropathy (NAION) is the leading cause of acute optic neuropathy in patients over 50 years of age. OCT helps identifying early and late structural changes in the optic nerve head, but interpretation can be subjective and hindered by edema in the acute phase of NAION. Therefore, evaluating the reliability of subjective OCT parameters in NAION is essential.

Methods:
This retrospective observational study included NAION patients diagnosed at Rigshospitalet, Denmark, between August 2021 and August 2023. Patients were selected if they had radial OCT and dense enhanced depth imaging (EDI) OCT scans of the optic nerve head OCT performed in the acute phase, i.e. within one month of onset. Interrater reliability was assessed using Cohen's Kappa for optic disc edema, peripapillary hyperreflective ovoid mass-like structures (PHOMS), and optic disc drusen (ODD). Intraclass correlation coefficient (ICC) analyses assessed anterior lamina cribrosa depth (ALC) and Bruch's membrane opening (BMO).

Results:
We included 19 patients, resulting in 20 eyes with NAION, as one patient presented with bilateral NAION. Only 13 patients had dense EDI-OCT scans in the acute phase, therefore, assessment of ALC and ODD was limited to these cases. Interrater reliability of BMO as well as ALC showed excellent agreement (ICC = 0.953, $p < 0.001$, and ICC=0,928, $p < 0.001$, respectively), while Cohen’s kappa indicated fair agreement for PHOMS (kappa=0,286, kappa=0,197), fair agreement for edema (kappa=0,241, p=0,212) and none to slight agreement for ODD (kappa=0.198, p=0.416).

Conclusions:
Although interpretation of optic nerve head OCT can be subjective and hindered by edema in acute NAION, ALC and BMO showed excellent interrater reliability. The reliability was low for ODD which needs to be explored further.

References: None provided.

Keywords: Neuroimaging, Optic neuropathy, Retina

Financial Disclosures: Sedra Al Yousef; Lea Lykkebirk: I have received research grant for my PhD: - Fight for Sight - Denmark - Synoptikfonden - VELUX Foundation; Anastasiia Skliarova; Simon Joel Lowater; Steffen Hamann

Grant Support: None.

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AI-Assisted Diagnosis and Grading of Papilledema from Fundus Photographs: A Comparative Study of Neuro-Ophthalmologists and ChatGPT

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Introduction:
Papilledema management often involves taking fundus photos to monitor disease severity. Recently, interest has grown in using Artificial Intelligence (AI) programs, such as OpenAI's ChatGPT (GPT)1, to improve diagnostics throughout medicine. This study compares GPT's ability to grade papilledema in fundus photos to that of a practicing neuro-ophthalmologist (PNO).

Methods:
Fundus photos (n=26) from patients with papilledema at a large academic medical center were retrospectively identified. GPT's Image Analyzer model and a PNO graded photos for optic disc pallor (0-3), Frisen scale (0-5), vessel tortuosity (0-3), cup-to-disc ratio (CDR), and RNFL thickness. True CDRs and RNFL thickness measurements were collected from same-day OCTs. GPT and PNO performance were compared using Cohen's Kappa test (pallor, Frisen, tortuosity; $p < 0.05$). GPT and PNO estimates of CDR, and GPT estimates of RNFL thickness were compared to OCT measurements using paired sample t-tests ($p < 0.05$).

Results:
Comparisons between GPT and PNO grading revealed poor agreement for pallor ($\kappa = 0.037$, 95% CI -0.069 – 0.143), Frisen score ($\kappa = 0.092$, 95% CI -0.042 – 0.225), and tortuosity ($\kappa = 0.204$, 95% CI -0.044 – 0.451), with none reaching statistical significance. 5/26 of GPT Frisen scores aligned with PNO, and 15/26 were within 1 point. GPT's average estimated RNFL thickness was significantly different from OCT ($p < 0.001$). GPT's average estimated CDR was significantly different from OCT ($p < 0.001$), whereas the PNO's was not significantly different from OCT ($p = 0.28$).

Conclusions:
GPT performed poorly compared to a PNO when grading fundus photos for papilledema severity, highlighting GPT's limitations in fundus photo analysis and the need for further model refinement. GPT was also unable to match the performance of a PNO in grading CDR compared to OCT measurements. Future iterations of GPT should be studied to determine analytic capabilities and ultimately aid in medical management.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Ophthalmic Manifestations and Management of Cerebral Venous Thrombosis

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Introduction:
Cerebral venous thrombosis (CVT) may be associated with neuro-ophthalmic complications including papilledema and ocular motility disorders. The efficacy of intracranial pressure-lowering medications such as acetazolamide in CVT is not well described, and surgical options are limited in the setting of anticoagulation and CVT. We identify the prevalence, duration, severity, and management of papilledema from CVT.

Methods:
A retrospective review of patients diagnosed with CVT from June 2021 to January 2024 was conducted in Alberta, Canada using the province-wide EPIC electronic medical record.

Results:
Of 193 patients with CVT, 35 (18.1%) had an ophthalmology consultation and 36 (22.8%) endorsed visual symptoms without an ophthalmic examination. Among those with ophthalmic exams, 82.6% (n=29/35) had visual acuity 20/50 or better, 17.1% (n=6/35) had visual field deficits, 20% (n=7/35) had ocular motor abnormalities, and 60% (n=21/35) had papilledema with an average retinal nerve fiber layer (RNFL) thickness of 224.6 microns. Papilledema was mild-moderate (/= Frisén Grade 4) in 9.5% (n=2/21), while 38.1% (n=8/21) did not have a documented grading. All patients were treated with anticoagulation and intracranial pressure-lowering medications including acetazolamide, topiramate, and/or furosemide. Of the 21 patients with papilledema, 4 patients (19%) received surgical management including ventriculoperitoneal shunt and craniotomy. Papilledema resolved at an average of 151.4 [27-365] days.

Conclusions:
In this retrospective study of patients with CVT in Alberta, the majority of patients with ophthalmic exams did not have significant vision loss or visual field deficits at initial presentation. While follow-up data were limited, significant visual loss, visual field deficits and RNFL thinning were rare. Importantly, less than 20% of patients with CVT had an ophthalmic examination suggesting the need for greater interdisciplinary collaboration.

References: 1. Park MG, Roh J, Ahn SH, Park KP, Baik SK. Papilledema and venous stasis in patients with cerebral venous and sinus thrombosis. BMC Neurol. 2023;23(1):175. Published 2023 Apr 28. doi:10.1186/s12883-023-03228-0 2. Saposnik G, Barinagarrementeria F, Brown RD Jr, et al. Diagnosis and management of cerebral venous thrombosis: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2011;42(4):1158-1192. doi:10.1161/str.0b013e31820a8364

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Lesion Location Along the Optic Nerve: Clinical and Radiographic Correlations in Myelin Oligodendrocyte Glycoprotein Antibody Disease

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Introduction:
Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD) often presents with optic nerve lesions, leading to varying clinical and radiographic patterns. While these correlations are known, the impact of lesion location on diagnosis and management warrants further study.

Methods:
A retrospective, observational study was conducted on adult MOGAD patients (n=45) with optic nerve lesions, analyzing segments involved. The analysis compared clinical symptoms, radiographic findings, and demographics to assess for significant associations.

Results:
Patients with ON lesions reported more diminished vision (100% vs. 41.2%, n=27 vs n=17, p< 0.001) and eye pain (55.6% vs. 11.8%, n=27 vs n=17, p=0.004). MOG titers ≥1:160 (47.6% vs. 0%, n=21 vs n=12, p=0.004) were more frequent, while neuropathic pain (29.6% vs. 82.4%, n=27 vs n=17, p< 0.001) and weakness (14.8% vs. 58.8%, n=27 vs n=17, p=0.002) were lower. Intraocular ON lesions showed higher bilateral ON involvement (83.3% vs. 26.3%, n=6 vs n=19, p=0.013) and fewer brain lesions (16.7% vs. 63.2%, n=6 vs n=19, p=0.047). Intraorbital ON lesions had increased bilateral involvement (52.6% vs. 0%, n=19 vs n=6, p=0.002), but lower cervical and ON involvement (12.5% vs. 75%, n=16 vs n=4, p=0.010). Intracanalicular ON lesions were linked to more intracranial ON lesions (78.6% vs. 27.3%, n=14 vs n=11, p=0.010) and increased cervical and ON involvement (41.7% vs. 0%, n=12 vs n=8, p=0.035).

Conclusions:
Intraocular and intraorbital lesions show distinct bilateral involvement and reduced brain lesions, while intracanalicular lesions involve more extensive cervical and intracranial ON involvement, highlighting lesion location's importance in MOGAD evaluation.

References: None provided.

Keywords: Demeylinating disease, Neuroimaging, Optic neuritis, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None

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The Presence of Vitritis on Multimodal Imaging in Patients with Syphilitic Optic Neuropathy

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Introduction:
Syphilitic optic neuropathy may or may not be accompanied by vitritis and is often not directly analyzed by multimodal ocular imaging. Therefore, the purpose of this investigation is to determine whether multimodal imaging (optical coherence tomography, fluorescein angiography, or B-scan ultrasound) is sensitive enough to determine the presence of vitritis in patients with syphilitic optic neuropathy.

Methods:
A total of 10 patients (15 eyes) that were diagnosed with syphilitic optic neuropathy were included in this study. Demographic information, presenting and final visual acuity after treatment, RPR/FTA-ABS/VDRL reactivity, clinical exam findings, and multimodal imaging were collected for each patient. Statistical analyses were conducted using GraphPad Prism software (Version 5.1).

Results:
Of the 10 patients included in this study, 9 were male and 1 was female. The average age (Mean ± SD) was 48.7 ± 11.7 years and with a racial breakdown of 50% Black, 30% White, and 20% Hispanic. Eye laterality was roughly equal with 54% and 46% of right and left eyes respectively. Presenting visual acuity ranged from 20/25 to light perception (LP), with an average logMAR of 2.1. Of the 10 patients, 9 had a positive RPR and all 10 had a positive FTA-ABS. Only 6 patients had a positive CSF VDRL. 13 of the 15 eyes had clinically significant vitritis. Of the patients that underwent optical coherence tomography and B-scan ultrasound, all had evidence of vitritis. The one patient that had fluorescein angiography had focal areas of hyperflourescence with leakage around the optic nerve. All patients were treated with IV penicillin with resolution of clinical vitritis and improvement of visual acuity to logMAR 0.80 ($p < 0.05$).

Conclusions:
Vitritis observed on multimodal imaging was grossly consistent with clinical exam findings. Multimodal imaging can be reliably used to confirm the presence of vitritis in cases of syphilitic optic neuropathy.

References: None provided.

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

Financial Disclosures: Marko Oydanich; Siri Uppuluri; Rashika Verma; Roger Turbin: Research investigator for Viridian Therapeutics, Inc. I am currently receiving research support to my institution and advisory board status, past travel support, and own a small equity position below federal approved thresholds. My conflicts have all been thoroughly declared and approved by my institution.; Larry Frohman

Grant Support: None.

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Optic nerve sheath meningiomas: a retrospective cohort study comparing outcomes in treated versus observed patients

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Introduction:
The rarity of optic nerve sheath meningiomas (ONSMs) complicates the guidelines surrounding optimal treatment strategies and prognostic factors. There is limited data on the visual outcomes of those treated with radiotherapy versus those observed without treatment. This study aims to characterize the clinical and radiographic presentations of patients diagnosed with ONSMs and to identify factors predicting improvement in visual function after treatment.

Methods:
This is a retrospective case series of 26 patients who presented to two tertiary neuro-ophthalmology practices over ten years with the presumptive diagnosis of ONSM. Demographic, clinical, investigative, radiologic, treatment and outcome data was collected. Visual improvement was defined as VA improvement by ≥2 Snellen lines or VF MD improvement by ≥2 decibels. Statistical analyses were performed to compare patients who experienced improvement in visual function and those who did not post-stereotactic radiotherapy to identify pre-treatment predictors of visual recovery.

Results:
17 patients underwent radiotherapy, and four elected observation. Five were lost to follow-up. Visual function improvement was seen in ten patients who underwent radiotherapy. Pre-treatment visual acuity, tumor size, and a decrease in tumour size post-radiotherapy were significantly associated with objective visual improvement.

Conclusions:
Pre-treatment visual acuity and tumor size may predict improvement in visual function in patients with ONSMs treated with radiotherapy. Future larger-scale studies that include this data may be able to draw more definite conclusions.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None

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Adherence to Biologic Therapies Among Patients with Neuromyelitis Optica Spectrum Disorder (NMOSD) in the United States

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Introduction:
Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune demyelinating disease characterized by relapses and risk of disability accumulation. Adherence to therapy among patients with NMOSD on approved biologics remains to be extensively characterized. The objective was to assess adherence to approved biologics among patients with NMOSD in the US.

Methods:
A retrospective cohort study was conducted among adult patients with NMOSD treated with approved biologics (inebilizumab, eculizumab, or satralizumab) using the Komodo Research Database (2020 – 2023). Adherence to treatment was assessed as percentage of days covered (PDC), measured as a continuous and binary variable (PDC≥80%=adherent), from treatment initiation to data availability. Difference in continuous PDC (ΔPDC) was assessed using fractional regression adjusting for demographic characteristics (age, sex, race, region, health plan) and NMOSD-associated conditions (neuropathic pain, bladder dysfunction, hemiplegia/paraplegia) at baseline.

Results:
In total, 111 patients were included in analyses: 45% inebilizumab, 28% eculizumab, 27% satralizumab. Patients were, on average, 43.0 years-old, 85.6% female, and 34.2% Black/African American. Common baseline NMOSD-associated conditions included neuropathic pain(43.2%), bladder dysfunction (18.0%), and hemiplegia/paraplegia (17.1%). Prevalent comorbidities during the study period included hypertension(36.9%), obesity(30.6%), and depression(29.7%). Mean duration of follow-up was 17.3±6.9 months and varied by treatment: inebilizumab (16.4±6.3 months), eculizumab (20.6±7.4 months), and satralizumab (15.5±6.6 months). Adherence was substantially higher among patients on inebilizumab (mean PDC=85.2%±19.0; adherent=72.0%) than on eculizumab (mean PDC=73.2%±21.5; adherent=45.2%) and satralizumab (mean PDC=66.5%±30.0; adherent=53.3%). Fractional regression adjusting for covariates revealed patients on inebilizumab had significantly higher adherence as compared to satralizumab (ΔPDC=20.8%, p=0.005) and higher as compared to eculizumab (ΔPDC=10.2%, p=0.090).

Conclusions:
Among NMOSD patients treated with approved biologics, patients on inebilizumab had substantially higher adherence to treatment as compared to those on eculizumab and satralizumab. Further research assessing the impact of adherence on patient outcomes, including relapses and treatment persistence, can further elucidate important evidence to guide effective clinical decision-making.

References: None provided.

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

Financial Disclosures: Bruce A. C. Cree: Personal compensation for consulting from Alexion, Atara, Autobahn, Avotres, Biogen, Boston Pharma, EMD Serono, Gossamer Bio, Hexal/Sandoz, Horizon, Immunic AG, Kyverna, Neuron23, Novartis, Sanofi, Siemens and TG Therapeutics and received research support from Genentech.; Kristina R. Patterson: Employee and stockholder of Amgen Inc.; Andrea Meyers: Employee and stockholder of Amgen Inc.; Patrick Gagnon-Sanschagrin: Employee of Analysis Group, a consulting company that has provided paid consulting services to Amgen Inc.; Jessica Maitland: Employee of Analysis Group, a consulting company that has provided paid consulting services to Amgen Inc.; Jenny Y. Park: Employee and stockholder of Amgen Inc.

Grant Support: None.

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Meningococcal Infection With Eculizumab Or Ravulizumab In Patients With Generalized Myasthenia Gravis Or Neuromyelitis Optica Spectrum Disorder: An Analysis Of United States Clinical Practice

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[1] *Alexion, AstraZeneca Rare Disease*

Introduction:
Eculizumab and ravulizumab are effective treatments for generalized myasthenia gravis (gMG) and neuromyelitis optica spectrum disorder (NMOSD). Safety mitigations, including vaccinations, are used to reduce the risk of Neisseria meningitidis (Nm) infection associated with these treatments. Here, we evaluate US exposure-adjusted Nm infection and mortality in eculizumab- or ravulizumab-treated patients with gMG and NMOSD using postmarketing pharmacovigilance data (Nm case counts) and commercial data (exposure).

Methods:
The US Alexion safety database was searched for eculizumab and ravulizumab (data cutoff: December 2022) across approved indications (gMG, NMOSD, paroxysmal nocturnal hemoglobinuria, atypical hemolytic uremic syndrome) using the MedDRA High Level Term "Neisseria infection." Only Nm-associated cases were included. Reporting rates were calculated cumulatively per 100 patient-years.

Results:
US Nm infection and mortality annual reporting rates in eculizumab-treated patients remained stable over 15 years across approved indications (2022: 0.13 and 0.01, respectively; exposure: 29,758.4 patient-years). In 2022, US postmarketing Nm infection reporting rates in eculizumab-treated patients with gMG and NMOSD were 0.02 (exposure: 8,042.0 patient-years) and 0.07 (exposure: 1,470.1 patient-years), respectively. At data cutoff, there were no Nm infections among ravulizumab-treated patients with gMG. No Nm fatalities were noted for eculizumab- or ravulizumab-treated patients with gMG and NMOSD.

Conclusions:
Nm infection and mortality reporting rates for patients with gMG and NMOSD remained stable despite increasing eculizumab and ravulizumab exposure over time. These results suggest US Nm-related risk mitigation strategies are effective in patients receiving eculizumab or ravulizumab.

References: None provided.

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

Financial Disclosures: Shirali Pandya: SP is an employee of Alexion, AstraZeneca Rare Disease, and holds stock or stock options in AstraZeneca.; Lokesh Jha: LJ is an employee of Alexion, AstraZeneca Rare Disease, and holds stock or stock options in AstraZeneca.; Imad Al-Dakkak: IAD is an employee of Alexion, AstraZeneca Rare Disease, and holds stock or stock options in AstraZeneca.; Feifei Yang: FY is an employee of Alexion, AstraZeneca Rare Disease, and holds stock or stock options in AstraZeneca.; Vidya Chitikireddi: VC is an employee of Alexion, AstraZeneca Rare Disease, and holds stock or stock options in AstraZeneca.; Hua Zhang: HZ is an employee of Alexion, AstraZeneca Rare Disease, and holds stock or stock options in AstraZeneca.; Arshad Mujeebuddin: AM is an employee of Alexion, AstraZeneca Rare Disease, and holds stock or stock options in AstraZeneca.

Grant Support: This study was sponsored by Alexion, AstraZeneca Rare Disease.

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Neuro-Ophthalmic Manifestations of Pachymeningitis

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Introduction:
Pachymeningitis is an uncommon entity characterized by thickening of the dura mater, localized or diffuse, due to a primary or secondary process. We hereby aim to showcase its different etiologies and common neuro-ophthalmic presentations.

Methods:
This is a retrospective review of patients found to have pachymeningitis at a single quaternary referral academic center between 1/2000 and 7/2023. A review of the database yielded 38 patients. Medical records and imaging were reviewed to confirm the diagnosis. We describe herein the demographic characteristics, neuro-ophthalmic manifestations, and relevant pathology.

Results:
Among the patients identified, three were excluded based on imaging, and two due to subsequent diagnoses (meningioma and intracranial hypotension). Of the remaining 33 patients, 23 were women (69.7%), and 16 were white (48.5%). All patients were adults (range: 27-81 years old, average: 55.1). Twenty-seven (81.8%) patients had neuro-ophthalmic manifestations at presentation: 13 (39.4%) had decreased vision, 11 (33.3%) diplopia, and three (9.1%) eye pain. Uveitis/scleritis was documented in four patients (12.1%) either prior to or after presentation, three of which had either proven or suspected sarcoidosis. Optic nerve involvement was noted at presentation or follow up in 23 (69.7%) patients, from optic nerve infiltration/compression, optic neuritis/perineuritis, optic disc infiltration/edema, papilledema, or unspecified optic neuropathy. Eighteen (54.5%) had other cranial nerve involvement, single or multiple. While biopsy was performed in 22 patients, including 15 dural based, an etiology was identified in nine (yield: 40.9%, 27.3% of total): neurosarcoidosis (4), IgG4-pachymeningitis (2), eosinophilic meningitis (1), Rosai-Dorfman (1), granulomatosis with polyangiitis (1).

Conclusions:
Pachymeningitis can present with varied neuro-ophthalmic manifestations, and the initial differential diagnosis is broad. Prior literature is limited to case reports or etiology-specific disease. MRI findings are nonspecific, and other laboratory evaluations and biopsy are often required for a conclusive diagnosis, though many cases remain idiopathic.

References: None provided.

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

Financial Disclosures: Reeda Bou Said; Florian Guillot; Amanda Henderson: None related to this submission: Horizon Therapeutics/Amgen.; Andrew Carey: None related to this submission: Horizon Therapeutics/Amgen, Bristol-Myers-Squibb, Springer publishing.

Grant Support: None.

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Epidemiology of Double Vision and Falls in Spinocerebellar Ataxia

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Introduction:
Spinocerebellar ataxias (SCAs) are inherited neurodegenerative disorders characterized by muscle coordination, balance, and gait difficulties. Studies have independently found a high prevalence of diplopia and falls in the SCA population. This analysis aims to determine the prevalence and risk factors for diplopia in spinocerebellar ataxias (SCA) and its association with frequent falls in the SCA population.

Methods:
We analyzed data from participants aged 18 or older in the Clinical Research Consortium for the Study of Cerebellar Ataxia (CRC-SCA), a multicenter natural history study of people with SCA types 1, 2, 3, 6, 7, 8, and 10. Pre-ataxia genetic carriers with a baseline total Scale for the Assessment and Rating of Ataxia score < 3 and subjects with unknown SCA types or missing demographic data were excluded. Diplopia was ascertained at baseline, and fall questionnaires were completed at baseline and follow-up visits. We measured the prevalence of diplopia overall and by SCA type and used logistic regression to identify characteristics associated with diplopia prevalence. Using mixed effects logistic regression models, we also investigated the relationship between diplopia and frequent falls, defined as two or more falls to the ground over 12 months.

Results:
Of 747 eligible CRC-SCA participants, 280 (37.5%) reported experiencing at baseline. SCA 3 (OR 4.93, 95% CI 2.76-8.78), SCA 6 (OR 2.81, 95% CI 1.46-5.40), and SCA 8 (OR 2.67, 95% CI 1.05-6.83) were associated with an increased prevalence of diplopia compared to SCA1. Diplopia was not associated with frequent falls cross-sectionally (OR 0.94, 95% CI 0.53-1.65) or longitudinally (OR 0.96, 95% CI 0.42-2.18).

Conclusions:
Diplopia is common in the SCA population and is associated with SCA type but not increased fall prevalence, functional limitation severity, ataxia severity, or disease duration.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Adult strabismus with a focus on diplopia

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Time to Vaccination after Rituximab Discontinuation in Patients with Anti–Aquaporin–4 Antibody–Positive Neuromyelitis Optica Spectrum Disorder: A Post-hoc Analysis of the CHAMPION-NMOSD Trial

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[1] Departments of Neurology and Ophthalmology, Programs in Neuroscience and Immunology, University of Colorado, [2] Alexion, AstraZeneca Rare Disease, [3] Brigham and Women's Hospital and Harvard Medical School, [4] University of Cincinnati Gardner Neuroscience Institute, [5] Massachusetts General Hospital and Harvard Medical School, [6] Mayo Clinic

Introduction:
Rituximab (RTX) is often prescribed off-label for patients with AQP4-Ab+ NMOSD, and patients may transition to ravulizumab, an approved therapy. Vaccination against Neisseria meningitidis (Nm) is the primary risk-mitigating strategy for complement inhibitors. Although meningococcal vaccines trigger a T-cell response, prior anti-B-cell therapy may attenuate responses to clinically relevant vaccines. CHAMPION-NMOSD (NCT04201262) is a global, open-label, phase 3 study evaluating ravulizumab in patients with AQP4-Ab+ NMOSD, approximately one-third of whom had RTX exposure. The objective was to characterize the time from last RTX dose to first administered meningococcal vaccine in patients from the CHAMPION-NMOSD trial.

Methods:
Descriptive post-hoc analyses were performed in a subgroup of patients on ravulizumab who received meningococcal vaccinations (MenACWY or MenB) after their last RTX dose (N=19). Clinical laboratory parameters, vaccine administration, and time to first meningococcal vaccination and ravulizumab dose post-RTX are summarized.

Results:
Patients were primarily White (63.2%), North American (68.4%), and female (94.7%). Lymphocytes were within normal limits in most patients (13/14, 92.3%); lymphocyte subsets were not collected in this study. All patients received ≥1 meningococcal vaccine ≥2 weeks prior to ravulizumab initiation. Most patients (68.4%) received their first meningococcal vaccinations either 0–3 months (15.8%) or 3–6 months (52.6%) after the last dose of RTX prior to ravulizumab. Most patients (84.2%) received both MenACWY and MenB vaccinations at the same visit; 4 patients (21.0%) received multiple doses of either vaccine. There were no reports of meningococcal infection in patients whose initial Nm vaccination occurred after their last dose of RTX.

Conclusions:
Most patients received a meningococcal vaccination ≤6 months after their last dose of RTX, with MenACWY and MenB vaccines at the same visit. Total lymphocyte counts were normal in most patients with no reports of meningococcal infection or NMOSD attacks in patients who received their initial Nm vaccination after their last RTX dose.

References: None provided.

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

Financial Disclosures: Jeffrey Bennett: JB has received personal compensation for serving as a consultant for Alexion Pharmaceuticals, Amgen, Beigene, Reistone Bio, Chugai, Genentech, ImCyse, Immpact Bio, Mitsubishi Tanabe, Novartis, and Roche; serving on a Scientific advisory or data safety monitoring board for CorEvitas, MIAC, and Roche; serving on a Speakers Bureau for Alexion Pharmaceuticals, Efficient LLC, Touch IME, and Vindico; serving as an expert witness for Marie Bush, Pavich Law, Marks Gray, and Knight, Nicastro, MacKay; received institutional research support from Alexion Pharmaceuticals; received intellectual property interests from a discovery or technology relating to health care; and received publishing royalties from a publication relating to health care; Ukwen Akpoji: UA is an employee of Alexion, AstraZeneca Rare Disease and holds stock in Alexion Pharmaceuticals.; Shamik Bhattacharyya: SB has received research support from Alexion Pharmaceuticals, NIH, Roche, and UCB; publishing honoraria from American Academy of Neurology and UpToDate.; Aram Zabeti: AZ has received research funding from Alexion Pharmaceuticals, Biogen, Chugai, Genentech, Medimmune, NIH, and PCORI, and; honoraria for speaker bureau or advisory board from Biogen, Celgene/Bristol Myers Squibb, Genentech-Roche, Merck-Serono, Novartis, Teva Pharma, Sanofi-Genzyme, Viela Bio/Horizon/Amgen, and TG therapeutics.; Michael Levy: ML has received fees from Alexion Pharmaceuticals, Genentech, Inc., and Horizon Therapeutics; Kerstin Allen: KA is an employee of Alexion, AstraZeneca Rare Disease and holds stock in Alexion Pharmaceuticals; Sean Pittock: Sean J. Pittock has received personal compensation for serving as a consultant for Roche/Genentech, Sage Therapeutics, Arialys and Astellas. He has received personal compensation for serving on scientific advisory boards or data safety monitoring boards for F. Hoffman-LaRoche AG, Genentech, Arialys and UCB. His institution has received compensation for serving as a consultant for Astellas, Alexion, and Viela Bio/MedImmune. All compensation is paid to Mayo Clinic. He has received research support from Alexion, Viela Bio/MedImmune, Roche/Genentech and Adimmune. He has a patent, Patent# 8,889,102 (Application#12-678350, Neuromyelitis Optica Autoantibodies as a Marker for Neoplasia)—issued; a patent, Patent# 9,891,219B2 (Application#12-573942, Methods for Treating Neuromyelitis Optica (NMO) by Administration of Eculizumab to an individual that is Aquaporin-4 (AQP4)-IgG Autoantibody positive)-issued and from which he has received royalties and a patent for GFAP-IgG; Septin-5-IgG; MAP1B-IgG; Kelch-like protein 11; PDE10A pending. He is working as a consultant in the Mayo Clinic Neuroimmunology laboratory clinical service. The Mayo Clinic Neuroimmunology Laboratory commercially offers MOG-IgG testing, but revenue accrued does not contribute to salary, research support, or personal income

Grant Support: None.

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Incidence of Relapses After Meningococcal Vaccination In Clinical Trials And Real-World Evidence Of Eculizumab And Ravulizumab In Anti-Aquaporin-4 Antibody-Positive Neuromyelitis Optica Spectrum Disorder

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Introduction:
Ravulizumab and eculizumab are complement component C5 inhibitor therapies (C5ITs) approved for anti-aquaporin-4 antibody-positive (AQP4-Ab+) neuromyelitis optica spectrum disorder (NMOSD). Because C5ITs are associated with increased Neisseria meningitidis infection risk, patients are generally advised to be vaccinated ≥2 weeks before receiving C5ITs; however, vaccination may further activate the complement pathway. Because of this, patients with complement-mediated diseases, including NMOSD, may experience increased signs and symptoms of their underlying disease when vaccinated before C5IT initiation. In this study, we aim to report on relapses occurring within 4 weeks of meningococcal vaccination before initiating (1) ravulizumab in patients screened in CHAMPION-NMOSD (NCT04201262), (2) either eculizumab or placebo in patients enrolled in PREVENT (NCT01892345), and (3) eculizumab in a regulatory-mandated postmarketing surveillance (PMS) study of patients with AQP4-Ab+ NMOSD in Japan.

Methods:
Analysis included vaccination data from patients (1) screened in CHAMPION-NMOSD, irrespective of screening outcome, (2) randomized to placebo or eculizumab in PREVENT, and (3) included in the Japanese PMS study from approval (November 2019) to data cutoff (October 2023). Outcomes were physician-reported relapses occurring within 4 weeks of last meningococcal vaccination and before ravulizumab, eculizumab, or placebo initiation.

Results:
This analysis included 70 patients from CHAMPION-NMOSD (57 enrolled; 13 screen failures), 2.9% (2/70) of whom experienced a relapse per analysis criteria; both patients were screen failures. In PREVENT, 3.1% (3/96) of eculizumab-treated and 10.6% (5/47) of placebo-treated patients had a relapse. In the Japanese PMS study, 0.7% (1/151) of patients experienced a relapse.

Conclusions:
This retrospective analysis of both clinical trial and real-world data indicates a low relapse incidence (0.7%–3.1%) within 4 weeks of meningococcal vaccinations before C5IT initiation and 10.6% for those randomized to placebo. Available information precludes determination as to whether relapses observed are attributable to meningococcal vaccination or inherent relapse risk among patients with AQP4-Ab+ NMOSD.

References: None provided.

Keywords: Myasthenia, Neuro-ophth & infectious disease (eg, AIDS, prion), Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Demeylinating disease, Optic neuritis

Financial Disclosures: Sami Fam: SF is an employee of Alexion, AstraZeneca Rare Disease and holds stock options in AstraZeneca; Becky Parks: BP is an employee of Alexion, AstraZeneca Rare Disease and holds stock options in AstraZeneca; Kerstin Allen: KA is an employee of Alexion, AstraZeneca Rare Disease and holds stock in Alexion Pharmaceuticals

Grant Support: This study was sponsored by Alexion, AstraZeneca Rare Disease.

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Persistent Visual Field Defects Despite Excellent Visual Acuity Recovery in Optic Neuritis Associated with Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease

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Introduction:
Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a rare autoimmune demyelinating disorder. In adults, optic neuritis (ON) is the most common clinical manifestation. MOGAD-ON can severely affect visual acuity (VA) and cause visual field (VF) deficits. VA typically improves rapidly with treatment, but little is known about VFs at follow-up. To address this, we analyzed VFs in MOG-ON patients.

Methods:
We conducted a multicenter international retrospective review of MOGAD-ON patients. VFs were obtained at presentation and follow-up at least three months later and before the next relapse. VF severity was based on the mean deviation (MD) measurements graded as mild, moderate, or severe. Specific VF deficit patterns and shapes were assessed by a single-blinded neuro-ophthalmologist (as per Optic-Neuritis-Treatment-Trial Group). Time to treatment was also assessed.

Results:
39 eyes of 28 patients were included (mean age 39.68 ± 12.9 years, 13 males). The average MD nadir from all eyes was -14.18 (±9.8 dB) and -3.02 (±3.2 dB) at follow-up. At follow-up, 46% of the eyes developed permanent VF deficits with a MD below -2 dB. (41% with a recognizable VF deficit pattern) despite recovery to an average VA of 6/6.

Conclusions:
In contrast to visual acuity, visual fields showed poorer recovery with persistent deficits in MOGAD patients with optic neuritis despite treatment. The mean deviation appeared to be affected by treatment timing, with delays associated with worse severity gradings.

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Keywords: Optic neuritis, Demeylinating disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Perimetry, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.
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Temporal Artery Ultrasound in the Diagnosis of Giant Cell Arteritis: Experience from a Single US Tertiary Center

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Introduction:
Temporal artery ultrasound (TAUS) is a minimally invasive test in the diagnosis of giant cell arteritis (GCA). There is a range of reported sensitivity (3% to 100%) and specificity (40% to 100%) of TAUS. We evaluate the sensitivity and specificity of TAUS compared to the gold standard of TAB in the diagnosis of GCA.

Methods:
Retrospective cohort study of 50 patients with clinically suspected GCA evaluated with TAUS and TAB after January 2023 at one US tertiary center. All pertinent clinical and laboratory data were collected within a 14-day period before any steroid dose increases. Ophthalmic examination findings were noted if available. TAUS positivity was defined as the presence of a halo sign. Sensitivity and specificity of ipsilateral TAUS (i.e., ipsilateral to TAB site) and bilateral TAUS were calculated. Fisher's exact test was used to compare clinical and laboratory findings between false positive and true positive TAUS.

Results:
Of 50 patients, 33 were female. Mean age was 70.8 (SD: 8.9, Range: 44-86). 38 were Caucasian, 9 were African American, 2 were Asian, and 1 was "other" race. Sensitivity and specificity of ipsilateral TAUS was 100% and 76.7%, respectively. Sensitivity and specificity of bilateral TAUS was 100% and 88.4%, respectively. Of the 10 cases with false positive TAUS, 4 maintained follow-up for 6 months or greater. Of these, the final diagnosis was a non-GCA entity in 3 patients and GCA in 1 patient. There was no significant difference between false positive TAUS and true positive TAUS in ESR elevation ($p = .60$), CRP elevation ($p = .49$), nor fundoscopic findings ($p = .22$).

Conclusions:
TAUS shows high sensitivity and specificity in the diagnosis of GCA when compared to TAB and bilateral TAUS shows higher diagnostic specificity than ipsilateral TAUS. At our center, the 100% sensitivity of TAUS makes it a promising GCA screening tool.

References: None provided.

Keywords: Vascular disorders, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Visual Pathway Structure and Function in Pediatric-Onset Multiple Sclerosis (POMS): Are Social Determinants of Health (SDOH) Related?

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Introduction:
Recent advancements in MS have demonstrated that SDOH (socioeconomic status, race, ethnicity, insurance type) are associated with adverse clinical outcomes, but less is known about the impact of SDOH on POMS. Visual function is a fundamental dimension of MS; Optical coherence tomography (OCT) has provided a non-invasive structural marker and has brought the optic nerve to the forefront of early MS diagnosis. SDOH, however, may also affect clinical severity and timing of presentation, especially in POMS. In this study, we investigate the relation of clinical visual function tests and OCT measures to social determinants of health (SDOH) in pediatric-onset multiple sclerosis (POMS).

Methods:
This was a cross-sectional study of neuro-ophthalmic clinical measures, OCT, and volumetric MRI measures in patients with POMS at a pediatric MS center. Patient data were included if both a volumetric MRI and a neuro-ophthalmologic or ophthalmologic evaluation had been performed. Self-identified race, ethnicity, and current insurance type (commercial versus Medicaid) were collected. Potential SDOH were identified as minority status (non-White or Hispanic/Latino) and Medicaid insurance.

Results:
Among 72 patients (144 eyes), median age was 19 years (range 10-27) with a median disease duration of 4 years (0-16) at time of MRI. Minority status was associated with worse high-contrast visual acuity ($p=0.006$, generalized estimating equation [GEE] models, accounting for age at diagnosis and adjusting for within-patient inter-eye correlations). Non-white race was associated with reduced ganglion cell layer thickness ($p< 0.001$) and worse visual acuity ($p=0.002$). Having Medicaid insurance was also associated with worse visual acuity ($p=0.005$) and worse Ishihara color testing ($p=0.01$).

Conclusions:
Like other dimensions of MS, visual outcomes of structure/function may be adversely affected among pediatric-onset patients with SDOH that are markers for social vulnerability. Future investigations should examine these associations in context of timing and type of MS therapy and other factors that influence disease activity.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Pediatric neuro-ophthalmology, Demeylinating disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Optic Atrophy Predominant WFS1 Disorder – A Case-Control Study

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Introduction:
Wolfram Syndrome Type 1 (WFS), also known by DIDMOAD (Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy, and Deafness, OMIM #222300) is a rare neurodegenerative disorder resulting from homozygous or compound heterozygous autosomal recessive (AR) mutations in the WFS1 gene.1-3 Isolated optic atrophy (OA) with late-onset, milder phenotypes in WFS is rare and typically associated with biallelic autosomal recessive mutations.4-8 Here, we describe five cases of patients with WFS1 mutations presenting with a non-syndromic, late-onset OA and compare to other OA-predominant genetic syndromes.

Methods:
A retrospective review was performed after identifying records of patients seen at our institution from January 1, 2020 through December 31, 2024 with optic atrophy secondary to mutations in OPA1 (n=4), WFS1 (n=5), as well as mtDNA mutations causing LHON (n=5) or other genetic causes (n=4). Patients with non-genetic causes of OA were excluded. Clinical data including logMAR visual acuity, Humphrey visual field (HVF) mean deviations, foveal sensitivities, and optical coherence tomography (OCT) measures of ganglion cell complex (GCC), and peripapillary retinal nerve fiber layer (RNFL) thicknesses were analyzed comparing worst eyes at presentation. This study was granted exempt status by our institutional IRB.

Results:
The LHON group presented with the worst logMAR acuity (1.58, p=0.01), often with positive family history. OPA1 mutations presented with a trend toward better preserved acuity (0.7, p=0.07) and foveal sensitivities (28.00 decibels, p=0.11). POLG mutations predominantly affected the papillomacular bundle, showing reduced foveal sensitivity (8 decibels, p=0.05) with temporal RNFL thinning and a trend toward significant GCC thinning (58.7 microns, p=0.13). Four WFS1 cases presented after age 40 with biallelic mutations, exhibiting dyschromatopsia with variable HVF changes.

Conclusions:
This series expands the clinical spectrum of WFS1 to include isolated OA phenotypes and highlights key differences from other genetic forms of optic atrophy, despite the unclear role of Wolframin in OA pathogenesis.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.
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The impacts of thyroid eye disease (TED) extend beyond signs/symptoms, and patients want to discuss more with their physicians: Results from the ElevaTED survey

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Introduction:
TED is a chronic, debilitating autoimmune disease. Although the signs and symptoms are well known, its effects on quality of life (QoL), mental health, and daily living require more attention.

Methods:
ElevaTED, a 30-minute online survey, was designed to improve understanding of key issues affecting adults diagnosed with TED. It was distributed to members of multiple patient advocacy organizations and a national panel of patients. Questions focused on QoL, activities of daily living, pain, sleep, depression, anxiety, work productivity, and treatment experience and goals.

Results:
204 respondents qualified and completed the survey. Mean age was 50 years; 74% were female. Broad ranges of race/ethnicity (53% White) and geographical location (42% suburban, 43 states in U.S.) were represented. The mean (SD) times since first symptoms and diagnosis were 2.7 (4.4) and 2.2 (3.7) years, with 93% reporting symptoms of any severity and 72% reporting moderate-to-severe symptoms in the last month. The average number of symptoms experienced was 6 at any time and 3 in the past month. For the 146 patients with moderate-to-severe symptoms in the past month, the most frequent were eye pressure/pain (38%), red/swollen/burning eyes (35%), and dry/gritty eyes (32%); the single most bothersome was eye pressure/pain. Negative impacts were reported in QoL (GO-QOL, TED-QoL, and EQ-5D-5L), sleep (overall and Jenkins Sleep Score), depression (PHQ-9), anxiety (GAD-7), work (WPAI), and specific activities of daily living (most frequently using electronic devices, being outside, and reading). Over 80% of respondents were worried about symptoms returning/worsening regardless of prior treatments; the majority want to discuss symptoms and QoL/impacts with their physicians.

Conclusions:
TED is a chronic condition with persistent effects on QoL and mental health. As the TED treatment landscape continues to evolve, increased understanding of TED's impact on daily activities and mental health will improve multidisciplinary care and enable more informed treatment decisions.

References: None provided.

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

Financial Disclosures: Jody Abrams: Jody Abrams is a research investigator and serves on the advisory board for Viridian Therapeutics, Inc., and is a speaker for and serves on the advisory board for Amgen.; Christine Gustafson: TED Community Organization has received financial sponsorships from Viridian Therapeutics, Amgen Rare Disease, Immunovant, Tourmaline, Leapcure, argenx, ACELERIN, Lassen, and Sling Therapeutics.; Julie Ulloa; Sherry Danese; Jennifer Helfer: Jennifer Helfer is an employee of Viridian Therapeutics and holds stock in the company.; Shula Pollard: Shula Pollard is an employee of Viridian Therapeutics, Inc.; Kimberly Cockerham: I am a Principal Investigator and consultant for Viridian, Amgen, Genentech, Immunovant, Lassen, Tourmaline and ArgenX.

Grant Support: None.

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Association of Ocular Cranial Nerve Palsies and Risk of Future Strokes – A Systematic Review and Meta-Analysis

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Introduction:
Ocular Cranial Nerve Palsies (OCNP) occur commonly due to risk factors such as diabetes, hypertension and hyperlipidaemia. Strokes, which share similar risk factors, are a leading cause of morbidity and mortality. While some studies have reported a link, not all studies concur. As it remains a crucial public health strategy for early identification of high risk groups, our study aims to summarise evidence surrounding the association between OCNP and the subsequent risk of stroke.

Methods:
PubMed, Embase and Cochrane Library databases were searched from inception to 12 August 2024 for observational studies on OCNP in association with stroke in adults, diagnosed through validated methods. This review was prospectively registered on PROSPERO (CRD42024579166). Two independent authors selected relevant articles, extracted data and evaluated risk of bias using the Newcastle-Ottawa Scale (NOS). Using a random-effects model, maximally covariate-adjusted estimates were pooled as Hazards Ratios (HR). Heterogeneity was measured using I2. Further subgroup analysis by the type ocular cranial nerve involved, as well as sensitivity and influence assessments were conducted.

Results:
This study included six studies with a pooled cohort of 168,169 participants. All studies had a low-moderate risk of bias. Patients with OCNP had a 89% higher risk of developing stroke than patients without OCNP (HR:1.89;95%CI:1.29-2.76;I2=85%). The risk of stroke was highest among patients with oculomotor nerve palsy (HR:2.46;95%CI:1.46-4.14;I2=39%), followed by abducens nerve palsy (HR:2.27;95%CI:1.38-3.73;I2=49%), and trochlear nerve palsy (HR:2.06;95%CI:1.24-3.44;I2=0%). These findings remained robust to various sensitivity and influence analyses. The incidence of stroke was 4% higher for OCNP patients (Proportion:8%;95%CI:3-18%;I2=99%) than those without OCNP (Proportion:4%;95%CI:2-8%;I2=100%).

Conclusions:
This study found that OCNP is associated with an increased risk of future strokes, highest amongst oculomotor, abducens then trochlear nerve palsies. Further research could explore the feasibility of OCNPs treatment as a possible strategy for primary stroke prevention.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Genetic Associations of Non-Arteritic Anterior Ischemic Optic Neuropathy

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Introduction:
This systematic review aims to synthesise the available literature on possible genetic associations of NAION using observational studies that fit our pre-determined selection criteria. Non-arteritic anterior ischemic optic neuropathy (NAION) describes acute optic nerve ischemia and is a common cause of visual loss in patients over 50. Several risk factors have been proposed for NAION, including atherosclerosis, diabetes mellitus, and hypertension. However, the precise mechanism and pathogenesis of NAION remain ill-defined, and treatment options for this disease are limited.

Methods:
We queried studies from the electronic databases PubMed, Embase, Google Scholar, DOAJ, Scopus, Web of Science, TRIP, and the grey literature to aggregate a list of observational studies related to NAION genetic associations. Data retrieved includes an odds ratio of either greater than or less than one or a mean difference in case-control studies.

Results:
After selection, 20 articles remained, and from these studies, 921 patients with 20 unique genes were found to be associated with NAION. Of 20 genes, 21 genotypes had a statistically significant impact ($p< 0.05$). Based on these studies, our meta-analysis indicates a statistically significant association between genetic polymorphisms and the risk of NAION (OR = 2.57, 95% CI: 2.11-3.13, $p < 0.05$).

Conclusions:
Individual analysis suggests polymorphisms of several gene candidates (ATOH7, EDN1, SELP, G6PD, GSTM1, F5, ACE, ITGB3, GP1BA, and APOE) may increase susceptibility to developing NAION. Future research is needed, however, to define the exact role of genetic factors in NAION.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Characterizing the Use of Remote Interpretation of Optical Coherence Tomography in Neuro-Ophthalmology

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Introduction:
Neuro-ophthalmology faces a shortage of physicians with a median wait time for a neuro-ophthalmologist appointment estimated at 6 weeks. Strategies to alleviate this burden for physicians and patients include teleophthalmology in which diagnostic testing such as optical coherence tomography (OCT) can be interpreted in remote settings without the patient seeing a neuro-ophthalmologist. The purpose of this cross-sectional study is to characterize the use of remote interpretation of OCT at a single academic center.

Methods:
Interpretation-only OCTs done in 2022 were identified through billing codes. Patients were excluded if they were < 18 years old, lacked Minnesota Research Authorization, or the OCT had significant artifact.

Results:
Of 533 patients with interpretation-only OCTs, 56 patients were excluded for a total of 477 OCTs. The referring departments were neurology (95.2%), neurological surgery (4.6%), and endocrinology (0.2%). The most frequent indication for OCT was multiple sclerosis (55.3%), demyelinating disease of the central nervous system (31.4%), and abnormal brain MRI (6.3%). Of the 477 patients with OCT, 273 (57.2%) were confirmed to have multiple sclerosis. There were 69 patients with a clinical history of optic neuritis (ON), of which 68 cases were confirmed by OCT. OCTs also identified 58 cases of subclinical ON. There were 4 cases of binasal ganglion cell-inner plexiform layer (GC-IPL) thinning to suggest prior chiasmal involvement and 11 cases of homonymous GC-IPL thinning to suggest prior optic tract involvement. Four patients were recommended for in-person neuro-ophthalmology appointment for reasons such as elevated retinal nerve fiber layer thickness.

Conclusions:
Considering neuro-ophthalmology faces an estimated 20% workplace shortage, this study highlights the potential role for remote interpretation of OCTs to complement diagnostic workup. In addition, with OCT and optic nerve being incorporated into the upcoming McDonald criteria for MS, these findings highlight the potential usage of remote OCT interpretations in helping confirm a diagnosis of MS.

References: None provided.

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

Financial Disclosures: Jessica Trinh; Deena Tajfirouz; Kevin Chodnicki; Negar Moheb; Sabrina Poonja; W. Oliver Tobin: Dr. Tobin reports receiving research funding from the National institutes of Health, Mayo Clinic Center for Multiple Sclerosis and Autoimmune Neurology and Mallinckrodt Inc. He receives royalties from the publication of “Mayo Clinic Cases in Neuroimmunology” (OUP).; Sean Pittock: Sean J. Pittock has received personal compensation for serving as a consultant for Roche/Genentech, Sage Therapeutics, Arialys and Astellas. He has received personal compensation for serving on scientific advisory boards or data safety monitoring boards for F. Hoffman-LaRoche AG, Genentech, Arialys and UCB. His institution has received compensation for serving as a consultant for Astellas, Alexion, and Viela Bio/MedImmune. All compensation is paid to Mayo Clinic. He has received research support from Alexion, Viela Bio/MedImmune, Roche/Genentech and Adimmune. He has a patent, Patent# 8,889,102 (Application#12-678350, Neuromyelitis Optica Autoantibodies as a Marker for Neoplasia)—issued; a patent, Patent# 9,891,219B2 (Application#12-573942, Methods for Treating Neuromyelitis Optica (NMO) by Administration of Eculizumab to an individual that is Aquaporin-4 (AQP4)-IgG Autoantibody positive)-issued and from which he has received royalties and a patent for GFAP-IgG; Septin-5-IgG; MAP1B-IgG; Kelch-like protein 11; PDE10A pending. He is working as a consultant in the Mayo Clinic Neuroimmunology laboratory clinical service. The Mayo Clinic Neuroimmunology Laboratory commercially offers MOG-IgG testing, but revenue accrued does not contribute to salary, research support, or personal income; Eoin Flanagan: The institution of Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Alexion. Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Genentech. Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Horizon Therapeutics. The institution of Dr. Flanagan has received personal compensation in the range of $10,000-$49,999 for serving on a Scientific Advisory or Data Safety Monitoring board for Roche. Dr. Flanagan has received personal compensation in the range of $500-$4,999 for serving on a Speakers Bureau for Pharmacy times. The institution of Dr. Flanagan has received personal compensation in the range of $5,000-$9,999 for serving on a Speakers Bureau for UCB. The institution of Dr. Flanagan has received research support from Viela Bio. The institution of Dr. Flanagan has received research support from UCB. The institution of Dr. Flanagan has received research support from Roche. Dr. Flanagan has received publishing royalties from a publication relating to health care. Dr. Flanagan has a non-compensated relationship as a Member of medical Advisory Board with The MOG Project. Dr. Flanagan has a non-compensated relationship as a Editorial board member with Journal of The Neurologic Sciences. Dr. Flanagan has a non-compensated relationship as a Editorial board member with Neuroimmunology Reports. Dr. Flanagan has a non-compensated relationship as a Editorial Board Member with Neurology, Neuroimmunology Neuroinflammation (N2) Journal.; John Chen

Grant Support: None.

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Genetic Risk Scores for Prediction of Multiple Sclerosis and Other Immune-mediated Inflammatory Disease in Uveitis: Exploratory UK Biobank Study

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Introduction:
Uveitis, an inflammatory eye condition, is frequently associated with immune-mediated inflammatory disorders (IMIDs), including multiple sclerosis (MS). This latter association poses a particular problem for use of anti-TNFα biologics in patients with refractory uveitis, as treatment may precipitate demyelination. We previously demonstrated that multiple sclerosis genetic risk score (MS-GRS) aids in predicting MS in optic neuritis, offering an opportunity for genomic-based risk stratification. In this study we explored the utility of GRS in predicting future IMIDs in patients with undifferentiated uveitis.

Methods:
We utilised United Kingdom Biobank (UKBB), a longitudinal cohort of 500,00 individuals with phenotypic and genetic data. We defined 14 phenotypes, including 3,562 uveitis and 2,369 MS cases. Utilising published and unpublished genome wide association studies, we generated GRS for eight IMIDs: MS, ankylosing spondylitis (AS), ulcerative colitis, Crohn's disease, psoriasis, systemic lupus erythematosus, rheumatoid arthritis, and sarcoidosis. We assessed whether GRS improved IMID prediction using survival models adjusted for age and sex over a median follow-up of 16.3 years. We initiated replication of our models in Regeneron-DiscovEHR cohort.

Results:
During follow-up, 9.9% (n=353) of uveitis patients developed an IMID. GRS significantly predicted the onset of five IMIDs in patients with undifferentiated uveitis. Adjusted Hazard Ratios per SD increase in GRS ranged from 1.3 for Psoriasis-GRS (95%CI: 1.1–1.6, $p < 0.05$, c-index=0.63) to 2.4 for MS-GRS (1.6–3.5, $p < 0.0001$, c-index=0.79), with the AS model showing the strongest predictive performance (c-index=0.81) and an aHR of 1.8 (1.5–2.0, $p < 0.0001$).

Conclusions:
Our study demonstrates that models incorporating GRS can aid prediction of IMIDs in patients with uveitis. MS-GRS differentiates uveitis patients at low MS risk from those at higher risk. Integrating GRS into clinical practice could guide decision-making and facilitate timely interventions, improving outcomes and reducing disability. Validation of these models in diverse populations and clinical settings is essential to assess their utility.

References: Loginovic, P., Wang, F., Li, J., ... Oram ,R., & Braithwaite, T. Applying a genetic risk score model to enhance prediction of future multiple sclerosis diagnosis at first presentation with optic neuritis. Nature communications, 15(1), 1415. 2024

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

Financial Disclosures: Pavel Loginovic: Masters (MSc) Health Data Science Scholarship from Randox Ltd, not directly related to submitted work; Jiang Li; Lauric Ferrat; Uyenlinh Mirshahi; Qian Zhang; Tim Raine; Matthew Brown; Axel Petzold: A. P. reports personal fees from Novartis, Heidelberg Engineering, Zeiss, grants from Novartis, outside the submitted work; and is part of the steering committee of the OCTiMS study which is sponsored by Novartis and the Angio-OCT steering committee which is sponsored by Zeiss. He does not receive compensation for these activities.; Harry Green; Michael N. Weedon; David Carey; Richard Oram: R.O. is a co-investigator on a Randox Laboratories R&D research grant and receive translational industry academic funding from Randox Laboratories R&D relating to autoimmune GRS for prediction and classification of disease. There are no established patents, loyalties, or licensing agreements relating to this grant. It is a 3-year grant (February 2022–2025). The approximate value is a £2.2 million program grant on GRS across autoimmune disease. No funding is directly related to the submitted work; Tasanee Braithwaite

Grant Support: None.

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Isolated third cranial nerve palsy: Etiologies, demographic data, and clinical characteristics of 207 subjects

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Introduction:
The etiologies of isolated third cranial nerve palsy (TCNP) can be varied. Moreover, demographic and clinical features may be different among each etiology. Therefore, we aimed to evaluate the etiologies, demographic data, and clinical characteristics of isolated TCNP.

Methods:
Subjects diagnosed with isolated TCNP from January 2004, through October 2022 were included in this retrospective study. The etiologies, demographic data, and clinical characteristics of isolated TCNP were reviewed.

Results:
We identified 207 subjects with isolated TCNP. Overall, the most common etiology was microvasculopathy (64 subjects, 30.92%), followed by intracranial aneurysm (40 subjects, 19.32%) and intracranial neoplasm (34 subjects, 16.43%). Of all etiologies, microvasculopathy displayed the highest age at onset (median (interquartile range) 66.71 (57.52, 75.70) years) and intracranial aneurysm showed the highest female preponderance (female 29/40 subjects, 72.50%). The highest proportion of subjects with eye pain, categorized by etiology, was demonstrated in inflammation (12/17 subjects, 70.59%). Based on etiology, the highest proportion of subjects with headaches was revealed in intracranial infection (4/5 subjects, 80.00%). Of the total 207 subjects, bilateral involvement of isolated TCNP were found in 4 subjects (1.93%); 2 subjects were categorized in congenital etiology, while the others were categorized in trauma (1 subject) and intracranial infection (1 subject) etiologies. The highest proportion of subjects with pupillary involvement, based on etiology, was found in intracranial aneurysm (40/40 subjects, 100.00%).

Conclusions:
In our study, most isolated TCNP were due to microvasculopathy. Microvasculopathy displayed the highest age at onset and intracranial aneurysm showed the highest female preponderance. Eye pain and headaches were most commonly found in inflammation and intracranial infection etiologies, respectively. In spite of the rarity, bilateral involvement of isolated TCNP can be demonstrated, which were mostly due to congenital etiology. Pupillary involvement was most commonly revealed in intracranial aneurysm etiology.

References: None provided.

Keywords: Pupil, Adult strabismus with a focus on diplopia

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Phase 1 Healthy Volunteer Results Show Potential for Subcutaneous Administration of VRDN-003, a Half-life Extended Full Antagonist Monoclonal Antibody to IGF-1R, for Thyroid Eye Disease

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Introduction:
VRDN-003 and veligrotug (VRDN-001) are full antagonist monoclonal antibodies to IGF-1 receptor (IGF-1R). They have the same binding domain, and VRDN-003 contains half-life extension to optimize subcutaneous (SC) administration. Phase 3 data in patients with active TED (THRIVE, NCT05176639) showed statistically significant improvements in clinically meaningful endpoints (proptosis, CAS, diplopia) after 5 IV infusions of veligrotug (10 mg/kg) administered Q3W. Here we show phase 1 data comparing the safety and pharmacokinetics/pharmacodynamics (PK/PD) of VRDN-003 vs veligrotug administered as an SC injection.

Methods:
In separate studies, 24 healthy volunteers (HVs) received either VRDN-003 SC (n=16; 1 dose 300 mg [n=6]; 1 dose 600 mg [n=6]; or 1 dose 600 mg followed by 1 dose 300 mg [n=4]) or veligrotug SC (n=8; 1 dose 300 mg). Preliminary data including adverse events (AEs), PK, and PD (increases in IGF-1 serum levels) were assessed, and simulated exposures were generated for repeat VRDN-003 SC dosing.

Results:
AEs were reported in 31% (5/16) of HVs for VRDN-003 vs 38% (3/8) for veligrotug, with no treatment-related discontinuations, no hearing-related AEs, and no serious AEs. Half-life was ~40-50 days for VRDN-003 vs ~10-12 days for veligrotug. IGF-1 serum levels were similar for both antibodies (>4-fold above baseline) but sustained longer for VRDN-003 (>40 days). Dosing simulations indicated VRDN-003 SC could be administered as infrequently as Q8W while achieving exposures in the range of those obtained with veligrotug IV dosing Q3W.

Conclusions:
At 2 dose levels, single and repeat SC injections of VRDN-003 in HVs were well tolerated, had 4-5 times longer half-life than veligrotug, and demonstrated sustained increases in IGF-1 levels—potentially enabling low-volume SC dosing as infrequently as Q8W. The safety and efficacy of VRDN-003 SC administered Q4W and Q8W for 20 weeks are being assessed in clinical studies enrolling patients with active TED (REVEAL-1) and chronic TED (REVEAL-2).

References: None provided.

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

Financial Disclosures: Raghu Mudumbai: Clinical Trial Support: Stoke Therapeutics, Viridian Therapeutics, Nicox; Jody Abrams: Jody Abrams is a research investigator and serves on the advisory board for Viridian Therapeutics, Inc., and is a speaker for and serves on the advisory board for Amgen.; Tom Ciulla: Thomas Ciulla is an employee of Viridian Therapeutics, Inc.; Brent Dickinson: Brent Dickinson is an employee of Viridian Therapeutics, Inc.; Jyothi Vijayaraghavan: Jyothi Vijayaraghavan is an employee of Viridian Therapeutics, Inc.; Cathy Michalsky: Cathy Michalsky is an employee of Viridian Therapeutics, Inc.; Vahe Bedian: Vahe Bedian is an employee of Viridian Therapeutics, Inc.

Grant Support: None.

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New Onset Giant Cell Arteritis In Confirmed COVID-19 Infections: A Retrospective Study

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Introduction:
Giant cell arteritis (GCA) is an immune-mediated vasculitis that affects large arteries, usually the vessels of the face and head, in people over the age of 50. Currently, the exact cause of GCA is unknown. GCA may result in ischemia, which can be detrimental to vision if not treated immediately. During the first wave of the COVID-19 pandemic, there was an increase in GCA cases of 118%; however, the association between GCA and COVID-19 remains unknown. In this study, we investigated the relationship between confirmed COVID-19 infections and new-onset GCA.

Methods:
In this retrospective cohort study, patients' information, such as demographics, characteristics, comorbidities, and information detailing the timing of their COVID-19 diagnosis and neuro-ophthalmology diagnosis, were collected and recorded in an IRB-approved University of Missouri database. Average age, time between COVID-19 positive test and diagnosis, and associated risk factors were reported for a total of 7 patients with confirmed diagnosis of GCA.

Results:
The average age of diagnosis was 71 years. Of the 7 patients with confirmed GCA diagnosis post-COVID infection, 3 were female (42.9%) and 4 were male (57.1%). Four of the patients are smokers, two with diabetes, and 5 have a hypertension diagnosis. Only 3 of the patients had a pre-COVID ophthalmology evaluation with no diagnosis of GCA prior to COVID-19 infection.

Conclusions:
The data above is inconclusive to extrapolate any conclusions. However, given the inflammatory effects of the COVID-19 on the eye and nerves, there may exist a relationship between the COVID-19 infection and GCA. More research is needed to investigate this relationship further and examine the risk factors.

References: None provided.

Keywords: Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Optic Atrophy in Wolfram Syndrome: Prevalence and Use as a Diagnostic Indicator

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Introduction:
Wolfram syndrome is a predominantly autosomal recessive condition with classic symptoms of juvenile-onset diabetes mellitus (DM), diabetes insipidus, sensorineural hearing loss, and optic nerve atrophy. This study aims to characterize the symptoms observed in Wolfram syndrome, particularly the prevalence and timing of optic atrophy, to facilitate early diagnosis.

Methods:
A retrospective chart review was completed for 41 patients diagnosed with genetically confirmed Wolfram syndrome who were seen at an endocrinology and neuro-ophthalmology clinic at a single institution. Patients received a neuro-ophthalmic evaluation by a single attending physician. OCT imaging was conducted using a Zeiss machine at a single testing center and interpreted by the same physician. Linear regression with slope fitting was done using Prism. Statistical significance was defined as $P < 0.05$. Additionally, 5 patients with Wolfram syndrome evaluated at another institution will be included in the final analysis, bringing the total cohort size to 46.

Results:
Among 41 patients included in the analysis thus far, 33 had DM and only 4 had all four cardinal Wolfram symptoms. Vision loss affected 35 patients; in 3, vision loss was their only major symptom, and in 8, it preceded DM onset. Five patients had 20/20 vision. Of those with vision loss, 21 had moderate-to-severe vision impairment (20/60 or worse in the better-seeing eye). Visual impairment severity was inversely correlated with ganglion cell complex but not retinal nerve fiber layer thickness, age of visual symptom onset, or optic atrophy duration.

Conclusions:
In this cohort, vision loss and DM are the most prevalent symptoms, with some patients experiencing vision loss as their only or earliest symptom. About half have moderate-to-severe visual impairment that could negatively impact quality of life. Thus, it is important to consider screening for Wolfram syndrome in patients with unexplained vision loss and optic nerve pallor, even if they lack other classic symptoms.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Autonomic Symptoms Differentiate Lambert–Eaton Myasthenic Syndrome from Myasthenia Gravis among Patients with Certain Ocular Signs

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Introduction:
Ocular findings are common in both myasthenia gravis (MG) and Lambert-Eaton myasthenic syndrome (LEMS), which can manifest with autonomic dysfunction. We assessed how autonomic signs can be used to distinguish LEMS from MG in a real-world cohort.

Methods:
We conducted a retrospective cohort study using de-identified U.S. claims data (Symphony Health's PatientSource®). Eligible patients had ≥2 MG or LEMS claims ≥30 days apart between 3/1/2014 - 4/30/2022. Ocular (diplopia, ptosis, or abnormal saccades) and autonomic findings (anhidrosis, anisocoria, dry eyes, dry mouth, dry skin, constipation, urinary retention, erectile dysfunction, orthostatic hypotension, tonic pupil, Horner's syndrome, or other autonomic disorders) occurred if ≥1 claim was present. Claims for autonomic findings following pyridostigmine therapy were excluded. Statistical methods included chi-square tests, two-sample t-tests, and Firth logistic regression.

Results:
Among 130,362 patients with MG and 2,013 patients with LEMS, 42,702 (32.8%) and 311 (15.5%) had ocular signs, respectively. In patients with any ocular sign, ptosis was less frequent in LEMS than in MG (48.2% vs 58.5%, p=0.0003), while constipation (24.1% vs 12.3%, p< 0.0001), dry eyes (16.4% vs 12.4%, p=0.0327), urinary retention (10.9% vs 4.7%, p< 0.0001), other autonomic disorders (8.0% vs 2.1%, p< 0.0001), orthostatic hypotension (7.7% vs 2.6%, p< 0.0001), and dry mouth (3.2% vs 0.8%, p< 0.0001) were more frequent. In multivariate analysis, autonomic signs predictive of LEMS relative to MG included dry mouth (OR: 2.74; 95% CI: 1.44-5.19, p=0.002), other autonomic disorders (OR: 2.57; 95% CI: 1.65, 3.99, p< 0.0001), urinary retention (OR: 1.89; 95% CI: 1.29-2.75, p= 0.001), orthostatic hypotension (OR: 1.79; 95% CI: 1.14-2.80, p= 0.0112), and constipation (OR: 1.66; 95% CI: 1.25, 2.19, p= 0.0005).

Conclusions:
In a real-world cohort of MG and LEMS patients with ocular signs, autonomic signs predicted LEMS.

References: None provided.

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

Financial Disclosures: Andrew Lee; Guy Shechter: Consultant to Catalyst Pharmaceuticals; Luis Lay: Employee, Catalyst Pharmaceuticals; Regina Grebla: Consultant to Catalyst Pharmaceuticals

Grant Support: None.

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REVEAL-1 and REVEAL-2, Randomized Placebo-Controlled Clinical Trials in Thyroid Eye Disease of Subcutaneous Administration of VRDN-003, a Next-Generation Full Antagonist Monoclonal Antibody to IGF-1R

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Introduction:
VRDN-003 and veligrotug (VRDN-001) are full antagonist monoclonal antibodies to IGF-1 receptor (IGF-1R). They have identical binding domains, but VRDN-003 contains half-life extension to optimize subcutaneous (SC) administration. Phase 3 data in patients with active thyroid eye disease (TED; THRIVE, NCT05176639) showed statistically significant improvements in TED symptoms after 5 intravenous (IV) infusions of veligrotug (10 mg/kg) administered Q3W. Phase 1 data for VRDN-003 in healthy volunteers showed its half-life is 4-5 times longer than that of veligrotug, potentially enabling low-volume SC dosing as infrequently as Q8W while achieving exposures in the range of those observed with veligrotug IV dosing Q3W. The safety and efficacy of VRDN-003 SC are being evaluated in 2 ongoing randomized placebo-controlled clinical trials in patients with moderate-to-severe active TED (REVEAL-1) and chronic TED (REVEAL-2).

Methods:
The studies are evaluating VRDN-003 vs placebo administered as SC injections where patients are randomized (1:1:1) to VRDN-003 Q4W, VRDN-003 Q8W, and placebo. For REVEAL-1, patients must have a clinical activity score (CAS) of ≥4 and onset of signs/symptoms within 15 months of enrollment; for REVEAL-2, patients can have any CAS and must have onset of signs/symptoms at least 15 months prior to enrollment.

Results:
Efficacy assessments include measures of proptosis, diplopia, CAS, eyelid retraction, and quality of life. The primary endpoint will be assessed at 24 weeks, with safety and tolerability followed through the full study period, up to 1 year. Patients who do not meet responder criteria at 24 weeks may be eligible to receive a full course of open-label VRDN-003 SC.

Conclusions:
VRDN-003 is in development as an SC treatment for TED with the goal of reducing the treatment burden currently associated with IV infusions. The REVEAL-1 and REVEAL-2 randomized double-masked, placebo-controlled trials will be the first to assess VRDN-003 SC in patients with TED.

References: None provided.

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

Financial Disclosures: Roger Turbin: Research investigator for Viridian Therapeutics, Inc. I am currently receiving research support to my institution and advisory board status, past travel support, and own a small equity position below federal approved thresholds. My conflicts have all been thoroughly declared and approved by my institution.; Abhijit Narvekar: Abhijit Narvekar is an employee of Viridian Therapeutics, Inc.; Tom Ciulla: Thomas Ciulla is an employee of Viridian Therapeutics, Inc.

Grant Support: None.

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Differentiating Myasthenia Gravis and Cranial Nerve Palsies through Saccadic Eye Movement Analysis: A Prospective Cross-Sectional Study

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Introduction:
Myasthenia gravis (MG) is an autoimmune disorder characterized by fatigable muscle weakness due to the autoimmune destruction of neuromuscular junctions, while cranial nerve palsies (CNP) result from damage to the third, fourth, or sixth cranial nerves, leading to ocular movement impairments. Both conditions can present with similar ocular symptoms, such as diplopia and ptosis, making differential diagnosis crucial for appropriate treatment. This study aims to evaluate the effectiveness of video-oculography (VOG) in analyzing saccadic eye movements as a diagnostic tool to differentiate MG from CNP.

Methods:
In this prospective cross-sectional study, 93 patients with MG, 40 patients with sixth cranial nerve palsy, and 86 age- and sex-matched healthy controls (HC) were assessed using VOG. Saccadic eye movements within a ±15° range were recorded, focusing on parameters such as saccadic range, peak velocity, latency, and duration from onset to target after repetitive saccadic movements.

Results:
MG patients exhibited a decremental saccadic range after repetitive saccadic movements, indicating oculomotor fatigability, whereas CNP patients showed a decreased saccadic range from the first saccadic eye movement, which remained consistent throughout the session. The duration to reach the target significantly increased after consecutive eye movements in MG patients compared to CNP and HC groups. While the peak velocity in MG patients was comparable to that of the HC group, the CNP group exhibited a significant decrease in peak velocity compared to both MG patients and HCs.

Conclusions:
The quantification of saccadic eye movements shows potential as a disease-specific oculomotor biomarker, effectively diagnosing and differentiating MG from CNP. This enhances diagnostic accuracy and improves patient outcomes. VOG-based oculomotor recordings provide a non-invasive, repeatable, accurate, and practical tool for distinguishing MG from cranial nerve palsies.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Design Of A Phase 3 Randomized, Double-Blinded, Placebo-Controlled Study Evaluating Subcutaneous Efgartigimod PH20 Administered By Prefilled Syringe In Adults With Ocular Myasthenia Gravis

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Introduction:
An unmet need exists for approved, effective treatments for patients with ocular myasthenia gravis (oMG). Efgartigimod is an immunoglobulin G (IgG)1 antibody Fc-fragment that selectively reduces IgG levels by blocking neonatal Fc receptor (FcRn)-mediated IgG recycling and is approved in the US for the treatment of adults with generalized myasthenia gravis (gMG) and chronic inflammatory demyelinating polyneuropathy (CIDP). Retrospective analyses of data from pivotal studies in patients with gMG indicated an improvement in ocular symptoms in this population. The Phase 3, randomized, double-blind, placebo-controlled study, ADAPT OCULUS (NCT06558279), will investigate the efficacy and safety of subcutaneous (SC) efgartigimod PH20 (coformulated with recombinant human hyaluronidase PH20) in patients with oMG.

Methods:
Adults with confirmed oMG and a Myasthenia Gravis Impairment Index (MGII) patient-reported outcome (PRO) subcomponent ocular score ≥6 who are on stable MG therapy will be randomized 1:1 to receive 4 once-weekly efgartigimod PH20 SC 1000 mg or placebo injections administered via prefilled syringe (PFS), followed by 4 weeks of follow-up. Participants may continue in the up-to-2-year open-label extension part of the study evaluating long-term efgartigimod PH20 SC efficacy and safety in oMG.

Results:
The primary endpoint is change in MGII PRO ocular score from baseline to Week 4. Key secondary endpoints include changes from baseline to Week 4 in MGII ocular score (PRO plus physical examination), Myasthenia Gravis Activities of Daily Living ocular domain score, and MGII total score. Statistical analyses for efficacy endpoints will be conducted in hierarchical order at a 1-sided significance level of α=.025. Safety assessments include adverse event incidence and severity.

Conclusions:
This is the first Phase 3 clinical trial evaluating the safety and efficacy of efgartigimod PH20 SC in patients with oMG that addresses the unmet need for treatment in oMG.

References: None provided.
Keywords: Myasthenia, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: Julie Dela Cruz: JDC is an employee of argenx.; Carolina Barnett-Tapia: CB-T has served as an advisory board member for argenx, Alexion, UCB, and Janssen; been a consultant for argenx, Janssen, and UCB; received research support from US Department of Defense, Muscular Dystrophy Canada, MGNet, Grifols, and Octapharma; and is the primary developer of the MGII and may receive royalties.; James F. Howard Jr.: JFH has received research support (paid to his institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, NMD Pharma, PCORI, and UCB Pharma; honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, Amgen, argenx, Biohaven, Ltd., Biologix Pharma, CheckRare CME, Curie.bio, F. Hoffmann-LaRoche Ltd, Medscape CME, Merck EMB Serono, Novartis Pharma, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, TG Therapeutics, UCB Pharma, and Zai Labs; nonfinancial support from Alexion AstraZeneca Rare Disease, argenx, Biohaven Ltd., Cartesian Therapeutics, Toleranzia AB, UCB Pharma. and Zai Labs.; Jeffrey Guptill: JG is an employee of argenx.; Rosa Jimenez: RJ is an employee of argenx.; Fien Gistelinck: FG is an employee of argenx.; Sophie Steeland: SS is an employee of argenx.; Fien Verhamme: FV is an employee of argenx.; Sui H. Wong: SHW has received research support (paid to her institution) from Visual Snow Initiative, myaware, and MGFA; honoraria/consulting fees from argenx and Immunovant.

Grant Support: None.
Contact Information: None provided.

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Neuro-Ophthalmologic Manifestations Of Intracranial Aneurysms

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Introduction:
Intracranial aneurysms may present with neuro-ophthalmologic signs and symptoms. At present, there is a lack of updated information on this topic1,2. This study provides an epidemiological, clinical and paraclinical description of the afferent, efferent or mixed neuro-ophthalmological manifestations of intracranial aneurysms

Methods:
This is a longitudinal, observational, descriptive retrospective cohort study. We included 33 patients diagnosed with an intracranial aneurysm with neuro-ophthalmologic manifestations followed from 2019 to 2023 at a referral ophthalmological center.

Results:
33 patients with confirmed intracranial aneurysms and neuro-ophthalmologic manifestations were analyzed. 87.8% were female, median age at presentation was 64(±)14 years. 66%(22 patients) presented afferent manifestations, post-treatment retrochiasmatic pathway lesions were the most frequent in 27%(9 patients), followed by compressive anterior lesions in 24%(8 patients). 33%(11 patients) presented with efferent manifestations, and among these, isolated third nerve palsy represented 64% (7 patients). In 52%(17 patients) the neuro-ophthalmic syndrome was the presenting symptom, mean symptom duration was 245.85(±)504.89 weeks, symptom duration was not related to a larger aneurysmal size (r=0.06, p>0.05). 30%(10 patients) presented as aneurysmal post-treatment complications; among these, 80% were afferent and 20% were efferent in nature. 12%(4 patients) presented aneurysmal rupture. 76%(25 patients) of the aneurysms were in the anterior circulation and the most frequent affected artery was the ophthalmic segment of the internal carotid artery - 21%(7 patients). Mean aneurysm size was 14.1(±)6.66 mm in the anterior circulation vs 16.1(±)8.02 mm in the posterior circulation (p=0.20).

Conclusions:
Afferent visual pathway lesions represent two-thirds of the neuro-ophthalmic manifestations due to intracranial aneurysms. Three-quarters of these aneurysms arise from the anterior circulation. Overall, the most common initial neuro-ophthalmic manifestation was a disturbance along the anterior visual pathway (39%) in contrast to the more recognized third nerve palsy (22%) cited in the literature; among isolated third nerve palsies only two were secondary to the classical posterior communicating artery aneurysm.

References: 1. Dailey EJ, Holloway JA, Murto RE, Schlesinger N; Evaluation of ocular signs and symptoms in cerebral aneurysms. Arch Ophthalmol, 71, 463-474, 1964. 2. Kowsalya A, Sangeetha R, Jayashree N, Saidheera M; Neuro ophthalmologic manifestations of intracranial aneurysms: A case series. Kerala J Ophthalmol, 35, 76-78, 2023.

Keywords: Vascular disorders, Optic neuropathy, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Evaluating Microperimetry in Multiple Sclerosis: A Cross-Sectional Study of Disease Stages Compared to Healthy Controls

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Introduction:
Multiple sclerosis traditionally affects vision by causing optic neuritis. Many studies have documented foveal dysfunction independent of optic neuritis. MS has also been shown to cause fixation instability. This study evaluates the commercial microperimeter as a biomarker for MS stage measuring both foveal sensitivity and gaze fixation stability simultaneously .

Methods:
In this prospective, observational study, 70 eyes without optic neuritis from 42 people (25 relapsing MS, 5 progressive MS, 12 control) completed full threshold microperimetry (Nidek MP-3, 4-2 strategy) using Goldmann size I and III stimuli. Mean retinal sensitivity was calculated as the average sensitivity across 9 points in a 1mm region centered on the fovea. Fixation was measured using 1st ,2nd, 3rd standard deviation Bivariate Contour Ellipsoid area.

Results:
Though race/ethnicity were similar between groups, RMS group had more females (84% vs 40%) and MS subjects were older (PMS 59.2 ± 15 years, RMS 42.7 ± 10, control 30.7 ± 7). There was no difference in the fixation indices between MS and control eyes or RMS and PMS eyes. Control eyes had a higher mean sensitivity than MS eyes using Goldmann stimulus size I(1.97, 95% C.I of 0.34 & 3.61, p= 0.018, GEE) and III (1.54, 95% CI of 0.42 & 2.67, p = 0.007, GEE). There was no difference in mean sensitivity between RMS and PMS eyes using either stimulus size.

Conclusions:
Compared to control eyes, MS eyes had similar fixation indices and lower mean retinal sensitivity with Goldmann I and III stimuli. Compared to Relapsing MS group, progressive MS group had similar fixation indices and mean retinal sensitivity with Goldmann I and III stimuli. Further research in age matched groups is needed to confirm this observation. The sensitivity parameters obtained from the commercially available microperimeter may be useful as a biomarker for foveal dysfunction in multiple sclerosis.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: NIH R01 EY033475, DOD exploratory award, NIH P30 EY026877, Research to Prevent Blindness

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Impact Of Visual Snow Syndrome On Daily Life

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Introduction:
Understanding the specific factors that impact quality of life in patients with visual snow syndrome (VSS) is vital for developing personalized care strategies that effectively address their unique needs and challenges.

Methods:
We conducted a survey study of patients with VSS diagnosed by neuro-ophthalmologists at a tertiary referral center. Potentially eligible patients ≥18 years of age with VSS were identified by searching the medical records and called to assess interest in participation. After informed consent was obtained, surveys were administered and included the open-ended question, “how does visual snow syndrome affect your daily life?” The responses were coded independently by two team members using a modified grounded theory approach.

Results:
Of the 115 eligible patients, 28 (24%) completed the survey. Participants’ ages ranged from 21–52 years (Mean = 30, SD = 8). Most were women (n=21, 75%) and self-identified as White (n=24, 86%). Many (n=8, 29%) reported that receiving a VSS diagnosis led to heightened perception/worsening of symptoms (“Now that I know it isn't 'normal,' I tend to be more cognizant of the symptoms”). The most significant impacts on daily life included decreased independence, primarily due to an inability to drive (n=12, 43%, “I rely on my husband to drive.”), difficulties with daily tasks (n=13, 46%, “I have to remember where things are located in my house, how many stairs are on the porch . . . I cannot rely on my vision all the time.”), heightened sensory perceptions (n=12 [43%], light/environmental sensitivity; n=4 [14%] pain), and non-pain brain-mediated symptoms (n=8, 29% “depression, anxiety,” brain fog).

Conclusions:
Effective treatments for VSS need to improve independence, daily task execution, and address the numerous non-visual symptoms impacting patients' lives. Additional educational and psychological resources may be needed to support patients receiving a VSS diagnosis and lessen the potential for worsening symptoms.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Plasma calprotectin: A Blood Biomarker for Identifying Giant Cell Arteritis

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Introduction:
We evaluated if plasma calprotectin at time of first clinical presentation could predict the final clinical diagnosis of giant cell arteritis (GCA) as evaluated at follow-up after six months.

Methods:
Blood samples were drawn at presentation in consecutive patients suspected of GCA. Plasma calprotectin was measured using the Gentian GCAL® Calprotectin Reagent Kit. The final diagnosis of GCA was given at six-months follow-up.

Results:
Of 110 patients reviewed, 104 were eligible for data analysis, from whom 77 had plasma calprotectin analysis available. Of these 77, 45 (58.4%) had a final diagnosis of GCA, 31 (40.3%) had no GCA, and one case (1.3%) as inconclusive. There was a significant difference in plasma median calprotectin concentration (P=0.0001508) between those with and without GCA. By comparing the upper reference limit of the Gentian CGAL® (≥0.970 mg/L) with the final clinical diagnosis, plasma calprotectin performed with sensitivity 65% (95%CI: 48–79%) and specificity 75% (95%CI: 55–89%). The area under the receiver operating characteristics curve (AUC) was 0.70 (95%CI: 0.57–0.83). Accuracy was 69% (95%CI 57–80%). By using an upper reference limit of >0.635 mg/L, test statistics reached sensitivity 85% (95%CI: 70–94%), specificity 61% (95%CI: 41–79%), AUC 0.73 (95%CI: 0.60–0.86), and accuracy 75% (95%CI: 63–85%).

Conclusions:
Plasma calprotectin concentration was higher in GCA. The value of plasma calprotectin in the diagnosis of patients with suspected GCA warrants further studies.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: Synoptik Foundation and The Danish Rheumatism Association

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Associations Between Eye Pain, Vision Loss, and Imaging Findings in Myelin Oligodendrocyte Glycoprotein Antibody Disease

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Introduction:
Myelin Oligodendrocyte Glycoprotein Antibody Disease (MOGAD) is a rare, autoimmune demyelinating disorder often presenting as optic neuritis. The relationships between patient-reported symptoms, such as diminished vision and eye pain, and imaging findings are underexplored. This study investigates these associations in MOGAD patients at initial evaluation.

Methods:
A retrospective study of adult MOGAD patients (n=45) was conducted using electronic health records. Symptoms of vision loss and eye pain were compared with MRI findings, demographics, and other clinical features. Data analysis involved a comparison of proportions to assess statistically significant associations.

Results:
Patients with diminished vision (DV) had a higher prevalence of eye pain (50% vs 0%, n=34 vs n=11, p = 0.003), lower male prevalence (29.4% vs 72.7%, n=34 vs n=11, p=0.011), and higher Hispanic prevalence (50% vs 0.91%, p=0.016). MRI findings showed fewer cervical (28.6% vs 63.6%, n=28 vs n=11, p=0.043) and thoracic lesions (31.8% vs 70%, n=22 vs n=10, p=0.044), but more optic nerve lesions (79.4% vs 0%, n=34 vs n=10, p< 0.001). Eye pain (EP) was linked to more optic nerve lesions (88.2% vs 44.4%, n=17 vs n=27, p=0.004) and bilateral optic nerve involvement (64.3% vs 16.7%, n=14 vs n=12, p=0.014), and lower rates of neuropathic pain (29.4% vs 64.3%, n=17 vs n=28, p=0.023) and weakness (11.8% vs 46.4%, n=17 vs n=28, p=0.017).

Conclusions:
In MOGAD patients, diminished vision and eye pain are associated with specific MRI findings. Demographic differences may influence clinical and radiographic correlations, warranting further study with larger cohorts.

References: Jeyakumar, N., Lerch, M., Dale, R.C. et al. MOG antibody-associated optic neuritis. Eye 38, 2289–2301 (2024). https://doi.org/10.1038/s41433-024-03108-y

Keywords: Demeylinating disease, Neuroimaging, Optic neuritis, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None

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Prognostic Factors of Favorable Aneurysmal Third Cranial Nerve Palsy Recovery

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Introduction:
Data regarding prognostic factors of recovery in Thai aneurysmal third cranial nerve palsy (TCNP) patients is scarce. Therefore, we aimed to identify prognostic factors of favorable TCNP recovery in Thai aneurysmal TCNP subjects.

Methods:
Forty subjects with aneurysmal TCNP were included. Demographic data, clinical and radiographic characteristics, treatment, follow-up period, and recovery of TCNP were retrospectively reviewed. A favorable TCNP recovery was defined as subjects who achieved all of the following conditions: absence of ptosis, equal pupillary size (impaired pupillary light reflex was not considered), and normal ocular motility in all directions.

Results:
All subjects had unilateral TCNP. The median margin reflex distance 1 and mean anisocoria were -2.0 (interquartile range (IQR): -4.0, 0.0) mm and 2.49(standard deviation: 1.11) mm, respectively. All subjects had diffuse ophthalmoplegia (defined as ophthalmoplegia in all of the following directions: supraduction, infraduction, and adduction), of which 20 subjects (50.00%) were complete (defined as duction completely abolished in all 3 directions: supraduction, infraduction, and adduction). Posterior communicating artery aneurysm was the most common location of aneurysm(23 subjects, 57.50%). The median time from initial symptoms onset to treatment was 6.50(IQR: 3.00, 30.00) days. Twenty-eight subjects(70.00%) underwent cerebral angiogram with coil embolization and the remaining 12 subjects(30.00%) underwent craniotomy with aneurysm clipping. The median follow-up period was 24 (IQR: 14, 36) months. Eleven subjects (27.50%) achieved a favorable TCNP recovery. Incomplete diffuse ophthalmoplegia and time from initial symptoms onset to treatment of ≤ 5 days were significant factors associated with favorable TCNP recovery (odds ratio (OR) 57.14, 95% confidence interval (CI): 3.11, 1,049.19, p = 0.006 and OR 85.59, 95% CI: 4.82, 1,520.91, p = 0.002, respectively).

Conclusions:
Incomplete diffuse ophthalmoplegia and time from initial symptoms onset to treatment of ≤ 5 days were the significant prognostic factors of favorable TCNP recovery in Thai aneurysmal TCNP subjects.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Diagnostic Yield of Neurogenetic Evaluation for Patients With Undiagnosed Optic Neuropathy

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Introduction:
Genetic disorders represent an increasingly recognized etiology of undiagnosed optic neuropathy, especially given diagnostic advances. However, diagnostic limitations persist with one recent study showing a 31% yield of genetic testing. This retrospective single institution study seeks to characterize integration of the neuro-ophthalmic work-up with genetic testing as an approach to undiagnosed optic neuropathy.

Methods:
All patients seen by the Neurogenetics Division at a single institution between August 2021 and January 2024 were reviewed with the following search criteria: “optic neuropathy”, “vision loss”, “optic atrophy”, “blurry vision”, “neuro-ophthalmology.” 159 charts were reviewed to identify 21 patients with an optic neuropathy diagnosis who had appropriate neuro-ophthalmology work up. Clinical features, including best corrected visual acuity (logMAR), peripapillary retinal nerve fiber layer (pRNFL) thickness, and Ishihara color plates, were recorded for two groups based on whether testing confirmed or refuted a genetic basis of optic neuropathy. Two-sample t tests were performed comparing clinical features between groups. Wilcoxon rank-sum tests were performed for comparing color testing.

Results:
A molecular genetic diagnosis was identified in 9 out of 21 patients corresponding to a diagnostic yield of 43%. Causative variants in NDUFS7 (1), WFS1 (2), IBA57 (1), ATXN8OS (1), MPZ (1), MT-ND4 (2) and MT-ND6 (1) mutations were identified. There was a statistically significant difference in mean change in Ishihara color plates between the 1st and 3rd visit with the negative group improving by 2.1 plates compared to the confirmatory group worsening by 1.6 plates (p=0.03). There was no statistically significant difference for other measures or for those with unilateral and bilateral optic neuropathy.

Conclusions:
In our cohort, variants associated with optic neuropathy were confirmed among 43%. Characteristics of optic neuropathy were similar for patients with and without identified causative variants. Genetic testing should be considered among patients with unclear etiology of optic neuropathy.

References: Fiorini C, Ormanbekova D, Palombo F, et al. The Italian reappraisal of the most frequent genetic defects in hereditary optic neuropathies and the global top 10. Brain 2023;146:e67-e70.

Keywords: Optic neuropathy, Genetic disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Large Language Models in Neuro-ophthalmology: A Comparative Analysis of Diagnostic Accuracy

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Introduction:
With recent advancements in consumer-accessible generative artificial intelligence (AI), large language models (LLMs) have shown potential to assist in medical decision-making. However, the effectiveness of LLMs in diagnosing complex medical conditions, particularly in specialized fields like neuro-ophthalmology, remains underexplored. This study aims to evaluate and compare the diagnostic accuracy of GPT-4o and GPT-3.5 in challenging neuro-ophthalmology cases.

Methods:
Fifty published UPFRONT and clinical correspondence cases from the Journal of Neuro-Ophthalmology from 2015 to 2024 were utilized. Case information was input into GPT-4o and GPT-3.5 with increasing amounts of information given, history alone; history and physical; and history, physical and imaging. The AI was then asked, “what is the most probable diagnosis?” Between the two models, 300 generated answers were compared for accuracy against established clinical diagnoses. Results were statistically analyzed using Chi-squared tests on SPSS 29.0.2. Significance was set at $p< 0.05$.

Results:
GPT-4o had an overall diagnostic accuracy of 55%, and GPT-3.5, 43% ($p< 0.0001$). GPT-4o was significantly more accurate when prompted with history alone (30% vs 22%, $p< 0.05$) and history and physical (42% vs 28%, $p< 0.01$). With a full workup of history, physical, and imaging, GPT-4o remained more accurate than GPT-3.5 (92% vs 78%; $p< 0.01$). Both GPT-4o and GPT-3.5 were significantly more accurate when prompted with more information. The only exception was for GPT-3.5; adding only physical examination to the history did not significantly impact diagnostic accuracy ($p=0.08$).

Conclusions:
We found that GPT-4o was significantly more accurate at diagnosing neuro-ophthalmological conditions than GPT-3.5. The increase in diagnostic accuracy with increasing amounts of input information highlights the potential of LLMs to support clinical decision-making in this complex medical field. Further research is warranted to explore the integration of these models into clinical practice.

References: Madadi Y, Delsoz M, Lao PA, Fong JW, Hollingsworth TJ, Kahook MY, Yousefi S. ChatGPT Assisting Diagnosis of Neuro-ophthalmology Diseases Based on Case Reports, medRxiv [Preprint], 2023. Kenney RC, Requarth TW, Jack AI, Hyman SW, Galetta SL, Grossman SN. AI in Neuro-Ophthalmology: Current Practice and Future Opportunities. J Neuroophthalmol. 2024. Lee AG, Zapletal A, Charoenkijkajorn C, et al. Artificial Intelligence in Neuro-Ophthalmology. Available at: https://eyewiki.org/Artificial_Intelligence_in_Neuro-Ophthalmology, 2023.

Keywords: Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Evaluation of potential inequities in patient outcomes following a STAT outpatient neuroimaging for evaluation of optic nerve swelling

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Introduction:
Previously, our group piloted an innovative outpatient STAT neuroimaging pathway for patients with optic nerve swelling. These patients are commonly referred to the emergency department (ED) for urgent neuroimaging. The STAT pathway is an alternative that facilitates urgent outpatient MRIs, avoiding significant wait times and costs associated with ED visits without compromising clinical outcomes.[1] This study aims to assess for demographic and BMI-based inequities in STAT pathway efficacy and clinical outcomes.

Methods:
A retrospective chart review was performed for patients who received STAT outpatient or ED-based neuroimaging for optic nerve swelling between 2020-2024. Data were collected on demographics, BMI, and clinical characteristics at presentation and latest follow-up, and for the STAT cohort only, on whether MRIs were scheduled and completed promptly. Wilcoxon rank tests evaluated for outcomes differences between STAT patients from different demographic groups. Multivariate regressions examined predictors of changes in ophthalmologic measures over time. T- and Fisher's exact tests compared demographic characteristics of STAT and ED patients.

Results:
We examined 50 STAT and 63 ED patients. Among STAT patients, females were relatively younger with higher BMIs, baseline VF MDs, and baseline RNFL thickness ($p< 0.05$ for all). Blacks were younger compared with whites ($p< 0.01$). There were no significant demographic or BMI-based differences in clinical outcomes or in MRI scheduling/completion rates among STAT patients. Multivariate models revealed no significant predictors of changes in ophthalmologic measures over time for STAT patients. The STAT and ED cohorts had similar demographic profiles.

Conclusions:
There were no demographic variations in outcomes within the STAT cohort or differences in the demographic composition between the STAT and ED cohorts. The efficacy of MRI scheduling and completion were similar among different demographic groups. These findings support the STAT protocol as an equitable alternative to ED-based care for a subgroup of patients presenting with optic nerve swelling.

References: 1.Gibbons AB, Huang P, Sklar M, Kim P, Henderson AD. Evaluation of a STAT MRI Protocol for Emergent Ophthalmology Patients. J Neuroophthalmol. 2023 Dec 5. doi: 10.1097/WNO.0000000000002053. Epub ahead of print. PMID: 38051953.

Keywords: Neuroimaging

Financial Disclosures: Apurva Dev; Florian Guillot; Amanda Henderson: None related to this submission: Horizon Therapeutics/Amgen.

Grant Support: None.

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Utilizing Simulation-Based Trainings to Enhance Neuro-Ophthalmological Examination Proficiency in Neurology Residents

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Introduction:
Developing neuro-ophthalmological exam skills is crucial for accurate diagnosis and avoiding potential pitfalls in many urgent, vision- and life-threatening conditions. However, neurology residents often receive limited formal training in this subspecialty. Simulation-based training (SBT) has proven to be an effective method for improving clinical skills by offering a controlled, feedback-rich environment. Here, we present pretest and posttest results from a cohort of neurology residents over the past year, demonstrating the positive impact of simulation (SIM) neuro-ophthalmology exam workshops on their performance.

Methods:
In the last one year, we conducted three in-person SIM sessions to enhance neurology residents' neuro-ophthalmology exam skills. Residents took a pre-SIM test on neuro-ophthalmology skills knowledge, participated in hands-on SIM scenarios covering key exam techniques, and received feedback from clinical faculty. A post-SIM test, identical to the pre-test, was given to assess performance and knowledge improvement. Statistical analyses were performed to compare pre- and post-workshop scores.

Results:
Of the 17 participants, most were PGY4 residents (n=7). Pre-SIM scores averaged 41.2%, ranging from 20% to 60%. Post-SIM scores improved to an average of 69.4%, with a range of 40% to 100%, showing significant skill improvement.

Conclusions:
The implementation of neuro-ophthalmology exam simulation sessions resulted in marked improvement in neurology residents' examination skills. Post-SIM test scores consistently outperformed pre-SIM scores, highlighting the effectiveness of the in-person training and feedback provided. Effective training of the residents is essential to avoid diagnostic pitfalls that can be caused by limited neuro-ophthalmology skill set. We encourage the adoption of this simulation-based model in other residency programs to improve resident competency in essential neuro-ophthalmology skills.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Miscellaneous, Retina, Pupil, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Use Of A Virtual Reality Visual Field Device To Improve Quality Of Care In The Emergency Department And Inpatient Setting

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Introduction:
Automated visual field testing is an essential diagnostic and disease monitoring tool for many neuro-ophthalmic disorders. Most commonly, automated devices are stationary and located in ophthalmology clinics. As a result, formal visual field testing has been limited in the hospital setting until the recent availability of virtual reality visual field testing. In this study, we report our experience with the use of a virtual visual field (VVF) device in the emergency department (ED) and inpatient hospital settings.

Methods:
We performed a retrospective chart review of our use of a VVF device in the ED and inpatient hospital setting from February 2020 to March 2022. We report our experience and the impact on patient care with use of the VVF.

Results:
110 patients (ages 10 to 85 years) and 128 visual field encounters were identified. Patients were most commonly located on the hospital floor (50.8%), followed by the intensive care unit (32.0%), and ED (17.2%). The VVF prevented the need for a trip to the outpatient ophthalmology clinic in 100% of encounters of patients with vision threatening papilledema and those with lumbar drains. Use of the VVF provided a more detailed, baseline exam at bedside in 67.2% of all encounters. A bedside pre/post-operative visual field assessment was achieved in 12.0% of encounters. The VVF did not change management in 17.2% of encounters.

Conclusions:
In our experience, use of the VVF has improved the quality of care of patients with neuro-ophthalmic conditions. A significant impact of the VVF was increased safety by preventing the need for transport of patients with vision-threatening papilledema and lumbar drains to the outpatient setting for visual field monitoring. Due to increased quality of patient care, the VVF device has become a mainstay of the examination of patients in the ED and hospital.

References: None provided.

Keywords: Visual fields, Perimetry, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease, Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Refining skills: Using Self-Assessments to Gauge the Transformative Impact of Neuro-Ophthalmology Rotations on Essential Skill Mastery in Neurology Residency

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Introduction:
Developing neuro-ophthalmological skills, such as direct ophthalmoscopy, can be challenging for neurology residents due to limited exposure during their residency training. We conducted a pre-and post-survey of 17 neurology residents (PGY 2-4) over a three-year period, assessing the impact of a neuro-ophthalmology clinic rotation. During this rotation, residents engaged in hands-on practice with patients, receiving guided instruction and individualized feedback. The study evaluated the effect of this experience on the residents' self-assessed competency in performing neuro-ophthalmological examinations.

Methods:
Residents completed self-assessments before and after a neuro-ophthalmology rotation, rating their comfort with nine core competencies, including direct ophthalmoscopy, papilledema grading, RAPD detection, eye movement/diplopia/Maddox rod evaluation, and interpreting OCT and visual fields. Improvements were measured by comparing pre-and post-rotation scores, raw score changes, and percentage improvements. Pearson correlation coefficients assessed the relationship between rotation days and skill improvement.

Results:
Of the 17 participants, most were PGY2 residents (n=9), spending an average of 3.5 days on rotation. Pre-rotation scores averaged 40.7% and improved to 66.9% post-rotation, indicating a 64% increase in score. Direct ophthalmoscopy skills improved by 63%, papilledema grading by 71%, and OCT interpretation by 87%. Strong correlations were noted between days on rotation and skill improvement in papilledema grading (r=0.37) and HVF (r=0.35). Weaker or negative correlations were observed for eye movement (r=-0.10) and cover-uncover tests (r=-0.07), indicating less consistent improvement with additional rotation days. This may be attributed to varying baseline competencies among the cohorts.

Conclusions:
Our findings indicate that residents' self-reported competencies improved after the neuro-ophthalmology rotation. Seven of nine skills showed positive correlations between time spent on rotation and improvement, with varying impact across areas. This highlights the value of incorporating much-needed neuro-ophthalmology rotations into neurology residency programs to learn critical neuro-ophthalmology skills.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Visual fields, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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PHOMS-up Thickness: A novel OCT based method for discriminating between true papilledema and pseudopapilledema

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Introduction:
A peripapillary hyperreflective ovoid mass-like structure (PHOMS) is an OCT biomarker of nonspecific axoplasmic stasis seen on optical coherence tomography (OCT) scans of the optic nerve head (ONH), associated with both true papilledema and pseudopapilledema. Discriminating these conditions is crucial due to their differing underlying causes and management strategies, as true papilledema can be both vision- and life-threatening. This study aimed to test a simple method for differentiating pseudopapilledema from true papilledema using OCT measurements of the ONH.

Methods:
This was a comparative cross-sectional study of patients who underwent OCT scanning following ODDS Consortium guidelines. Patients were categorized into two groups: Group 1 had true papilledema due to IIH (33 eyes of 33 patients), and Group 2 had pseudopapilledema (44 eyes of 44 patients) due to optic disc drusen (n=38) and myopic tilted discs (n=6). Data assessment was performed on Heidelberg ONH OCT, measuring the retinal thickness above the PHOMS, specifically from the anterior limit of the inner nuclear layer perpendicular to the internal limiting membrane. This thickness was termed the PHOMS-up Thickness (PupT).

Results:
While PHOMS were equal in height and width between groups, PupT was significantly larger in the true papilledema group compared to the pseudopapilledema group (PupT 298µm (±52µm) vs 173µm (±40µm), $p < 0.001$). Furthermore, we identified a potential new qualitative marker of true papilledema resembling hyperreflective droplets in the outer nuclear layer lateral to PHOMS present in 44% of individuals in the true papilledema group and 0% in the pseudopapilledema group.

Conclusions:
The significantly larger PupT in true papilledema compared to pseudopapilledema supports the hypothesis that true papilledema involves both intra-axonal and interstitial fluid stasis, while pseudo-papilledema only involves axoplasmic intra-axonal stasis. This study shows promise that PupT can be used as a simple, rapid, OCT-based metric to differentiate pseudopapilledema from true papilledema.

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Keywords: Optic neuropathy, Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Canadian Practice Patterns for Acute Central Retinal Artery Occlusion

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Introduction:
Central retinal artery occlusion (CRAO) causes acute monocular vision loss and shares a common pathophysiology with cerebral stroke. [1] CRAO requires urgent investigations to reduce the risk of subsequent stroke, and current evidence is supportive of intravenous thrombolysis to improve visual outcomes when offered within a therapeutic window. [2] This is the first study to describe current practice patterns for non-arteritic CRAO management at academic teaching hospitals in Canada.

Methods:
A 13-question survey was distributed to the residents of Canadian Ophthalmology training programs. Analysis was performed using descriptive statistics based on geography (Ontario, Quebec, or East) and by size of the nearest urban center (large, medium, and small).

Results:
The response rate was 13/15 ophthalmology programs. Patients were referred most frequently by emergency physicians (57.2%) and optometrists (30.8%). On average each program received 20.4 referrals annually and 14.6% of patients presented within six hours of symptom onset. At larger centres 46% of patients presented within the 6-hour window. Conservative treatments such as massage and intraocular pressure lowering medications were offered by 30.7% programs, but not anterior chamber paracentesis. All programs uniformly arranged appropriate vascular neuroimaging, and 69.2% of programs arranged stroke neurology or internal medicine consultation within 24 hours. Six centers “occasionally” offered intravenous thrombolysis for acute CRAO, with two “frequently” offering it. Only two programs utilize a pre-existing Eye Stroke pathway, and no programs have access to fundus photography within the emergency room for rapid identification of CRAO.

Conclusions:
This is the first study to describe the landscape for CRAO management at Canadian academic centers. A coordinated approach to acute CRAO may be facilitated by interdisciplinary partnerships between emergency physicians, ophthalmologists, and stroke neurologists by way of an “Eye Stroke” pathway. Use of ophthalmic imaging within the emergency room may facilitate early diagnosis and management.

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Keywords: Vascular disorders, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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The Increasing Prevalence of Neuro-Ophthalmology Emergency Department and Inpatient Consultations in an Academic Quaternary Care Center

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Introduction:
Ophthalmology and neuro-ophthalmology consultations (NOC) in emergency departments (EDs) and hospitals increased during the COVID pandemic, with a change in referral patterns. The shortage of neuro-ophthalmologists, combined with difficult patient access to ophthalmologists in many under-served areas, contribute to many patients self-referring to general EDs or being referred/transferred to EDs/hospitals with access to neuro-ophthalmologists. We compared our institution's ED/inpatient-NOC patterns from year 2024 [after implementation of non-mydriatic ocular imaging (NMFP-OCT) in our general ED] to the 494 ED/inpatient-NOCs seen in year 2022 [prior to implementation of NMFP-OCT in the ED] at the same institution with the aim to determine if the burden of ED/inpatient-NOCs continues to increase over time and to evaluate the impact of ED/NMFP-OCT.

Methods:
Prospective observational study with systematic collection of consecutive ED/inpatient-NOCs at one academic center. Referral patterns and need for outpatient neuro-ophthalmology follow-up were collected and compared with previously-published data prospectively obtained during year 2022.

Results:
Of 478 consecutive in-person NOCs between 01/01/2024-10/01/24, there were 348 ED-NOCs (68%) and 131 inpatient-NOCs (27%). 76/348 ED NOCs (22%) occurred on weekends/holidays; 129/348 ED-NOCs (37%) at night. 212/348 ED consultations (45%) were referred by an outside eye-care specialist [103/212 (49%) ophthalmologists, 109/212 (51%) optometrists). The most common ED-NOC was for papilledema (94/348, 27%). 345/478 NOCs (72%) required outpatient neuro-ophthalmology follow-up. During the same period, 187 additional patients had papilledema ruled-out remotely in real-time on NMFP-OCT obtained in the ED.

Conclusions:
During only the first 10 months of 2024, there were 478 in-person ED/inpatients NOCs compared to 494 consultations over 12 months in 2022, confirming the increasing number of ED/inpatient-NOCs. Over the same 10 months in 2024, 187 additional ED-NOCs had papilledema ruled-out remotely on NMFP-OCT (without in-person NOC), thereby decreasing the burden of NOCS in the ED. The results for the entire year-2024 will be presented at the NANOS meeting.

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

Financial Disclosures: Amy (Mung Yan) Lin; Michael Dattilo; Andrew Pendley; James Greene; Hetal Ray; Avital Okrent Smolar; Etienne Bénard-Séguin; Nithya Shanmugam; Jessica McHenry; Matthew Keadey; David Wright; Nancy Newman: Consultant for GenSight, Chiesi, Neurophth (all involved with the treatment of Leber hereditary optic neuropathy. Research support as PI to my institution from GenSight for clinical trials.; Valérie Biousse: Consultant for Topcon which commercializes fundus cameras. The current research is completely independent from Topcon and is not funded by the company.

Grant Support: None

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Epidemiological, Clinical, and Prognostic Features of Optic Neuritis in Latin American Population in a Tertiary-Care Ophthalmology Center.

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Introduction:
Optic neuritis (ON) is a major contributor to visual impairment, frequently affecting younger individuals. This study outlines the demographic, clinical and paraclinical characteristics, and outcomes of ON patients within both pediatric and adult Latin American cohorts in our hospital.

Methods:
This is an observational, longitudinal, and comparative, retrospective cohort study reviewing patients between January 2021 and February 2024 that were admitted while experiencing a current ON event. Infectious and other optic neuritis, considered atypical, were not excluded. We considered atypical optic neuritis (AtON) is characterized as neuritis that does not fulfill the criteria for typical optic neuritis, which include the following: unilateral involvement, pain with eye movements, age between 20 and 45 years, lack of recovery within 4 weeks of onset, and progression beyond 3 weeks of onset.

Results:
125 (12 [96%] children, 113 [90.4%] adults) were included in the study; 72 (57.6%) were female. The median age at diagnosis was 31 years (±10.6). 122 (97.6%%) were first-ever optic neuritis episodes, while 7 (5.6%) where recurrent episodes or presented recurrence during follow-up. 66 (52.8%) were classified as AtON. Onset, was different ($p< 0.05$) by seasonal occurrence: winter (33.3%), spring (26.1%), summer (20.6%) and fall (18.2%). Pain with eye movements was reported in 99 (79.2%) patients, present in 60.6% of AtON and in all patients with typical ON ($p< 0.05$). 60 (48%) patients had optic disc edema at presentation, among the anterior ON, 34 (56.6%) were AtON ($p= 0.43$). 88 (70.4%) patients had a VA < 20/200 at the first consult in the affected eye, in the case of the 10 (8%) patients that presented simultaneous bilateral AtON the eye with the worst VA was considered.

Conclusions:
A study could highlight these epidemiological variations and improve disease recognition and management in this population.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Slow Rise in Platelet Count as a Predictor of GCA in Patients With and Without PMR

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Introduction:
Thrombocytosis is often seen or described as an acute phase reaction in GCA, while in reality it is usually a gradual increase over 6 months to a year culminating often in profound visual loss in one or both eyes. Mild anemia also develops over the same time period. This slow criss cross in the lab values is a useful tool especially in patients with or without PMR who present with minimally elevated sedimentation rates or c reactive protein levels

Methods:
Retrospective chart review was performed at one institution. Statistical analysis was performed to compare patients with Giant Cell Arteritis with vision loss and PMR to patients without PMR regarding change in their hemoglobin, hematocrit and platelet counts over a 1 year period. These groups were compared to patients who suffered from NAION.

Results:
Slow escalation of platelet counts and drop in H/H was found to be a diagnostic predictor of patients who developed GCA with acute visual loss but not in patients who were diagnosed with PMR alone. No escalation in platelet count was noted in patients who presented with NAION.

Conclusions:
In patients with or without PMR, a gradual escalation of platelet count should be a red flag in patients who may go on to GCA with devastating visual loss. The rise is often not acute as previously believed but actually gradual over 6 months to a year. The slow downward trend in H/H Is also an important finding. This awareness is especially important in patients who already carry the diagnosis of PMR who have not yet developed symptoms of visual loss whether amaurotic in nature or in the form of vasculitic optic neuropathy. Any older patient who presents with headache, visual loss or diplopia should have their CBC's over the past year reviewed.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Can Mesopic Virtual Reality Detect Changes Prior to Traditional SITA Humphrey Visual Fields in Neuro-Ophthalmology Patients?

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Introduction:
Traditional Humphrey visual fields can be uncomfortable. They are difficult to obtain in hospital patients. We analyzed seven patients and seven controls longitudinally to determine if virtual reality visual fields (VR) using a unique mesopic paradigm were comparable or additive to longitudinally performed Humphrey visual fields (HVF). HVFs use the Swedish Interactive Threshold Algorithm (SITA), a photopic (cone-dominated) background. The commercially available "VF3" VR device uses Block's Optimal Luminance Thresholding (BOLT), a mesopic background (stimulating rods and cones).

Methods:
We evaluated seven controls (14 eyes) and seven patients (13 eyes) longitudinally with both HVF and VR on the same day. All tested an average of eight weeks (between 1-20 weeks) after their initial test to evaluate the reproducibility of the VF3 to HVF. Reliability indices, mean deviation (MD), and correlation of total deviation p-values of 0.05 (indicating a visual field defect in a given location) were recorded. A questionnaire determining overall preference, enjoyability, comfort, understanding, and focus was administered.

Results:
All 14 normal eyes changed similarly for total deviation p-value abnormalities on VR and HVF between visits. Eight of 13 patient eyes changed similarly between VR and HVF tests based on total deviation p-values. Of the 5 eyes that didn't change similarly, VR showed earlier change than HVF did. The HVF did eventually demonstrate the similar pattern of change at a follow-up visit. Changes in MD were similar in 10 of 13 patient eyes. HVF was preferred in 4/7 normals. VR was preferred in 6/7 patients.

Conclusions:
Based on these pilot data, the VF3 device has the potential to detect visual deficits earlier than HVFs, perhaps based on use of a mesopic background. Further prospective studies are needed to determine the ultimate longitudinal testing value of VR.

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Keywords: Visual fields, Pseudotumor cerebri, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Novel Computer Vision Progression Analysis for Humphrey Visual Field Testing and Machine-Learning Applications

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Introduction:
Glaucoma management requires rigorous tracking of visual field progression, with guided progression analysis (GPA) being the standard approach for visual assessment; however, some studies have brought into question the consistency of GPA in classifying clear progression. In 2022, the University of Washington released an open-source Humphrey visual field dataset (UWHVF), which contains 28,943 visual fields from 7,248 eyes of 3,871 patients. This study leverages this dataset to develop a novel computer vision-based progression analysis using machine learning (ML) to enhance detection and classification of visual field changes and progression.

Methods:
Linear regression analysis of mean total deviation (MTD) values in the UWHVF dataset was performed to categorize progression into four classes: no progression (progression > 0 dB/year), slow (-0.5 < progression < 0), moderate (-1 < progression < -0.5), and fast progression (progression < -1). Visual field progression was evaluated using topographic analysis, quantifying the prevalence of peaks and valleys, respectively, in visual field data as well as the sizes of peaks and valleys. ML classification models were developed to classify progression using the topographic metrics, including a Decision Tree (DT) classifier, Random Forest (RF) classifier, and Multi-layer Perceptron (MLP) classifier. A convolutional neural network (CNN) deep learning (DL) model was developed to classify visual field progression using raw visual field data, as well.

Results:
The DT classifier achieved an accuracy of 0.796 (sensitivity 0.777, specificity 0.812) in classifying visual field progression using the extracted topographic metrics, RF classifier had an accuracy of 0.844 (sensitivity 0.815, sensitivity 0.871), and MLP classifier had 0.849 accuracy (sensitivity 0.808, specificity 0.892). CNN DL model achieved 0.970 accuracy (sensitivity 1.00, specificity 0.947).

Conclusions:
This study presents a robust and novel approach to visual field progression analysis using computer vision and ML using an open-source visual field dataset, with promising results for managing glaucoma and neuro-ophthalmic diseases.

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Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Evaluation of EyeMirage for Visual Acuity, Color Vision, and Visual Field Testing

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Introduction:
Eye and brain impairments affect millions worldwide, significantly contributing to disability and reduced quality of life. Despite their high prevalence, access to timely and accurate eye care remains a challenge due to a shortage of specialists and their uneven geographical distribution. EyeMirage, a virtual eye examination technology powered by artificial intelligence (AI), has the potential to transform eye care by providing innovative solutions for remote and efficient assessments. This study aims to validate the effectiveness of EyeMirage in evaluating visual acuity, color vision, and visual fields compared to standard clinical tests.

Methods:
Twenty-four participants underwent visual acuity, color vision, and visual field assessments using EyeMirage. The results were statistically analyzed to compare with those obtained from conventional clinical testing methods, evaluating the device's accuracy and reliability.

Results:
The t-test analysis showed that the SPS counts from EyeMirage's AI system were statistically equivalent to those from expert clinicians. The AI system demonstrated greater reliability in counting eye movements when the saccade interval was under 500 ms.

Conclusions:
EyeMirage offers reliable SPS counts comparable to expert evaluations, with particular accuracy for faster saccade intervals. By providing an accessible, cost-effective tool for concussion assessments, EyeMirage has the potential to reduce healthcare costs, decrease patient wait times in emergency departments and clinics, and alleviate the burden on healthcare systems struggling with specialist shortages.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Visual fields, Perimetry, Miscellaneous, Stroke

Financial Disclosures: Behzad Mansouri: The author is the president of Neuroptek Corporation Inc. which has made EyeMirage device.; Neda Anssari: She is the shareholder of Neuroptek Corporation Inc. that builds the EyeMirage device.

Grant Support: NRC-IRAP No. 989496 IGP-Economic Development, Investment and Trade

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Where's the Vision? Introducing MULES and SUN to Concussion Testing in a Youth Ice Hockey Cohort

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Introduction:
Vision comprises 50% of brain pathways; these are frequently involved in concussion. Yet, vision assessment is limited in current concussion testing. The MULES (Mobile Universal Lexicon Evaluation System, picture naming) and SUN (Staggered Uneven Number) tests are quick, simple and accessible vision-based rapid automatized naming tasks. These tests were developed for concussion yet also identify patients with mild cognitive impairment, multiple sclerosis, and Parkinson's disease. MULES and SUN have not been introduced for baseline and sideline testing in sports. We administered MULES and SUN to youth ice hockey athletes and examined the relation of time scores to age, ranging from 5-17 years.

Methods:
Laminated 8.5x11-inch test card versions of MULES and SUN were administered in a youth hockey league during pre-season. Two trials of each test were completed; the best (fastest) of the test times was recorded as baseline.

Results:
Among 103 youth athletes (median age 12 years [range=5-17]), average best times were 51 seconds (range=28-163) for MULES and 68 seconds (range=36-330) for SUN. Learning effects, common for timed measures, were noted between trials 1 and 2 for MULES (median improvement 8.1 seconds [range=-31-58], $p< 0.001$, Wilcoxon signed-rank test). Learning effects for SUN, however, were, on average, absent (median improvement=0 [range=-94-58], $p=0.39$). While both MULES and SUN showed progressively faster times with increasing age (R-squared=0.59, $p< 0.001$ for MULES; R-squared=0.81, $p< 0.001$ for SUN, nonparametric regression models), associations of younger age with slower test times were substantially greater for MULES (model effect=-5.4) vs. SUN (model effect=0).

Conclusions:
MULES and SUN are practical vision tests to add to current concussion testing. Pre-season baseline scores should be obtained given substantial associations of young age with slower test times. Differences in age related times on MULES vs. SUN provide evidence that picture and number naming capture separate aspects of complexity and function of brain pathways.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Trauma, Higher visual functions, Ocular motility, Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Right Or Left? A Deep Learning Approach To The Electrophysiology Of Saccadic Preparation.

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Introduction:
How early can we detect an impending saccade in humans? We developed a deep learning approach to identify preparatory signals for prosaccades and antisaccades on event-related EEG recordings.

Methods:
Twenty healthy participants performed separate blocks of 500 prosaccades and 550 antisaccades to the left or right while EEG was recorded. Fixation and stimulus onset were automatically marked using a BioSemi Trigger Interface. There were two analyses: one time-locked to stimulus onset, and one time-locked to saccade onset. We asked, first, during which bins the classifier could predict the direction of the upcoming saccade. Second, we compared across blocks to see when it could predict that the response would be a prosaccade or an antisaccade.

Results:
We analyzed a total of 8387 prosaccades and 8723 antisaccades. The mean time from stimulus to saccade onset was 172ms for prosaccades and 229ms for antisaccades. For data time-locked to stimulus onset, discrimination between directions started at 90ms for prosaccades and 95ms for antisaccades, and the AUC increased to 0.86 for prosaccades at 100ms. When time-locked to saccade onset, discrimination started at 65ms before prosaccades and 120ms before antisaccades. The AUC was better when the neural network was trained with prosaccades pooled from all subjects rather than a single person, but the reverse was true for antisaccades, suggesting more between-subject variability in the latter. The classification of prosaccades vs. antisaccades was evident during the entire trial. This indicates a constant 'antisaccade mindset' that distinguished the blocks.

Conclusions:
Our classifier detected a stimulus-linked signal just before 100ms after stimulus onset, and a direction-specific preparatory signal 65ms before a prosaccade and 120ms before an antisaccade. A constant pro- vs. antisaccade difference was evident in this block design, suggesting persistent inhibitory control rather than recruitment just prior to the saccade.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Higher visual functions, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: The Neurological Foundation of New Zealand

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Comparison of Olleyes Virtual Reality VF Testing and Humphrey VF Testing in Detecting Visual Field Defects in Neurosurgical Patients

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Introduction:
Visual field testing plays an integral role in determining timing of neurosurgical intervention. Frequently patients present to the hospital after hours when office based visual field testing is not available. We aimed to determine if head mounted virtual reality visual field testing was comparable to Humphrey visual field testing in detecting visual field defects among neurosurgical patients.

Methods:
Patients referred to the neuro-ophthalmology clinic with neurosurgical diagnoses were randomized to complete either the standard Humphrey visual field (HVF) or the Olleyes (OE) visual field first, followed by the other test. Reliability indices, completion time, mean deviation (MD), pattern standard deviation (PSD) and foveal thresholds results of the two tests were compared using Wilcoxon rank sum tests. The sensitivity and specificity of the Olleyes device for detecting an abnormal HVF test were calculated. Results from both tests were assessed for clinical significance and compared.

Results:
49 tests from 47 patients were analyzed. 25 patients were male, average age was 54. 24/49 tests had the HVF administered first. The most common diagnoses were pituitary adenoma (49%), followed by meningioma (23%), and craniopharyngioma (11%). There was no significant difference for MD, PSD and fixation losses between HVF and OE. There were higher false positives, lower false negatives, higher foveal thresholds, and longer test duration in HVF compared to OE. 34/49 tests were abnormal on HVF. An abnormal OE test was 76% sensitive and 60% specific in detecting an abnormal HVF.

Conclusions:
OE is a reasonable screening tool for identifying visual field defects in neurosurgical patients, especially when HVF is not available. Clinical context is important for interpreting results. When clinical suspicion is high, HVF should be done if OE results are not as expected.

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Keywords: Visual fields, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Perimetry, Tumors, Skull base

Financial Disclosures: The authors had no disclosures.

Grant Support: Unrestricted departmental grant from Research to Prevent Blindness VisuALL - S device donated by Olleyes

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A novel machine learning-aided risk stratification tool for NAION in patients with OSA

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Introduction:
Non-arteritic anterior ischemic optic neuropathy (NAION) is a leading cause of sudden vision loss above the age of 50. While numerous risk factors are associated with NAION, there is no way to reliably predict who is at risk for NAION. Obstructive sleep apnea (OSA) is one of the most well-documented risk factors for NAION. Pooled analysis has reported OSA to have an odd's ratio of 6.2 for NAION. Thus, it seems reasonable that there may be a subset of OSA patients who are at high risk for NAION. This study aims to develop a risk-scoring calculator for NAION in patients with OSA.

Methods:
This was a retrospective cohort study of patients evaluated by neuro-ophthalmologists at the Massachusetts Eye & Ear Infirmary and Massachusetts General Hospital from December 1, 2017 through October 10, 2024, found by using internal diagnostic codes related to OSA and NAION. We employed an ensemble prediction model that leveraged gradient boosting and random forest to develop a risk-scoring tool.

Results:
142689 cases of OSA were found, of which 232 were diagnosed with NAION. The overall age and sex adjusted incidence was 16.3 per 10000 individuals diagnosed with OSA (95% confidence interval [CI]: 12.8-20.3). The risk factors with the highest association with NAION were CVA (RR 2.0, 1.2-2.7), diabetes (RR 1.5, 1.2-1.8), atrial fibrillation (RR 1.4, 1.1-1.6), and hypertension (RR 1.3, 1.1-1.5). Protective factors for NAION included aspirin use (RR 0.8, 0.5-1.1). In patients with OSA, this (preliminary) algorithm was able to predict the occurrence of NAION with a positive predictive value of 29% and a negative predictive value of 81%.

Conclusions:
This study proposes a risk-scoring tool to predict which patients that are diagnosed with OSA are high risk for developing NAION. Identifying patients who are high risk will facilitate future investigations into developing primary prevention strategies for NAION.

References: None provided.

Keywords: Optic neuropathy, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Area-Modulation Strategy Improves Signal/Noise Ratio and Expands Dynamic Range In a Smartphone Perimeter

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Introduction:
Because standard automated perimeters are expensive, non-portable, and ergonomically challenging, head-mounted (HMD) systems could increase access to perimetry. Smartphone display hardware imposes limits on the dynamic range of standard luminance-modulation perimetry. Area-modulation uses a fixed stimulus luminance and instead modulates the area of the stimulus, and has been shown to improve the signal-to-noise ratio for detecting reduced retinal sensitivity. Because smartphone displays have high spatial resolution, we hypothesized that area-modulation could be a better fit for the hardware, while capitalizing on the inherent advantages.

Methods:
59 healthy observers and 7 glaucoma patients underwent perimetric testing using a modified 24-2 grid with additional central locations. Each subject was tested twice with the HMD using an area-modulation strategy (AMS), and twice using a luminance-modulation strategy (LMS), as well as on bowl perimeter using LMS. [Stimuli were white-on-white, Goldmann-V for LMS, 5cdm-2 AMS, Background 10cdm-2] Mean and pointwise variability was calculated. Sensitivity decreases with eccentricity, so the difference between the sensitivity of peripheral and central locations in each eye (signal) was pooled for each test and divided by the pointwise variability of the test (noise) to calculate a signal/noise ratio. A normative dataset was generated for each strategy.

Results:
Mean differences between central and peripheral locations in normal subjects were greater with area-modulation (4.06±2.14dB HMD-AMS vs 0.96±0.99dB HMD-LMS, 1.38±1.13dB SAP [$p < 0.0001$ 1-way ANOVA]). Pointwise retest variability was also higher for AMS, but to a lesser extent (repeatability coefficient: 5.37dB HMD-Area, 3.19dB HMD-luminance, 3.2dB SAP). Signal/Noise ratio was still highest for area-modulation (0.79 HMD-Area vs 0.31 HMD-luminance, 0.45 SAP). Bland-Altman comparison in glaucoma patients illustrates that the dynamic range on the HMD was improved using AMS.

Conclusions:
The relative increase in signal magnitude with area modulation was greater than the relative increase in pointwise variability, suggesting that an area-modulation strategy may improve detection of disease.

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Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Perimetry, Visual fields, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: VA Merit Review Grant (I01 RX-001821-01A1), and by an unrestricted grant to the University of Iowa Department of Ophthalmology from Research to Prevent Blindness, New York, N.Y., USA.

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A New and Improved Double Maddox Rod: Design Concept and Clinical Implications

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Introduction:
In this study, we sought to design a novel pair of Double Maddox Rod (DMR) glasses with permanent, integrated lenses with cyclotorsional precision of one degree and to test the new glasses compared to gold standard DMR testing using trial frames and loose filter lenses to validate our design.

Methods:
We collaborated with senior mechanical engineering students to create adult frames with integrated lenses for DMR testing. After multiple interviews with pediatric and adult strabismus surgeons, a neuro-ophthalmologist, and an orthoptist, the frames were designed using computer-aided design. The frames were 3-D printed out of polyethylene terephthalate glycol filament and the lenses were secured into place onto a bevel-gear with laser etched 1-mm markings with a level attached at the nasal bridge. In the trial phase of the study, the novel 3-D printed glasses were compared to standard DMR testing using trial frames by measuring torsion in patients presenting to neuro-ophthalmology clinic with vertical strabismus. The measurements with the novel glasses were checked twice in each participant to evaluate test-retest reliability.

Results:
Five adult frames were designed and constructed with unique features including integrated red and white filter lenses, a level on the nose bridge, and laser-etched markings to measure torsion in one-degree increments. The trial phase remains ongoing but measurements in over ten patients thus far show consistency between the two methods of DMR testing and adequate test-retest reliability.

Conclusions:
These novel, integrated DMR glasses are lighter than trial frames and should facilitate ease of taking measurements and improve accuracy compared to current techniques. The trial phase will be conducted and completed over the following two months with a goal of testing at least 50 patients with both our novel glasses and trial frame method for DMR testing in order to validate our design.

References: None provided.

Keywords: Ocular motility, Adult strabismus with a focus on diplopia, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Distinguishing Papilledema from Pseudopapilledema with the Aid of Deep Learning Variational Autoencoders Trained on the Idiopathic Intracranial Hypertension Treatment Trial

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Introduction:
We sought to determine whether the spatial patterns encoded by a bi-channel deep-learning variational autoencoder (biVAE) model of retinal nerve fiber layer thickness and total retinal thickness from OCT in papilledema and normal subjects can improve OCT-based classification of papilledema vs pseudopapilledema.

Methods:
A biVAE model was previously trained using 1498 optical coherence tomography (OCT) scans of 125 subjects over time from the Idiopathic Intracranial Hypertension Treatment Trial (IIHTT). An independent test data set of 371 eyes from 193 papilledema subjects and 21 eyes from pseudopapilledema subjects from our institution was collected, and the two latent variables (i.e., d1 and d2; low-dimensional representation) that the biVAE used to reconstruct the retinal nerve fiber layer (RNFL) thickness maps were collected from the model. We generated three binary logistic regression models to distinguish papilledema from pseudopapilledema based on the following parameters: 1) peripapillary RNFL thickness (pRNFLT), 2) latent variables d1 and d2 from the biVAE model and 3) latent variables from the biVAE plus optic nerve head volume (ONHV). Models were trained with a 2:1 papilledema:pseudopapilledema ratio of training images using leave-one-subject-out cross-validation. Area under the receiver operating characteristic (ROC) curves for classification from each group were compared.

Results:
ROC curves for each of the three classification models and their area under curves (AUCs) were generated. Model 1 incorporated only the pRNFLT and produced an AUC of 0.45. Model 2 incorporated only spatial information contained within latent variables d1 and d2 and produced an AUC of 0.71. Model 3 included spatial information contained within the latent variables and the ONHV and produced the highest AUC of 0.75.

Conclusions:
Spatial information encoded by the biVAE latent variables are able to perform modest discrimination of papilledema from pseudopapilledema, indicating that RNFL patterns represented by the model preserve their clinical meaning.

References: None provided.

Keywords: High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Self-Paced Saccade Testing Using EyeMirage as a Concussion Biomarker

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Introduction:
Concussions are a common neurological injury, with millions of cases each year worldwide. Diagnosing and managing concussions remains challenging due to limited access to neuro-ophthalmology specialists and their uneven geographic distribution. Ocular examination and particularly the Self-paced saccade (SPS) testing are promising biomarkers for concussion diagnosis and recovery monitoring. EyeMirage, an AI-powered device by Neuroptek, aims to automate eye movement recording and SPS analysis to enhance diagnostic accuracy and accessibility. This study evaluates EyeMirage's performance in capturing eye movements and counting SPS as a potential concussion biomarker.

Methods:
Twenty-four participants were assessed using EyeMirage to perform SPS tests. The device reliably captured eye movements and counted SPS using its AI system. A t-test was used to compare the AI system's SPS counts with those from two expert clinicians, validated against ground truth data.

Results:
The t-test analysis showed that the SPS counts from EyeMirage's AI system were statistically equivalent to those from expert clinicians. The AI system demonstrated greater reliability in counting eye movements when the saccade interval was under 500 ms.

Conclusions:
EyeMirage offers reliable SPS counts comparable to expert evaluations, with particular accuracy for faster saccade intervals. By providing an accessible, cost-effective tool for concussion assessments, EyeMirage has the potential to reduce healthcare costs, decrease patient wait times in emergency departments and clinics, and alleviate the burden on healthcare systems struggling with specialist shortages.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Higher visual functions, Ocular motility, Ocular manifestations of vestibular disorders, Stroke

Financial Disclosures: Neda Anssari: She is the shareholder of Neuroptek Corporation Inc. that builds the EyeMirage device.; Behzad Mansouri: The author is the president of Neuroptek Corporation Inc. which has made EyeMirage device.

Grant Support: IRAP-Proof of concept for remote and portable screening of concussion IGP-Economic Development, Investment and Trade

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Differences in OCT findings of the NFL and GCL between patients with optic neuropathy due to chiasmatic compression and patients with a diagnosis of glaucoma.

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Introduction:
Differentiation of compressive optic neuropathies and glaucoma in early stages has proven to be a challenge in many patients due to similar characteristics in visual field defects and OCT characteristics. Further analysis of nerve fiber layer (NFL) and ganglion cell layer (GCL) OCT may prove to be a useful tool to aid early diagnosis, prevent wrongly administered treatments and further optic nerve damage.

Methods:
This was a retrospective, cross section study, with the review of 102 OCT studies of the optic nerve. The sample was divided into two groups: A compressive optic neuropathy group and a glaucoma group. The obtained numerical data was analyzed with the use of the SPSS software.

Results:
The obtained variables “average GCL”, “superior GCL”, “inferior GCL, “superonasal GCL”, “NFL/CGL Ratio”, “NFL/inferior CGL Ratio” and “nasal GCL” showed a statistically significant difference between both groups, being useful to discriminate between pathologies through a quantitative study of the OCT.

Conclusions:
We did not find a direct or reliable association to differentiate these two groups with the average/vertical cup-to-disc ratio. However, new and easily applicable variables are offered, which could have clinical relevance when applied as a new useful and non-invasive tool for early differentiation between these two etiological groups.

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Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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"Features & surgical mangement of acquired esotropia associated with high myopia"

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[1] University of Colorado, [2] Moorfields Eye Hospital, [3] National Hospital for Neurology & Neurosurgery

Introduction:
The increase in myopia prevalence has led to a concurrent rise in the incidence of acquired esotropia in myopia or 'heavy-eye-syndrome(HES)' presenting to neuro-ophthalmologists. There are no accepted diagnositic criteria nor concordance reagarding best surgical management in HES. MRI metrics (particularly the angle between the lateral and medial rectii(LR:SR)) have been proposed to aid diagnosis and muscle union procedures (e.g.Yokoyama) as effective treatment. The purpose of this study is to present, for the first time, the largest cohort of patients with HES yet described in the literature in order to answer the important question: what diagnostic features are important in this increasingly common condition and how best to treat it?

Methods:
A retrospective case note review of adults seen in the Moorfields hospital system between 2018 and 2023. N=69 cases were identified as: age >18, spherical equivalent(SE) >6.00DS, a esotropia diagnosis and availability of MRI orbit images. Demographics, orthoptic measurements at presentaion, refraction, examination - particularly myopic features & LR:SR angle were recorded along with surgical technique and three-month post-operative outcomes.

Results:
At presentation, the median age was 50.8(IQR36.6to63.7) years, median SE-9.00DS(IQR-6.75--13.00DS). Deviation at near 18PD(IQR6–40) and distance 20PD(IQR15–40) was significantly different (ANVOA,P< 0.01) without significant correlation between SE and esodeviation (beta=-1.10,P=0.07). Right eye LR:SR =111.0±10.6o; Left eye LR:SR =110.1±37.7o. 43%(n=29) underwent surgery: n=21 adjustable-horizontal, n=6 fixed-horizontal, n=2 Yokoyama. Mean postoperative esodeviation was 6PD(IQR1-12), N=5 required a second procedure.

Conclusions:
This is now the largest clinically and radiographically characterised cohort of HES patients in the literature, many with surgical outcomes data. It concludes that measured myopia and size of deviation may not directly corrolate, that SR:LR angles may be less obtuse than in previosuly reported and that unilateral recess-resect procedures may provide good outcomes. This will have great impact in informing the evidence-based diagnosis and treatment of this rapidly increasing clinical problem.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Comparing and explaining deep-learning torsional nystagmus detection.

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Introduction:
Nystagmus is spontaneous repetitive ocular oscillations due to injury to vestibular and ocular motor neural circuitry. Of particular interest is torsional nystagmus – the result of damage to central and peripheral vertical-torsional eye muscle circuitry. The presence, degree or direction of torsional nystagmus can provide clues on central versus peripheral lesional localization, especially in the emergency setting. Timely diagnosis enables efficient interventions in the setting of central (stroke) causes of torsional nystagmus. Expert eye movement and vestibular specialists are scarce, and non-experts, like emergency room providers, may struggle with subtle eye movements. Current torsional detection relies on unreliable iris tracking due to eye closures and mobile device video quality.

Methods:
To address this challenge, we utilized a small dataset of simulated torsional infrared video-oculography (VOG) to develop video-based deep learning models for remote torsional sensing without the need for traditional pupil or iris tracking. This dataset comprised torsion labels for clips of 500ms, 750ms, and 1s, with degrees of torsion ranging from 0.5-10.0 degrees. These models were trained using the ResNet architecture and incorporated 2D, 2.5D, and 3D convolutional layers. These models were compared to a small cohort of clinicians who classified 100 videos of the test set. We also applied explainable AI methods, including gradient-weighted class activation mapping (Grad-CAM), to enhance model interpretability.

Results:
Our models achieve 93.05% accuracy, using ocular features and neurophysiology-supported phenomena as evidenced by the Grad-CAM. Furthermore, when compared to the clinician, the model boasted a 90% overall accuracy compared to a 75% from the clinician.

Conclusions:
Our study illustrates that machine learning techniques can precisely identify small amplitude torsional nystagmus, offering a promising avenue for the early detection of pathological vestibular disorders that outperforms expert neuro-otologist.

References: None provided.

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

Financial Disclosures: Krishna Mukunda: Summer Student Fellowship 2024, Institute for Data Intensive Engineering; Tianyi Ye; Yi Luo; Asimina Zoitou; Kyungmin (Esther) Kwon; Richa Singh; JiWon Woo; Nikita Sivakumar; Joseph L. Greenstein; Casey Overby Taylor; Amir Kheradmand; Kemar Green

Grant Support: None.

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Neuro-Ophthalmology Mobile App to Improve Diagnosis of Afferent/Efferent Disorders

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Introduction:
Numerous video resources exist to facilitate learning and teaching of afferent/efferent disorders. Although mostly free and readily accessible, their usage in the novice learner may be limiting for several reasons; extensive search results can be daunting to choose from, multiple steps/clicks required to access resource, variable videographic quality, drawn-out timeframe from video initiation to sign appreciation, difficulty identifying salient findings and incorrect interpretation of eye movement signs (more so with non-expert YouTube videos). These can all compound and hamper the time-sensitive learning experience.

Methods:
Several prominent Neuro-ophthalmology textbooks and video libraries were reviewed, yielding a list of 59 afferent/efferent disorders. Of these, 50 were ultimately chosen (vestibulopathies excluded due to complexities with accelerometer calibration). From these, 75 animations were developed to account for ipsilateral/contralateral lesions. Adobe Animate (vector-based animation software) was used to create ethnic/gender neutral eyes animated alongside 'ground-truth' resources to depict salient changes (e.g. nystagmus waveforms) precisely. Two versions of each animation were made, a shortened animation for the time-sensitive quiz, and a longer version for teaching/demonstration purposes. 200 single-best-answer questions were created to promote deep learning and high-yield facts. Comprehensive 'library' descriptions of each pathology were developed to promote ad-hoc learning. Figma (vector-based graphics tool) was then used to build a testable iPhone/Android mobile app.

Results:
14 beta-testers with differing levels of expertise (students, residents, fellows and neuro-ophthalmologists) rigorously evaluated the app. Likert ratings significantly reflected the ease of navigation, comprehensiveness of pathologies, accurate animated depictions, engaging quiz interface and helpful explanations ($p < 0.05$). Anecdotally it was also a fun resource to use.

Conclusions:
Neuro-ophthalmologic disorders are numerous and can be daunting to the uninitiated. The development of an animation-based mobile app created to promote pattern recognition and knowledge of afferent/efferent disorders has been met with enthusiastic response, further fostering interest and understanding of this unique subspecialty.

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Keywords: Ocular motility, Nystagmus, Pupil, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Ophthalmologic Cranial Nerve Palsies and COVID-19 Infection: A Retrospective Analysis

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Introduction:
COVID-19 has been shown to cause neurological manifestations in 45.5% of patients, but its role in cranial nerve (CN) palsies is underreported. An observed increase in cranial nerve palsies in neuro-ophthalmology patients suggests a possible association between CN palsies (primarily CN3, 4, and 6) and COVID-19. This study aims to investigate the relationship between confirmed COVID-19 infection and new-onset cranial nerve palsy, including the impact of risk factors such as hypertension, diabetes, and vaccination status.

Methods:
This retrospective cohort study included 22 patients diagnosed with cranial nerve palsy following confirmed COVID-19 infection. Patient demographics, co-morbidities, vaccination status, and timing of COVID-19 diagnosis relative to cranial nerve palsy onset were collected from an IRB-approved University of Missouri database. A linear regression analysis was performed to assess the relationship between time to onset and age, hypertension, diabetes, and vaccination status.

Results:
The average time between COVID-19 infection and CN palsy onset was 387 days (range: 28 to 982 days). Linear regression showed age increased the time to onset ($\beta = 23.51$), while hypertension ($\beta = -13.06$) and vaccination ($\beta = -13.06$) shortened it. Diabetes significantly delayed onset ($\beta = 83.64$). Hypertension was present in 50% of patients, and 22.7% had diabetes. Only 18.2% had received the COVID-19 vaccine.

Conclusions:
COVID-19 may be linked to delayed cranial nerve palsies, with time to onset influenced by age, hypertension, diabetes, and vaccination. Patients with diabetes had a longer onset delay, while vaccination and hypertension shortened it. Larger studies are needed to validate these findings and compare the incidence of idiopathic CN palsies in the general population versus post-COVID.

References: None provided.

Keywords: Pupil, Ocular motility, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Risk of Oculomotor and Trochlear Nerve Palsies Following Covid-19 Vaccination

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Introduction:
To investigate the prevalence and risk of new-onset oculomotor and trochlear nerve palsies following COVID-19 vaccination compared to COVID-19 infection, influenza vaccination, and TDAP vaccination.

Methods:
This retrospective, population-based study analyzed patient data from the COVID-19 Research Network of TriNetX using the TriNetX Analytics platform. Patients who received COVID-19, influenza, or TDAP vaccinations were identified through Common Procedural Technology codes. Newly diagnosed oculomotor and trochlear nerve palsies within 21 days of vaccination were recorded.

Results:
Of the 6,195,183 patients (mean age 46.8 ± 21.2 years) who received the mRNA COVID-19 vaccine, < 10 patients developed oculomotor nerve palsy and 13 developed trochlear nerve palsy within 21 days of the first dose. Propensity score matching was performed to balance the cohorts. The relative risk for new oculomotor nerve palsy following first dose of COVID-19 vaccination was compared to that after influenza vaccination (RR, 1, [0.416,2.402]), Tdap vaccination (RR, 1 [0.416,2.402]), second COVID-19 dose (RR, 1 [0.416-2.403]) and COVID-19 infection (RR, 0.192 [0.098,0.378]). For trochlear nerve palsy, the relative risk following first dose of COVID-19 vaccination was compared to that after influenza (RR, 0.833 [0.36,1.929]0.36,1.929)), Tdap (RR, 1 [0.416,2.402]), the second COVID-19 dose (RR, 1 [0.416,2.403]) and COVID-19 infection (RR, 0.5 [0.234,1.068]).

Conclusions:
The risk of new oculomotor and trochlear nerve palsies after COVID-19 vaccination is similar to other vaccines. The risk of new oculomotor nerve palsy after COVID-19 vaccination is lower than after COVID-19 infection. There is a similar risk of new trochlear nerve plasy after COVID-19 vaccination compared to COVID-19 infection. There is no evidence to suggest a causal relationship between COVID-19 vaccination and the development of oculomotor or trochlear nerve palsies.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Fixational Microsaccades In Patients With Parkinson's Disease

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Introduction:
Fixational microsaccades (FM) encompass the involuntary, small-scale movements of the eye that occur as we attempt to fixate on a single point. These movements are crucial for maintaining a steady visual perception despite the constant, subtle changes in our gaze. FM are significant because they can serve as an indicator of central nervous system disorders; for example, altered FM correlated with multiple sclerosis disability level and disease worsening. This study aims to determine FM in patients with Parkinson's disease (PD) compared to age-matched healthy controls.

Methods:
A total of 14 older adults (age 71.0 ± 7.2 years, 6 females) with PD and 17 controls (age 73.4 ± 4.4 years, 15 females) were recruited. Retinal motion traces were recorded using a tracking scanning laser ophthalmoscopy (RetiTrack, C.Light Technologies, Medford, MA). The number of FM, saccade amplitude, velocity, peak velocity, and frequency were measured.

Results:
All FM measurements were significantly different between PD patients and controls (P values < 0.05): the number of saccades (18.01 ± 10.97 vs. 12.02 ± 15.08, P = 0.004), average amplitude (0.42 ± 0.16 vs. 0.36 ± 0.15, P = 0.023), average velocity (7.26 ± 1.51 degrees vs. 6.69 ± 1.44, P = 0.019), average peak velocity (10.10 ± 3.13 degrees vs. 8.98 ± 3.00, P = 0.028), and saccade frequency (1.80 ± 1.10 vs. 1.25 ± 1.54 Hz, P = 0.009). These results indicated that PD patients had larger, more frequent and quicker microsaccades.

Conclusions:
This is the first study to explore and characterize FM using the RetiTrack in patients with PD. The results suggest an impairment in fixational microsaccades in PD patients, specifically highlighting a fixational instability.

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Keywords: Ocular motility

Financial Disclosures: Daniela Teijelo; Kirill Stremousov; Yunhai Dai; Byron Lam: Research Support: National Eye Institute, United States Department of Defense, Foundation Fighting Blindness, Atsena Therapeutics, Beacon Therapeutics, Endogena Therapeutics, Nanoscope Therapeutics, Ocugen Inc., PYC Therapeutics, Sparingvision, Spark Therapeutics, Splicebio, Stoke Therapeutics; Consulting: BlueRock Therapeutics, Johnson & Johnson, Splicebio, Spulbio; Christy Sheehy: This study was supported by NIH Center Grant P30 EY014801, UM Team Science Award, McKnight Brain Institute Pilot Award, and a grant from Research to Prevent Blindness (RPB). co-founder of C. Light Technologies & inventor of Retitrack.; Joseph Signorile; Jianhua Wang: This study was supported by NIH Center Grant P30 EY014801; NINDS 1R01NS111115.; Hong Jiang: This study was supported by UM Aging Team Science Award, the Ed and Ethel Moor Alzheimer's Disease Research Program, Florida Health, 20A05.

Grant Support: This study was supported by NIH Center Grant P30 EY014801, UM Team Science Award, McKnight Brain Institute Pilot Award, and a grant from Research to Prevent Blindness (RPB).
Contact Information: None provided.

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The 180-Degree Swivel Chair Test: A Novel Clinical Exam Maneuver to Evaluate Cerebellar Nodulus Function

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Introduction:
Case Description: A 27 year-old woman reported turning-induced vertigo and oscillopsia after Chiari decompression. When asked to reproduce symptoms, actively turning 180° rightward triggered vertigo and left-beating nystagmus lasting >30 seconds. Turning left produced comparable vertigo and right-beating nystagmus. On our examination, passive 180° rotations in a swivel chair at ~50°/s elicited similar responses. Head-impulse-testing was normal and did not trigger symptoms. Examination demonstrated saccadic pursuits and gaze-evoked & rebound nystagmus. Review of presurgical MRI revealed compression of both cerebellar tonsils and uvula/nodulus. Neuroscientific Correlate: Nodular Purkinje neurons provide GABA-mediated inhibitory signals to vestibular nuclei which augment the velocity storage mechanisms (VSMs). The VSMs improve responses to prolonged low-frequency movements by perseverating peripheral vestibular signals after semicircular afferent signals decay. VSM disinhibition can cause central patterns of head-shaking nystagmus and periodic alternating nystagmus (PAN). We propose turn-induced-nystagmus may reflect perseverated vestibular signals from disinhibited VSMs, a possible manifestation of nodulus impairment on a spectrum with PAN.

Methods:
This is an ongoing prospective study. Thus far ten patients with cerebellar ataxia and two with dizziness but no cerebellar ataxia were tested. Subjects were seated on a swivel chair with room light, rotated en bloc 180°/s for 1 second, stopped, and the presence and duration of nystagmus was recorded.

Results:
Nine patients with cerebellar ataxia exhibited prolonged (5-10 seconds) nystagmus after the 180° turn. Patients without cerebellar ataxia exhibited no nystagmus after the turn. Notably, the one cerebellar ataxia patient without nystagmus had severe vestibular loss.

Conclusions:
Inspired by observations from a patient with cerebellar ataxia and pre-operative nodulus compression, the swivel-chair test may help identify patients with clinically significant nodulus impairment. Patients with cerebellar ataxia should be asked about turn-induced dizziness, and the presence/absence of this sign may help localization and/or guide therapeutics (e.g., trial of GABA-ergic medication such as baclofen).

References: None provided.

Keywords: Ocular manifestations of vestibular disorders, Nystagmus, Vestibular disorders, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Multivariate Prediction Model for Suspected Ocular Myasthenia Gravis: Development and Validation

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Introduction:
Diagnosing ocular myasthenia gravis (OMG) remains challenging despite recent diagnostic advances. We addressed this challenge by developing and validating a multivariate prediction model that estimates the OMG probability given the results of any partial selection of available diagnostic tests.

Methods:
The source data for our model were retrieved from our blinded prospective diagnostic accuracy study at a tertiary care center. Patients with ptosis and/or diplopia whose presentation was suspicious for OMG underwent comprehensive diagnostic testing. An independent neuromuscular specialist made the final diagnosis. This data was used to fit and validate a Bayesian network model against additional retrospective patient data from two tertiary care centers. The primary outcome was to predict the likelihood of a positive OMG diagnosis given the available diagnostic tests. For any set of tests, the model returns an OMG probability together with 95% credible intervals indicating the prediction uncertainty.

Results:
Of 89 patients included in the development of the model, 39 were diagnosed with OMG. The following variables were the most useful predictors in descending order: Edrophonium-test, acetylcholine-receptor antibodies (anti-AChR), single-fiber EMG, repetitive nerve stimulations (RNS) facial/accessory nerve, Besinger-score, ice-test, Simpson-test, dysarthria, dyspnea, dysphagia, diplopia, ptosis, age, and sex. The model was validated by determining the mean error rate and the area under the curve (AUC) by 10-fold cross-validation and prediction on the retrospective validation data consisting of 69 and 24 patients, respectively. Of all variables, edrophonium (sensitivity 94%, specificity 90%) and anti-AChR testing (sensitivity 85%, specificity 96%) showed the highest predictive value during validation with an AUC of 0.912 and 0.872, respectively. Incorporating more predictors reduced the predictive error in both validation datasets.

Conclusions:
Our prediction model serves as a basis to predict the OMG likelihood. It underwent successful internal and external validation and can be used to assist in clinical decision-making.

References: None provided.

Keywords: Myasthenia, Ocular motility, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

Financial Disclosures: Armin Handzic; Marius Furter; Brigitte Messmer; Magdalena Wirth; Yulia Valko; Fabienne Fierz; Edward Margolin; Konrad Weber: Konrad Weber has previously acted as a paid consultant for Alexion Pharmaceuticals but declares no non-financial competing interests. Alexion Pharmaceuticals also provided some study equipment (spirometer).

Grant Support: None.

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Multimodal deep learning-based ocular myasthenia classification from video-oculography

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Introduction:
Myasthenia gravis (MG), an autoimmune disorder affecting neuromuscular junctions, can lead to muscle weakness and double vision. Using deep learning (DL) algorithms to analyze eye movement data offers a promising approach for swift and accurate diagnosis, especially for ocular MG, which can be challenging to diagnose early.

Methods:
Ocular videos were collected from 20 participants, equally split between MG patients and healthy controls, using infrared video-oculography goggles as they tracked a moving stimulus. Sequential eye recordings enabled optokinetic nystagmus analysis and generated corresponding waveform data. The dataset was split 70:30 to train/test a ResNet-3D video classifier and a custom convolutional and recurrent neural network waveform classifier. A multimodal classifier combined both model outputs with a final linear layer. We use different sampling strategies (random, uniform, consecutive) to extract frames from videos, considering the varying phase information in each time segment. External validation data was collected using Microsoft HoloLens, where patients tracked a moving stimulus in virtual reality while eye position was recorded for ~120 seconds.

Results:
For the video classifier, consecutive sampling with both 32 frames and 300 frames delivers consistently high performance, achieving accuracy of 97.35% and 97.36% and sensitivity of 95% and 100% respectively. The waveform classifier performs best when using all frames, achieving the highest accuracy (97.37%) and perfect specificity (100%). Models trained using random and uniform sampling approaches, especially with fewer frames, generally exhibit lower accuracy and sensitivity. Notably, the multi-modal classifier, which combines video and waveform data, performs with a comparable accuracy of 92.10%, sensitivity of 85% and specificity of 100%.

Conclusions:
Although clinical, serological, and electrodiagnostic tests are available for diagnosing myasthenia gravis (MG), their efficacy drops significantly for ocular MG. Given its high sensitivity and specificity, our noninvasive DL approach may become a valuable tool for early and accurate diagnosis of ocular MG.

References: None provided.

Keywords: Myasthenia, Ocular motility

Financial Disclosures: Preetham Bachina; Aimon Rahman; Goknur Kocak; Andrea Corse; Adatepe Nuren; Vishal Patel: Provisional patent for method of generating synthetic eye and head movement data for deep learning neurologic disease phenotyping.; Kemar Green

Grant Support: None.

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315

Autonomous Detection of Eye and Head Movements for Neurologic Assessment using AR/VR Platforms: A Feasibility Study

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Introduction:
Accurate detection of eye and head movements plays a crucial role in diagnosing neurological disorders . Manual assessments, such as the Head Impulse, Nystagmus, and Test of Skew (HINTS), are sensitive for detecting brainstem lesions but are limited by the need for specialized expertise. Emerging augmented and virtual reality (AR/VR) systems present an opportunity to automate and remotely administer such assessments. This study introduces an AR/VR-based system that autonomously detects eye and head movements for neurologic screening, reducing reliance on in-person expert evaluations.

Methods:
We developed an automated testing interface utilizing Microsoft HoloLens 2 to record head and eye movements with built-in sensors. The system guides users through tasks, such as nystagmus and head impulse tests, via instructional text and voice commands. The collected data is transmitted in real-time to an interconnected provider interface for visualization and verification. In preliminary testing, we evaluated the system on three participants, collecting eye-tracking data at 60 Hz and calculating head velocities above 120°/sec to ensure clinical validity. Data analysis was conducted using MATLAB to assess movement accuracy and detect abnormal responses.

Results:
The system successfully captured high-quality head and eye movement traces, with head impulse velocities meeting the clinical threshold. Simulated nystagmus waveforms closely matched physiological patterns. The eye movement data demonstrated precise alignment, supporting vertical skew detection. Users found the platform easy to navigate, and the system maintained connectivity with minimal latency.

Conclusions:
This study showcases the feasibility of using AR/VR platforms to automate eye and head movement detection for neurologic assessments, reducing the need for specialized personnel. Future developments will focus on enhancing real-time analysis with AI and expanding capabilities to include visual field testing and pupillometry. The platform aims to transform remote diagnostics and monitoring for conditions like vestibular disorders and brainstem lesions.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Ocular motility, Vestibular disorders, Miscellaneous, Nystagmus

Financial Disclosures: Haochen Wei: co-inventor of TeleAutoNeuro: an autonomous remote head and eye AR/VR/XR sensing for neurologic screening, diagnosing and disease monitoring; Justin Bosley: co-inventor of TeleAutoNeuro: an autonomous remote head and eye AR/VR/XR sensing for neurologic screening, diagnosing and disease monitoring; Peter Kazanizides: co-inventor of TeleAutoNeuro: an autonomous remote head and eye AR/VR/XR sensing for neurologic screening, diagnosing and disease monitoring; Kemar Green

Grant Support: None.

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Demographic and Clinical Characteristics of Patients with Acquired Isolated and Multiple Cranial Neuropathies in a Referral Hospital.

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Introduction:
Acquired cranial nerve palsies are commonly seen in the ophthalmology practice and clinical presentation and course varies widely between patients. This study aims to differentiate the clinical presentation between patients with isolated versus multiple cranial neuropathies.

Methods:
We reviewed 1,895 medical records of patients referred to our hospital with isolated and/or multiple third, fourth, fifth and sixth cranial nerve neuropathies from 2020 to 2024. 1733 patients were excluded for not attending their neuro-ophthalmology appointment or if a diagnosis different to oculomotor neuropathy, like myasthenia gravis or orbitopathy, was encountered.

Results:
A total of 162 patients were included, 67 (41.4%) female and 95 (58.6%) male patients. 139 (85.8%) patients presented isolated neuropathies while 23 (14.2%) presented multiple cranial neuropathies. Of those, 81 (49.7%) had sixth nerve palsy, 70 (43.2%) third nerve palsy, 32 (19.8%) fourth nerve palsy, and 11 (6.8%) trigeminal neuropathy. The most common etiology was microvascular (n=93, 56.8%). 29 (20.9%) patients with isolated neuropathies manifested pain versus 10 (43.5%) patients with multiple cranial neuropathies (p=0.01). Third nerve palsy was commonly associated with pain (n=19, 13.7%) versus fourth (n=2, 1.4%) and sixth (n=8, 5.8%) nerve palsy (p=0.01). The chief symptom of presentation was diplopia in 114 (70.4%). The majority of the female patients presented sixth nerve palsy (n=35, 53.8%) while in males third nerve palsy was the most commonly affected nerve (n=31, 63.3%) (p=0.36).

Conclusions:
Sixth cranial nerve was the most commonly affected in our study and pain was an important feature in patients with isolated cranial neuropathies similar to other studies. Reports demonstrate an association of pain with third nerve palsy and in our study this association was statistically significant.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Relations Between Retinal Microstructure, Microvasculature and Microcirculation in Patients with Parkinson's Disease

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Introduction:
The present study aimed to investigate the relationships between retinal microstructure, microvasculature, and microcirculation in patients diagnosed with Parkinson's Disease (PD).

Methods:
A total of twenty patients with clinically diagnosed PD were recruited, and successful retinal imaging was conducted on 17 participants (mean age 72.2 ± 7.2 years; 9 females). Inclusion criteria included: (1) age 55 years and older, (2) a Montreal Cognitive Assessment (MoCA) score > 18, (3) Hoehn & Yahr Stages 1-3 of PD, (4) ability to walk at least 50 feet with or without an assistive device, and (5) ability to get up/down from the floor with minimal assistance. Retinal capillary perfusion density (CPD) and tissue volume (RTV) were assessed within a 2.5 mm diameter disk centered on the fovea using optical coherence tomography angiography (OCTA). RTV encompassed the inner retinal layers including the retinal nerve fiber layer (RNFL), ganglion cell-inner plexiform layer (GCIPL), inner nuclear layer (INL), and outer plexiform layer (OPL). Retinal blood flow (RBF) was measured using a retinal function imager (RFI). Pearson correlation analyses were employed to assess relationships between variables.

Results:
No significant relationship was found between CPD and RBF ($r = 0.028$, $P = 0.92$) or between CPD and RTV ($r = 0.20$, $P = 0.46$). Additionally, RBF showed no significant correlation with RTV ($r = 0.008$, $P = 0.976$).

Conclusions:
This study represents the first investigation into the relationships among retinal microstructure, microvasculature, and microcirculation in patients with PD. The findings indicate that these components of the neurovascular system may exhibit distinct characteristics. Concurrent imaging of these elements may enhance the development of ocular biomarkers for patients with PD.

References: None provided.

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

Financial Disclosures: Potyra Rosa; Kirill Stremousov; Yunhai Dai; Joseph Signorile; Jianhua Wang: This study was supported by NIH Center Grant P30 EY014801; NINDS 1R01NS111115.; Hong Jiang: This study was supported by UM Aging Team Science Award, the Ed and Ethel Moor Alzheimer's Disease Research Program, Florida Health, 20A05.

Grant Support: This study was supported by NIH Center Grant P30 EY014801; NINDS 1R01NS111115 (Wang); UM Aging Team Science Award, the Ed and Ethel Moor Alzheimer's Disease Research Program (Florida Health, 20A05, to Jiang); and a grant from Research to Prevent Blindness (RPB).

Contact Information: None provided.

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Non-Mydriatic Ocular Fundus Imaging On Consecutive Headache Patients In An Emergency Department (ED)

Kevin Yan [1], George Alencastro [1], Andrew Pendley [1], Nithya Shanmugam [1], Jessica McHenry [1], Stuart Duffield [1], Daniel Adamkiewicz [1], Duyen Vo [1], Jordan Prosky [1], Matthew Keadey [1], David Wright [1], Michael Dattilo [2], Andrew Fischer [1], Mung Yan Lin [1], Nancy Newman [3], Valérie Biousse [1]

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Introduction:
Papilledema is a red-flag in the evaluation of headache but is often missed in EDs where ocular fundus examination is rarely performed. Our goal was to determine how often non-mydriatic ocular fundus photographs with OCT (NMFP-OCT) show relevant fundus findings in a consecutive cohort of patients with headaches in a general ED.

Methods:
Quality improvement project, prospective over 16 consecutive days/nights. NMFP-OCT OU [table-top Maestro2/Topcon-Japan] was ordered for all patients presenting to our ED with headaches [as primary (Group1) or secondary complaint (Groups2/3)], or with history of headaches of any kind (Group4). Demographic information, headache classification, final diagnosis and NMFP-OCT findings were collected.

Results:
Of 1838 ED visits over 16 days/nights, 194 patients had headaches and 149 underwent NMFP-OCT in the ED. Group1: 46 patients presented for isolated headache evaluation/treatment; 40 had NMFP-OCT [1 papilledema, 1 dilated retinal vessels from carotid-cavernous fistula, 2 non-relevant findings]; 6 patients without NMFP-OCT in the ED [1 unable to sit, 4 discharged prior, 1 refused]. Group2: 46 patients presented for a neurologic/neurosurgical issue with associated headache; 37 had NMFP-OCT [4 papilledema, 4 relevant retinopathies, 3 optic atrophy, 7 non-relevant findings]; 9 patients without NMFP-OCT in the ED [6 unable to sit, 3 admitted/discharged prior). Group3: 77 patients presented for a non-neurologic issue and had headache; 52 had NMFP-OCT and none had papilledema. Group4: 25 patients with previous history of headache but no active headache (3 with neurologic/neurosurgical issue, 22 with non-neurologic/neurosurgical issue); 20 had NMFP-OCT [no papilledema, 1 optic atrophy].

Conclusions:
NMFP-OCT obtained in the ED in consecutive patients with active headaches allowed for rapid diagnosis of papilledema in 5/86 (5.8%) and other relevant findings in 8/86 (9.3%), with 15 (17.5%) not having NMFP-OCT in the ED. None of the patients with headaches or history of headaches who presented to the ED for other reasons had papilledema.

References: Do TP, et al. Red and orange flags for secondary headaches in clinical practice: SNNOOP10 list, Neurology, 92(3):134-144, 2019.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), High intracranial pressure/headache

Financial Disclosures: Kevin Yan; George Alencastro; Andrew Pendley; Nithya Shanmugam; Jessica McHenry; Stuart Duffield; Daniel Adamkiewicz; Duyen Vo; Jordan Prosky; Matthew Keadey; David Wright; Michael Dattilo; Andrew Fischer; Mung Yan Lin; Nancy Newman: Consultant for GenSight, Chiesi, Neurophth (all involved with the treatment of Leber hereditary optic neuropathy. Research support as PI to my institution from GenSight for clinical trials.; Valérie Biousse: Consultant for Topcon which commercializes fundus cameras. The current research is completely independent from Topcon and is not funded by the company.

Grant Support: None.

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Retinal Microstructural Changes in Aging Rhesus Macaques

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Introduction:
Human studies have demonstrated progressive retinal thinning with aging, and rhesus macaques undergo similar physiological and behavioral changes. Alterations in their maculae can be visualized non-invasively and with high resolution using optical coherence tomography (OCT). This study aims to evaluate the retinal microstructural changes in aging rhesus macaques as measured by OCT.

Methods:
We obtained spectral-domain OCT images from 36 eyes of 18 geriatric rhesus macaques (12 females, mean age 22±3 years) using the Heidelberg Spectralis®. A customized segmentation algorithm was employed for automatic retinal layer thickness measurements, which were then manually corrected for accuracy. The layers measured included the retinal nerve fiber layer (RNFL), ganglion cell layer-inner plexiform layer (GCL-IPL), inner nuclear layer (INL), outer plexiform layer (OPL), outer nuclear layer (ONL), inner segment (IS), outer segment (OS), retinal pigment epithelium (RPE), and total retinal thickness (TRT). Simple linear regression and descriptive statistics were performed using Prism GraphPad to analyze the relationship between retinal layer thickness and age.

Results:
TRT had the strongest significant association with age and retinal thickness (β=-1.84, 95% CI: -3.18 to -0.51). GCL-IPL (β=-0.62, 95% CI: -1.18 to -0.05), INL (β=-0.55, 95% CI: -0.82 to -0.28), and RNFL (β=-0.45, 95% CI: -0.81 to -0.09) also showed significant associations. OPL (β=-0.02, 95% CI: -0.16 to 0.13), ONL (β=-0.36, 95% CI: -0.93 to 0.21), IS (β=-0.06, 95% CI: -0.27 to -0.14), OS (β=0.15, 95% CI: -0.14 to 0.44), and RPE (β=0.06, 95% CI: -0.24 to 0.36) were nonsignificant. Statistically significant age-related decreases were observed in the RNFL (p=0.016), GCL-IPL (p=0.033), INL (p=0.0002), and TRT (p=0.008) suggesting that these layers progressively thin with age.

Conclusions:
Rhesus macaques experience age-related retinal thinning like humans which may serve as markers of aging. Future studies should use a larger cohort of macaques and include behavioral correlations to identify potential retinal biomarkers for Alzheimer's Disease.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Retina

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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In Vivo Two-Photon Microscopy in Thy1-GcAMP Transgenic Rats Demonstrates that Electric Field Stimulation Directly Modulates Retinal Ganglion Cells

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Introduction:
Numerous electromagnetic stimulation (EMS) techniques, from trans-corneal to trans-cranial EMS, are being investigated to treat several neuro-ophthalmic conditions with variable reported outcomes. However, it has yet to be shown which neural structures are activated by these different stimulation strategies, which vary in electrode positioning and waveform parameters. In this study, we investigated in-vivo retinal ganglion cell (RGC) activation by various electrodes using two-photon microscopy in transgenic Thy1-GcAMP rats. This allows for direct visualization of intracellular calcium and, thus, electrical activity.

Methods:
Four electrodes were implanted in adult rats: 1) a circum-scleral, 2) a peri-optic-nerve, 3) an intracranial, and 4) a supraoccipital electrode. EMS tolerance testing was performed, followed by in-vitro studies to map out efficacious parameter space. Thy1-GcAMP rats underwent two-photon transpupillary imaging to quantify RGC activation in response to stimulation with various waveforms and electrode combinations.

Results:
Preliminary results revealed that biphasic stimulation via circum-scleral and peri-optic-neural electrodes directly activates RGCs (n = 2). For 1000 Hz at 800 µA, there was a mean fluorescence change (ΔF/F0) of 10.9% across 10 seconds of stimulation. For 100 Hz at 800 µA, mean ΔF/F0 was 39.6%, while at 1200 µA it was 70.7%.

Conclusions:
For the first time, this study provides direct visualization of EMS on retinal activation in vivo and demonstrates that trans-scleral stimulation can directly modulate RGCs. More studies, including in-vivo cortical imaging via a cranial window, are pending and will provide insight as to whether trans-scleral stimulation leads to V1 activation or trans-cranial stimulation leads to RGC activation. This study will demonstrate how different EMS stimulation strategies activate different parts of the visual pathway and may shed light on the mechanism underlying visual improvement with EMS.

References: None provided.

Keywords: Neuroimaging, Retina, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease, Higher visual functions

Financial Disclosures: The authors had no disclosures.

Grant Support: Research to Prevent Blindness (RPB) - Individual Medical Student Award (Nicholas Householder only)

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Features of intraretinal and subretinal fluid in non-arteritic anterior ischemic optic neuropathy

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Introduction:
Intraretinal fluid (IRF) and subretinal fluid (SRF) may occur in non-arteritic ischemic optic neuropathy (NAION) and cause diagnostic ambiguity. This cross-sectional study aimed to characterize the prevalence and severity of IRF and SRF in NAION, as well as investigate their associations with demographics, clinical characteristics, and visual function.

Methods:
Patients seen for acute NAION at a tertiary neuro-ophthalmology center between July 2022 and July 2024 underwent optic disc cube 200x200 and macular cube 512x128 spectral-domain optical coherence tomography scans. Two neuro-ophthalmologists assessed scans for SRF (pSRF), peripapillary IRF (pIRF), and foveal SRF (fSRF). Pairwise associations were evaluated using non-parametric tests.

Results:
Sixty-eight eyes (median age 65.0 years, 32.4% female) were included. pSRF was present in 5 (7.4%) of cases (height range 57.0-216.0 µm), pIRF in 32 (47.1%, height range 103.0-504.0 µm), and fSRF in 6 (8.8%, height range 51.0-288.0 µm). pSRF extended ≤25% of the distance from the disc margin to the fovea in all cases, while pIRF extended beyond 50% of the distance in 9 (28.1%) cases. Compared to patients without pIRF, patients with pIRF had a greater baseline pRNFL thickness (P=.02) and smaller vertical CDRs in the unaffected eye (P<.001). The presence of fSRF was associated with the presence of pIRF (P=.008), greater pIRF height (P=.003), longer pIRF extension (P=.003), and smaller average CDR in the fellow eye (P=.045). Visual acuity and visual field mean deviation at baseline and follow-up were not associated with IRF and SRF features.

Conclusions:
pIRF occurs in almost half of acute NAION cases but pSRF and fSRF are less common. Patients with smaller cup-to-disc ratios and more severe optic disc edema may be more likely to develop pIRF and fSRF. The presence and degree of IRF and SRF do not affect initial visual function nor visual prognosis.

References: None provided.

Keywords: Optic neuropathy, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Non-Mydriatic Ocular Fundus Imaging on Consecutive Neurologic and Neurosurgical Patients in an Emergency Department (ED)

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Introduction:
Examination of the ocular fundus is part of the standard neurologic examination. However, bedside ophthalmoscopy is rarely performed, especially in EDs, with risk of missed/delayed diagnoses/inappropriate triage. Our goal was to determine how often funduscopic examination with non-mydriatic ocular fundus photographs/OCT nerve/macula (NMPF-OCT) may be possible/helpful in a consecutive cohort of patients with neurologic/neurosurgical disorders seen in a general ED.

Methods:
Quality improvement project, prospective over 16 consecutive days/nights. NMFP-OCT OU [table-top Maestro2/Topcon-Japan] was ordered for all patients presenting to our ED with any neurologic/neurosurgical disorders. Demographic information, neurologic diagnosis, presence of headache and NMFP-OCT findings were collected.

Results:
Of 1838 ED visits over 16 days/nights, 449 (24.4%) patients reported neurologic/neurosurgical disorders, including headache; 247 underwent NMFP-OCT. 115/202 (57%) patients without NMFP-OCT were medically unable. -64/247 had neurologic complaints without active headaches [NFMP-OCT: 2 papilledema, 3 other disc edema, 4 optic atrophy, 36 normal]. -54/247 with past neurologic/neurosurgical disorders presented for another reason without headache [2 papilledema, 1 other disc edema, 2 optic atrophy; 40 normal]. -37/247 had neurologic complaints and headaches [NMFP-OCT: 4 papilledema, 1 other disc edema, 3 optic atrophy, 3 relevant retinopathy; 19 normal]. -52/247 presented for non-neurologic issues but also had headaches [NMFP/OCT: no papilledema]. -40/247 patients with NMFP-OCT presented for primarily headaches without focal neurologic symptoms [NMFP-OCT: 1 papilledema, 1 vasculopathy from carotid-cavernous-fistula; 36 normal].

Conclusions:
NMFC-OCT obtained in the ED in patients presenting with neurologic/neurosurgical disorders allows for rapid/reliable diagnosis of papilledema (9/247) and ruling-out papilledema (233/247), often remotely. It also facilitates diagnosis of other causes of optic neuropathies with disc edema (5/247), optic atrophy (9/247), relevant retinopathy (4/247). Overall, 27/247 (10.9%) had relevant findings, confirming that NMFP-OCT is useful in patients with neurologic/neurosurgical disorders. However, 115/449 (25.6%) patients were too sick and could not have NMFP-OCT, reinforcing the need for funduscopic examination in neurology/neurosurgery patients.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Vascular disorders, Tumors, High intracranial pressure/headache, Stroke

Financial Disclosures: Stuart Duffield; Kevin Yan; George Alencastro; Andrew Pendley; Nithya Shanmugam; Jessica McHenry; Daniel Adamkiewicz; Duyen Vo; Jordan Prosky; Matthew Keadey; Michael Dattilo; Andrew Fischer; Mung Yan Lin; David Wright; Nancy Newman: Consultant for GenSight, Chiesi, Neurophth (all involved with the treatment of Leber hereditary optic neuropathy. Research support as PI to my institution from GenSight for clinical trials.; Valérie Biousse: Consultant for Topcon which commercializes fundus cameras. The current research is completely independent from Topcon and is not funded by the company.

Grant Support: None.

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Non-Mydriatic Ocular Fundus Imaging in a General Emergency Department: Feasibility and Findings

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Introduction:
Despite having non-mydriatic ocular fundus photographs with OCT (NMFP-OCT) implemented in our general ED, not all eligible patients are imaged. We investigated the feasibility of systematic ocular imaging of consecutive patients presenting to our ED with chief complaints for which fundoscopic examination is standard of care.

Methods:
Quality improvement project, prospective over 16 consecutive days/nights. NMFP-OCT [table-top Maestro2/Topcon-Japan] was ordered for consecutive patients presenting to our ED with vision complaints, headaches, neurologic/neurosurgical disorders, hypertensive crisis, diabetes mellitus, end-stage renal disease. NMFP-OCT were obtained in the ED by trained researchers 24/7. Demographic information, indication for NMFP-OCT, findings, reason why NMFP-OCT not taken were documented.

Results:
1838 ED visits over 16 days, with orders for NMFPs placed for 801 patients (43.6%). 410/801 patients with NMFP-OCT (51%) compared with 391/801 patients without NMFP-OCT (49%): 99/410 (24.2%) vs 23/391 (5.9%) vision complaints[p< 0.0002], 116/410 (28.3%) vs 167/391 (42.7%) neurological/neurosurgical disorders[p< 0.0002], 60/410 (14.6%) vs 0/391 papilledema/papilledema rule-out[p< 0.0002], 37/410 (9%) vs 33/391 (8.4%) headaches[NS], 19/410 (4.6%) vs 2/391 (0.5%) dizziness/vertigo[p< 0.0002], 3/410 (0.7%) vs 3/391 (0.8%) hypertensive crisis [NS], 63/410 (15.4%) vs 130/391 (33.2%) diabetes[p< 0.001], 10/410 (2.4%) vs 33/391 (8.4%) ESRD[p< 0.001]. Demographics were similar across groups. 216/391 (55.3%) didn't have NMFP-OCT for medical reasons [181/391 (46.3%) too sick/unable to sit, 35/391 (9%) infectious precautions]. The remainder 175/391 (44.7%) did not have NMFP-OCT because of process problems [54/391 (13.8%) admitted prior to imaging, 51/391 (13%) discharged prior to imaging, 15/391 (3.8%) camera-room unavailable, 50/391 (12.8%) patients refused (23 with recent normal eye examination), 5/391 (1.3%) ED team refused.

Conclusions:
Despite 24/7 coverage of the ED by our team, 49% of patients could not have NMFP-OCT for reasons related to underlying patient illness or specific to the ED-setting. Realistic expectations are needed when considering the feasibility of implementation of new technology in an ED setting.

References: None provided.

Keywords: Neuroimaging, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Miscellaneous

Financial Disclosures: Nithya Shanmugam; Mung Yan Lin; Jessica McHenry; Kevin Yan; Stuart Duffield; Andrew Pendley; George Alencastro; Daniel Adamkiewicz; Duyen Vo; Jordan Prosky; Matthew Keadey; David Wright; Andrew Fischer; Michael Dattilo; Nancy Newman: Consultant for GenSight, Chiesi, Neurophth (all involved with the treatment of Leber hereditary optic neuropathy. Research support as PI to my institution from GenSight for clinical trials.; Valérie Biousse: Consultant for Topcon which commercializes fundus cameras. The current research is completely independent from Topcon and is not funded by the company.

Grant Support: None.

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The use of prompt engineering in a Vision-Language Model (VLM) for disc swelling identification from fundus photos

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Introduction:
The use of artificial intelligence (AI) to detect and classify optic disc swelling (ODS) on fundus images has applications for expediting the diagnosis of severe ophthalmic or neurological conditions. To date, work in this area has relied on convolutional neural networks (CNN). Vision Language Models (VLM) are an extension of Large Language Models (LLM). These generative models can learn simultaneously from images and text, with minimal training required, and provide the ability to interact with the image through text, often in the form of prompt engineering. We aimed to study if a pre-trained generic VLM can be used to identify ODS in fundus photos.

Methods:
Cropped optic disc-centered fundus images consisting of 779 normal optic discs and 295 images of swollen discs were obtained from an open-source Kaggle database. Using BLIP-2, an open-source VLM that is compute-efficient, we first generated a description for each image without any prompting and assessed the accuracy of the description. Next, we guided the model by prompting it to name the anatomical structure seen in the photo. Lastly, we specifically prompted the model to identify if the image shows ODS.

Results:
Without any prompts, BLIP-2 was able to identify that the image was of an eye in most cases (99.7%). When prompted for an anatomical structure, the most common label was “iris” (75%) followed by “retina” (22.9%). In no case, did it identify the image as an optic disc. When prompted that the image was an optic disc and asked if it was swollen, it achieved a sensitivity of 66.8% and specificity of 20.8%.

Conclusions:
Using a non-specialty trained VLM applied to fundus photographs of the optic disc, we demonstrate an ODS identification sensitivity of 66.8% through prompt engineering alone. This demonstrates the potential for VLMs for neuro-ophthalmic diagnosis.

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Keywords: High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: NIH P30 026877, unrestricted grant from research to prevent blindness

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Machine Learning-Based Papilledema Detection Leveraging the Quantification of Optic Disc Margin Clarity

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Introduction:
Optic disc margin blurring is an established sign of papilledema; to date, no clear definitions or thresholds for the degree of optic disc margin clarity have been established. This study expanded upon a previously-presented work on the quantification of optic disc margin clarity, leveraging additional computer vision methods to obtain enhanced results for a machine learning (ML)-based, automated detection of papilledema. This study also provides an overview of the clinical interplay between ML and neuro-ophthalmology practice, demonstrating the clinical correlation between ML, explainability analysis of ML, and clinical practice.

Methods:
Using a publicly-available fundus photograph dataset, transfer learning was employed utilizing a VGG-19 model pre-trained on the ImageNet database. Computer vision techniques such as region adjacency graphs (RAGs) and histogram of oriented gradients (HOGs) were performed for the quantification of optic disc margin clarity and model explainability. Image segmentation techniques were utilized for the automatic detection and orientation of optic disc centers for the calculation of rate of change in radial pixel intensity, as well.

Results:
The VGG-19 model achieved 92.8% accuracy in classifying normal optic discs, pseudopapilledema, and papilledema; edge detection methods demonstrated significant differences between the optic disc margin clarity of the three classes ($p < .001$) and ML models achieved 94.7% classification accuracy utilizing the extracted metrics. Saliency/attention heatmaps generated in explainability analysis highlighted model focus surrounding relevant retinal features, namely the optic disc margin and surrounding vasculature.

Conclusions:
Thresholds of clinical significance for papilledema detection can be established by leveraging the quantification of optic disc margin clarity aided by machine learning. Explainability analysis yields insights on the classification reasoning of deep learning models, providing a bridge between deep learning image analysis and clinical practice.

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Keywords: High intracranial pressure/headache, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Visual Field Threshold Changes in Normal Pressure Hydrocephalus Patients With and Without Primary Open-Angle Glaucoma

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Introduction:
While Normal Pressure Hydrocephalus (NPH) and Primary Open-Angle Glaucoma (POAG) both affect visual function, their combined impact remains unclear. Recent retrospective studies have suggested a significant glaucoma risk in NPH patients. This study aimed to compare visual field threshold value changes in NPH patients with and without POAG.

Methods:
We conducted a retrospective study using OPUS, a system developed at Mayo Clinic's Department of Ophthalmology. The study included age-matched patients with at least two reliable visual field tests for both eyes. We compared 59 NPH+POAG patients (average follow-up: 7.7 years) with 235 NPH patients without POAG (average follow-up: 1.7 years). Visual field data was retrieved in DICOM format, converted to PDF, and analyzed using custom software with Optical Character Recognition (OCR) to extract threshold values. Changes in visual field threshold values between the first and last tests were compared between groups.

Results:
The mean visual field threshold for the NPH+POAG group was 22.75dB at the first test and 20.4dB at the last test, while the NPH-only group showed 24.87dB and 24.85dB, respectively. The difference in visual field thresholds was -2.35dB for the NPH+POAG group and -0.02dB for the NPH-only group. An independent samples t-test revealed a significant difference between the two groups ($p=0.005$). The NPH-only group demonstrated less change overall, contrasting with the more pronounced deterioration in the NPH+POAG group.

Conclusions:
NPH patients with concomitant POAG exhibited significantly greater visual field deterioration compared to NPH patients without POAG. Interestingly, NPH patients without POAG showed stability in their visual fields. This finding suggests that POAG presence in NPH patients may result in visual field loss, highlighting the importance of careful monitoring and management in this patient population.

References: None provided.

Keywords: Orbit/ocular pathology, Optic neuropathy, Perimetry, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Differentiating Compressive Optic Neuropathy from Primary Open Angle Glaucoma Using the Macular Naso-Temporal Ratio

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Introduction:
Distinguishing compressive optic neuropathy (CON) from primary open angle glaucoma (POAG) clinically can be difficult but is crucial given their markedly different treatment approaches. Prior studies suggest that CON and POAG can be discriminated by patterns identified on OCT imaging. This study evaluates patterns of macular ganglion cell and inner plexiform layer (mGCIPL) loss in CON versus POAG.

Methods:
We retrospectively reviewed POAG and preoperative CON patients seen at an academic, quaternary medical center between 1/1/2013 and 6/31/2023. POAG was defined using the United Kingdom Glaucoma Treatment Study (UKGTS) criteria, excluding those with cranial mass lesions. CON was defined by UKGTS visual field criteria, inter-eye asymmetry in retinal nerve fiber layer or mGCIPL, or intra-eye asymmetry in mGCIPL. A Zeiss Cirrus optical coherence tomograph was used to derive the macular naso-temporal ratio (mNTR). Differences between mNTRs were explored using Wilcoxon rank sum tests, multivariable linear regression, and the area under the receiver operating characteristic curve (AUC).

Results:
194 CON and 121 POAG eyes with mGCIPL data were identified. POAG patients had significantly thinner mGCIPL than CON with a respective median [IQR] of 63 [55-69] versus 68 [62-74] µm ($p< 0.001$). mNTR was higher in POAG, with a median [IQR] of 1.04 [0.97-1.13] versus 0.90 [0.82-0.98] in CON ($p< 0.001$). This relationship held true when isolating the superior and inferior components of mNTR. Controlling for age, sex and average mGCIPL thickness, mNTR was 0.14 higher in POAG ($p< 0.001$). mNTR showed moderate ability to discriminate POAG and CON, with an AUC of 78.4%. Optimal mNTR threshold was 1.0072, achieving 63.6% sensitivity and 80.2% specificity.

Conclusions:
Both mGCIPL thickness and mNTR were significantly different in POAG and CON, with mNTR demonstrating moderate ability to distinguish between the two conditions. Further research is needed to validate the clinical application of mNTR for differentiation of these conditions.

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Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Optic neuropathy, Tumors, Retina

Financial Disclosures: Lucy Chen; Setu Mehta; Florian Guillot; James Davis; Altug Ay; Amanda Henderson: None related to this submission: Horizon Therapeutics/Amgen.; Andrew Carey: None related to this submission: Horizon Therapeutics/Amgen, Bristol-Myers-Squibb, Springer publishing.

Grant Support: None

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Validating Averaged OCT as a Tool for Identifying Scattering Features in the Retinas of People with MS

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Introduction:
Scattering features (SF) in the inner retina at the foveal avascular zone (FAZ) of people with multiple sclerosis (MS) have been reported using Adaptive Optics Scanning Laser Ophthalmoscopy (AOSLO). These features may serve as ocular biomarkers for MS, but AOSLO is time-consuming, requires pupil dilation, specialized training, and complex image processing. Similar features have been observed in the maculas of people with MS using averaged Optical Coherence Tomography (aOCT), but aOCT's ability to reliably detect AOSLO-identified features has not been validated. This project aims to assess whether aOCT can serve as an alternative tool for detecting these features, using AOSLO as the gold standard.

Methods:
AOSLO images (2.0-degree Field of View) from people with MS in an ongoing study served as the gold standard for identifying scattering features by group consensus. Macula OCT B-Scans (Avanti, Optovue) were segmented 3 µm above the inner limiting membrane (ILM) to create en face foveal images. Four to 11 scans per eye were selected based on quality, registered with OCTA, and averaged to improve the signal-to-noise ratio. Two raters, blinded to AOSLO results, independently classified SF on aOCT as Yes (detected) or No/Equivocal (not detected). Inter-rater agreement, sensitivity, and specificity of aOCT were calculated.

Results:
17 eyes from 9 people with MS were included (9 Yes, 5 No, 3 Equivocal for AOSLO features). Inter-rater agreement for aOCT was 100%. Sensitivity and specificity were 56% and 100%, respectively. The 4 false-negative aOCT scans matched AOSLO scans with ≤2 features, while all true positives had ≥2 features. No false positives were found.

Conclusions:
Averaged OCT shows excellent interrater agreement, high specificity, and low sensitivity for detecting SF in MS foveas. While it may have limited use in excluding features, it offers advantages over AOSLO in speed and ease of image acquisition and processing.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: NIH R01 EY033475, Department of Defense, NIH P30 026877, Research to Prevent Blindness

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Retinal vascular signs in intracranial atherosclerotic stenosis

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Introduction:
To investigate the associations of retinal vascular signs with intracranial atherosclerosis stenosis (ICAS) that might provide clues to the pathology of ICAS and new biomarkers.

Methods:
In this multi-center, cross-sectional study, we recruited participants who were at least 30 years old and had examinations of computed tomography angiography (CTA), or magnetic resonance angiography (MRA) and fundus photography from three general hospitals. Intracranial atherosclerosis stenosis was evaluated by the CTA or MRA. Qualitative assessment of retinal vascular signs were assessed from fundus images by ophthalmologists who were masked to the patients' clinical details. Retinal vascular parameters were quantitatively measured by using an automatic retinal vessels segmentation and parameter calculation (ARVSPC) method (China Patent Application No: CN202211272854.6).

Results:
A total of 531 participants including 272 participants with ICAS and 259 participants without ICAS in three hospitals were included in this study. Participants with ICAS were more likely than participants without ICAS to have focal arteriolar narrowing (14.3 vs 7.7 %, p=0.015), enhanced arterial light reflex (34.2 vs 22.8 %, p=0.004) and any retinal vessel wall signs (46.0% vs 30.9%, p=0.001) and wider retinal venules (212.96 um vs 206.7 um, p=0.015). In multivariate-adjusted analyses, focal arteriolar narrowing [OR, 2.35, 95% CI (1.27-4.37)], enhanced arteriolar light reflex[OR, 2.31, 95% CI (1.49-3.58)], and any retinal vessel wall signs were [OR, 2.52, 95% CI (1.67-3.8)] independently associated with ICAS, particularly in participants with hypertension and diabetes and participants with a history of stroke.

Conclusions:
Retinal arteriolar wall signs were closely associated with ICAS. Our findings suggest that retinal vessel wall signs may be an early manifestation of intracranial atherosclerosis stenosis, which might have implications for the early screening and treatment of ICAS.

References: None provided.

Keywords: Retina, High intracranial pressure/headache, Neuroimaging, Ocular manifestations of vestibular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Comparative Image Quality of Slit Scan vs Xenon Flash Photography in Screening Afferent Visual System Pathologies

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Introduction:
Ocular fundus screenings are critical for diagnosing afferent visual system pathologies, especially in vulnerable patient populations. Achieving optimal image quality is essential for accurately identifying both glaucomatous and non-glaucomatous optic neuropathies, whether through human interpretation or artificial intelligence (AI) algorithms.

Methods:
A total of 284 participants aged 18 and over attending the an urban eye screening event in Chicago consented to and participated in the study. Fundus imaging without pupil dilation was performed using two camera platforms. Each participant had images taken with the standard handheld camera using xenon flash (CamA) and a transportable camera using slit-scan technology (CamB). Images were independently graded by two masked qualified eye care professionals (Examiner1 and Examiner 2) using a five-point image quality scale (Figure1) while analyzing the image quality factors (Figure 2). Image quality was compared using the Wilcoxon signed-rank test for paired data.

Results:
For examiner 1, the median score for CamA was 3 and for CamB was 4. The median scores for image quality differed significantly between CamA and CamB ($P < 0.0001$). For examiner 2, the median score for image qualtiy for CamA was 2 and for Cam B was 4, with a statistically significant difference ($P < 0.0001$).

Conclusions:
This study shows the superiority of slit scan fundus photography as compared to standard hand-held xenon flash image quality. Transportable slit-scan cameras should be considered for maximizing image quality for the detection of neuro-ophthalmic afferent system disorders in community eye screenings as superior image quality is crucial for optimal clinical and AI interpretation of fundus images.

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Keywords: Optic neuropathy, Retina, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Rapid Automatized Naming and Retinal Neurodegeneration in Multiple Sclerosis and Neuro-Myelitis Optica Spectrum Disorder

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Introduction:
Performance on the Mobile Universal Lexicon Evaluation System (MULES), a rapid automatized naming (RAN) task engaging visual and cognitive network pathways, has demonstrated impairment in neurological conditions such as multiple sclerosis (MS), concussion, Parkinson's and Alzheimer's diseases. Optical coherence tomography (OCT) and low-contrast letter acuity (LCLA) have demonstrated changes in retinal structure and visual function in MS and neuro-myelitis optica spectrum disorder (NMOSD). This study investigates the relationship of cognitive-visual performance, as measured by MULES, and retinal integrity and afferent visual function as quantified by OCT and LCLA, in patients with MS and NMOSD.

Methods:
The MULES test, consisting of 54 color photographs of various objects (fruits, animals, and random objects), OCT and high- and low-contrast letter acuity (LCLA) testing were administered to 54 people with MS, 15 with NMOSD, and 15 healthy controls (HC). People with MS included those with clinically isolated syndrome, relapsing remitting MS (RRMS) and progressive MS. OCT imaging of the peripapillary retinal nerve fiber layer (pRNFL) and the macular ganglion cell + inner plexiform layer (GCIPL) were performed. Average pRNFL and GCIPL thickness between both eyes of participants, as well as inter-eye thickness differences, were calculated.

Results:
Greater MULES time scores, indicating worse performance, were associated with lower average pRNFL thickness in NMOSD ($p=0.004$, linear regression accounting for age), lower average GCIPL thickness in NMOSD ($p=0.019$) and higher inter-eye GCIPL thickness differences in RRMS ($p=0.003$) and HC ($p=0.045$). Longer MULES times were also associated with worse binocular high- and low-contrast letter acuity scores in both MS and NMOSD ($p< 0.05$).

Conclusions:
The MULES test of rapid picture naming enhances visual screening when evaluating patients with MS and NMOSD. Greater degrees of retinal neurodegeneration were associated with worse RAN task performance. Inter-eye GCIPL difference is the best OCT predictor of worse RAN task performance in MS.

References: None provided.

Keywords: Demeylinating disease, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Optic neuropathy, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Lower retinal arteriolar and venular fractal dimension are associated with higher risk of incident dementia - The UK Biobank (n=65,727)

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Introduction:
There is an urgent need for the identification of scalable biomarkers for Alzheimer's disease and related dementias. The retina is postulated a window to the brain and may be informative of changes in the central nervous system, including degenerative changes of the microvasculature. The objective of this study was to examine whether degeneration of the retinal microvasculature, represented by lower fractal dimension, was associated with risk of incident dementia (primary outcome) and Alzheimer's disease (secondary outcome).

Methods:
Data on 65,727 participants from UK Biobank, a prospectively designed population-based study, were used (mean age (SD) 56.7 (8.2) years; 45% men). Arteriolar and venular fractal dimension were extracted from fovea-centered fundus photos using AutoMorph software. Dementia diagnosis was assessed using electronic health-care records. Cox regression was used to examine associations of arteriolar and venular fractal dimension (in tertiles) with incident dementia, with adjustment for potential confounders (sociodemographic factors and cardiovascular and lifestyle factors). Results were expressed as hazard ratio with 95% confidence interval. In interaction analyses we examined whether associations differed as a function of age, ethnicity, or APOE4 genotype status.

Results:
Over a median follow-up time of 11.4 years (interquartile range 11.2-11.5 years) there were745 incident dementia cases. After maximal adjustment, lowest versus highest tertile of arteriolar and venular fractal dimension was associated with higher risk of incident all-cause dementia (HR 1.31 (1.02, 1.68) and HR 1.28 (1.01, 1.63), respectively). Similar associations were observed for middle versus highest tertile (HR 1.34 (1.02, 1.68) and HR 1.28 (1.01, 1.63), respectively). These associations did not differ as a function of age, ethnicity, or APOE4 genotype. Similar findings were obtained in analyses of Alzheimer's disease.

Conclusions:
Retinal microvascular dysfunction may precede the onset of dementia. Retinal imaging tools may be informative biomarkers for the study of the early pathophysiology of dementia.

References: None provided.

Keywords: Retina, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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The Relationship of Optical Coherence Tomography with Visual Outcomes in Children with Sellar Tumors

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Introduction:
Pediatric sellar tumors can compress visual pathways causing irreversible vision loss in children. Although retinal nerve fiber layer (RNFL) has been demonstrated to correlate with visual field loss, there is not enough data on the prognostic value of the ganglion cell layer (GCL) in predicting visual outcomes in children with sellar tumors. In this study, we evaluated the relationship of GCL with visual field defects and visual acuity (VA) in children with sellar tumors.

Methods:
This is a retrospective study included 176 eyes (88 patients) treated for sellar tumors. VA, RNFL, and GCL data were extracted. Mixed-effect linear models were used to investigate the relationship between VA and optical coherence tomography (OCT) parameters in both eyes. Generalized estimating equations binary logistic regression was used to assess to relationships between OCT parameters and the presence of a visual field defect in both eyes.

Results:
88 patients (59% female, 41% male) with a median age of 12.7 years (IQR 6.8, 15.9) at diagnosis were included: craniopharyngioma (48), pituitary adenoma (26), pituitary germinoma (5), pituitary stalk lesion (2), teratoma (2), indeterminate pituitary lesions (2), dermoid tumor (1), Rathke's cleft cyst (1), and glioma (1). At the last follow-up after surgical treatment, 41 eyes had visual field deficits. The median final GCL was 1.01 mm3 (IQR: 0.74, 1.10); RNFL, 85 microns (IQR: 57, 104); and logMAR VA of 0.02 (IQR: 0.00, 0.18). Both RNFL and GCL were significantly associated with the presence of a visual field defect ($p<.001$ and $p<.001$, respectively). Both RNFL and GCL were significantly associated with VA ($p<.001$), with a stronger correlation found between VA and GCL than with RNFL (pseudo-r-square=0.227 vs. 0.141).

Conclusions:
Both GCL and RNFL are associated with visual field defects. GCL is strongly correlated with VA in patients with sellar tumors and may offer greater prognostic value than RNFL.

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Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Pediatric neuro-ophthalmology, Tumors, Visual fields, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None

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Age differences in clinical manifestation and prognosis of orbital apex syndrome

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Introduction:
To examine clinical differences in the manifestation, course, treatment, and prognosis of orbital apex syndrome (OAS) between younger and older patient populations.

Methods:
This retrospective study included patients diagnosed with OAS between 2017-2023 at a tertiary neuro-ophthalmology practice. Charts were reviewed to extract data containing details of neuro-ophthalmic examination on presentation, imaging findings, final etiology, treatment offered, and visual prognosis for all patients. Non-parametric tests were performed to compare clinical characteristics between Group 1 (patients aged < 45 years, N=18) and Group 2 (patients aged ≥45 years, N=17).

Results:
The most common cause of OAS among younger patients was inflammation (55% of Group1 versus 19% of Group 2, p=0.02) while the most common cause among older patients was neoplasia (Group 2 with 60% versus Group1 with 33%, p=0.05). Among older OAS patients with neoplasia, metastasis (18%) was the most frequent cause followed by nasopharyngeal carcinoma (15%). In younger patients optic disc edema (28%) and optic atrophy (33%) were more frequent at initial presentation compared to the older group (p=0.03), whereas older patients were more likely to have diplopia (53% vs. 27%, p=0.048) and cavernous sinus involvement on MRI (57% versus 39%, p=0.06). The mean follow-up time was 36 months (±7.7). Recurrence was more prevalent among group 1 (55% vs. 17%, p=0.001) while worse final visual acuity (0.40 logMAR versus 0.25 logMAR , p=0.04) and death attributed to the underlying disease (7% vs. 0%, p=0.12) were more common among group 2.

Conclusions:
OAS has different aetiologies and clinical features depending on the age at presentation. Inflammation is the most common ethology in younger patients while neoplasia is the most common one in older ones. Older patients had less risk of occurrence but poorer visual prognosis and higher disease morbidity.

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Keywords: Optic neuropathy, Tumors, Adult strabismus with a focus on diplopia, Orbit/ocular pathology, Orbit

Financial Disclosures: The authors had no disclosures.

Grant Support: there is no grant support

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Extraocular Muscle Enlargement in Graves' Orbitopathy: A Systematic Review and Meta-Analysis

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Introduction:
The likelihood of individual EOM enlargement in GO is typically thought to occur in an "IMSLO" pattern with the inferior rectus(IR) being affected the most often and to the greatest extent, followed by the medical rectus(MR), superior rectus(SR), inferior rectus(IR), and lastly oblique muscles. This study investigated the patterns of EOM enlargement in GO across the reported literature.

Methods:
A comprehensive search of MEDLINE, EMBASE, and Cochrane Library was conducted in May 2024 for studies on GO including measurements of EOMs with a control group. Meta-analysis was completed using random effects models to estimate standard mean differences. The main outcomes of interest were the mean diameters and/or cross-sectional areas of each EOM in GO and control groups, as well as the proportion of each EOM demonstrating enlargement in GO compared to a control group.

Results:
There were 2196 studies identified by the outlined search criteria. After title and abstract screening 157 studies underwent full-text review. In total, 22 studies reported data on EOM enlargement in GO compared to a control group, and were included. Data from 2545 orbits with GO, and 1243 control eyes was reported. There were 766 female patients(73.7%). Across studies, the ratio of GO to control EOM maximum diameter(n=1345) for the IR was 1.55:1(standard mean difference(SMD):1.64, 95% confidence interval(CI):1.05-2.23), SR was 1.34:1(SMD:1.11, CI:0.98-1.24), MR was 1.39:1(SMD:1.68, CI:0.48-2.89), and LR was 1.46:1(SMD:0.69, CI:0.17-1.21). The ratio of GO to control EOM volume(n=774) for the IR was 1.89:1(SMD:1.63, CI:1.40-1.86), SR was 1.87:1(SMD:2.91, CI:0.84-4.98), MR was 1.70:1(SMD:2.17, CI:0.38-3.96), and LR was 1.59:1(SMD:1.23, CI:-0.14-2.59). The percentage of EOM affected in each orbit(n=327) was IR 53.3%, SR 52.8%, MR 54.2%, and LR 38.3%.

Conclusions:
EOM enlargement in GO was not shown to follow the typically taught IMSLO pattern. The pattern of EOM enlargement extent for diameter was found to be IR>LR>MR>SR, and for volume was IR>SR>MR>LR.

References: None provided.

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

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Retrospective Study of Orbital Tumors in the Modern Era

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Introduction:
This study examines types of orbital tumors and their impact on vision loss at our institution over the past 14 years. Orbital tumors can lead to significant complications, including diplopia, ptosis, pain, and visual impairment, making it essential to understand their characteristics and outcomes. Given evolving treatment options for malignant orbital tumors, updated prognostic data is needed. The primary objective of our study is to investigate factors affecting vision and survival outcomes to inform treatment strategies and improve patient counseling.

Methods:
A retrospective chart review was conducted on patients presenting with orbital tumors since January 2010 and data were retrieved from electronic medical records, imaging studies, and diagnostic tests. From an initial review of approximately 1,000 charts, 283 qualifying patients were identified.

Results:
Preliminary results analyzed 146 tumors: 30 orbital metastases, 21 lacrimal gland tumors, 25 primary lymphomas, 17 secondary lymphomas, and 53 meningiomas. When comparing post-treatment visual acuity (LogMAR) between orbital metastases, lymphomas, and meningiomas, there was a significant difference (1.05 vs 0.33 vs 1.12 respectively, p=0.041). However, there were no significant differences between the percentage of patients with diplopia (p=0.834) or proptosis (p=0.150) among these tumors. The overall 5-year survival was 88.1% (95% CI 79.6%-93.2%). 5-year survival was < 50% for orbital metastases, 100% for meningiomas, and >87% for primary lymphomas, secondary lymphomas, and lacrimal gland tumors. Patients with orbital metastases treated with chemotherapy or chemoradiation had a longer mean survival (29.49 and 26.94 months respectively) than those treated with only radiation (15.91 months), but the difference was not significant (p=0.709). These differences in survival may reflect a predilection for the use of palliative radiation in patients whose cancer has further progressed.

Conclusions:
In conclusion, this study provides updated insights into the visual effects and survivability of orbital tumors, emphasizing the need for ongoing research to enhance outcomes.

References: None provided.

Keywords: Orbit, Orbit/ocular pathology, Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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LX-101, a Novel Payload-bearing Insulin-like Growth Factor-1 Receptor Targeted Therapy, Inhibits Thyroid Eye Disease Inflammation

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Introduction:
In thyroid eye disease (TED), excessive inflammation driven by activated orbital fibroblasts (OFs) and infiltrating T lymphocytes leads to orbital tissue expansion, pain, diplopia, vision impairment, and potentially sight-threatening outcomes. Teprotumumab, an insulin-like growth factor 1 receptor (IGF-1R) antibody approved for TED, validated IGF-1R as an important target in TED, but suboptimal responses, relapses, and side effects underscore the need for additional therapeutic options. LX-101 is a next-generation, targeted therapy directed to the IGF-1R that delivers a methotrexate payload, a drug used to treat many autoimmune diseases. This study evaluated the efficacy of LX-101 in dampening the inflammatory response driven by IGF-1R+ T lymphocytes and OFs in TED.

Methods:
Primary OFs and donor-matched T lymphocytes derived from TED patients were treated separately or in OF-T lymphocyte co-cultures with LX-101 (0.01 - 2.5 μM). Cell viability was measured using redox sensitive dyes, and Western blot was used to evaluate markers of apoptosis. Scratch assays were used to assess cell migration. Inflammatory cytokine levels were analyzed by Luminex assay, ELISA, and RT-qPCR.

Results:
OFs and T lymphocytes from TED patients expressed high levels of IGF-1R. LX-101 induced T lymphocyte apoptosis as demonstrated by increased expression of cleaved PARP, and T lymphocyte viability was reduced by LX-101 with an IC50 of 14 nM. While OFs maintained viability in the presence of LX-101, LX-101 inhibited PDGFbeta-mediated OF migration. In addition, LX-101 treatment significantly inhibited OF production of IL-6, IL-8 and MCP-1 induced by co-culture with T lymphocytes or by T lymphocyte conditioned media.

Conclusions:
These results demonstrate that LX-101 has potent activity against TED T lymphocytes and effectively blocks OF production of key inflammatory mediators that drive TED pathogenesis. These findings suggest LX-101 may represent a promising therapeutic approach and support clinical development of LX-101 in TED.

References: None provided.

Keywords: Graves' disease, Orbit/ocular pathology, Orbit

Financial Disclosures: Collynn Woeller: My laboratory received research support from Lirum Therapeutics.; Farha Husain; Elisa Roztocil; Charkira Patrick; Steven Feldon; Matt Hoberman: Employee and shareholder of Lirum; Peter McDonald: Employee and shareholder of Lirum

Grant Support: This work was supported by a research grant from Lirum Therapeutics.

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Teprotumumab Efficacy and Safety in an Open-label (OL) Extension in Patients with Chronic Thyroid Eye Disease (TED)

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Introduction:
Thyroid Eye Disease (TED) can lead to chronic and symptomatic disease with pain and proptosis. Teprotumumab has demonstrated efficacy in patients with acute and chronic TED. In the first placebo-controlled, double-blind trial (NCT04583735) in patients with chronic TED (2-10 years disease duration and clinical activity score ≤1), teprotumumab improved proptosis and visual function-quality of life. We report teprotumumab safety and efficacy in the open-label extension of this trial.

Methods:
Proptosis non-responders (< 2 mm improvement) from the randomized period of the trial could receive open-label teprotumumab (8 infusions over a 24-week treatment period).

Results:
Of 24 patients in the open-label extension, 12 patients who were previously treated with placebo received a first course of teprotumumab (PBO/TEP) and 12 patients who were previously treated with teprotumumab received a second course (TEP/TEP). At week 24 of the open-label extension, mean (SD) proptosis change from pre-teprotumumab was -2 (1.2) mm for PBO/TEP and -1.6 (1.2) mm for TEP/TEP; and 7/12 (58.3%) PBO/TEP and 5/12 (41.7%) TEP/TEP were proptosis responders. Adverse events (AEs) were reported in 11 (91.7%) PBO/TEP and 8 (66.7%) TEP/TEP patients, with no serious AEs or deaths. No TEP/TEP patients and 3 PBO/TEP patients reported hearing AEs (eustachian tube dysfunction, hypoacusis, tinnitus).

Conclusions:
Delayed treatment (PBO/TEP) had similar outcomes as teprotumumab in first 24 weeks. Additional teprotumumab therapy (TEP/TEP) proved beneficial without added safety concern in about 40% of patients with prior non-response.

References: Raymond S Douglas, Steven Couch, Sara T Wester, Brian T Fowler, Catherine Y Liu, Pet al. Efficacy and Safety of Teprotumumab in Patients With Thyroid Eye Disease of Long Duration and Low Disease Activity, Journal of Clinical Endocrinology & Metabolism, 109(1), 25-35, 2024.

Keywords: Graves' disease, Orbit/ocular pathology, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)
Financial Disclosures: Prem Subramanian: P. S. Subramanian is a consultant for Gensight, Amgen (formerly Horizon) and Viridian. His institution received funds from Horizon (now Amgen) to perform the trial on site.; Steven Couch: His institution received funds from Horizon (now Amgen) to perform the trial on site.; Sara Wester: S.T. Wester received research funding from Horizon (now Amgen, Sling, and Immunovant, and is consultant for Amgen (formerly Horizon), Immunovant, and Lassen.; Brian Fowler: B. T. Fowler is a consultant to Amgen (formerly Horizon). His institution received funds from Horizon (now Amgen) to perform the trial on site.; Catherine Liu: C. Y. Liu receives royalties from Wolters Kluwers Health and her institution has received research support from Lassen as well as funds from Horizon (now Amgen) to perform the trial on site.; Rosa Tang: R. Tang is a consultant for Viridian, Alexion, Valenza, and Acelyrin, an investigator for Horizon (now Amgen), Viridian, Novartis, Immunovant, Vasaragen, Sling Therapeutics, Lassen, Roche, ArgenX, Tourmaline Bio and a speaker for Serono journal club. Her institution received funds from Horizon (now Amgen) to perform this trial on site.; Robi Maamari: R.N. Maamari was a sub-investigator in the Horizon (now Amgen) teprotumumab clinical trials: HZNP-TEP-403, HZNP-TEP-402, and subcutaneous Phase 1b. His institution received funds from Horizon (now Amgen) to perform these trials on site.; Kate Hsu: K. Hsu is an employee of and holds stock in Amgen.; Michael Karon: M. Karon is an employee of and owns stock in Amgen.; Marius Stan: M. N. Stan's institution has received research support from Horizon (now Amgen), Immunovant, ValenzaBio, Sling Therapeutics and Lassen Therapeutics and he is a consultant for Septerna Inc, Third Rock Ventures LLC, Genentech, ArgenX US Inc, Tourmaline Bio, Ortho Clinical Diagnostics, OSE Immunotherapeutics and Roivant Sciences.
Grant Support: Horizon Therapeutics (now Amgen) funded this study, and the authors' institutions received funds from Horizon (now Amgen) to perform the trial on site.
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Systemic Effects of Teprotumumab Treatment on Thyroid Function in Patients with Thyroid Eye Disease: A Retrospective Study

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Introduction:
Teprotumumab, an IGF1-R inhibitor delivered systemically in the treatment of thyroid eye disease (TED), poses uncertainties regarding its systemic impact on thyroid hormone levels. This study aims to assess alterations in thyroid laboratory values among patients receiving teprotumumab treatment.

Methods:
A retrospective chart review was conducted for patients undergoing teprotumumab treatment for TED at UC San Diego between January 2020 and December 2023. Inclusion criteria comprised patients receiving at least four infusions of teprotumumab, with pre- and post-treatment thyroid-stimulating hormone (TSH) measurements.

Results:
Forty-six patients met the inclusion criteria, with a mean age of 55.9 (±14.6) years. Thirty patients presented with hyperthyroidism, 13 with hypothyroidism, and 3 with euthyroidism. The majority were female (n=37), and the mean pre-treatment Clinical Activity Score (CAS) was 4.3 (±0.9), significantly reduced post-treatment to 1.2 (±0.9) ($p< 0.001$). The mean number of infusions was 7.5 (±1.1). Although there was a trend towards increased TSH levels post-treatment (mean: 2.2 ± 5.1) compared to pre-treatment (mean: 1.3 ± 2.6), this was not statistically significant (p=0.266). However, free thyroxine (T4) levels significantly decreased post-treatment (mean: 1.3 ± 0.4) compared to pre-treatment (mean: 1.7 ± 1.2) (p=0.049). Among patients with stable thyroid labs and medication (levothyroxine/methimazole) dosages for at least 6 months prior to treatment (n=23), a substantial proportion (n=12) required adjustments during teprotumumab therapy, indicating a lack of correlation between pre-treatment stability and stability during treatment (p=0.353).

Conclusions:
IGF1-R is expressed in many tissues, including in isolated thyroid epithelial cells. Teprotumumab treatment for TED was associated with a trend towards increased TSH levels and decreased free T4 levels, irrespective of pre-treatment medication stability. Thyroid medication adjustment was required in over half of patients who were medically stable pre-treatment. These findings underscore the importance of close endocrine monitoring during teprotumumab therapy for TED.

References: None provided.

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

Financial Disclosures: Rafaella Penteado; Leo Meller; Marissa Shoji; Eman Al-Sharif; Don Kikkawa: Consultant for Horizon, Immunovant and Lassen Therapeutic, royalties from Elsevier Publishing.; Bobby Korn: Consultant for Immunivant.; Catherine Liu: Grant funding from Horizon, royalties from Wolters Kluwers Health.

Grant Support: None.

Contact Information: None provided.

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Impact of Insurance Coverage on Healthcare Access and Coordination for Patients with Thyroid Eye Disease

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Introduction:
The average time to diagnosis of thyroid eye disease (TED) is 9 months and can be misdiagnosed up to 58% of the time (1). Delay in TED management can impact a patient's vision and quality of life. We sought to determine whether different insurance plans affect the time to diagnosis, specialists, and treatments for TED patients.

Methods:
Thirty-seven patients over 18 years old with TED with follow-up at safety-net and tertiary private hospital in one year period were identified through retrospective chart review. Primary/secondary insurance types (e.g., Medi-Cal, Medicare, HMO, PPO, self-pay) were recorded. Time from symptom onset to diagnosis (TTD), time to ophthalmology sub-specialist (TTS), time to initial TED treatment (TTT), and time to teprotumumab treatment (TTP) were quantified. Initial and most recent clinical activity scores (CAS) obtained to represent TED severity.

Results:
Patients with PPO plans had significantly lower TTS (mean TTS=40.7 days, p=0.02) than those without PPO. Patients with Medi-Cal had higher TTS (mean TTS=152.1 days) than with PPO (mean TTS=40.7 days, p=0.03) and HMO (mean TTS=50.5 days, p=0.07). Patients with Medicare had significantly lower TTP (mean TTP = 48.4 days) than those without Medicare (mean TTP=248.7 days, p=0.002) and Medi-Cal (mean TTP=144.6 days, p=0.03), specifically. Differences in TTD and TTT were present between insurance types, although not statistically significant. Tertiary private hospital patients had significantly lower TTS (mean TTS=56.5±66 days, p=0.03) than safety-net hospital patients (mean TTS = 194.6±183 days). No differences were present between active and inactive TED for all metrics.

Conclusions:
Private insurance (e.g PPO, HMO) is associated with more efficient coordination to ophthalmology specialty care. Medicare coverage is associated with shorter time to teprotumumab, suggesting more efficient access to treatment in the setting of severe TED. Further research may elucidate other modifying sociodemographic factors and self-perceived barriers that contributed to delays in TED care.

References: 1. Dosiou C, Kossler AL. Thyroid Eye Disease: Navigating the New Treatment Landscape. J Endocr Soc, Volume 5, Issue 5, 2021.

Keywords: Orbit, Graves' disease

Financial Disclosures: Shaili Davuluru; Nikta Saeedi; Rasika Sudharshan; Sandy Zhang-Nunes: Sandy Zhang-Nunes is a Research Investigator for Amgen, consultant/advisor for Amgen, consultant/advisor for Tarsus.

Grant Support: None.

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Interleukin-6 Receptor Signaling Inhibition With Satralizumab in Thyroid Eye Disease: Phase 3 SatraGO-1 and SatraGO-2 Trial Design

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Introduction:
Thyroid eye disease (TED) is an inflammatory orbitopathy that can cause facial disfigurement and sight-threatening complications. There is a significant need for disease-modifying treatments for active TED as current therapies may be ineffective, cause relapses, and/or have considerable side effects. Inactive TED is primarily treated through surgical methods. Interleukin-6 (IL-6) and its receptor (IL-6R) may play a key role in TED pathogenesis. Satralizumab, a humanized monoclonal anti–IL-6R antibody, utilizes innovative recycling technology to enhance IL-6 suppression and effectively manage inflammation and its consequences, with subcutaneous administration every 4 weeks (Q4W). We describe the design of the SatraGO-1 and SatraGO-2 trials evaluating satralizumab in TED.

Methods:
SatraGO-1 (NCT05987423) and SatraGO-2 (NCT06106828) are identical, global, phase 3, randomized, double-masked, placebo-controlled, 72-week multicenter studies that will recruit ~120 participants at ~70 sites across 20 countries. Participants ≥18 years with moderate-to-severe active TED or stable, chronic inactive TED are eligible provided the systemic disease is under control (euthyroid or mild hyper-/hypothyroidism). Participants will be randomized 1:1 to subcutaneous satralizumab or placebo at weeks (W) 0, 2, and 4 (loading doses) and then Q4W through W20 (maintenance doses). Based on the W24 proptosis response, nonresponders will receive satralizumab Q4W and responders re-randomized 1:1 to satralizumab or placebo Q4W through W44.

Results:
Primary endpoint: proportion of active TED participants achieving a proptosis response (≥2 mm proptosis improvement from baseline in study eye) at W24. Secondary endpoints include proptosis response in active/chronic TED participants and overall response (≥2-point improvement in clinical activity score from baseline and proptosis response in study eye) in active TED participants. Safety outcomes include incidence, seriousness, and severity of adverse events.

Conclusions:
SatraGO-1 and SatraGO-2 are designed to investigate IL-6R inhibition via satralizumab in TED. Satralizumab offers a potential disease-modifying treatment in TED while minimizing safety risks associated with current treatments.

References: None provided.
Keywords: Graves' disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Orbit

Financial Disclosures: Madhura Tamhankar: Financial Disclosures: Advisor: Amgen, Roche, Viridian; Royalty: Chapter in UpToDate; Daniel Ezra; Atif Collins: Financial Disclosures: Unpaid Member of Study Review Committee; Marius Stan: M. N. Stan's institution has received research support from Horizon (now Amgen), Immunovant, ValenzaBio, Sling Therapeutics and Lassen Therapeutics and he is a consultant for Septerna Inc, Third Rock Ventures LLC, Genentech, ArgenX US Inc, Tourmaline Bio, Ortho Clinical Diagnostics, OSE Immunotherapeutics and Roivant Sciences.; Zdenka Haskova: Financial Disclosures: Employment and Stocks or Stock Options: Genentech, Inc.; Thomas Kuenzel: Financial Disclosures: Employment and Stocks or Stock Options: F. Hoffmann-La Roche Ltd.; Miriam Triyatni: Financial Disclosures: Employment and Stocks or Stock Options: F. Hoffmann-La Roche Ltd.; Oluwatobi Idowu: Financial Disclosures: Employment and Stocks or Stock Options: Genentech, Inc.

Grant Support: None.
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Preliminary Safety, Efficacy, and Quality of Life Outcomes of Subcutaneous Lonigutamab (Anti–IGF-1R) from a Phase 1/2 Study of Thyroid Eye Disease (TED)

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Introduction:
This phase 1/2 study evaluated subcutaneous lonigutamab, a high-affinity anti–IGF-1R monoclonal antibody, in patients with TED (NCT05683496).

Methods:
Eligible patients had proptosis ≥3mm above normal range in the study eye and Clinical Activity Score (CAS) ≥4 (7-item scale). Cohort 1 received lonigutamab 40mg or placebo Q3W (2 doses); week 6 and 12 data are shown. Cohort 2 received lonigutamab 50mg (loading dose), then 25mg weekly (11 doses); week 6 data are shown.

Results:
In cohort 1 (N=8 [lonigutamab, n=6; placebo, n=2]), 3/6 (50%) lonigutamab-treated patients had a proptosis response (vs 0% for placebo) at weeks 6 and 12; 1/4 (25%) lonigutamab-treated patients with baseline diplopia had a diplopia response (vs 0% for placebo). With lonigutamab, 6/6 (100%) patients achieved a ≥2-point reduction in CAS at weeks 6 and 12 (vs 0% for placebo). Mean (SD) overall Graves' Ophthalmopathy Quality of Life (GO-QoL) change from baseline was 12.9 (13.9) and 12.3 (9.7) at weeks 6 and 12 with lonigutamab (vs −15.6 for 1 placebo-treated patient; higher scores indicate better health). In cohort 2, 4/6 (67%) patients had a proptosis response, 2/5 (40%) had a diplopia response, and 5/6 (83%) achieved a ≥2-point reduction in CAS at week 6. Mean (SD) overall GO-QoL change from baseline was 21.1 (15.0). Treatment-emergent AEs were grade 1-2 (cohort 1: lonigutamab, 4/6 [67%], placebo, 2/2 [100%]; cohort 2: 5/6 [83%]), with no serious AEs. Tinnitus occurred in 3 lonigutamab-treated patients (cohort 1; no audiogram changes).

Conclusions:
These are the first reported proof-of-concept results of subcutaneous anti–IGF-1R in patients with TED (cohort 1). Patients achieved early clinical responses that were maintained over time, including at week 12 (off-treatment). Evidence from cohort 1 suggests lonigutamab was well tolerated and displayed clinical efficacy and QoL responses, which was further substantiated by cohort 2 data.

References: None provided.

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

Financial Disclosures: Shoaib Ugradar: Shoaib Ugradar has served as a consultant for ACELYRIN, INC., Amgen, Lassen Therapeutics, and Viridian Therapeutics.; David A Kostick: David A Kostick has served as a principal investigator for ACELYRIN, INC. and participated in a speakers' bureau for Amgen.; Jane Spadaro; Anita Grover: Anita Grover is an employee and shareholder of ACELYRIN, INC.; So Jung Imm: So Jung Imm is an employee and shareholder of ACELYRIN, INC.; Roberta Vespignani: Roberta Vespignani is an employee and shareholder of ACELYRIN, INC.; Shephard Mpofu: Shephard Mpofu is an employee and shareholder of ACELYRIN, INC.; Jwu Jin Khong: Jwu Jin Khong has received consulting fees from ACELYRIN, INC., and Amgen; received funding from the Centre for Eye Research Australia; participated in an advisory board for ACELYRIN, INC.; and served as a member on the RANZCO Victoria branch and the Royal Victorian Eye and Ear Hospital ethics committees

Grant Support: This study is sponsored by ACELYRIN, INC.

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Smartphone-based artificial intelligence system for measurement of ptosis and other oculofacial measurements

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Introduction:
Ptosis is a common clinical presentation that may be associated with vision and life-threatening conditions. Assessments of ptosis have often been subjective in nature, which can negatively impact care and obscure recognition of a potentially serious diagnosis. The objective of this study was to develop and validate a new low-cost artificial intelligence (AI) smartphone application that can accurately measure ptosis and other oculofacial measurements. OphthoRuler, a free smartphone application powered by AI and image processing techniques to automatically detect eyelid margins can calculate margin to reflex distance 1 (MRD1) and margin to reflex distance 2 (MRD2).

Methods:
We validated the app against 120 healthy control images from the Chicago Face Database. App measurements were compared to manual photographic measurements obtained using an image analysis tool (ImageJ). Descriptive analyses were conducted in Python using the Pingouin statistical package. Agreement was assessed using Bland-Altman difference plots. Subgroups of controls were compared to assess for equal reliability of measurements across Male, Female as well as Asian, Black, Latino, and White participants.

Results:
Using the current version of our AI model, the mean difference was 0.75mm [95% CI 0.65mm, 0.85mm] for MRD1, -0.58mm [95% CI -0.71mm, -0.45mm] for MRD2, 0.16mm [95% CI 0.01mm, 0.31mm] for palpebral fissure height, and -0.37mm [95% CI -0.61mm, -0.13mm] for palpebral fissure width. There were no notable differences in reliability of measurements across Male, Female or Asian, Black, Latino, and White participants as demonstrated in Bland-Altman plots.

Conclusions:
We developed a novel app for automated ptosis measurements and present case examples to illustrate functionality as well as data assessing the app's reliability against manual photographic measurements. The findings of our study demonstrate the feasibility and accuracy of using a novel smartphone-based AI system for ptosis measurements. Our next objective is to validate the app for the detection of ptosis in neuro-ophthalmic conditions.

References: None provided.

Keywords: Orbit/ocular pathology, Neuroimaging, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

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Evaluation of Topological Data Analysis in Detecting Papilledema Using Oral Fluorescein Angiography in Children

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Introduction:
Oral fluorescein angiography (FA) has been used in children to differentiate papilledema from pseudopapilledema. A previous study that used expert readers demonstrated lower than expected accuracy. We have been exploring the use of topological data analysis (TDA) to improve the precision of the diagnosis.

Methods:
Topology-based analysis, particularly persistence diagrams, is able to process complex images and to extract features of the image that exhibit interesting properties. We developed an algorithm that pinpoints certain points of retinal images using the concept of persistence homology. Relaying on persistence diagrams, we isolate points on the retina whose topology corresponds to a certain area in the persistence diagram. FA's of patients with pseudopapilledema exhibit more of these points of interest than those of patients with papilledema.

Results:
We evaluated 42 images of oral FA's of papilledema and 145 images of pseudopapilledema using TDA. When considering the number of interesting topological points, we can predict whether the disease is present or not by simply counting those points. We identified a point count that produced zero false negatives in those 187 analyzed images. Using that count as threshold, the accuracy is 40% , although there are other thresholds that trade-off false negatives for accuracy as high as 70%.

Conclusions:
TDA is an additional tool for improving the accuracy of diagnosing papilledema and avoiding expensive testing in patients with pseudoedema. It has application both for patient care and for teaching because the topological points of interest appear to coincide with certain blood vessels of the retina.

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Keywords: Pediatric neuro-ophthalmology, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: N/A

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Assessing Visual Saliency in Children with Cerebral/Cortical Visual Impairment (CVI) Using Generative AI and Eye Tracking

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Introduction:
Cerebral/cortical visual impairment (CVI) is a leading cause of pediatric visual impairment. Objective metrics to assess higher-order visual processing in developmentally delayed children with CVI are needed. We developed a novel method using a combination of eye tracking and a generative artificial intelligence (AI) model (SegCLIP) to analyze higher-order visual characteristics in pediatric CVI.

Methods:
34 children with CVI (≤12 years old) and 29 age-matched controls were recruited. Participants viewed a series of images on a computer monitor while direction of eye gaze was recorded. We excluded participants whose visual acuity was insufficient to resolve images on the screen, based on Fourier analysis to calculate the spatial frequency of these images. SegCLIP generated saliency maps of each image, highlighting areas of interest pertaining to specific visual characteristics. Fixations were aligned to these saliency maps to calculate fixation saliency values, which were compared between CVI and control participants.

Results:
Mean age was 4.9 years, and mean binocular visual acuity was 8.9 cpd by preferential looking. Compared to age-matched controls, CVI participants fixated less on human faces, 2-dimensional representations of depth, still depictions of motion, and visually complex stimuli (< 0.001).

Conclusions:
Eye tracking combined with AI-enabled saliency analysis indicates that children with CVI generate fewer fixations to image characteristics that require higher-level visual processing. Future research is necessary to determine whether eye tracking findings correlate with functional vision. This approach could potentially be used to guide individualized interventions and serve as an outcome measure in future clinical trials for CVI.

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Keywords: Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

Grant Support: NIH NEI K23EY033790

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Impact of Neonatal Hyperbilirubinemia on Optic Nerve Parameters in Children: A Cross-sectional Study

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Introduction:
Jaundice affects over 60% of full-term and 80% of premature infants[1, 2]. Hyperbilirubinemia, the primary cause of newborn readmissions, typically manifests in the first week [3]. Elevated unconjugated bilirubin levels can lead to neurological damage, including in the auditory and visual pathways [4, 5]. This study aims to assess the impact of neonatal hyperbilirubinemia on the optic nerve, focusing on retinal nerve fiber layer (RNFL) thickness and optic cup-to-disc ratio.

Methods:
This cross-sectional study was conducted at a tertiary care center, targeting children aged 6-18 years. A total of 62 patients were enrolled, including 31 with a history of neonatal hyperbilirubinemia and 31 without such a history (control group). The groups were matched for sex and age. Optical coherence tomography (OCT) imaging was performed on all participants, and data were analyzed using SPSS software.

Results:
The mean age of participants is 9.32 years. There was no significant difference in average RNFL thickness ($p=0.81$), RNFL quadrants, or optic cup-to-disc ratio ($p=0.17$) between the control and hyperbilirubinemia groups. No significant differences in visual acuity were found between groups (p-value=0.27, control vs hyperbilirubinemia). A sub-analysis within the hyperbilirubinemia group revealed higher RNFL measurements in severe cases compared to mild ones ($p< 0.05$). The average cup-to-disc ratio was significantly higher in mild hyperbilirubinemia cases compared to severe ones ($p< 0.001$).

Conclusions:
This study reveals no significant differences in optic nerve characteristics between children with and without neonatal hyperbilirubinemia. However, cases of severe hyperbilirubinemia demonstrate greater RNFL thickness compared to mild cases, indicating possible localized effects, potentially through a neurotoxic mechanism that promotes neural regeneration and increased thickness. Further research with larger sample sizes and longitudinal follow-up is needed to better understand the relationship between hyperbilirubinemia and optic nerve changes.

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Keywords: Neuroimaging, Optic neuropathy, Pediatric neuro-ophthalmology, Visual fields, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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The Rates of Retinal Nerve Fiber Layer Change in Children with Optic Disc Drusen

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Introduction:
Optic disc drusen (ODD) are calcified deposits in the prelaminar portion of the optic nerve head. Although often asymptomatic, it can damage optic nerve fibers, resulting in irreversible vision loss. This study evaluates rates of structural changes in children with ODD and risk factors associated with faster rates of retinal nerve fiber layer (RNFL) thinning.

Methods:
This was a retrospective cohort study including 40 eyes of 22 children with ODD and 40 eyes of 20 age-, gender-, and race-matched glaucoma suspects. Subjects were required to have at least 3 optical coherence tomography (OCT) tests and a minimum of 18 months between the first and last OCT. Linear mixed models estimated RNFL changes over time. Univariable and multivariable models assessed the effect of clinical variables on rates of change.

Results:
Children with ODD were followed for an average of 4.1 ± 2.5 years. Eyes with ODD had rates of RNFL change significantly faster than the glaucoma suspect group (-2.01±1.53 µm/year versus -0.07±0.47 µm/year, P< 0.001). The multivariable model revealed older age and higher RNFL at baseline significantly associated with faster rates of RNFL thinning, with 0.37 µm/year faster loss for each year older (P= 0.040) and 0.07 µm/year faster loss for each µm higher RNFL at baseline (P= 0.030).

Conclusions:
Children with ODD demonstrate significant rates of RNFL thinning over time. Knowing the distribution of RNFL change attributable to ODD in children will enable clinicians to identify rapid progressors and/or alternative etiologies of optic nerve injury.

References: None provided.

Keywords: Pediatric neuro-ophthalmology, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Optic neuropathy

Financial Disclosures: Tais Estrela; jacqueline jeon-chapman; Gena Heidary; Eric Gaier: Luminopia Inc. (advisor, equity, patent), Stoke Therapeutics Inc (consultant), Neurofieldz Inc (consultant); Ryan Gise

Grant Support: none

Contact Information: None provided.

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Pediatric Idiopathic Intracranial Hypertension with Venous Sinus Stenosis and Congenital Sinus System Anomalies: Outcomes Following Medical Management

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Introduction:
To investigate outcomes following medical management of pediatric patients with idiopathic intracranial hypertension (IIH) who show dural venous sinus stenosis and congenital venous anomalies.

Methods:
34 pediatric patients diagnosed with IIH who showed dural venous sinus stenosis and/or congenital venous anomalies at a tertiary referral center were reviewed. Clinical features, imaging characteristics (OCT RNFL, MRI, MRV), and outcomes following medical management were noted.

Results:
Mean age at diagnosis was 14 years (range, 6 to 19), with 24(71%) patients female. All 34(100%) had papilledema on clinical examination with mean RNFL thickness of 242 um (range, 128 to 372). Average body mass index was 34.2 kg/m2 with 32(94%) patients in >90th percentile. On MRV, all patients were noted to have stenosis of dural venous sinus(es). 32 patients (94%) had junctional stenosis localized to transverse sinus, with 18 patients (53%) having unilateral and 14 patients (41%) having bilateral stenosis. 2 patients (6%) had stenosis of sigmoid sinus. Additional findings including right/left dominant transverse/sigmoid sinus system and high riding jugular bulb were noted in 8(24%) cases. All 34(100%) were treated with acetazolamide (Diamox). Treatment response was noted in all with 29(85%) showing resolution of papilledema within 3 months and all 34(100%) showing complete resolution within 9 months. Clinical response was correlated using OCT RNFL showing significant decrease in RNFL thickness. Recurrence was noted in 5(15%) patients with 80% attributed to compliance issues. Recurrence was successfully managed in all 5(100%) using oral treatment. Patients were followed up for (mean) 31 months (range, 8 to 48), with none requiring venous sinus stenting.

Conclusions:
Pediatric IIH with venous sinus stenosis can be managed medically with favorable outcomes without need for venous sinus stenting, including in cases where congenital venous system anomalies exist. Given possible complications, cautious use of venous sinus stenting is advised in pediatric population with IIH.

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Keywords: Pediatric neuro-ophthalmology, Neuroimaging, High intracranial pressure/headache, Interventional neuroradiology, Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None

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Treatment of increased intracranial pressure secondary to Otitic Hydrocephalus with corticosteroids and factors associated with treatment failure leading to procedural intervention.

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Introduction:
Otitic hydrocephalus is a rare complication of acute mastoiditis that may lead to significant visual morbidity. Given that no standardized treatment exists, this study aims to evaluate the impact of corticosteroids on visual outcomes.

Methods:
This was a retrospective chart review of children < 18 years old diagnosed with otitic hydrocephalus evaluated by ophthalmology between July 2022 to July 2024 at a quaternary children's hospital. Data from ophthalmologic visits, clinic and surgical treatments were recorded. Unpaired T-test was used for statistical analysis.

Results:
Fourteen patients (9 male) were identified. The average age was 5.6 years (range 2-9). All patients were treated with acetazolamide, anticoagulation and antibiotics. Papilledema was reported in all patients at presentation and progressed in seven patients (50%), despite improving clot burden. Two patients (14%) were treated with only surgery, including otologic (e.g. mastoidectomy) and ventriculoperitoneal shunt. Twelve patients had corticosteroid treatment initially, and four (29%) of these patients required further neurosurgery to control papilledema. For the patients who improved on corticosteroids, papilledema improved in five (63%) of these patients and three required acetazolamide increase. Visual acuity at was a risk factor for failure of steroid therapy (p=0.01). Final visual outcome, Frisen grade at presentation and time to initiation of steroids were not significant in predicting corticosteroid failure. Patients who received corticosteroids had a significantly (p< 0.01) reduced duration of hospital stay (17 days), when compared to patients who needed further surgery (28 days).

Conclusions:
This case series highlights the value of corticosteroids as an important part in the treatment of otitic hydrocephalus. It plays a role in reducing hospital admission duration. It also demonstrates the need for close follow up, especially in patients with poorer visual acuity, as surgical intervention for increased intracranial pressure may still be needed for visual preservation.

References: None provided.

Keywords: Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Visual Hallucinations, Quality of Life, and Psychological Distress in Visually Impaired Adolescents with Charles Bonnet Syndrome

Alison Martin [1], Sachin Iyer [2], Deepta Ghate [2], Sachin Kedar [1]

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Introduction:
We studied the prevalence, clinical features, and impact of Charles Bonnet Syndrome (CBS) on quality of life (QoL) and psychological distress in visually impaired adolescents.

Methods:
Adolescent patients (age 10-19 years; WHO definition) with low vision (better visual acuity 20/70 or worse) seen in the eye clinic between 7/1/2024 and 8/31/2024 were included. Those with known psychotic disorder, on antipsychotic medications, developmental delay, or impaired communication were excluded. Eligible and consented subjects were administered: Chicago Hallucination Assessment Tool (CHAT) to assess visual hallucinations; K-10 to assess psychological distress; PedEyeQ5-11 (ages 10-11), PedEyeQ12-17 (ages 12-17), and NEI-VFQ-25 (ages 18-19) to assess vision-related QoL. Nineteen (17 with CBS and 2 without CBS) completed the interview.

Results:
Of 57 low vision adolescents, 19 (33%) had visual hallucinations. The CBS group included 8 (42%) males and 11 (58%) females. The average age was 14.8 years (10-19). Visual acuity in the better eye varied, from 20/70 to light perception. Glaucoma (32%), retinal detachment (16%), and chronic anterior uveitis (11%) were the most common causes of vision loss. Hallucinations included spots of light or color (11.8%); simple forms, shapes, or lines (70.6%); poorly formed objects or human-like figures (23.5%); fully formed detailed humans, animals, or objects (5.9%). Hallucinations were black and white for 41% and colored for 59%, with red being the most common color. The age-appropriate vision-related QoL domain and composite scores were worse for CBS compared to non-CBS adolescents. K10 psychological distress scores were worse in CBS (19.5) compared to non-CBS (13.5) adolescents.

Conclusions:
Contrary to our current understanding, the 33% prevalence of CBS among low vision adolescents is similar to the adult population. Adolescents with low vision should be screened for visual hallucinations given the adverse impact of CBS on QoL and psychological distress in this vulnerable group.

References: None provided.

Keywords: Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Differences In The Diagnostic Approach Of Medical Trainees To A Case Of Pharmacologic Anisocoria

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Introduction:
The importance of history taking in correctly diagnosing neuro-ophthalmological problems has been previously reported1, but medical trainees may rely on diagnostic testing over history relative to attending physicians2. This study examined medical trainees' diagnostic approach to a case of pharmacologic anisocoria.

Methods:
31 medical students, ophthalmology residents, and neurology residents completed a simulated case of glycopyrronium-induced anisocoria. The number of history questions asked, exam maneuvers performed, and tests ordered by each participant was compared between these three groups, as well as between trainees who did vs did not reach the correct diagnosis.

Results:
Pharmacologic anisocoria was correctly diagnosed by 26% of participants (1 student, 7 residents). Medical students trended towards ordering more diagnostics on average than either neurology or ophthalmology residents (8.0 vs 6.1 vs 3.0, p=0.08), but also asked more history questions (22.5 vs 19.6 vs 11.0, p=0.03). Trainees who correctly diagnosed the patient ordered significantly fewer tests (1.8 vs 7.4, p=0.0007) and did not ask more questions (13.8 vs 19.9, p=0.13).

Conclusions:
Medical students did not spend less time on history taking than residents but were less likely to recognize the correct diagnosis and ordered more testing. In line with prior reviews that identified "intolerance of diagnostic uncertainty" as contributing to overtesting3, all trainees who arrived at the correct diagnosis ordered far fewer tests. Furthermore, our results highlight the importance of taking a relevant history rather than simply a comprehensive one. With the increasing use of topical anticholinergics for hyperhidrosis, awareness and accurate recognition of pharmacologic mydriasis among trainees will help their patients avoid the financial burdens of unnecessary and potentially invasive testing.

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Keywords: Pupil

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Delivering Neuro-Ophthalmic Care Around the World [2.00]

Moderators: Michael Lee, MD & Steffen Hamann, MD, PhD

Introduction: *Michael Lee, MD & Steffen Hamann, MD, PhD*
Neuro-Ophthalmology Practice and Healthcare Accessibility in Korea, *Hyun Jin Shin, MD, PhD*
Neuro-Ophthalmology in the Global South: What Works Where Resources are Limited, *Umapathi Thirugnanam, MD*
Delivering Neuro-Ophthalmic Care: The United States Experience, *Kevin E. Lai, MD*
Neuro-Ophthalmology in Latin America, *Alvaro Mejia-Vergara, MD*
Interdisciplinary Neuro-Ophthalmology and Neuro-Otology Patient Care – the Zürich Model, *Konrad P. Weber, MD*
Neuro-Ophthalmology Workforce/Pipeline in South Asia, *Aastha T. Kapila, MD, DM*
Innovative Care Models: Group Consultations in IIH and Quality Improvement Implementation, *Sui H. Wong, MBBS, MD, FRCP*
Keynote: Workforce Challenges in Ophthalmology and Beyond, *Stephen McLeod, MD*

This symposium will highlight how neuro-ophthalmic care varies domestically and internationally. Speakers will discuss the unique challenges and opportunities particular to their region. In addition, the symposium will address specialized clinical care models for idiopathic intracranial hypertension and dizziness. The symposium concludes with a keynote address discussing workforce challenges in ophthalmology by the Chief Executive Officer of the American Academy of Ophthalmology, Stephen McLeod, MD.

Upon completion of this session, participants should be able to:
(1) Identify challenges facing ophthalmology in the United States.
(2) Discuss innovative care models for idiopathic intracranial hypertension and dizziness.
(3) Describe neuro-ophthalmic care in Latin America, South Korea, and Singapore.

NEURO-OPHTHALMOLOGY PRACTICE AND HEALTHCARE ACCESSIBILITY IN KOREA

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LEARNING OBJECTIVES

1. Identify that the types of diseases commonly seen in outpatient clinics in East Asia differ from those frequently encountered in Western countries.
2. Discuss practical tips for neuro-ophthalmologic care in Korea, with a focus on efficiently managing a high volume of patients.
3. Recognize ways to promote neuro-ophthalmology in countries where it is still under-recognized to ensure more patients can benefit from this subspecialty.

CME QUESTIONS

1. Select the statement that correctly describes the characteristics of neuro-ophthalmology in Korea.

   A. The neuro-ophthalmology fellowship training system is well-established.
   B. Due to high medical costs, it is often difficult for patients to visit the hospital on time.
   C. Korean neuro-ophthalmologists often face pressure to treat many patients quickly.
   D. Professions such as Optometry and Orthoptics are well-equipped to deliver prompt and effective neuro-ophthalmic care
   E. All of the above

2. The proportion of patients with giant cell arteritis and idiopathic intracranial hypertension (IIH) is large in neuro-ophthalmology clinics in Korea
   A. True
   B. False

KEYWORDS

1. Practice patterns
2. Infrastructure
3. Korean medical crisis

HIGHLIGHTS

- Differences Between East Asia and Western Countries
  - Neuro-ophthalmology in East Asia has distinct differences from Western countries. For instance, diseases like idiopathic intracranial hypertension (IIH) and giant cell arteritis (GCA), which are prevalent in Western neuro-ophthalmology clinics, are relatively rare in East Asia.
  - In East Asia, the proportion of optic neuritis cases caused by multiple sclerosis (MS) is lower than that in Western countries. As a result, when East Asian patients who have immigrated to the West present with vague or nonspecific neurological symptoms and non-specific white matter abnormalities on brain imaging, they are sometimes mistakenly diagnosed with MS.

- Neuro-ophthalmology care in Korea
  - Generally, medical care in Korea is relatively accessible due to low medical costs and the high number of ophthalmologists

- In Korea, neuro-ophthalmologists often have dual specialization, with many also practicing pediatric ophthalmology and strabismus. As a result, a significant proportion of patients visiting neuro-ophthalmology clinics present with issues related to double vision or eye movement disorders.
- Many neuro-ophthalmologist perform surgery, mostly strabismus surgery, and some oculoplastic surgery. The advantage of this approach is that streamlined care is possible when patients visit the neuro-ophthalmology clinic without needing to see multiple ophthalmologists. For example, a patient with thyroid-associated ophthalmopathy (TAO) and compressive optic neuropathy can conveniently receive all care from the same physician including intravenous steroid therapy, orbital decompression surgery, and strabismus surgery.
- In Korea, neuro-ophthalmology clinics have developed efficient methods to care for a large number of patients. They use mobile messaging apps for quick communication and to send medical questionnaires to patients in advance, allowing them to fill them out at home before their appointments. Additionally, patients receive notices with QR codes that provide more information about their eye conditions when scanned with their phones. This approach not only saves time but also enhances patients' understanding and engagement in their own care, making the overall process faster and more effective for everyone involved.

- Research
  - Our research team has developed a set of innovative devices for measuring extraocular muscle tension. These tools are specifically designed to enhance the precision of strabismus surgery, particularly benefiting patients who suffer from double vision. The user-friendly interface and compact design of these devices make them easy for ophthalmologists to integrate into their daily practice

- Challenges in Korean Neuro-ophthalmology
  - Korea lacks professions such as optometry and orthoptics, so there is a lack of specialized support for visual rehabilitation. Additionally, there is no formal neuro-ophthalmology fellowship training program in Korea, which poses a challenge for specialized training in this field. Neuro-ophthalmology is less recognized as a distinct subspecialty by the general public and even some healthcare professionals, which can lead to delayed referrals and underutilization of neuro-ophthalmology services.
  - Since the establishment of the Korean Neuro-Ophthalmology Society in 2009, many young doctors have pursued specialized neuro-ophthalmology training abroad and have attended NANOS meetings to expand their knowledge and actively participate in the field.
  - Resources like NOVEL (Neuro-Ophthalmology Virtual Education Library), neuro-ophthalmology webinars, and educational YouTube videos are highly beneficial in training doctors in countries where neuro-ophthalmology remains underrecognized. These resources help bridge knowledge gaps, offering accessible, specialized education to improve understanding and practice in the field.

- 2024 South Korean medical crisis
  - The 2024 South Korean medical crisis occurred when new government policies announced significantly increasing medical student quotas. Thousands of residents and interns have since resigned, which has resulted in medical school professors working to cover for residents
  - As a result, many university hospital emergency rooms operate at reduced capacity. This has severely impacted patient care, particularly for those with urgent needs. For instance, patients requiring immediate treatment like optic neuritis caused by neuromyelitis optica (NMO) have faced delays in receiving timely care.
  - The crisis also has taken a toll on medical professionals. Many university hospital professors reported experiencing burnout as they struggle to manage their own duties while also covering for absent residents. This intense pressure has led several experienced professors to leave their positions at universities, creating a gap in medical expertise and experience. The repercussions of this crisis are expected to have long-lasting effects on the Korean healthcare system. The loss of experienced personnel and the disruption to medical education and patient care are likely to create challenges that will persist for a prolonged time, well after the immediate crisis is resolved.

SUMMARY

Neuro-ophthalmology in East Asia, especially in Korea, has distinct features compared to Western regions. Conditions like idiopathic intracranial hypertension, giant cell arteritis, and optic neuritis related to multiple sclerosis are less

common here. Many Korean neuro-ophthalmologists hold dual subspecializations, often blending their practice with pediatric ophthalmology and strabismus. Korean clinics have also created streamlined ways to handle a high volume of patients, utilizing mobile messaging for fast communication and sending out pre-appointment medical questionnaires, allowing patients to complete them from home. Patients also receive QR codes linked to information about their eye conditions.

However, the field encounters challenges, such as a limited number of specialized professionals and the lack of formal neuro-ophthalmology fellowship programs. Separate from these issues, the 2024 medical crisis in Korea has worsened healthcare availability, with widespread resignations among residents and interns, leading to reduced hospital capacity and delays in neuro-ophthalmologic care.

CME ANSWERS

1. **C**
2. **B**

NEURO-OPHTHALMOLOGY IN THE GLOBAL SOUTH: WHAT WORKS WHERE RESOURCES ARE LIMITED.

Umapathi Thirugnanam
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Singapore

LEARNING OBJECTIVES

1. Describe the challenges to optimal neuro-ophthalmology practice in the developed world
2. Discuss the challenges of applying evidence-based medicine in resource limited settings.
3. Recognize the basis of creative "disruptive" initiatives to enable patients in the Global South to achieve outcomes similar to those in the developed world

CME QUESTIONS

1. The "fortune at the base of the pyramid" in economic terms, refers to the untapped economic potential in developing countries.
    A. True
    B. False

2. Clayton Christensen's idea of "disruptive innovation" refers to technologies that disrupt creativity.
    A. True
    B. False

3. The key to achieving clinical outcomes similar to developed countries is via innovative care delivery.
    A. True
    B. False

KEYWORDS
1. Specialist expertise
2. Base of the pyramid
3. Democratization of evidence production
4. Disruptive innovation
5. Innovative care delivery

HIGHLIGHTS
Articles 3 and 1 of the Universal Declaration of Human Rights state:

Everyone has the right to life, liberty and security of person,
All human beings are born free and equal in dignity and rights.
They are endowed with reason and conscience and should act towards one another in a spirit of brotherhood.

Yet tremendous disparity exists in the provision of life, limb and vision threatening health-care in different parts of the world,

SUMMARY
I speak largely from my personal experience gleaned from working in various under-served regions.

There is an unmet need for specialist expertise, such as neuro-ophthalmologists, to complement the development of general clinical medicine in developing countries. The limited resources make evidence-based medicine as important for those living in the economic "base of the pyramid", as their counterparts in the developed world. Evidence collection should therefore be made more democratic and not ignore the unique needs of the significant segment of the global population that live in under-resourced areas.

I discuss "disruptive" enabling initiatives and technologies that improve the care provided by clinicians working in the Global South. Whenever possible, I shall use illustrative case studies and real examples; for instance initiatives to make indispensable diagnostic tests like aquaporin antibodies more widely accessible.

"These unhappy times call for the building of plans that rest upon the forgotten, the unorganized but the indispensable units of economic power, for plans like those of 1917 that build from the bottom up and not from the top down, that put their faith once more in the forgotten man at the bottom of the economic pyramid." Franklin Roosevelt 1932

CME ANSWERS

1. A
2. B
3. A

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DELIVERING NEURO-OPHTHALMIC CARE AROUND THE WORLD: THE UNITED STATES EXPERIENCE

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LEARNING OBJECTIVES

1. Review the workforce distribution and demands within the United States population
2. Describe various practice settings of clinical neuro-ophthalmologists within the United States
3. Identify unique challenges to clinical neuro-ophthalmology practice within the United States

CME QUESTIONS

1. As of June 2024, what states lack an actively practicing neuro-ophthalmologist?
   A. Delaware, Montana, South Dakota, Wyoming
   B. Delaware, New Mexico, Maine, Montana, South Dakota, Wyoming
   C. Maine, South Dakota, Wyoming
   D. Alaska, Montana, Wyoming

2. Based on a 2019 survey of United States NANOS members actively practicing neuro-ophthalmology, what is the approximate average amount of time, in weekly half-days, respondents spent in clinical neuro-ophthalmology?
   A. 2.5 half-days (0.25 FTE)
   B. 5 half-days (0.5 FTE)
   C. 7.5 half-days (0.75 FTE)
   D. 10 half-days (1.0 FTE)

3. Approximately what is the average travel time (by car) to the nearest neuro-ophthalmologist in the United States?
   A. 15 minutes
   B. 30 minutes
   C. 45 minutes
   D. 60 minutes

KEYWORDS

1. Neuro-Ophthalmology
2. United States
3. Healthcare Access
4. Workforce
5. Pipeline

HIGHLIGHTS

- Neuro-ophthalmology practice in the United States is characterized by marked heterogeneity in practice and regional diversity.
- United States neuro-ophthalmologists are generally concentrated in larger population centers, with patients typically traveling to a referral center. The wide variance in geography and population distribution results in partially imbalanced access to neuro-ophthalmic care, which is exacerbated by workforce shortages.
- Challenges to healthcare access include geographic limitations, insurance coverage, and wait times.

SUMMARY

Diversity is a common feature of life in the United States. Likewise, neuro-ophthalmologists in the United States can choose from many permutations to stylize their practice. This heterogeneity offers the freedom for neuro-ophthalmologists to choose their practice based on personal preferences. However, it also limits the extent of analysis on the state of neuro-ophthalmic practice on a national level.

Neuro-Ophthalmology Workforce Shortages in the United States Have Been Developing Over Decades

In 2024, the North American Neuro-Ophthalmology Society (NANOS) Workforce and Patient Access Committee conducted a peer-based review of all United States physicians providing at least 0.1 clinical full-time equivalents (CFTE) of neuro-ophthalmic care. They found that 446 physicians provided neuro-ophthalmic care and that Alaska, Montana, and Wyoming were the only states without a neuro-ophthalmologist.[1] Larger metropolitan areas, such as Los Angeles (14) and New York City (22), had a higher number of neuro-ophthalmologists. In many states, neuro-ophthalmologists were based in the state's largest cities. These results support other methodologies that have been used recently for assessing the neuro-ophthalmology workforce, such as by self-reported survey,[2] NANOS's "Find a Neuro-Ophthalmologist" public directory,[3] other public directories,[4] and claims-based data analysis.[5] These studies highlight the overall scarcity of neuro-ophthalmic care across the US, which has been a focus of concern for nearly two decades.[6–11]

Neuro-Ophthalmology Practices Vary Widely

Career flexibility is one of the many appeals to practicing neuro-ophthalmology in the US. Debusk et al. found that the average US NANOS member spent 70% of their clinical time (56% of their total work time) on neuro-ophthalmology and that 41.3% have fellowship-level training in at least one other subspecialty of neurology or ophthalmology.[2] Solomon et al. found that among recent graduates of neuro-ophthalmic fellowships, 67% reported maintaining surgical practices, including 33% who performed cataract surgery (n=51).[12]

US neuro-ophthalmologists may practice in academic institutions, solo private practice, group private practice, private hospital-based systems, or government-based institutions (local or federal). They may be affiliated with ophthalmology, neurology, or neurosurgical departments. They may hold teaching positions as adjunct academic faculty or be employed by the university. In addition to their clinical duties, neuro-ophthalmologists often engage in clinical education and research. Some neuro-ophthalmologists are involved in their institution's administration. Many neuro-ophthalmologists consult with industry, may be retained as subject-matter experts for legal work, speak at continuing education events, and review clinical records for third parties. Neuro-ophthalmologists may serve in local, national, and international organizations, such as the American Academy of Neurology (AAN) or the American Academy of Ophthalmology (AAO).

Although these opportunities can attract trainees to include neuro-ophthalmology in their careers, they can also skew the analysis of workforce needs, as the actual number of physicians required for sufficient neuro-ophthalmic coverage may be much higher than reported.[13]

There Are Many "Deserts" of Neuro-Ophthalmic Care

Xue et al. found many geographic "deserts" within the US, where travel times to the nearest neuro-ophthalmologist may be 120 minutes or longer.[3] Stunkel et al. found similar results in an analysis of neuro-ophthalmology patients referred to a single tertiary neuro-ophthalmology referral center.[14] Despite the rapid adoption of telehealth services in response to the coronavirus-19 (COVID-19) pandemic, the promise of telemedicine to reduce barriers to healthcare may have worsened socioeconomic disparities instead.[15–16]

Wait times may also produce an access "desert" in certain regions; a 2019 NANOS survey noted a median wait time of 6 weeks for a new neuro-ophthalmology consult. 23% of the respondents reported wait times of 12 weeks or longer.[2]

Insurance coverage may also produce access "deserts" contributing to socioeconomic disparities in care. Because insurance coverage in the US varies based on employment, age, income, and personal choice, some populations may have

greater access to care than others based on affordability. Studying this disparity is challenging due to many factors, including referral bias and lack of data transparency.

CME ANSWERS

1. **D** The NANOS Workforce and Patient Access Committee conducted a neuro-ophthalmology peer-based review of all United States physicians providing at least 0.1 clinical full-time equivalents (CFTE) of neuro-ophthalmic care and found that Alaska, Montana, and Wyoming were the only states without any neuro-ophthalmology providers.

   Debusk et al (2019) reported no NANOS members in Delaware, New Mexico, Maine, Montana, South Dakota, and Wyoming.

   Pakravan et al. (2024) published a review of self-reported neuro-ophthalmologists listed in four public databases in 2023. They found that Maine, South Dakota, and Wyoming were the only states without any neuro-ophthalmologists.

   Xue et al. (2023) noted that Delaware, Montana, South Dakota, and Wyoming had no NANOS members based on the 2020 member directory.

2. **B** Debusk et al. reported that, on average, respondents spent 70% of their clinical time devoted to neuro-ophthalmology, or about 56% of a full-time work week, approximately 5.6 half-days (0.56 FTE).

3. **C** Xue et al. calculated the average time to the nearest neuro-ophthalmologist to be 46.50 minutes, with the average distance being 40.90 miles (65.82 kilometers). There was wide variation in time and distance based on location, with western plains and mountain regions having travel times of 120 minutes or longer.

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NEURO-OPHTHALMOLOGY IN LATIN AMERICA

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LEARNING OBJECTIVES

1. Describe the history of Neuro-ophthalmology in Latin-America.
2. Differentiate the practice patterns of Neuro-ophthalmology in some of the Latin-American countries.
3. Recognise the barriers for Neuro-ophthalmology expansion in Latin-America.

CME QUESTIONS

1. The availability of Neuro-Ophthalmology in Latin-America is
   A. 1 for every 100.000 people
   B. 1 for every 1.000.000 people
   C. 1 for every 5.00.000 people
   D. 1 for every 10.000.000 people

2. Neuro-Ophthalmic practice in Latin-American is more commonly
   A. Ophthalmology trained in an academic setting
   B. Ophthalmology trained in a mixed academic plus private practice
   C. Ophthalmology trained in a private setting
   D. Neurology trained in an academic setting

3. The major barrier for neuro-ophthalmic practice in Latin-America is
   A. Reimbursement
   B. Training opportunities
   C. Technological lag
   D. Unawareness of the scope of Neuro-ophthalmology by other medical professionals

KEYWORDS
1. Latin-America
2. Latin American Neuro-Ophthalmology Club (CLAN)
3. Scope of Practice

SUMMARY
The field of neuro-ophthalmology in Latin America has experienced significant growth since the late 1980s, marked by the establishment of the Latin-American Neuro-Ophthalmic Club (CLAN). What began with three members in 1988 has now expanded to include 70 fellowship-trained members, with an additional 40 fellowship-trained providers not affiliated with the CLAN. In total, 110 individuals are practicing neuro-ophthalmology across the region, with the majority in Chile, Argentina, Mexico, Brazil, Colombia, Peru, Ecuador, Panamá, and Venezuela. The current ratio of neuro-ophthalmic care providers to inhabitants is approximately 1:5,000,000.

Despite the growth of neuro-ophthalmology in Latin America, there are significant challenges in training and access to care. Most physicians are concentrated in their respective countries' major cities, leaving rural areas underserved. 82% of the providers are ophthalmology trained and work in a mixed-type practice with academic and private components. The academic appointments are usually at university hospitals catering to government-run medical insurance, with many patients and resident-training responsibilities. While neuro-ophthalmic training has become mandatory for most ophthalmology programs in Latin-America, it is optional in neurology residency programs, highlighting a need for further integration and collaboration.

Currently, most young neuro-ophthalmologists are locally trained. Mexico, Colombia, Chile, Argentina, and Brazil have 8-10 fellowship spots yearly. Interest in fellowship training has increased in the past ten years. 90% of the trainees come from ophthalmology residencies. The lack of knowledge of the pathologies and scope of Neuro-Ophthalmology in

Medical Schools and Neurology residencies is the major barrier to the expansion of neuro-ophthalmic care in Latin-America. Up to 60% of the patients in Colombia had an erroneous diagnosis at referral, and the median time to neuro-ophthalmic evaluation was 365 days from symptom onset, illustrating a significant gap in timely access to specialized care. Local groups have implemented innovative strategies, such as monthly case discussions in Colombia and monthly virtual lectures accessible to comprehensive ophthalmology and general neurologists in Mexico and Peru.

CME ANSWERS

1. C
2. B.
3. D

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INTERDISCIPLINARY NEURO-OPHTHALMOLOGY AND NEURO-OTOLOGY PATIENT CARE – THE ZÜRICH MODEL

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LEARNING OBJECTIVES

1. Identify a framework for establishing an interdisciplinary neuro-ophthalmology and neuro-otology center
2. Discuss hurdles to overcome in setting up the center
3. Recognize clinical challenges in the daily operation of the center

CME QUESTIONS

1. What are the advantages of an interdisciplinary center for neuro-ophthalmology and neuro-otology?

    A. Integrated patient care
    B. Pooled clinical expertise
    C. Better patient satisfaction
    D. Improved reputation and visibility
    E. All of the above

2. The smallest hurdle in setting up an interdisciplinary center is

    A. Administrative
    B. Clinical
    C. Financial
    D. Political

3. What are the most important factors for the smooth operation of an interdisciplinary center?

    A. Flat hierarchy and right chemistry between the different sub-specialists
    B. Spacial integration of the different clinics
    C. Careful triage and preparation of the consultations in advance (reports, MRI images, etc.)
    D. Shared administration for running the center
    E. All of the above

KEYWORDS

1. Neuro-Otology
2. Interdisciplinary center
3. Integrated patient care
4. Patient satisfaction

HIGHLIGHTS

The *Interdisciplinary Center for Vertigo and Neurological Visual Disorders*, located at the University Hospital Zurich, is a specialized clinical, teaching, and research center focused on diagnosing and treating complex cases of balance and neuro-ophthalmological disorders. Unique in its integrated approach, the center brings together a team of neurologists, ophthalmologists, ENT specialists, physiotherapists, psychiatrists, orthoptists, and specialized technicians who collaborate closely in a joint unit to provide holistic and patient-centered care.

SUMMARY

1. Patient Coordination
The key to efficient patient workup is careful triage to order all the necessary tests before the medical consultation. This involves obtaining records and previous ancillary examinations, including MRIs based on the referral letters by a common patient coordination office. Before the consultation, patients are given a tablet to take a structured history, including past medical history, medications, and relevant clinical scores. This not only supports the writing of the medical letter but can also be used for retrospective studies.

2. Facilities
Our center is located in a dedicated unit where all the specialists work in close proximity. All different sub-specialties offer comprehensive examination units and a wide range of ancillary tests:

Neuro-Ophthalmology Unit
- Slitlamp examination unit
- OCT
- Auto-refractometer, lens meter
- Static and kinetic perimetry
- Binocular pupillometry
- Comprehensive orthoptic examination unit
- Binocular video oculography (INO, strabismus, nystagmus measurement)
- Non-mydriatic fundus camera (incl. measurement of ocular counter-roll)
- Edrophonium test facility

Comprehensive vestibular test battery (examination of all 6 sub-organs of the labyrinth)
- Video head impulse test (all 6 semicircular canals)
- Ocular vestibular-evoked myogenic potentials (oVEMPs, utriculus test)
- Cervical vestibular-evoked myogenic potentials (cVEMPs, sacculus test)
- Audiogram (cochlear test)

Additional vestibular tests
- ENT examination unit
- Rotary chair (patient treatment for benign paroxysmal positional vertigo (BPPV))
- Caloric testing
- Computerized dynamic visual acuity (DVA)
- Subjective visual vertical (SVV)
- Sudoscan platform (small fiber polyneuropathy screening)
- Brainstem Auditory Evoked Response (BAERs)
- Digital volume tomography of the petrous bone (DVT)

Physiotherapy and gait lab
- Posturography
- Treadmill for gait analysis
- Sensory Organization Test (SOT)
- Functional gait assessment (FGA)
- Vestibular Physiotherapy

3. Patient care
Patients at our center benefit from streamlined care that addresses not only neuro-ophthalmological but also neuro-otological aspects of their symptoms. The physician's perspective is also complemented by the views of our orthoptists, physiotherapists, and psychologists. The patient workup includes cutting-edge examination techniques, including video head impulse testing, video-oculography, and advanced imaging techniques as outlined above, which facilitate accurate assessments of ocular motor and vestibular function.

In daily patient care, subspecialists keep learning more about each other's disciplines, making it easier to recognize diagnoses from adjacent specialties so that patients can be swiftly referred internally. For example, patients with benign

paroxysmal positional vertigo (BPPV), bilateral vestibular loss, or (vestibular) migraine are commonly encountered among neuro-ophthalmology patients. Similarly, vestibular patients often suffer from refractive errors, strabismus, or ocular motor problems, and treating these problems can improve their balance problems.

Interdisciplinary Teaching
The interdisciplinary cluster of specialists allows for setting up interdisciplinary symposia and courses for physicians in private practice. At our center, we focus on interactive, hands-on teaching involving all the different professions. For example, since 2012, we have organized symptom-oriented courses in practical neuro-ophthalmology and neuro-otology.

Research
In addition to clinical services, our center is deeply involved in research. Most of the ancillary tests are custom-made, and our center strives to continually improve and develop new tools and therapies to advance the diagnosis and treatment of balance- and vision-related neurological conditions.

CME ANSWERS
1. E
2. B
3. E

DELIVERING NEURO-OPHTHALMIC CARE: WORKFORCE & PIPELINE
NEURO-OPHTH WORKFORCE/PIPELINE AROUND THE WORLD- SOUTH ASIA / INDIA

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LEARNING OBJECTIVES

1. Determine the availability of neuro-ophthalmic care in South Asia and describe the structural, economic and cognitive barriers to neuro-ophthalmology access.
2. Identify the gap between demand and supply of the neuro-ophthalmic workforce and describe the neuro-ophthalmology training matrix in South Asia.
3. Discuss changing paradigms, strategies and growing prospects in neuro-ophthalmology care.

CME QUESTIONS

1. The proportion of physicians in India who practice a significant amount of neuro-ophthalmology is
   A. 15.6/ million population
   B. 0.08/million population
   C. 5.05/ million population
   D. 20/ million population

2. Which of the following is true about patients referred for neuro-ophthalmology opinion in South Asia?
   A. Neuro-ophthalmology referral consists of around 5- 10% of patients referred for ophthalmic assessment.
   B. More than 50% of patients referred for neuro-ophthalmology care are incorrect referrals.
   C. The most common cause of referral is cranial nerve palsies accounting for around 60 to 70% of referrals.
   D. Optic nerve disorders consist of 10- 20 % of neuro-ophthalmic referrals.

3. What is not true about neuro-ophthalmology care in India?
   A. Physicians practising neuro-ophthalmology are either ophthalmology or neurology certified or both.
   B. Neurologists practising neuro-ophthalmology complete at least 5 to 6 years of clinical training after medical school (5 years).
   C. Waiting time to obtain neuroimaging (MRI) varies from a few weeks to months in most patients with neuro-ophthalmic diseases
   D. The use of multidisciplinary approaches, artificial intelligence-based models and tele-neuro ophthalmology is on the rise.

KEYWORDS
1. Neuro-ophthalmology workforce
2. South Asia
3. India
4. Career choice
5. Training

HIGHLIGHTS

The gap between the demand and supply of neuro-ophthalmologists is striking across the globe, including South Asia. The neuro-ophthalmic ecosystem in South Asia and India is unique with its distinctive patient profile, referral structure, triage system and training matrix. Indian neuro-ophthalmology has undergone huge strides in the last ten years (much more rapid as compared to the previous 50 years).

SUMMARY

South Asia (including the Indian subcontinent) comprises several countries, impressively diverse in culture, religion, history, language, social ethos, and political configurations. It is the most populous region of the world and houses a quarter of the world's population.(1) Varied social determinants of health, human resources, and non-uniformity in regional data flow give rise to obvious barriers to providing dedicated neuro-ophthalmic health care.

The prevalence of visual impairment due to any cause has steeply risen globally (91.46% increase from 1990) and the assessment of the prevalence and incidence of specific neuro-ophthalmic disorders remains a challenge worldwide.(2) This is especially conspicuous in the South Asian region, where a considerable gap between demand and supply of neuro-ophthalmic workforce exists.

NEUROOPHTHALMIC ECOSYSTEM IN INDIA

India is a country in transition and the 'patient' profile with neuro-ophthalmic disorders is unique. While there is a huge proportion of patients with infectious causes, a fair percentage is shared by immune, metabolic, vascular, toxic, and hereditary causes, underscoring the growing need for neuro-ophthalmology experts.

NEURO-OPHTHALMIC HEALTHCARE- PEARLS AND OYSTERS

The triage and referral system in neuro-ophthalmology is highly heterogeneous contributing to delays in diagnosis and management. The public healthcare system in India is largely pyramidal with primary healthcare centres at the base. These centres are bound by inherent challenges of resource scarcity (both infrastructure and human resources) and geographical barriers. This is in contrast to most tertiary care centres which are fully equipped with state-of-the-art facilities and cater to patients referred from various primary and secondary care centres. Neuro-ophthalmic healthcare in India is largely concentrated in these centres of excellence. The first neuro-ophthalmology unit was established at Madras (now Chennai) in 1954 and recent years have seen huge leaps with expert neuro-ophthalmology units being established in many regions of the country. (Two in north India, two in west India, one in east and four in south India).
Despite enormous patient load and limited awareness amongst the general public, the waiting period for a patient with a suspected neuro-ophthalmic disorder to meet a specialist is negligible at most centres (with most routine patients managing to get a neuro-ophthalmology opinion within one week and most emergency patients on the same day). Similarly, most investigations (including advanced imaging, antibody testing and advanced ophthalmic/ neurological investigations) and therapeutic modalities (intravenous immunoglobulins, plasmapheresis, biologicals) can be availed promptly during emergent situations in most public institutes at subsidised prices. The cost of Magnetic Resonance Imaging(MRI) is also variable and varies from as low as $30 in the public sector to $300 in the private or corporate sector. This holds affirmative even for patients below the poverty line, who avail monetary and health benefits using various government schemes and aids. Multidisciplinary teams are available in the public sector and institutes of national importance, where the poorest patients can also avail the most advanced medical treatment. The private health care system runs in parallel and provides advanced neuro-ophthalmology care. Multidisciplinary hospitals run by the corporate sector, hospitals managed by charitable trusts and independent hospitals/ clinics form this portion of the neuro-ophthalmic workforce in India. These healthcare systems (both public and private) also cater to international patients, mostly from other regions of Southeast Asia.

NEUROOPHTHALMIC WORKFORCE- THE GAP BETWEEN DEMAND AND SUPPLY

Wide geographic and socioeconomic disparities in neuro-ophthalmic care have been recognised the world over, however, the problems of the South Asian regions are unique.(3) The number of physicians who practice a significant amount of neuro-ophthalmology in India is very- low (0.08/million population).(4) Similarly, only a handful of physicians practice neuro-ophthalmology in the rest of South/Southeast Asia (42 in the Philippines, 19 in Vietnam, 20 in Singapore, 4 in Malaysia, 3 in Myanmar, none in Sri Lanka and Pakistan).

Most certified neuro-ophthalmologists in India come from ophthalmology background after completing 08 to 09 years of medical training and often combine it with paediatric ophthalmology, oculoplasty or general ophthalmology practice.(5) Dedicated fellowship, observership and short-term training are offered in around 8 ophthalmology centres.
Indian neurologists undergo a rigorous 11 to 12 years of medical training before joining a neuro-ophthalmology fellowship and usually combine it with general neurology or neuro-immunology practice. Although neuro-ophthalmology has emerged as an independent subspecialty of neurology, only one neurology centre is currently offering formal neuro-ophthalmology training. The challenges in patient care, recent advances and ease of combining with other subspecialties have shifted the curve, with many ophthalmologists and neurologists opting for neuro-ophthalmology as a career choice in recent decades.

THE EMERGING DATA- MORE TO COME

The neuro-ophthalmology community in India contributes significantly towards patient care, publishing available literature, organising regular conferences or academic updates, and enhancing social awareness of general neuro-ophthalmic disorders. There are two registered societies- 1. Indian Neuro-ophthalmology Society (INOS) (246 members) and 2. Neuro-ophthalmology subsection of the Indian Academy of Neurology (IAN)(89 members); which have taken the

lead in actively executing the above.(6)(7) Global collaboration and telemedicine have come up in a big way, supporting the neuro-ophthalmology workforce in India.

CME QUESTIONS

1. B
2. A
3. C

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INNOVATIVE CARE MODELS IN NEURO-OPHTHALMOLOGY: GROUP CONSULTATIONS IN IDIOPATHIC INTRACRANIAL HYPERTENSION AND QUALITY IMPROVEMENT IMPLEMENTATIONS

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LEARNING OBJECTIVES

1. Discuss the potential of Group Consultations in Neuro-Ophthalmic care, with a focus on Idiopathic Intracranial Hypertension.
2. Recognize how to incorporate peer-to-peer patient support and patient co-development of service care models, as part of a patient-centred approach to neuro-ophthalmic care
3. Implement quality improvement science in the evaluation of innovative care models

CME QUESTIONS

1. Group consultations (group clinics) are an untested model of medical care
   A. True
   B. False

2. Idiopathic intracranial hypertension is a condition can benefit from peer-to-peer support
   A. True
   B. False

3. Quality improvement science provides a framework to assess and implement innovative models of care
   A. True
   B. False

KEYWORDS

1. Group consultations
2. Patient peer support
3. Patient-centred care
4. Idiopathic intracranial hypertension
5. Quality improvement

HIGHLIGHTS/ SUMMARY

Dr Wong will discuss a quality-improvement approach in the development of innovative care models in Neuro-Ophthalmology, with a focus on group consultations (group clinics) for people with Idiopathic Intracranial Hypertension. The presentation will include how the delivery of these care models can be done as part of a scholarly effort with implementation of Quality Improvement science for the evaluation of service improvements. This includes an approach of patient-centred care with patients co-developing such models of care.

To illustrate this process, Dr Wong shares the development and delivery of a new model of care, with group consultations for people with Idiopathic Intracranial Hypertension. This model, which was co-developed with patients, includes a virtual pathway for ophthalmic assessment, group clinic for review of individual patient's progress and peer-to-peer patient support within the group clinic session. Lessons and challenges will be shared for attendees to develop this within their own service setting.

CME ANSWERS

1. **B**
2. **A**
3. **A**

REFERENCES

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Member Submitted Symposium: How to Implement a Non-Mydriatic Retinal Camera in General Emergency Departments and in Neurology Clinics [1.5 CME]

Director: Valerie Biousse, MD Speakers: Aubrey Gilbert, MD, Nancy Newman, MD, Oana Dumitrascu, MD, Mung Yan (Amy) Lin, MD, Kevin Yan, MD

This symposium will discuss the implementation of non-mydriatic fundus cameras (color and OCT) in general Emergency Departments (ED) and Neurology Clinics. This will be an interactive session moderated by speakers who have experience with such implementation. 8 Upon completion of this session, participants should be able to:

(1) Summarize the rationale supporting the need to deploy non-mydriatic ocular fundus cameras in non-ophthalmic settings such as Emergency Departments (ED) and Neurology Clinics where eye care providers are not readily available.

(2) Discuss the advantages and disadvantages of various types of cameras in the ED.

(3) Review potential outcome measures to assess the impact of non-mydriatic retinal cameras in EDs.

HOW TO IMPLEMENT A NON-MYDRIATIC RETINAL CAMERA IN GENERAL EMERGENCY DEPARTMENTS AND IN NEUROLOGY CLINICS

Moderators/Participants:

-Valérie Biousse, MD [Emory University School of Medicine, Atlanta GA]

-Nancy Newman, MD [Emory University School of Medicine, Atlanta GA]

-Aubrey Gilbert, MD, PhD [The Permanente Medical Group/Kaiser Permanente, CA]

-Oana Dumitrascu, MD [Mayo Clinic Alxy School of Medicine, Scottsdale, Arizona]

-Invited guest: Mung (Amy) Yan Lin, MD and Kevin Yan, MD [Neuro-ophthalmology fellows, Emory University School of Medicine, Atlanta GA]

LEARNING OBJECTIVES

1. Understand the rationale supporting the need to deploy non-mydriatic ocular fundus cameras in non-ophthalmic settings such as Emergency Departments (ED) and Neurology Clinics where eye care providers are not readily available.
2. Discuss the advantages and disadvantages of various types of cameras in the ED.
3. Review potential outcome measures to assess the impact of non-mydriatic retinal cameras in EDs.

CME QUESTIONS

1. Implementation of a non-mydriatic retinal camera in an emergency department may have the following impact:
   A. Facilitate on site ophthalmologic examinations
   B. Allow remote interpretation of pictures to rule-out papilledema
   C. Allow remote rapid diagnosis of acute central retinal artery occlusion
   D. Reintroduce the examination of the ocular fundus into routine ED and neurologic evaluations
   E. All of the above.

2. Obstacles to implementation of a non-mydriatic retinal camera in the ED include
   A. Lack of data showing that it is feasible
   B. Lack of evidence that a camera will be used by ED providers
   C. Belief that it is too expensive and will not be used enough
   D. Difficulty for ED staff to obtain fundus photographs
   E. Need to pharmacologically dilate the pupils to obtain high quality photographs

3. There is evidence in the literature that non-mydriatic fundus cameras:
   A. Can be implemented successfully in a general ED
   B. Can be used reliably by trained ED staff
   C. Can replace the direct ophthalmoscope
   D. Improve quality of care
   E. All of the above

KEYWORDS

1. Non mydriatic retinal camera
2. Non mydriatic optical coherence tomography
3. Emergency department
4. Ocular funduscopic examination
5. Central retinal artery occlusion

HIGHLIGHTS

This will be an interactive session between the 4 moderators and the audience to address common questions that arise when planning to implement a retinal camera in Neurology clinics and in general Emergency departments (EDs), especially those where there is no ophthalmology coverage.

All 4 moderators have extensive experience with implementation and use of various types of cameras in general EDs and in neurology clinics. They will be ready to discuss pros and cons as well as best practices to overcome inevitable issues and hurdles associated with implementation. We will ask the audience to submit questions in advance of the symposium at the NANOS conference.

Our invited guest is a current neuro-ophthalmology fellow who has taken many ophthalmology and neuro-ophthalmology calls in the Emory University Hospital ED before and after the camera was implemented. She will be able to address the impact of the camera on the diagnosis of ophthalmic emergencies by trainees, and rule-out of papilledema in the ED. She will also highlight the positive impact of having ocular imaging technology in the ED on resident wellness and performance.

SUMMARY

This 90-minute optional symposium will discuss the implementation of non-mydriatic fundus cameras (color and OCT) in general EDs and Neurology Clinics. Over the past year, a few NANOS members have had numerous discussions with the NANOS community regarding this topic and we anticipate interactive and lively discussions at the NANOS conference. This will be an interactive session moderated by NANOS members who have experience with such implementation. These moderators will set the stage by each addressing a specific issue in a few minutes, followed by interactive discussions with the audience. We will also have a current neuro-ophthalmology fellow who has personal experience with the use of such cameras while on call in the ED (both as a resident and as a fellow) participate in the discussion.

<u>We will specifically address:</u>

1. The rationale supporting the need to deploy non-mydriatic ocular fundus cameras in non-ophthalmic settings such as Emergency Departments (ED) and Neurology Clinics where eye care providers are not readily available.
2. How to convince your administration that such expense is beneficial for the hospital.
3. Advantages and disadvantages of various types of cameras in the ED, including color fundus photography versus OCT or both.
4. I have the money: what needs to be done to be successful – a step by step approach.
5. I have the camera: how to use the camera for remote diagnosis and Eye Stroke Protocols.
6. Metrics: measuring the benefits and the outcomes of having a camera in the ED.

Table 1: Possible outcome measures supporting the implementation of a non-mydriatic ocular fundus camera in a general emergency department. [Ref 7]

-Number of photographs/OCTs obtained by ED staff per week
-Number of photographs/OCTs obtained by tech in a Neurology Clinic
-Successful billing for all imaging studies
-Identification of prevented diagnostic errors
-Number of central retinal artery occlusions diagnosed within 6 hours of vision loss
-Number of central retinal artery occlusions treated with intravenous thrombolysis within 4.5 hours of vision loss or intraarterial thrombolysis within 6 hours of vision loss
-Length of stay in the ED for patients with papilledema or presumed papilledema
-Number of in-person ophthalmology consultations avoided by remote interpretation of ocular imaging studies obtained in the ED
-On call ophthalmology residents' satisfaction
-On call neurology residents' satisfaction
-ED staff's satisfaction
-ED providers' satisfaction
-Neuro-hospitalists/stroke specialists' satisfaction
-Outpatient neurologists' satisfaction
-Screening of various ocular diseases in the ED

ED: emergency department; OCT: optical coherence tomography

Table 2: Types of commercialized non-mydriatic ocular fundus cameras. Comparison of table-top and handheld non-mydriatic fundus cameras, detailing advantages and disadvantages. [Ref 7]

	Advantages	Disadvantages
Table-top models	• Robust • Higher quality camera optics providing high quality photographs, even without pharmacologic dilation of the pupils • Very user-friendly • Semi-automated image capture • Easy integration into EMR (most are DICOM compatible) • Possible combination of color fundus photographs and OCT images in hybrid models • Some models offer widefield imaging and autofluorescence imaging • Some models offer imaging of the anterior segment of the eye in addition to retinal imaging	• More expensive • Take space and require dedicated room in ED • Require specific table • Require that patients be able to sit up and cooperate
Handheld models	• Less expensive • Portable • Bedside use possible	• More difficult to use with steep learning curve, especially without pharmacologic dilation of the pupils • More fragile • Often lower quality photographs compared to table-top camera • Battery requires recharge • Not all handheld cameras have automated integration into EMR • No additional imaging modalities available (e.g., OCT) • Limited storage capacity

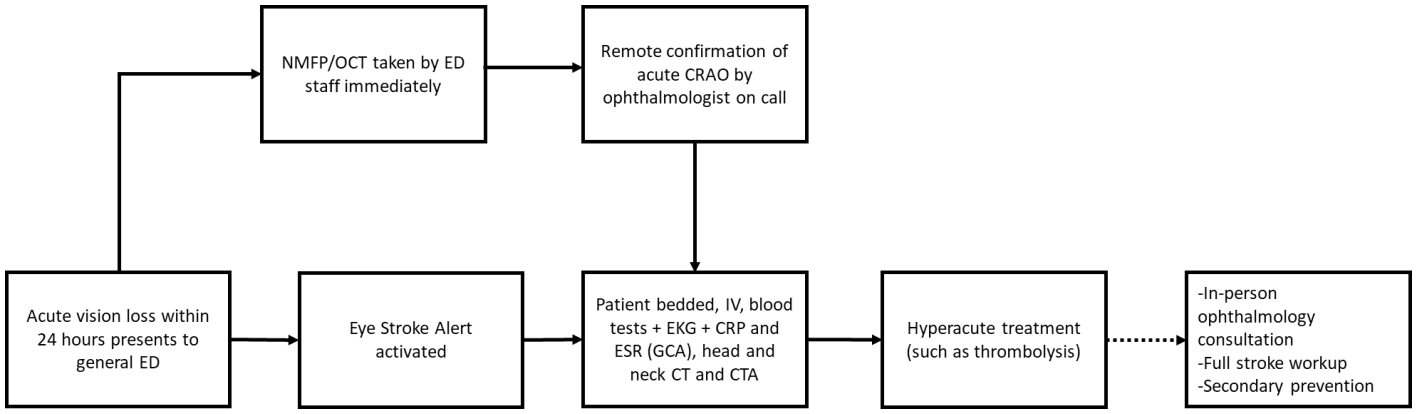
ED: emergency department; EMR: electronic medical record; DICOM: Digital Imaging and Communications in Medicine; OCT: optical coherence tomography

Table 3: General considerations prior to choosing non-mydriatic ocular fundus camera model for emergency department use. [Ref 7]

Basic requirements • Non-mydriatic • DICOM compatible • 45-degree view to image optic nerve and macula
Advisable options • Semi-automated (most user-friendly) • True color image • Integrated OCT • Other capabilities such as peripheral retina and anterior segment imaging

DICOM: Digital Imaging and Communications in Medicine; OCT: optical coherence tomography

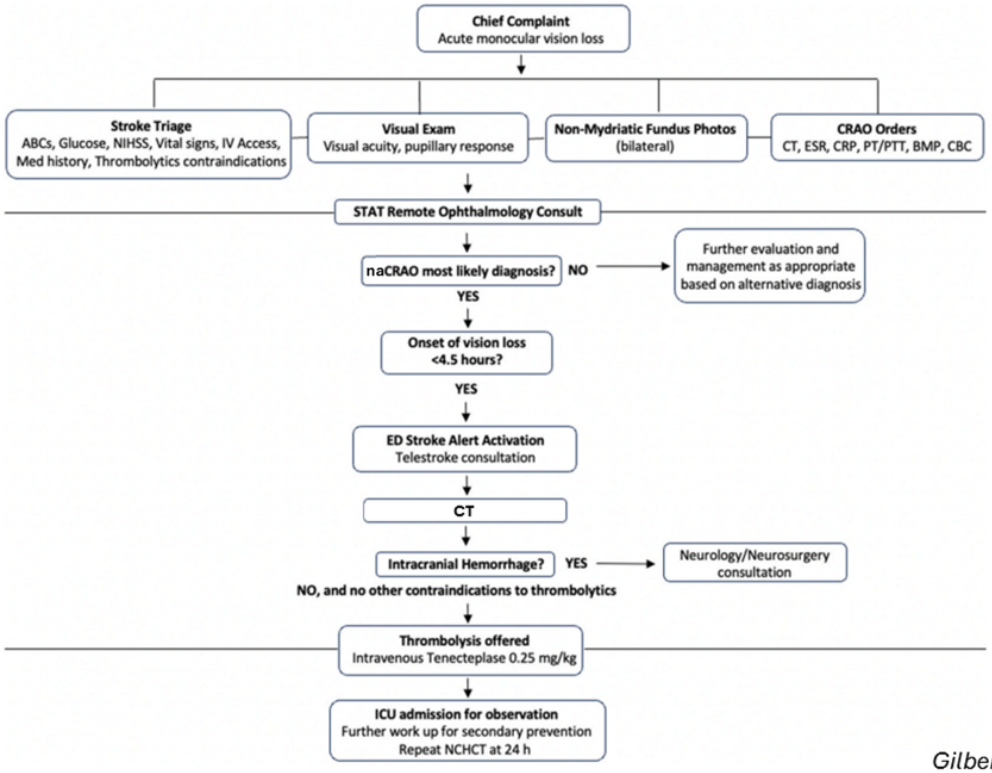
Figure 1: Example of Eye Stroke Protocol in a general ED (Emory University Hospital) [Ref 2]



NMFP/OCT: non-mydriatic color fundus photography with OCT pRNFL and macula
NMFP/OCT obtained by ED staff using the Topcon Maestro2 hybrid camera

Figure 2: Example of Acute Vision Loss Protocol in a general ED (Kaiser Permanente Medical Group). [Ref 12]

Management pathway for patients presenting within 4.5 hours of acute painless monocular vision loss

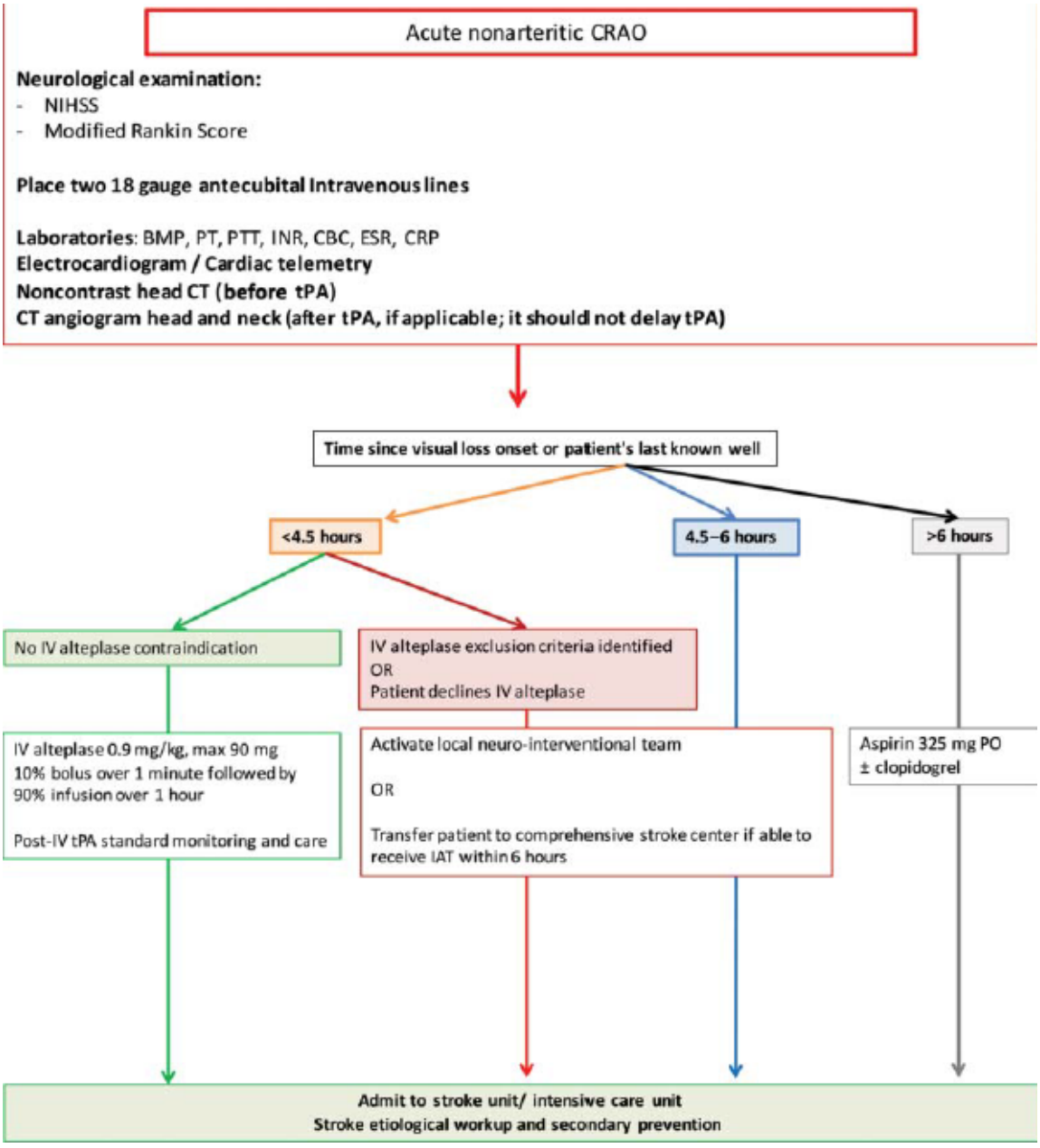


Gilbert et al. AJO CR 2024.

Color photographs obtained by ED staff using the non-mydriatic color fundus camera ICare DRS Plus

Figure 3: Example of Eye Stroke Protocol in a general ED (Mayo Clinic Arizona). [Ref 9]

1. BEFAST Code Stroke activated by ED/inpatient, for painless visual loss within 24 hours 2. VA (+ 10 diopter lens), IOP check by ED 3. Stroke Neurology: Handheld Optomed Aurora color photograph -> EMR (soon) 4. If within 6 hours & possible CRAO: Stroke Team activates Eye Stroke Code 5. Ophthalmology Consult



CME ANSWERS

1. **E**
2. **C**
3. **E**

ANNOTATED SELECTED REFERENCES DIRECTLY RELEVANT TO THIS TOPIC:

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The diagnosis of very acute CRAO may be difficult on ocular funduscopic examination or color fundus photographs, especially when there are no obvious retinal emboli. Macular OCT facilitates the diagnosis of very acute CRAO by demonstrating inner retinal layer hyperreflectivity and thickening withing minutes following the CRAO onset. This is why some EDs and stroke centers have chosen to implement OCTs or hybrid cameras (combining ocular fundus color photographs and OCT) instead of just color fundus photograph-capable cameras.

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Insight: The Science and Clinical Practice of Supporting Patients Through Vision Loss; Therapy When There is No Cure [2.0 CME]

Moderators: Melissa Ko, MD, MBA, FAAN & Guy Jirawuthiworavong, MD, MA

As neuro-ophthalmologists, we are frequently confronted with diagnosing and communicating to our patients the difficult news that their vision loss is irreversible and without cure. Patients seek our compassionate support as they journey through grief and loss of their visual impairment/blindness. Our expert panel comprised of a neuro-ophthalmologist/scientist/chaplain and a neuro palliative care physician will respectively provide didactics on the neuroscience of grief/loss along with compassion/mental training, the integration of palliative care into neuro-ophthalmology and the practical tools we can employ in clinic when caring for a distressed patient practice. This will be followed by video and live interviews with patients for our expert panel to discuss and to illustrate the principles of neuro palliative care in the neuro-ophthalmic setting.

Upon completion of this session, participants should be able to:

(1) Explain the neuroscience behind compassion and mental training.
(2) Identify patient distress and employ clinical tools to approach the distressed patient.
(3) Apply and integrate principles of neuro palliative care into neuro-ophthalmic practice.

Introduction, *Melissa Ko, MD, MBA, FAAN & Guy Jirawuthiworavong, MD, MA*
Integrating Palliative Care into Neuro-Ophthalmology Practice, *Benzi Kluger, MD, MBA, FAAN*
Neuroscience of Compassion, (Integrating Grief & Loss), *Agnes Wong, MD, PhD*
Adult Case Study (Video) With Panel Discussion, Case introduction: *Jeffrey Gluckstein, MD*
Pediatric Case Study with Parent Interview Followed by Panel Discussion, Case Introduction: *Sam Spiegel, MD*

INTEGRATING PALLIATIVE CARE INTO NEURO-OPHTHALMOLOGY PRACTICE

Benzi Kluger, MD, MS, FAAN, Professor of Neurology and Medicine Chief, Neuropalliative Care Service Director,
Palliative Care Research Center University of Rochester
Rochester, NY 14642

LEARNING OBJECTIVES

1. The attendee will be able to describe different models for integrating palliative care into neuro-ophthalmology practice.
2. The attendee will be able to identify the multiple dimensions of suffering that patients and families affected by neuro-ophthalmologic illness face.
3. The attendees will be able to identify opportunities to improve the lives of patients and families through palliative care approaches.

CME QUESTIONS

1. Primary (also known as generalist) palliative care refers to the upskilling of primary care providers to provide specialist palliative care.
   A. True
   B. False

2. Our healthcare system misses opportunities to assess and address many sources of suffering important to patients and families.
   A. True
   B. False

3. Neuro-ophthalmologists are already providing palliative care because most neurologic conditions are incurable.
   A. True
   B. False

KEYWORDS
1. Palliative care
2. Hospice
3. Neuro-ophthalmology
4. Neuropalliative Care
5. Suffering

OUTLINE

I. **Defining Palliative Care**
   - **a.** WHO definition
   - **b.** Palliative care and hospice
   - **c.** Myths

II. **Multidimensional Suffering and Gaps in Care**
   - **a.** The total pain of neurologic illness
   - **b.** Illness doesn't just affect one person (caregivers and family)
   - **c.** Opportunities to prevent and address suffering

III. **Models of Delivering and Integrating Palliative Care**
   - **a.** Primary/generalist palliative care
   - **b.** Consultative models
   - **c.** Integrated/embedded models

IV. **Opportunities to Improve Lives through Palliative Approaches**
   - a. Address current gaps in care
   - b. Increase your effectiveness as a provider
   - c. Find opportunities for joy, love and meaning

V. **Future Directions**
   a. Clinical care
   b. Education
   c. Research and advocacy
   d. Joining INPCS neuro-ophth group

CME ANSWERS

1. B
2. A
3. B

THE NEUROSCIENCE OF COMPASSION IN FACE OF GRIEF AND LOSS

Agnes Wong, MD, PhD, FRCSC, Professor of Ophthalmology, Neurology, and Psychology, University of Toronto; Staff Ophthalmologist and Senior Scientist, The Hospital for Sick Children, Toronto, Canada

LEARNING OBJECTIVES

1. To discuss the scientific evidence affirming that compassion is both innate and a trainable skill.
2. To understand the beneficial effects of compassion and mindfulness training.
3. Using these trainable skills to build inner resources in face of grief and loss.

CME QUESTIONS

1. Which of the following is NOT a component of compassion?
   A. Empathy
   B. Attention stability
   C. Perspective-taking
   D. Intention
   E. Attachment

2. Which of the following is FALSE about the default mode network?
   A. It is responsible for planning, reviewing, and remembering
   B. It is responsible for rumination and mind-wandering
   C. It is not activated in bereavement
   D. It consists of 4 major nodes
   E. If left unchecked, its activities have been associated with depression and anxiety

3. Which of the following is FALSE?
   A. Compassion is innate and trainable
   B. "Empathy fatigue" is a better term than "compassion fatigue" to describe the emotional exhaustion and distress when we are too identified with another's suffering
   C. Compassion training enhances positive emotions
   D. The brain networks for compassion and empathy are identical
   E. Compassion leads to the release of oxytocin

KEYWORDS

1. Compassion
2. Empathy
3. Mindfulness
4. Grief
5. Stress reduction

Compassion lies at the heart of all religious, ethical, and spiritual traditions. Scientific advances in recent decades have deepen our understanding of the neurobiology of compassion. Based on the three principles of neuroplasticity, epigenetics, and inborn goodness, compassion has been shown to be both innate and trainable.

Are we born compassionate?

From a biological perspective, there is now a wealth of evidence suggesting that humans are wired for compassion, which has evolved to promote social bonding and cooperation. It enables our ancestors to risk their own well-being to protect others from predators, to forgo immediate gratification to share food with others, and to invest in another's well-being even when the person being helped is a stranger.[1, 2] Indeed, studies have shown that infants as young as six months respond to the distress of others and choose puppets which help others experiencing difficulties, suggesting that the capacity for compassion is present from a very early age.[3]

The two emotion states

If humans are born with empathy and compassion, why is there so much hatred and violence in the world? This is where psychological science comes in, which tells us how we behave depends on our emotional state. When we feel safe and calm, our parasympathetic nervous system is active, which promotes helping behaviours, and we can be compassionate, kind, and selfless. However, when we perceive threat, it activates the sympathetic nervous system, leading to aversive behaviours, such as "fight" by being combative, "flight" by running away from it, or "freeze" by shutting down.[4] So, the key is to re-establish a sense of safety by shifting away from the threat system through self-regulation to promote compassion.

What is the difference between empathy and compassion?

It is crucial to clarify the difference between compassion and empathy, as these terms have often been conflated. Empathy refers to the ability to feel into the other's experience, to put oneself in someone else's shoes.[5] Healthy empathy requires us to be able to regulate our emotions, without being over-identified with other's suffering. While empathy is a component and often primes compassion, compassion differs in that it has three additional components: attention stability, perspective-taking, and motivation.[6, 7] Attention stability is the ability to be present for the experience of others rather than turning away; it involves meta-awareness, the ability to monitor where our mind is and what it is doing. Perspective-taking is the cognitive ability to take on the perspective of others to understand what they are experiencing. Most importantly, compassion entails the wish or motivation to alleviate another's suffering and to take actions if possible.

Why is compassion fatigue a misnomer?

Brain imaging studies further support this distinction between empathy and compassion.[8-10] When we observe others in pain, the same neural regions—the empathy network (including the anterior insula and anterior midcingulate cortex)—are activated as if we experience the pain ourselves. However, when we wish others to be happy and free from suffering, it activates other regions—the compassion network (including the medial orbitofrontal cortex, pregenual anterior cingulate cortex, globus pallidus, putamen, ventral striatum, nucleus accumbens, ventral tegmental area and substantia nigra)—which leads to positive emotions such as joy, love, and peace. It gives us a sense of pleasure and reward, and it enhances prosocial connections such as maternal bonding and romantic love through the release of oxytocin (the so-called "love hormone"). This also explains why compassion fatigue is a misnomer because compassion is associated with positive feelings and has a separate brain network distinct from the empathy network.[7, 11, 12] Therefore, empathy fatigue and empathic distress are better terms to describe the emotional exhaustion and distress when we are over-identified with another's suffering.

How to cultivate compassion and self-regulation?

How can we self-regulate better? Fortunately, there are various ways, some of which we learn in the normal course of our development, and some through intentional practice and meditation (e.g., focused attention, open monitoring, and loving-kindness/compassion training including Compassion Cultivation Training, Cognitively-Based Compassion Training, G.R.A.C.E. training, etc).[7, 13-16] Studies have shown that meditation and mindfulness practices can enhance emotion regulation, attentional stability, and meta-awareness,[17-20] all essential components of compassion. Research has also found that people who regularly practice compassion have increased activity in brain regions associated with positive feelings and decreased activity in areas related to stress and anxiety.[21] Indeed, spending as little as 30 minutes a day for only two weeks cultivating compassion is sufficient to rewire the brain to strengthen and activate the compassion network.[8] Compassion training has also been shown to increase longevity through epigenetic regulation of telomerase and telomeres.[22, 23]

A key neural network involved in mind wandering and ruminative mental activity is the default mode network (DMN).[24, 25] A well-balanced DMN helps us to plan tasks, review past actions, improve future behaviors, and remember pertinent life details. However, if left unchecked, it causes mental unrest (e.g., anxiety, obsession, major depression).[26-29] The DMN consists of four major structures: (1) the amygdala which generates emotions such as fear and stress; (2) the hippocampus which generates long-term memory; (3) the posterior cingulate cortex which adds a sense of self to emotionally relevant memory to form a narrative; and (4) the medial prefrontal cortex which evaluates and regulates emotional responses. Mindfulness training has been shown to decrease mind wandering and enhance emotion regulation and perspective-taking.[17-20]

Grief-related ruminations are a prominent feature in bereavement. They tend to center on five topics: (1) our negative emotional reactions; (2) the unfairness/injustice of the death; (3) our relationships with friends and family; (4) the meaning of the death; and (5) counterfactual thinking.[30] The posterior cingulate cortex in the DMN, which is responsible for retrieving emotional, autobiographical memories, has been found to be more activated during grief.[31] Mindfulness practices have been shown to improve executive control and emotion regulation, leading to less depressive symptoms in the bereaved. [32-34]

Why is self-compassion important?

Compassion is essential to humanity, yet for some, especially for those who work in healthcare, having compassion toward oneself may be difficult. We may castigate ourselves for our shortcomings, with our inner voice being our own harshest critic. The lack of self-compassion explains partly the triad of emotional exhaustion, depersonalization, and low personal accomplishment that characterizes burnout that is widespread.[35-38] Unfortunately, "self-compassion" has almost become a cliché in our society. For some, it connotes self-pity, selfishness, self-indulgence, or de-motivation, which are common misconceptions. So, what is self-compassion? It is the ability to turn inward toward oneself with understanding, acceptance, and love, rather than being self-critical.[39] Instead of feeling isolated, we could recognize our common humanity as we face our weaknesses, flaws, and limitations. Not ruminating about past events, upsets, or failures, we could plant ourselves firmly in the present with mindfulness. If we truly aspire to serve our patients, loved ones, and the world with compassion, we need to first cultivate kindness toward ourselves. As the 14th Dalai Lama said: "For someone to develop genuine compassion towards others, first he or she must have a basis upon which to cultivate compassion, and that basis is the ability to connect to one's own feelings and to care for one's own welfare...Caring for others requires caring for oneself."

CME ANSWERS

1. **E**
2. **C**
3. **D**

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Skills Session: Neuro-Otology meets Neuro-Ophthalmology [1.5 CME]

Moderators: Dan Gold, DO, Konrad Weber, MD & João Lemos MD, PhD

This will be a predominantly hands-on clinical skills transfer course, emphasizing the importance of the ocular motor examination in neuro-ophthalmology. This course will cover how to properly perform eye movement examination maneuvers, as well as their Interpretation. Participants will be assigned a starting station upon arrival and will rotate through each station during the session.

Upon completion of this session, participants should be able to:
(1) List the essential components of the eye movement examination.
(2) Apply the eye movement examination efficiently and effectively in patients with and without ocular motor dysfunction.
(3) Interpret the eye movement examination to distinguish normal from abnormal, and to assist with localization.

Station 1 (15 min): **OKN/Saccades,** *David Hale, MD & Caroline Froment, MD, PhD*
Station 2 (15 min): **Nystagmus:** *Jorge Kattah, MD & Shannon Beres, MD*
Station 3 (15 min): **Saccadic Intrusions,** *Janet Rucker, MD*
Station 4 (15 min): **Pursuit, VORS, vVOR,** *Anthony Brune, DO & Scott Grossman, MD*
Station 5 (15 min): **VOR/vHIT,** *Konrad Weber, MD, Kristen Steenerson, MD & Roksolyana Tourkevich, MD*
Station 6 (15 min): **Skew Deviation,** *João Lemos, MD, PhD, David E. Newman-Toker, MD, PhD, Dan Gold, DO*

NEURO-OTOLOGY MEETS NEURO-OPHTHALMOLOGY

Konrad Weber MD PhD, Departments of Neurology and Ophthalmology, University Hospital Zürich, Switzerland
João Lemos MD PhD, Coimbra University Hospital Centre, Coimbra, Portugal
Dan Gold DO, The Johns Hopkins University School of Medicine, Baltimore, MD

LEARNING OBJECTIVES

1. List the components of a comprehensive ocular motor and vestibular exam.
2. Differentiate eye movement abnormalities, including saccadic intrusions and nystagmus.
3. Demonstrate the head impulse test and other bedside maneuvers to evaluate ocular motor function.

CME QUESTIONS

All the following ocular motor abnormalities can be seen in a midbrain stroke, except one:
A. Slow vertical saccades
B. 3rd nerve palsy
C. 4th nerve palsy
D. Skew deviation
E. Horizontal gaze palsy

Which of the statements about covert saccades during the head impulse test is false?
A. Covert saccades can be measured with the video head impulse test
B. Covert saccades elicit less oscillopsia than overt saccades
C. Covert saccades can be detected by the naked eye
D. Covert saccades have shorter latencies than overt saccades
E. Covert saccades occur during the head movement; overt saccades occur after the head movement

The ocular tilt reaction consists of:
A. Skew deviation, head tilt, ocular-counterroll
B. Skew deviation, head tilt, subjective visual vertical tilt
C. Skew deviation, head bobbing, ocular-counterroll
D. 4th nerve palsy, head tilt, ocular-counterroll
E. 4th nerve palsy, head tilt, subjective visual vertical tilt

KEYWORDS
1. Nystagmus
2. Skew deviation
3. Vestibulo-ocular reflex
4. Saccadic intrusions
5. Saccades

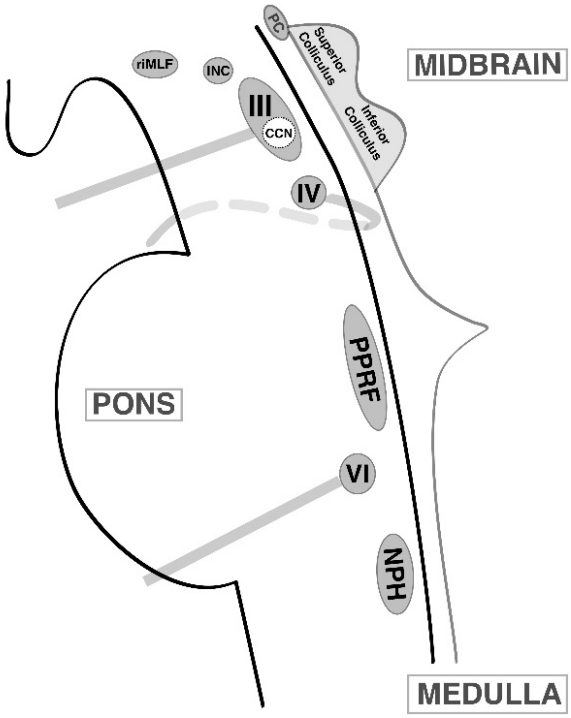
SUMMARY (to access videos, you can either 1) click the embedded "VIDEO" links below in the electronic version, or 2) use this link to access the original online document: https://collections.lib.utah.edu/ark:/87278/s64x9bq1)

1. Ocular Motor Examination

- Important anatomy (see Figure - https://collections.lib.utah.edu/ark:/87278/s6j13x04)
    - **Midbrain**: vertical/torsional burst neurons for saccades (rostral interstitial medial longitudinal fasciculus [riMLF]); vertical/torsional gaze-holding machinery (interstitial nucleus of Cajal [INC]); nuclei of IIIrd (including central caudal nucleus [CCN] and IVth nerves; posterior commissure (PC) which plays a role in upward gaze.

- **Pons**: horizontal burst neurons for saccades (paramedian pontine reticular formation [PPRF]); nucleus of VIth nerve.

- **Medulla**: horizontal gaze-holding machinery (nucleus prepositus hypoglossi [NPH] & medial vestibular nucleus [MVN]).



Complete ocular motor examination should consist of:

- **Range of movements** (VIDEO) – in 9 cardinal positions of gaze with both eyes viewing (versions). Check the range of each individual eye (ductions) if there is diplopia or if a motility deficit is suspected.
- **Convergence** (VIDEO) – may bring out or cause reversal of vertical nystagmus (e.g., bring out DBN in a cerebellopathy, transition from UBN to DBN in Wernicke's encephalopathy), or may exaggerate some acquired forms of nystagmus or damp congenital or infantile nystagmus. If the patient complains of binocular symptoms or double vision while reading and near viewing and the patient has a near point of convergence >10 cm, think about convergence insufficiency (particularly with parkinsonism [VIDEO] or TBI/concussion).
- **Alignment** (VIDEO) – start with alternate cover testing where one eye is occluded, and then the occluder (or examiner's hand) is moved to the fellow eye, and then back and forth as the patient continues viewing the same (usually distant) target. Look for a horizontal (when the eye under cover is crossed in so that it has to move outward when uncovered to take up fixation – ESO [VIDEO]; when the eye under cover is deviated outward so that it has to move inward when uncovered to take up fixation – EXO [VIDEO]) or vertical (generally named after the side of the higher eye – e.g., if the right eye is uncovered and has to come down to fixate on the target, this is a right hyperdeviation) movements of the uncovered eye. The eso-, exo-, hyper is further classified as a *tropia* (misalignment present with both eyes open – use a cover-uncover technique on each eye individually) or *phoria* (misalignment present when binocular vision is broken with alternate cover testing but no misalignment with cover-uncover). Any change in deviation or lack thereof helps in the localization. See examples below.
    - **Left 3rd** – due to left medial rectus paresis, exotropia in right gaze. Due to left superior rectus paresis, right hypertropia in up gaze. Due to left inferior rectus paresis, left hypertropia in down gaze.
    - **Left 6th** – an esotropia worse in left gaze suggests that there is an abduction deficit on the left; in the example of a left 6th nerve palsy, there is less left lateral rectus tone with normal medial rectus tone thereby resulting in crossing of the eyes (esotropia), and this will be maximal in the direction of the paresis (to the left).
    - **Left 4th –** due to left superior oblique (SO) paresis and given the actions of this muscle – primary – incycloduction; secondary – depression; tertiary – abduction – there will be left excycloduction,

hypertropia, and a V-pattern esotropia with bilateral 4ths (the tertiary action of abduction is generally not so clinically relevant with unilateral palsies, but when bilateral, an esotropia greatest in down gaze is seen), respectively. A left 4th nerve palsy is diagnosed using the 3-step test where the examiner identifies that there is a 1) left hypertropia that 2) increases in (contralateral) right gaze (the oblique muscles have greatest vertical action in adduction), and 3) increases in (ipsilateral) left head tilt. Because the SO is also a depressor, the left hypertropia will tend to increase in down gaze (at least with new-onset acquired palsies), and torsional measurements (e.g., double Maddox rod, bucket test, measuring the angle between the fovea and optic nerve) will demonstrate (ipsilateral) left excycloduction.

- **Skew deviation** (VIDEO) – a vertical, non-paralytic misalignment of the eyes from utricle-ocular motor pathway imbalance, which should be assumed to be central until proven otherwise. The vertical deviation (and vertical diplopia) is generally the same or similar in different directions of gaze.
  - **Low/Low –** the hypotropic (**low**er) eye will be ipsilesional if the injury occurs caudal to (**low**er than) the decussation of the utricle-ocular motor pathway. Accompanied by an ***ipsiversive*** ocular tilt reaction (OTR) – e.g., left Wallenberg causes left head tilt, ocular counterroll with top poles toward left ear
    - Examples: labyrinth and 8th cranial nerve (both are rare causes of a skew), vestibular nucleus (common cause)
  - **High/High** – the hypertropic (**high**er) eye will be ipsilesional if the injury occurs rostral to (**high**er than) the decussation of the utricle-ocular motor pathway. Accompanied by a ***contraversive*** OTR – e.g., left MLF lesion causes right head tilt, ocular counterroll with top poles toward right ear
    - Examples: MLF, INC
- **4th vs Skew**
  - **Head tilt –** patients with a 4th nerve palsy have a compensatory head tilt to the opposite side – e.g., a left 4th nerve palsy will cause a compensatory rightward head tilt. The reason is that by tilting the head to the right, the patient excites the right utricle which initiates the utricle-ocular motor reflex, resulting in minute elevation of the right eye and depression of the left eye and very slight ocular counterroll with top poles toward the left ear. This will help to minimize retinal image disparity resulting from the paretic left SO and improves diplopia. A patient with a left MLF lesion will have a contraversive OTR with right head tilt – in this case, the head tilt is pathologic, or an attempt to correct for an abnormal internal representation of where Earth vertical is located. In other words, with a left MLF lesion (where the utricle pathways that are injured originated in the right labyrinth, and the utricle pathways that originated in the left labyrinth are intact and are relatively hyperactive), the brain thinks that the head/body is tilting to the left (when in fact it is not) and attempts to compensate and bring the head to Earth vertical by tilting the head to the right.
  - **Cycloduction –** a patient with a left 4th will have left hypertropia and left excycloduction with no abnormal cycloduction in the right eye. A patient with a left MLF will have a left hypertropia and left incycloduction in addition to right excycloduction – this results from the ocular counterroll portion of the OTR.

- **Saccades** (VIDEO) – have the patient rapidly look back and forth between 2 visual targets, noting the speed, conjugacy, latency, and accuracy. First have the patient look between an eccentric target and the examiner's nose horizontally and vertically, making assessment of accuracy easier – e.g., overshooting the nose (hypermetria) or overshooting the nose (hypometria). Then have the patient make larger amplitude saccades horizontally and vertically, which makes assessment of speed and conjugacy (e.g., adduction lag suggest an internuclear ophthalmoplegia [INO]) easier. Saccade dysmetria is seen in cerebellar disease (or brainstem connections w/ cerebellum). Ipsilateral hypermetria and contralateral hypometria occurs in Wallenberg syndrome (VIDEO).
  - Slow saccades of normal amplitude occur in brainstem disease, typically involving burst neurons in the PPRF for horizontal saccades (e.g., SCA 1, 2, 3, 7 among others) or riMILF for vertical saccades (e.g., progressive supranuclear palsy, PSP VIDEO).
  - Slow saccades of restricted amplitude occur in motor nerve paresis or muscle weakness.
  - Slow adducting saccades are seen with an INO (lesion involving the MLF, commonly an INO is seen with an OTR/skew acutely – e.g., left MLF lesion with a left INO and left hypertropia, contraversive OTR), even when no adduction deficit is present (although at least an exodeviation in contralateral gaze is almost always noted). This is accompanied by abducting nystagmus. INO may be due to MS, stroke, or structural and metabolic injuries (VIDEO).
- **Smooth pursuit** (VIDEO) – have the patient slowly track a target and note saccadic (where saccades substitute for subnormal smooth pursuit gain to catch-up to the target) or "choppy" pursuit (VIDEO). Impaired pursuit

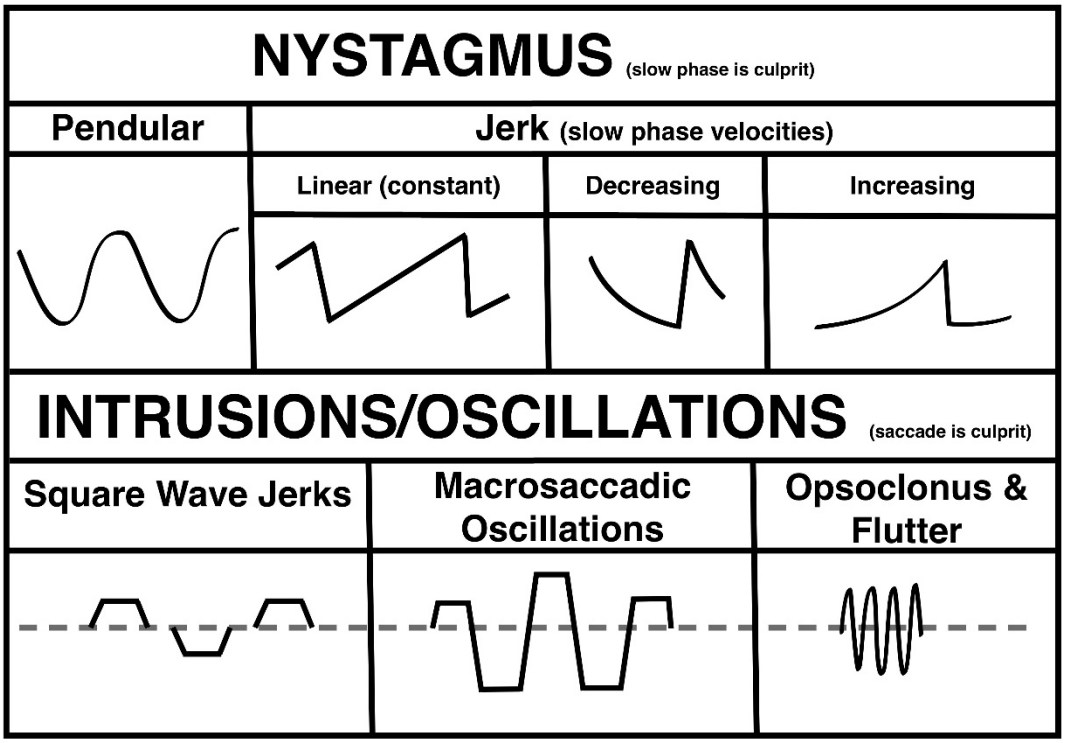
horizontally and vertically is typically seen in cerebellar disease (or its connections). If impairment of pursuit is asymmetric, think about an ipsilesional process – e.g., saccadic or choppy pursuit to the right due to a right hemispheric lesion.

- **Vestibulo-Ocular Reflex Suppression (VORS)** (VIDEO) – the VOR will need to periodically be suppressed or cancelled in certain situations – e.g,, sitting on a bus and reading a newspaper while the bus turns. The VOR is stimulated by the turning of the bus, but the VOR is suppressed and the eyes remain stable so the reader can continue to foveate the words on the page. VORS will generally be saccadic when pursuit is saccadic and vice versa (VIDEO). However, when pursuit is impaired and the VOR is lost (bilateral vestibular loss), VORS can look better than pursuit since there is no VOR to suppress (VIDEO).
- **Optokinetic nystagmus** (VIDEO) – at the bedside, using an optokinetic stimulus can assist in the evaluation of smooth pursuit and saccades. The slow phases represent smooth pursuit while the fast phases represent saccades. Since the bedside optokinetic stimulus used (optokinetic tape/flag, examiner's fingertips, or any alternating patterns/lines, optokinetic drum) does not involve full visual field stimulation like looking out the window at passing scenery from a moving train, the examiner is not really isolating the optokinetic system in this way.
    - Circumstances in which bedside OKN can be helpful
        - Rapid assessment of symmetry and presence/absence of pursuit/saccades in an uncooperative or difficult to examine patient
        - It can help to bring out a subtle adduction lag in INO
        - One of the first ocular motor signs of PSP is loss of the downward fast phase to an optokinetic stimulus directed upward (goes along with downward saccades being slightly slower than upward saccades initially, and downgaze being more affected than upgaze)
        - If nystagmus is seen in a patient with functional monocular (when the good eye is occluded) or binocular blindness, this suggests that the patient has at least some vision
        - Since upward saccades are often affected in dorsal midbrain (Parinaud's syndrome), vertical OKN can demonstrate this and convergence retraction nystagmus (when stimulus is directed downward).

2. Nystagmus

- **Observation for involuntary eye movements (nystagmus and intrusions - https://collections.lib.utah.edu/ark:/87278/s6hx56nc)**
    - **Saccadic intrusions** – saccades are the culprit
        - **With an intersaccadic interval (**VIDEO**)**
            - Square wave jerks are most common, mainly seen with basal ganglia and/or cerebellar pathology
        - **Without an intersaccadic interval (**VIDEO**)**
            - Ocular flutter (horizontal plane) and opsoclonus (horizontal, vertical and torsional planes)

    - **Nystagmus** – slow phases are the culprit
        - **Pendular** – back-to-back slow phases, giving a pendular appearance. Most commonly seen in multiple sclerosis (VIDEO) or with oculopalatal tremor (VIDEO).
        - **Jerk** – alternating slow and fast phases, where the slow drift is the pathological phase, although nystagmus is named for the direction the fast phase. Can be further localized by the slow phase velocity waveform (see figure below). Vestibular nystagmus tends to have a linear appearance; gaze-evoked nystagmus (due to impaired neural integrators) tends to have a velocity decreasing waveform; infantile nystagmus (and occasionally conditions causing an unstable neural integrator) tends to have a velocity increasing waveform.



- **Jerk nystagmus**
  - **Vestibular**
    - Spontaneous vestibular nystagmus implies imbalance of semicircular canal (SCC) afferents, either peripherally or centrally.
    - Fixation suppresses peripheral nystagmus, but occasionally central nystagmus too. Visual fixation can be removed by occlusive ophthalmoscopy, pen-light cover test, or using Frenzel lenses. Note that the actual direction of any horizontal or vertical spontaneous nystagmus is opposite of that seen with the ophthalmoscope (you are viewing posterior to the axis of rotation for horizontal and vertical movements), but is the same for torsional movements.
    - Peripheral nystagmus should be unidirectional, follow Alexander's law (intensity of the nystagmus increases in the direction of the fast phase) and acutely, has a mixed horizontal-torsional appearance (VIDEO). Central vestibular nystagmus can be indistinguishable from peripheral (VIDEO).
  - **Gaze-holding**
    - Have the patient maintain eccentric fixation in each of the other cardinal positions of gaze. If the eyes are unable to maintain eccentric fixation and instead drift back towards center (slow phase) and then quickly move back toward the intended direction of gaze, then this is referred to as gaze-evoked nystagmus (GEN). When GEN is present horizontally and vertically, this generally implies a disorder in the vestibulocerebellum (flocculus/parafloccculus, or its connections VIDEO). If only vertical GEN is observed, an INC (or medial longitudinal fasciculus or adjacent paramedian tract lesion(s) as these structures play a role in relaying vertical gaze position signals) should be suspected. If only horizontal GEN is observed, damage to the NPH-MVN complex should be suspected. Patients with GEN commonly have rebound nystagmus – e.g., the patient with GEN will have left-beating nystagmus (LBN) in left gaze and right-beating nystagmus (RBN) in right gaze, and when the patient is asked to look to the right (where there is RBN) and then back to primary gaze, the appearance of LBN will suggest rebound nystagmus. Again, this generally indicates flocculus/parafloccculus (or its connections) pathology.
    - Commonly, patients without posterior fossa pathology have a small amplitude, fatigable, physiologic end point nystagmus (EPN) in far lateral gaze, although this should abate when bringing the fixation target back to so that it can be viewed by both eyes, or at about ¾ lateral position. Rebound nystagmus should be absent.

3. **Vestibulo-ocular Reflex**

- **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 each head movement and the fovea 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 street due to impaired VOR, so the image appears to jump up and down (so-called *walking* oscillopsia https://collections.lib.utah.edu/details?id=1213442). The following are ways to evaluate VOR function at the bedside.
    - **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.
    - **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 due to 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.
    - **Head impulse test (HIT** VIDEO): With the patient fixating on the examiner's nose, perform a brief, rapid head rotation of 15-20º. 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).
    - **Vibration** (VIDEO): Vibration of the mastoids and vertex will induce an ipsilesional slow phase with unilateral vestibular loss, more so acutely than chronically.
    - **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 HSN without clear unilateral vestibular loss (VIDEO), think about a central process.

CME ANSWERS

1. **E**
2. **C**
3. **A**

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Skills Session: Chemodenervation meets Neuro-ophthalmology [1.5 CME]

Moderators: Lindsey DeLott, MD, MS & Billi Wallace, MD

Chemodenervation Meets Neuro-Ophthalmology is a hybrid didactic and hands-on skills transfer session. The didactic portion will discuss available toxins and techniques for several common and less common neuro-ophthalmic conditions including migraine, facial dystonias/spasms, and strabismus. The hands-on portion will allow participants to work in small groups to practice injection techniques on provided models and to participate in advanced discussion for less common toxin applications under the guidance of experienced group leaders. This course is designed for those who are interested in adding chemodenervation procedures to their clinical practice as well as those who have experience with chemodenervation but hope to further enhance their skills.

Upon completion of this session, participants should be able to:

(1) Discuss available toxins, appropriate injection preparation, and billing.

(2) Describe injection techniques, documentation, outcomes, and potential complications of toxin injection for facial spasm, headache/migraine, and other less common neuro-ophthalmic applications.

(3) Objective 3 Learners will identify injection sites, demonstrate proper injection techniques, and discuss less common applications in small group skills transfer sessions.

Overview, *Wayne Cornblath, MD*
Chemodenervation for Headache, *Judith Warner, MD*
Chemodenervation for Facial Spasms, *Neil Miller, MD*
Other Applications of Chemodenervation, *Kimberly Cockerham, MD*
Break out Session A, B or C (participant's choice)
Break out Session A, B, or C (participant's choice)

OVERVIEW OF CHEMODENERVATION: AVAILABLE TOXINS & MIXING

Wayne T. Cornblath, MD
W. K. Kellogg Eye Center
University of Michigan

LEARNING OBJECTIVES

1. Learn history and mechanism of botulinum toxin
2. Learn about the different available botulinum toxins
3. Learn how to mix and handle botulinum toxin

CME Questions

1. Botulinum toxin is reconstituted with
   A. Preservative free normal saline
   B. Bacteriostatic normal saline
   C. Preservative free half normal saline
   D. Bacteriostatic half normal saline

2. Different botulinum toxins have different FDA approved indications but can be used at physician discretion for non-approved uses
   A. True
   B. False

3. One botulinum toxin is superior to the rest
   A. True
   B. False

Botulinum Toxin

- Polypeptide toxin produced by bacteria *Clostridium botulinum*
- Most potent poison known
- Eight serotypes (A-G) (only A and B commerically available)
- Causes botulism (food-borne, wound, and infantile)
- Impairs neuromuscular transmission presynaptically
- Interferes with exocytic release of ACh vesicles
- Recovery eventually occurs when nerve fibers sprout and new neuromuscular junctions are established
- 1895 Clostridium botulinum identified
- 1920's Type A first isolated
- 1944 Dr. Edward Schantz starts to purify toxin
- 1946 Type A isolated in crystalline form
- 1950's Dr Vernon Brooks proves botulinum toxin blocks acetylcholine
- 1960's purification procedure improved
- 1978 Dr Alan Scott receives FDA approval to test botulinum toxin in humans (strabismus, BEB, HFS)

Botulinum Toxin Type A

- onabotulinumA (Botox) supplied by Abbvie in 100 unit and 200 unit vials
  - 1 unit = .05 nanograms of toxin
  - Each vial contains 5 nanograms of toxin (old batch 25 nanograms/100 units)

- 1 unit = LD50 for 20-g Swiss-Webster mouse with intraperitoneal injection
- LD50 for humans (70 kg) estimated at 3000 units
- Refrigerator storage

- abobotulinumA (Dysport) supplied by Ipsen in 300 unit and 500 unit vials
  - Refrigerator storage
- incobotulinumtoxinA (Xeomin) supplied by Merz in 50 unit, 100 unit and 200 unit vials
  - Room temperature storage (or refrigerator)
- daxibotulinumtoxinA, (Daxxify) supplied by Revance in 100 unit vials
  - Room temperature storage (or refrigerator)

Botulinum Toxin Type B

- Rimabotulinumtoxinb (Myobloc) supplied by Solstice Neuroscience
  - Comes as premixed solution
  - Vial sizes – 2500, 5000, 10000 units
  - Vials are overfilled about 10%
  - Refrigerator storage
  - Rimabotulinumtoxinb injections more painful than Botox/Dysport injections (acidic mixture)

FDA Approvals and Approximate Cost*

	BEB, HFS	Cervical Dystonia	Migraine	Strab	Rhytid	Spasticity	Bladder Spasm	Sialorrhea	Hyperhidrosis
Botox $565	X	X	X	X	X	X	X		X
Xeomin $435	X	X			X	X		X	
Dysport $672 100u=16		X			X	X			
Daxxify $452		X			X				
Myobloc $622 100u=50		X						X	

*Cost per 100 unit vial Botox, Xeomin, Daxify; Equivalent for Dysport and Myobloc

Common Off Label Uses

- TMJ/Bruxism
- Trigeminal neuralgia
- Trichodynia
- Hyperhidrosis other than axillae
- Weight loss (gastric injection)
- Plantar fasciitis
- Anal fissure
- Vaginismus

- Erectile dysfunction
- Cosmetic uses (outside of glabellar lines)

Handling and Dilution of Botulinum Toxin

- Reconstituted with 0.9% preservative free saline (per package insert)
- 1 cc, 2 cc, 4 cc, 5 cc dilution depending on use
- 30 gauge ½ inch needle for injection
- Refrigerator storage
    - good for 24 hours once reconstituted (package insert)
    - Daxxify 72 hours (package insert)
- Can be destroyed by vigorous shaking (long, fragile molecule)
- IncobotulinumA - Rotate bottle when mixing to get all the toxin

Controversies

- Good for weeks after opening if refrigerated or frozen (reference 1-6)
- Reconstitute with preserved saline (bacteriostatic) saline vs preservative free (reference 7-9)
- Don't need to use alcohol antisepsis (reference 10)

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BOTULINUM TOXINS FOR MANAGEMENT OF CHRONIC HEADACHE

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LEARNING OBJECTIVES

1. The participant will understand the indications, risks and benefits of botulinum toxin for chronic migraine
2. The participant will observe and gain hands on experience with the technical aspects of botulinum toxin for chronic migraine

CME QUESTIONS

1. Botulinum toxin has been approved for chronic migraine since:
   A. 1961
   B. 1991
   C. 2011
2. Botulinum toxin is typically injected for chronic migraine in:
   A. Face
   B. Temples
   C. Neck
   D. All of the above
3. Botulinum toxin injections for chronic migraine typically need to be repeated:
   A. Every 3 months
   B. Every week
   C. Every month

HIGHLIGHTS

The International Headache Society defines chronic migraine as headache occurring on 15 or more days per month for more than three months, where at least 8 of those headache days have migraine features:

- The pain is moderate or severe and often intense.
- The pain may be on one side or the head or both.
- The head pain causes a throbbing, pounding or pulsating sensation.
- The pain gets worse with physical activity or movement.
- The patient must have nausea, vomiting, and/or light and sound sensitivity along with the head pain.

Botulinum neuro-toxins (BoNT), primarily derived from *Clostridium botulinum*, have been extensively studied and utilized in the management of chronic migraine (1), after some receiving cosmetic treatment for forehead wrinkles reported improved migraine. BoNT inhibit acetylcholine release at the neuromuscular junction, leading to localized muscle paralysis. BoNT also modifies the release of neurotransmitters which are relevant in the transduction of pain such as substance P (2,3) or calcitonin gene-related peptide (4). It is thought that the inhibition of peripheral sensitization leads to an indirect inhibition of central sensitization and thus is a possible mechanism for the efficacy of BoNT in chronic pain (5).

In 2010, after a more than a decade of small trials with variable results, the PREEMPT (6,7) and PREEMPT2 (8) trials, both large randomized controlled trials demonstrated botulinum toxin type A's efficacy in reducing headache days per month. OnabotulinumtoxinA (Botox®) received FDA approval for the preventive treatment of chronic migraine in 2011. Other Botulinum toxin type A preparations include Dysport®, and Xeomin® but are not FDA approved for chronic migraine. For chronic migraine, BoNT treatment involves multiple injections in specified areas, including the forehead, temples, and neck, with intervals typically every three months.

Contraindications for the use of botulinum toxins include a history of hypersensitivity to any component of the formulation, active infection at the injection site, and neuromuscular disorders such as myasthenia gravis or Lambert-Eaton syndrome. Additionally, pregnant or breastfeeding individuals are advised against receiving botulinum toxin treatments due to the lack of conclusive safety data. While adverse effects are generally rare, they may include localized pain, muscle weakness, and transient headaches.

CME ANSWERS

1. **C**
2. **D**
3. **A**

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BOTULINUM TOXIN INJECTION FOR EYELID AND FACIAL SPASMS

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CME QUESTIONS

1. The pain associated with botulinum toxin injections can be reduced or eliminated by pretreating the areas to be injected with an ice pack.

   A. True
   B. False

2. How many days after botulinum toxins for eyelid and/or facial spasms do the effects usually begin.

   A. Immediately
   B. 3-5 days
   C. 7 days
   D. 14 days

3. Double vision that occurs in a patient following periorbital injections of botulinum toxin for eyelid spasms often is permanent.

   A. True
   B. False

OVERVIEW

- No other treatment satisfactory (although patients with Meige may benefit from bilateral stimulation of globus pallidus or subthalamic nucleus)

  – H-H Capelle et al. Neurology 60:2017, 2003
  – S Zhan et al. J Neurosurg 128:897-902, 2018
  – R Huh et al. Acta Neurochir 164:2287-902, 2022
  – H Xie et al. J Neurosurg 140:1650-1653, 2024

- Subcutaneous injections improve 95% of patients
- Pain of injection may be reduced by

  – Use of saline **with** preservative (controversial!)
  – Use of ice pack for about 5 minutes before injections
  – Use of anesthetic cream (eg, EMLA or 4% lidocaine) for 45 minutes before injections

Injection Technique

- Eyelids
  - Inject parallel to eye
  - Position just above lid margin
  - Bleb should form

- Forehead
  - 45 deg angle (thicker skin)

- Mid/Lower face
  - For Meige: Symmetric injections

Botulinum Toxin A for Essential Blepharospasm and Meige Syndrome

- Effects usually begin 3-5 days after injection (occ immediately!)
- Wear off usually rapid (1-2 days)
- Total dose required 50-100 units of Botox/Xeomin or 200-400 Units of Dysport every 2-5 months (ave 3 mos)
- Effective dose may need to be increased by 50% over time, depending on initial dosage
  - M Snir et al. Am J Ophthalmol 136:99, 2003
- Efficacy and safety maintained long-term (10-20 yrs)
  - OH Ababneh et al. Clin Exp Ophthalmol 42:254-261, 2014
  - F Vivancos-Matellano et al. Neuro-Ophthalmology 43:277-283, 2019
- Some patients whose BEB is relatively unresponsive to 100 total units of Botox may respond to higher doses (125-150 U)
  - RL Levy et al. Ophthalmology 113:1665-1668, 2006
  - AL-Y Pang et al. Clin Exp Ophthalmol 34:441-444, 2006

- Initial Injection
- Adequate preparation (explain what will happen)
- Call office in 1 week
- Artificial tear solution as needed
- Return in 1 month for assessment

- Potential Complications of Injections
- All are temporary but may last days to weeks (must inform patient!)
- Bruising/hematoma
- Ptosis
- Occurs about 10% of time
- Results from spread of medication to levator muscle (reason injections must be given far medial and far lateral in upper eyelid)
- May be hard to distinguish over phone from lack of effect of drug (ie, persistent spasm vs ptosis)--**may require exam**

- Double vision
- Results from spread of medication to one of the extraocular muscles
- Resolves when either eye is covered
- Usually from lower lid injection to inferior oblique muscle (vertical/oblique double vision)
- Rarely from spread of lateral injection to lateral rectus (horizontal double vision)
- Never permanent!
- May have to omit or reduce injection in area
- Dry eye
- From weak upper eyelid closure, lax lower lid, or both
- Usually responds to lubrication (drops during day/ointment or gel at night)
- Weakness of mid/lower face (smile)
  - – Results from spread of medication given in lower eyelid to mid/lower face
  - – Never permanent
  - – Omit lower lid injections or reduce amount injected

Hemifacial Spasm

- Occurs most often in middle-aged adults
- Women affected more often than men
- Can affect either side of the face
- More common contralateral to the dominant hand?

- Usually begins with involvement of the orbicularis oculi muscle
  - – Lower eyelid more often affected than upper
  - – Mimics eyelid myokymia
- Gradually spreads to affect mid and lower face on the same side
- At same time, affected side slowly becomes weak, esp lower face (must point out to pt before injection!)
- Affected patients may hear clicking noise in the ear on the side of the spasms

Botulinum Toxin A for Hemifacial Spasm

- ° Disorder can be cured by neurosurgical procedure (90-95% success rate)
- Botulinum toxin controls spasms in >90%
- Can be injected in periorbital region only or also in mid and lower face (risk of weakness)
- Total dose needed usually 20-25 units
- Complications same as for blepharospasm
- Effects last 3-12 months
- Dosage needed may increase by 50% over time depending on initial amount
- Initial Injection
- Adequate patient preparation (explain what will happen)
- Before injecting mid or lower face, point out any facial weakness!
- Call office in 1 week
- Lubrication as needed (?give sample)
- Return in 1 month for assessment

Summary

- Reconstitute Botox with saline **containing** preservative (injections less painful)
- Use small (30-gauge) needle
- Consider use of pre-treatment ice or anesthetic cream to reduce pain of injections
- One size does not fit all!!
  - Patient and physician **MUST WORK TOGETHER**
  - Patient must communicate with physician
  - Physician **MUST LISTEN TO PATIENT**
  - Physician must be flexible regarding dosage, location of injections, interval between injections (≥3 months for most)

CME Answers:

1. True

2. 3-5 Days

3. False

Oculoplastics-Orbit-Neuro-Ophthalmology
Chemodenervation Session

Kimberly Cockerham, MD, FACS
Senta Clinic
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CME Questions

1. What was the original FDA approval indication for Botox?
   A. Blepharospasm
   B. Hemifacial spasm
   C. Migraine
   D. Strabismus

2. What is the most common adverse outcome resulting from Botulinum A injection of the face?
   A. Bruising
   B. Numbness
   C. Ptosis
   D. Diplopia

3. The muscle that does not impact eyelid height is:
   A. Orbicularis
   B. Mueller's Muscle
   C. Levator aponeurosis
   D. Medical rectus muscle

Cosmesis Considerations in Hemifacial Spasm Indication:
Patients who are receiving botulinum A toxin for blepharospasm are receiving bilateral treatment that achieves a symmetric outcome, suppressing spasms bilaterally and suppressing eyelid rhytids symmetrically. In contrast, patients with hemifacial spasm receive the medical injections unilaterally resulting in suppression of the spasms but does not result in symmetry of facial form and function. Offering contralateral injections can enhance patient satisfaction and should be offered to optimize quality of life.
Technique:
I use a 1-2 cc dilution of normal saline/100 units reconstituted as previously described. Symmetric injections of similar dosing work in most patients but should be tailored to the patient's needs. Photos/video will be presented.
Dosing:
Symmetric injections as above.
Informed Consent:
All patients should discontinue blood thinners, if possible, to avoid bruising. Oral and topical Arnica can be utilized before and after to minimize bruising and swelling. Patients should be advised not to rub the treated area and to avoid hot tubs, working out as vasodilation may allow the medication to spread farther and create more complications. Botulinum toxin in patients with myasthenia gravis MAY be more likely to cause ptosis or diplopia.
Pitfalls:
Patients are often frustrated that insurance will not pay the cost of the toxin. I offer a discounted price compared to my strictly cosmetic patient's price.

Epiphora/Crocodile Tears Indication:
Tearing due to overproduction and/or under outflow can be combated by injecting the lacrimal gland. Technique:
I use a 0.5 cc dilution of normal saline/100 units reconstituted as previously described. The injection options are into the orbital or palpebral lobe of the lacrimal gland. Photos/video will be presented.
Dosing:
2-5 units initial injection. Follow up in two weeks to check on the outcome and potentially inject an additional dose.
Informed Consent:

All patients should discontinue blood thinners, if possible, to avoid bruising. Oral and topical Arnica can be utilized before and after to minimize bruising and swelling. Patients should be advised not to rub the treated area and to avoid hot tubs, working out as vasodilation may allow the medication to spread farther and create more complications. Botulinum toxin in patients with myasthenia gravis MAY be more likely to cause ptosis or diplopia.
Pitfalls:
If under dosed can re-inject, if overdose can cause dry eyes.

Tarsorrhaphy Indication:
Patients with corneal breakdown for any reason can benefit from a chemical closure of the eyelids. This allows ophthalmologists to check the status of the cornea in the ICU, hospital ward or office. Technique:
I use a 0.5 cc dilution/100 unit and inject directly into the Levator muscle of the upper lid through a transdermal approach.
Dosing:
5 – 10 units injected into superior aspect of Levator aponeurosis/muscle junction just below the superior orbital rim medially, centrally and laterally. The lecture will include photos and video demonstrations. Informed Consent:
All patients should discontinue blood thinners, if possible, to avoid bruising. Oral and topical Arnica can be utilized before and after to minimize bruising and swelling. Patients should be advised not to rub the treated area and to avoid hot tubs, working out as vasodilation may allow the medication to spread farther and create more complications. Botulinum toxin in patients with myasthenia gravis MAY be more likely to cause ptosis or diplopia.
Pitfalls:
Botulinum A lists neurologic disorders as a contraindication.
Eyelid Retraction Indication:
Eyelid retraction due to Thyroid Eye Disease, seventh nerve dysfunction, scarring due to prior surgery or trauma.
Technique:
I use a 0.5 cc dilution/100 unit and inject directly into the Mueller's muscle of the upper lid through a transconjunctival approach.
Dosing:
2 units are injected into Mueller's muscle medially, centrally and laterally. Will provide photos and video demonstration.
Informed Consent:
All patients should discontinue blood thinners if possible to avoid bruising. Oral and topical Arnica can be utilized before and after to minimize bruising and swelling. Patients should be advised not to rub the treated area and to avoid hot tubs, working out as vasodilation may allow the medication to spread farther and create more complications. Botulinum toxin in patients with myasthenia gravis MAY be more likely to cause ptosis or diplopia.
Pitfalls:
Under-correction, over correction, the need for surgical correction

Myogenic, Paralytic or Traumatic Ptosis Indication:
Eyelid ptosis due to Horner's syndrome (ptosis and inverse ptosis), aging (myogenic ptosis), or trauma (Levator disruption). Cranial nerve III related ptosis is usually too severe to benefit.
Technique:
I use a 0.5 cc dilution/100 unit and inject directly into the muscle of the upper or lower eyelid.
Dosing:
2 units are injected into muscle medially and laterally. The lecture will include photos and video demonstrations.
Informed Consent:
All patients should discontinue blood thinner -if possible- to avoid bruising. Oral and topical Arnica can be utilized before and after to minimize bruising and swelling. Patients should be advised not to rub the treated area and to avoid hot tubs, working out as vasodilation may allow the medication to spread farther and create more complications. Botulinum toxin in patients with myasthenia gravis MAY be more likely to cause ptosis or diplopia.
Pitfalls:
Under-correction, over correction, the need for surgical correction are all possibilities.

Spastic Entropion Indication:
Entropion due to aging, scarring due to prior surgery or trauma.
Technique:

Treatments Outside the Box [2.0 CME]

Moderators: Vivek Patel, MD & Zoe Williams, MD

The over-arching goal of this session is to highlight potential treatments and strategies to address common questions every neuro-ophthalmologist encounters in clinical practice. Relying on the expertise of our speakers, our moderators will lead a discussion in multiple areas including dietary factors relevant to neuro-ophthalmic conditions, the role of dietary supplements, potentially helpful in-office and surgical procedures such as botulinum toxin, therapeutic injections, vision therapy, and stem cell transplantation, optical strategies to correct diplopia, improve compensation for homonymous visual field loss, and address photophobia, topical agents for the treatment of ocular surface disorders resulting in eye pain, monocular diplopia, visual blurring, ptosis, presbyopia and anisocoria and potentially promising strategies for functional visual restoration using assistive devices and artificial vision technologies.

Upon completion of this session, participants should be able to:
(1) Evaluate evidence-based dietary changes to reduce vision loss, inflammation, and cognitive impairment.
(2) Discuss the role of stem cell transplantation and vision therapy.
(3) Describe optical techniques for managing patients with binocular vision disorders, nystagmus, and visual field loss.
(4) Describe pharmacologic options to address common clinical presentations including ptosis, anisocoria and presbyopia.

Introduction, Vivek Patel, *MD & Zoe Williams, MD*
Will Food Help Me? *Rudrani Banik, MD*
Will a Procedure Help Me? *Bradley Katz, MD, PhD*
Will Glasses Help Me? *Kimberly Winges, MD*
Will Eye Drops Help Me? *Jane Bailey, MD*
Will Devices Help Me? *Joseph Rizzo, MD*

WILL NUTRITION HELP ME? - DIET AND SUPPLEMENTS

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LEARNING OBJECTIVES

1. The attendee will be able to identify the key nutrients that play protective roles in eye and brain health.
2. The attendee will be able to discuss evidence from key clinical studies regarding the efficacy of specific vitamins and supplements.
3. The attendee will be able to assess the clinical utility of novel supplements (e.g., nicotinamide, biotin) in managing optic nerve or neurologic disorders.
4. The attendee will be able to integrate practical dietary guidance into patient care to support eye and brain health outcomes.

CME QUESTIONS

1. Which combination of nutrients was shown in the AREDS2 study to significantly reduce the risk of progression in age-related macular degeneration (AMD) was different than those used in the AREDS1 study formulation?

   A. DHA and EPA
   B. Vitamin C and E
   C. Lutein and zeaxanthin
   D. Zinc and copper

2. Riboflavin (Vitamin B2) has shown evidence in reducing the severity of which condition below?

   A. Thyroid Eye Disease
   B. Myasthenia Gravis
   C. Optic Neuritis
   D. Migraine

3. Nicotinamide (Vitamin B3) has gained interest in the treatment of optic neuropathy. What is its proposed mechanism of action?

   A. Reducing oxidative stress of Mueller cells
   B. Enhancing mitochondrial function
   C. Inhibiting amyloid-beta accumulation
   D. Reducing homocysteine levels

4. Supplementation with which of the following nutrients below has been shown in a prospective clinical studies to decrease the risk of stroke by 10%?

   A. Folic acid
   B. EPA
   C. Vitamin B12
   D. DHA

KEYWORDS

1. Macular carotenoids
2. Omega fatty acids
3. Nicotinamide
4. Biotin
5. Supplements for vision

HIGHLIGHTS

A considerable body of evidence indicates that nutrition has significant implications for the health of the eye and brain, influencing both acute conditions and chronic disease progression. Both the eye and brain are highly sensitive to oxidative stress,[1-3] mitochondrial dysfunction,[4] and inflammation,[5,6] and select nutrients may help shield these organs and their delicate tissues from damage. This review shares evidence-based findings related to the micronutrient demands of eye and neural tissues, exploring the effects of carotenoids, omega fatty acids, B vitamins, and phytonutrients on conditions such as age-related macular degeneration (AMD), dry eye, cognitive decline, and migraine. Additionally, emerging supplements, such as idebenone, nicotinamide, and biotin, are reviewed for their clinical utility for various optic neuropathies.

Perhaps the best studied nutrients for vision are the macular carotenoids - lutein, zeaxanthin, and meso-zeaxanthin. These xanthophyll carotenoids are potent antioxidants concentrated in the macula, all three being well established in their ability to decrease the risk of progression of macular degeneration. In one study, individuals who were in the highest quintile of dietary lutein and zeaxanthin intake based on food frequency questionnaires had a 43% reduced risk of progression to advanced AMD.[7] The Age-Related Eye Disease Study 2 (AREDS2) provided additional evidence supporting the role of supplements including lutein and zeaxanthin for AMD. In this randomized controlled trial with 4,203 subjects, AREDS2 found that the formulation with lutein (10 mg) and zeaxanthin (2 mg) reduced the progression of AMD by approximately 29%, similar to placebo (the original AREDS formulation that included beta carotene), that had a 31% risk reduction.[8]

The macular carotenoids also absorb short wavelength, high energy blue light and reduce phototoxic damage to retinal photoreceptors.[9,10] Clinical studies have demonstrated that supplementation with macular carotenoids increases macular pigment optical density (MPOD),[11] along with improved visual performance.[12] With respect to digital eye strain, in a placebo-controlled study of 48 healthy subjects with at least 6 hours of daily exposure to screens, macular carotenoid supplementation with lutein, zeaxanthin, and meso-zeaxanthin for 6 months was associated with decreased symptoms of eye strain and improved metrics of visual performance including glare, contrast sensitivity, and photostress recovery.[13]

In addition to their vision benefits, the macular carotenoids have been demonstrated to have cognitive benefits across all ages. In one prospective study, researchers found that supplementation with the three macular carotenoids, along with omega 3s and Vitamin E, when given for 24 months, improved working memory in older individuals age > 65 years.[14] A randomized double-blind, parallel placebo-controlled study of 60 children, ages 5-12 showed improved visual and cognitive performance.[15]

Astaxanthin, a red-pigmented carotenoid and potent antioxidant with higher antioxidant capacity than Vitamin C, A, and glutathione, has also garnered interest. It has potential eye health benefits with respect to AMD[17] and quenching inflammation post cataract surgery,[18] as well as potential neurologic benefits in conditions such as neurodegenerative disorders, cerebral ischemia, traumatic brain injury, and subarachnoid hemorrhage.[19] However, more research is necessary on astaxanthin, as large prospective clinical trials have not been performed.

The next class of nutrients extensively researched for vision and brain health include the omega fatty acids, particularly docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), both omega-3s essential for retinal and neuronal health. DHA forms the structural backbone of photoreceptor membranes and plays a critical role in brain cell function, while both DHA and EPA exhibit anti-inflammatory properties. Data from the Women's Health Study including over 32,000 individuals between the ages of 45-84 years of age showed that adequate dietary intake of the omega 3s in the form of fish two or more times per week was associated with a reduction in developing symptoms of dry eye.[20] The Dry Eye Assessment and Management (DREAM) study,[21] a double-blind placebo controlled study, yielded equivocal findings regarding symptom relief and objective findings on exam. However, it is important to note that olive oil, which contains oleic acid, an omega-9 fatty acid with anti-inflammatory properties, was used as the placebo in this study, and may have independent benefits for dry eye. A meta-analysis of 19 randomized controlled trials for omega 3s for dry eye found that overall, supplementation was beneficial, especially with higher doses of EPA and when given for extended periods of time.[22]

Other omega fatty acids, such as the anti-inflammatory omega-6, gamma linolenic acid (GLA),[23-26] and omega 7 (palmitoleic acid from sea buckthorn oil)[27] have also shown benefits for dry eye based on prospective clinical studies and meta-analyses.

With respect to AMD, although the AREDS2 study reported no significant impact of omega-3 supplementation (DHA 350 mg and EPA 650 mg) on AMD progression across the study population,[28] subsequent analysis revealed that higher dietary intake conferred a lower risk profile.[29]

The B vitamins, particularly riboflavin (B2), folic acid (B9), and vitamin B12, convey several benefits for various neuro-ophthalmic conditions. Riboflavin has received attention for its role in migraine prophylaxis, given its mitochondrial support function, and B2 deficiency being common in migraine. Two separate meta-analyses revealed that oral supplementation with high dose riboflavin (400 mg daily) for three months significantly reduces migraine frequency and severity.[30,31]

Elevated homocysteine, a byproduct of metabolic processes, is a known risk factor for neurovascular conditions associated with ischemia to the retina or brain. Select B vitamins, in particular folic acid and B12, and potentially B6, may effectively reduce homocysteine levels.[32] Dietary folate and supplementation with folic acid have been shown to lower the risk of neurologic ischemic events by 5% and 10%, respectively.[33,34]

Antioxidants like vitamins A, C, and E, alongside endogenous compounds such as glutathione, have been explored for their efficacy in preventing oxidative damage, particularly in relation to age-related cataracts and AMD. The antioxidants' primary mechanism involves neutralizing reactive oxygen species (ROS) generated by high metabolic demands in photoreceptor and neuronal cells, thereby limiting oxidative stress. AREDS confirmed that a high-dose antioxidant formulation containing these vitamins, in conjunction with zinc, contributed to a reduction in the progression of intermediate to advanced AMD.[35] However, the formulation conferred no benefit for cataract in the study population. Other studies have shown that populations with high intake of fruits and vegetables have lower incidence of cataract.[36]

Phytonutrients, including flavonoids from berries and curcumin from turmeric, have demonstrated neuroprotective and anti-inflammatory properties, and may support eye and brain health.[37] Flavonoids in berries are associated with a reduction in cognitive aging, as they appear to delay neurodegenerative changes by modulating antioxidant and anti-inflammatory pathways.[38] Similarly, curcumin has been studied for its potential to inhibit amyloid plaque accumulation in the brain[39] and to protect retinal pigment epithelium from inflammatory damage,[40-42] although its bioavailability remains a limiting factor in clinical use.

Emerging interest surrounds certain supplements, notably idebenone, nicotinamide (Vitamin B3) and biotin (B7). Idebenone, a synthetic analog of coenzyme Q10, has shown promise as a therapeutic intervention for Leber's Hereditary Optic Neuropathy (LHON), a mitochondrial disorder that leads to optic neuropathy with severe vision loss. Coenzyme Q10 enhances mitochondrial function by facilitating electron transport within the mitochondrial respiratory chain, bypassing complex I dysfunction and reducing oxidative stress.

The RHODOS study, a phase III double-blind, placebo-controlled trial, investigated the effects of idebenone in 85 patients with LHON.[43] The treatment group received idebenone at a dose of 900 mg/day (300 mg three times daily) over a 24-week period. The study, though it did not meet its primary endpoint, demonstrated a trend towards visual acuity improvement with idebenone ($p=0.046$). Additionally, patients receiving idebenone were less likely to experience further visual deterioration in both eyes. These findings suggest that idebenone has the potential to halt or even reverse visual loss in patients with LHON, particularly if treatment is initiated early in the disease course, and especially in those with discordant visual acuity.

A subsequent follow-up study, RHODOS-OFU (Open Follow-Up Study),[44] provided further insights into the long-term effects of idebenone in LHON patients. This observational study followed 56 patients from the original RHODOS cohort for an additional 30 months. The follow-up data revealed that visual gains achieved during the initial treatment period with idebenone were sustained over time. The study also confirmed the safety of long-term idebenone use, with no significant adverse events related to the drug reported during extended follow-up. These findings idebenone as an acute therapeutic treatment that can provides durable, long-term protection against visual deterioration in LHON patients.

Nicotinamide is a precursor to NAD+, a coenzyme involved in cellular energy metabolism, and has shown neuroprotective effects in preclinical studies in models of glaucoma.[45-47] A phase-2 randomized, double-blind placebo-controlled prospective clinical trial evaluated supplementation with nicotinamide (1000-3000 mg/day) and pyruvate (1500-3000 mg/day) for 2 months, noting improvements in visual field parameters, although the authors recommended larger-scale studies.[48]

Biotin has attracted attention for its role in mitochondrial function and nerve health, and may help in chronic disability in multiple sclerosis.A prospective double-blind placebo-controlled trial of high-dose, pharmaceutical grade biotin was given to subjects with optic neuritis, and did not show improvement in visual acuity, even after a 6 month open label period.[49] Case reports have also suggested that a biotin deficiency, due to a mutation in the biotinidase enzyme, may be linked to optic neuropathy and retinopathy.[50]

Dietary patterns that emphasize whole, minimally processed foods, particularly the Mediterranean and plant-predominant diets, have been consistently associated with lower risks of AMD and neurodegenerative conditions. These diets, which are rich in leafy greens, berries, and healthy fats, are naturally abundant in carotenoids, omega-3s, and flavonoids, as well as antioxidants and anti-inflammatory compounds. Longitudinal research supports the protective effects of these diets, associating them with slower cognitive decline[51-53] and lower incidence of AMD by 41%.[54]

In contrast, diets high in saturated fats, ultra-processed foods, and red meat have been correlated with increased risks of both AMD[55,56] and cognitive decline,[57,58] likely due to inflammation and oxidative stress triggered by their dietary compounds.

In summary, a number of nutrients such as the macular carotenoids and omega-3 and -6 fatty acids have shown benefit for vision and brain health when obtained via the diet or via supplementation. Supplementation with select micronutrients has shown benefits for eye and brain health, as seen with lutein, zeaxanthin, and meso-zeaxanthin and lower risk for advanced AMD, and folic acid and reduced risk for stroke. There is emerging evidence that other nutrients such as astaxanthin for macular degeneration or post cataract surgery, curcumin for AMD and Alzheimer's disease, and nicotinamide for glaucomatous optic neuropathy, may be helpful. However, more research into the impact of diet and supplementation for vision and neurologic conditions is needed, perhaps taking into account genetic variability that may affect bioavailability of these nutrients.

CME ANSWERS

1. C
2. B
3. D
4. A

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WILL A PROCEDURE HELP ME?

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LEARNING OBJECTIVES

1. The participant will be able to discuss the status of stem cell transplants with patients.
2. The participant will be able to describe to patients the Utah Electrode Array and its potential to restore vision.
3. The participant will be able to discuss the limitations of vision therapy for traumatic brain injury with patients.

CME QUESTIONS

1. Which of the following statements is TRUE?
   A. The regeneration of retinal ganglion cell axons does not necessarily lead to the restoration of visual function
   B. Stem cells cannot be induced to differentiate into non-mesenchymal derivatives such as neural cells
   C. Mesenchymal stem cells promote retinal ganglion cell survival by inhibiting mitochondrial function
   D. Mesenchymal stem cells lack the ability to secrete paracrine signalling factors
2. Which of the following statements is TRUE?
   A. The Utah Electrode Array is implanted in the retina
   B. The Utah Electrode Array is implanted in the optic nerve
   C. The Utah Electrode Array is implanted in the optic tract
   D. The Utah Electrode Array is implanted in visual cortex
3. Which of the following statements is TRUE?
   A. Vision therapy is effective for the treatment of convergence insufficiency
   B. Vision therapy is effective for the treatment of strabismus
   C. Vision therapy is effective for the treatment of amblyopia
   D. Vision therapy is effective for the treatment of visuospatial deficits

KEYWORDS

1. Vision therapy
2. Utah Electrode Array
3. Stem cell transplantation
4. Optic neuropathy
5. Optic atrophy

HIGHLIGHTS

- Optic neuropathies, including glaucoma, are associated with progressive retinal ganglion cell loss. Stem cells show promise for repairing optic nerve damage by differentiating into retinal ganglion cell-supportive environments. However, many challenges remain before these cells can be successfully transplanted into humans.
- A 2021 study demonstrated that chronic intracortical microstimulation via a 96-electrode array implanted in the visual cortex of a blind individual was safe and effective, enabling the participant to perceive visual information such as letters and object boundaries. The findings highlight the potential of this approach to restore functional vision in individuals with severe visual impairment.
- Optometric visual rehabilitation therapies are commonly used for post-trauma visual disorders, but their scientific basis is limited, relying mostly on case reports and series without controls. Providing physicians with guidance on the rationale and evidence for these therapies is essential to better inform patient care.

SUMMARY

Stem Cell Therapy
Emerging stem cell therapies show promise for protecting retinal ganglion cells (RGCs), preventing secondary degeneration, and promoting axonal regeneration, but challenges remain in restoring functional connections to the brain. For this reason, currently, RGC regeneration with stem cells does not necessarily restore visual function.

Mesenchymal stem cells (MSCs) show significant promise because they migrate to injury sites, support tissue regeneration, differentiate into neural cells, and enhance the survival of RGCs through the release of neurotrophic and neurogenic cytokines. Additionally, MSCs' paracrine effects, including secretion of growth factors and anti-inflammatory cytokines, offer synergistic benefits for RGC protection and axonal growth, making them a promising strategy for treating optic nerve injuries. MSC may improve mitochondrial function and attenuate oxidative damage by inhibiting reactive oxygen species (ROS) production and enhancing mitochondrial dynamics.

Utah Electrode Array
The Utah Electrode Array (UEA) is a 4mm x 4mm array of 96 electrodes, each 1.5mm long. It is designed to be implanted in striate cortex. When connected to a video camera, a signal processing device, and a microstimulation device, an experimental human subject was able to identify some letters and recognize object boundaries. These preliminary experiments indicate that the UEA may be able to restore rudimentary vision in patients with profound bilateral vision loss. Unlike retinal implants, the UEA “skips” the eye, optic nerves, tracts, and radiations. Patients whose visual impairments originate in these parts of the visual system may therefore benefit in the future from a variation of this technology.

Vision Therapy
Traumatic brain injury (TBI) is a leading global cause of disability and death, with mild TBI (mTBI), often referred to as concussion, posing significant diagnostic and economic challenges due to its subtle yet impactful neurological effects. Despite advances in imaging and biomarkers, mTBI diagnosis remains clinical, hampered by inconsistent definitions and potential misdiagnoses, which contribute to excessive healthcare costs and unnecessary treatments. Visual rehabilitation for symptoms like convergence insufficiency highlights the economic burden, with studies showing misdirected resources and frequent failure to meet diagnostic criteria.

Recommendations for improving therapeutic interventions for visual symptoms in mTBI emphasize the need for rigorous, unbiased research methodologies. Key unanswered questions include identifying patients at risk for persistent symptoms, evaluating the efficacy of visual rehabilitation compared to standard care, and determining the optimal timing for intervention. Therapies that improve convergence insufficiency are safe and effective. However, optometric vision therapies for the treatment amblyopia, strabismus, and visuospatial defects are unproven.

CME ANSWERS
1. A
2. D
3. A

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TREATMENTS OUTSIDE THE BOX: WILL GLASSES HELP ME?

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LEARNING OBJECTIVES

1. The attendee will be able to identify and describe low vision techniques for severe visual field loss.
2. The attendee will be able to list uses for specialized spectacles and/or contact lenses in low vision patients.
3. The attendee gain pearls for managing patients with binocular vision disorders and nystagmus.
4. The attendee will improve their knowledge of referral services available from low vision and polytrauma optometrists.

CME QUESTIONS

1. Monocular sector prisms are primarily used to:
   A. Move the non-seeing target into the seeing field
   B. Unify a vertically diplopic image
   C. Unify a horizontally diplopic image
   D. Dampen nystagmus

2. Which product is incorrectly paired with the symptom it is attempting to treat?
   A. Yoked prisms for nystagmus
   B. Contact paper for migraine
   C. Side shields for photophobia
   D. Neurolens® for headache

3. Contact lenses are used in low vision/polytrauma optometry to treat all the following conditions except:
   A. Nystagmus
   B. Photophobia
   C. Diplopia
   D. Visual field loss
   E. Dry eye

KEYWORDS
1. FL-41
2. Peli Lens™
3. Low vision
4. Glasses
5. Photophobia

Visual impairment, wherein functional changes occur because of anatomic changes to the visual system, and visual disability, the skills and abilities affected by the visual dysfunction, can benefit from visual aids and devices. The term "low vision" can be defined as "reduced visual function resulting from any disorder of the eye or visual system."[1] Glasses and other optical corrective devices may be used in these patients, as well as those who suffer from migraine, traumatic brain injury, diplopia, and other causes of photophobia, glare, or dyschromatopsia.

Different types of visual function deficits, such as peripheral vs. central field defects, require targeted approaches to visual aids. Tools as simple as a careful refraction may significantly improve a patient's visual quality of life. In this effort, a low vision optometrist, certified low vision therapist, and orientation and mobility specialist may all be needed in a visually disabled patient's care to work with other PT/OT specialists and prevent falls or injury.[2] Glasses and visual aids are part of the American Academy of Ophthalmology's Preferred Practice Pattern for Vision Rehabilitation Guideline for Adults, which states that "comprehensive vision rehabilitation assesses 5 areas: reading, activities of daily living, safety, continued participation despite vision loss, and psychosocial well-being." (3)

Since reading is such an essential part of our intensely visual world, its assessment is critical in the low vision patient, especially those with central vision loss. Determination of refractive error, near vision, and range of accommodation is important, as well as contrast sensitivity, magnification, reading speed, fixation behavior (ie. eccentric) and eye movements. (4) The minimum reading visual field spans 2 degrees in each horizontal direction and allows detection of words (not just individual optotypes). Fluent reading in Western writing requires 5 degrees (15 letters) to the right and 1.3-2 degrees (4-6 letters) to the left of fixation. (5) Optical correction for an individual with central visual impairment can involve spectacles, handheld and stand magnifiers, and telescopes aid in visualizing small print and near objects. Predicting the necessary strength of the reading add is often determined by the Kestenbaum rule: *"The add required can be estimated by the measured visual acuity, by dividing the denominator by the numerator."* For example, a patient with 20/400 vision should have a 400/20 = +20 D lens, with the material held at the focal point of the lens (1/20m, a.k.a. 5 cm).(1) Nevertheless, for patients with Leber hereditary optic neuropathy (LHON), the central scotomata are large and fenestrated, with a poor correlation between magnification need and reading speed. In these patients, the preferred retinal locus was found in one study to be within the fenestration and very unfavorable because the size was usually too small for fluent reading; therefore, eccentric viewing training is recommended in LHON patients. (6) Thus far, color filter overlays and prism spectacles have not shown any evidence of improving reading speed or visual quality of life in low vision patients. (7)

For those with permanent peripheral vision deficits--in particular, homonymous hemianopia—activities of daily living are greatly impacted, especially moving/orienting in one's environment, driving, and hand-eye coordination. Physically expanding a permanent field defect through therapy, or visual restitution training, has been controversial and deemed largely non-efficacious, at most delivering a placebo effect (8-10). The goal is then to improve functionality of existing field defects, and there are two general approaches: visual field enhancement or visual field expansion, both involving spectacle adaptations through prisms (2). Visual field enhancement utilizes techniques to enhance the use of remaining functional vision by moving objects from the non-seeing to seeing field or to trigger the patient to saccade into the blind field. In this category, sector (a.k.a. straight, spotting, or round "button") prisms applied in the non-seeing area are most popular and can be ground into spectacles, after a Fresnel prism trial applied monocularly (see Figure 1). Unfortunately, binocularly applied prisms (either yoked full or yoked sector prisms) create a scotoma at the prism apex (apical scotoma), which can be disabling when observed near fixation, as with yoked sector prisms (3,4). Yoked prism over the entire field may just induce a head turn rather than expanding the central visual field and therefore is of little practical use (11). Therefore, most sector prisms are applied monocularly, which allows the other eye to compensate for the apical scotoma in the eye with prism and keeps fixation central (fig. 1b and 1c). The disadvantage is diplopia when fixating through the prism, and no help when looking away from the prism. When used, most low vision practitioners start with a 15-prism diopter Fresnel press-on prism and increase the prism power (20 to 30Δ) depending on the patient's response and adaptation (12). Sector prism may also be used vertically in altitudinal field defects, generally starting with a smaller prism power. While definitive randomized clinical trial evidence is lacking with the above prisms, there is some evidence that binocular sector prisms do help spatial hemi-neglect to increase awareness in the neglected field (13). To assist with activities of daily living (ADLs), there is good evidence that prism adaptation testing, in which patients are trained with large angle prism glasses to perform reaching tasks while wearing base-left wedge prisms, can cause a persistent shift in the visual field to the right in patients with left hemifield neglect and help improve reaching tasks and improving hand-eye coordination to other ADLs.(13,14)

In contrast, visual field expansion uses prisms to expand the field of view into the non-seeing field. The best evidence for clinically useful field expansion comes from monocular peripheral prism segments. Temporary press-on Fresnel peripheral prism segments of 40Δ over the lens ipsilateral to the homonymous defect have proven useful in randomized-controlled trials (15). Furthermore, peripheral prisms showed longer-term utility through at least 1 year in patients in a community-based study (16), as well as other trials for obstacle avoidance (17) and even with obliquely placed peripheral prisms for driving (18). Peli Lens ™ prisms (Chadwick Optical, Inc., fig. 1d) are now commercially available permanent 40Δ segments that act as mobility aids by expanding peripheral field into the blind hemifield, while sparing central vision binocularity. They require some basic fitting and training, reviewed here:
https://youtu.be/CEubdVP_CXI?si=uKbEGBJjgPoeC3VZ

In patients with binocular diplopia, readers are very familiar with the two methods of prisms and occlusion. Fresnel and ground-in spectacle prisms are used to treat almost any cause of incomitant diplopia where vision is preserved adequately in both eyes (19-21). Comitant strabismus is also commonly assessed and treated with Fresnel, and then permanent prisms. For example, convergence insufficiency is commonly managed with bilateral base in prism fit onto or ground into separate near spectacles to compensate for the near exotropia (22). Prism trials for children with intermittent exotropia have been less successful, showing no difference between prism correction and refraction alone (23). Monovision correction with either contact lens or spectacle correction may help the patient ignore the second image and avoid

bifocals, learning to ignore the non-dominant image by adaptation, a process termed “suspension.” (24-26) To achieve monocular occlusion, one can use a quarter-sized piece of contact paper over the optical center of the non-dominant eye’s lens, allowing for a central unilateral scotoma with peripheral vision preservation. Bangerter occlusion foils, Mins lenses, or even slightly frosted over-the-counter tape can alternatively be placed over the area of diplopia on the eye-ward side of the lens, all of which are more discreet than eye patch or a dark occlusive filter (W. Jun, personal communication). “Scotogenic” contact lenses have also been developed to produce a central scotoma in one eye while sparing its peripheral vision (27). To restore fusion in primary gaze, prisms are required to prism contact lenses have been used for vertical realignment of the horizon or diplopia but are limited by positioning and stability. More recently, custom three-dimensional printed scleral lenses with horizontal prism were successfully used to treat a patient with decompensated esophoria (28) and technologic advances may lead to future prism correction with contacts.

In patients with nystagmus, a retinal image slip over 5 degrees per second is associated with decreased visual acuity and the goal is to minimize the amplitude and frequency while preserving voluntary extraocular movements. Yoked prisms can be used to reorient the image to the relative null point of nystagmus, improving visual acuity and assisting with the head turn (25). If the nystagmus is suppressed at near, prisms that induce convergence can decrease the oscillopsia, utilizing “spectacles with 7Δ base out Fresnel prism with -1 Diopter spherical correction so the associated forced accommodation is corrected.” (29) Infantile nystagmus syndrome dampens with contact lens use, through an as-yet unclear mechanism. High negative contacts can also be paired with high plus spectacles for up to 90% oscillopsia relief, using in a stationary environment to allow for the smaller field of view. (29)

In patients with photophobia from migraine, blepharospasm, traumatic brain injury, dry eye, and digital eye strain, a.k.a. “computer vision syndrome” (30), much attention and commercial interest has been paid to optical correction. Practical optical treatment of dry eye syndrome and photophobia uses contact lenses with tint or tinted periphery, scleral contact lenses, and glasses with side shields or moisture chambers. However, recent advances in the pathophysiology of photophobia related to trigeminal sensitization by intrinsically photosensitive retinal ganglion cells have led to the development of evidence-based glasses tints, most notably FL-41 tints (31,32). Clinical trial evidence supports their use in blepharospasm (33), dry eye (34) and in some patients with chronic ocular pain (35). In contrast, blue-blocking lenses that are widely commercially available and gained popularity for headaches, computer vision syndrome, sleep quality and glare prevention, have mixed or no evidence of true efficacy. (36,37) Neurolens® uses a proprietary “objective measurement technique” to measure dissociated phorias and fixation disparities, then applies a specialized contoured multi-prism lens to treat them. A recent RCT funded by the manufacturing company showed statistically significant improvement in subjective vision related headache scores by the HIT-6 Likert scale, but the trial did not reach clinical efficacy measures. (7) Despite this limitation, Neurolens® is being heavily marketed for headaches, photophobia, reading speed and work productivity improvement.

In summary, there are many neuro-ophthalmic conditions in which involvement of low vision and polytrauma optometry specialists may help provide optical correction to ameliorate symptoms and assist with activities of daily living, but caution should be taken in applying the best available evidence to real-world efficacy.

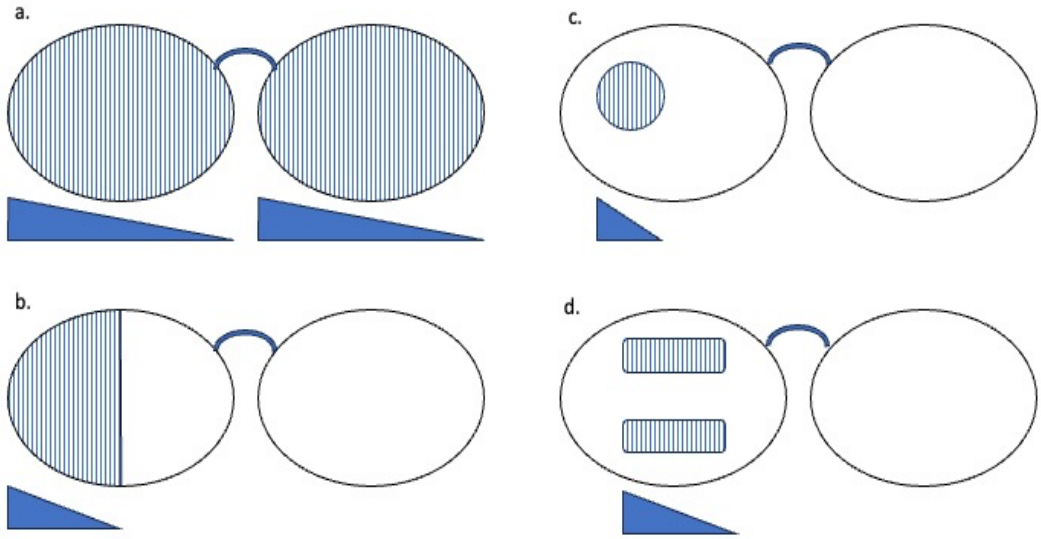

Figure 1. Various prism adaptive tools for patients with a right homonymous hemianopsia. Yoked prisms (a) are not useful for hemianopsia but are used to move the null point of fixation in nystagmus. Monocular sector (b) and round or "button" prisms provide extra peripheral input into one eye to avoid the apical scotoma, but they cause diplopia. Only monocular peripheral prism segments, marketed as Peli lenses™ (d), have been clinically proven to help visual field expansion and are most frequently used for permanent application.

CME ANSWERS
1. A
2. B
3. D

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WILL EYE DROPS HELP ME?

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LEARNING OBJECTIVES

1. Describe the mechanism of action of varenicline nasal spray to increase tear production.
2. Enumerate the ways in which recombinant human nerve growth factor promotes corneal healing.
3. Explain how preservative-free tears can be safely packaged in a bottle instead of single-use vials.

CME QUESTIONS

1. Pilocarpine drops can improve near vision by which of the following mechanisms:
   A. Dilating the pupil
   B. Blocking ciliary muscle contraction
   C. Creating a pinhole effect
   D. Stimulating the ciliary muscle
   E. C and D

2. Cenegermin is indicated to treat which of the following conditions:
   A. Neurotrophic keratitis
   B. Bell palsy
   C. Herpes simplex dendritic keratitis
   D. Presbyopia
   E. A and B

3. Varenicline increases basal tear film production stimulating which type of receptors:
   A. Alpha adrenergic receptors
   B. Acetylcholine receptors
   C. Beta adrenergic receptors
   D. Dopamine receptors
   E. GABA receptors

KEYWORDS
1. Oxymetazoline
2. Ptosis
3. Neurotrophic keratopathy
4. Varenicline
5. Pilocarpine

HIGHLIGHTS
Oxymetazoline is a topical alpha-adrenergic receptor agonist that was approved in 2020 for treating ptosis. Phentolamine was approved in 2024 for reversing dilation in the clinic. Dilute pilocarpine is available by prescription for improving near vision. Cenegermin drops are expensive but effective for promoting healing in patients with neurotrophic keratopathy. Varenicline intranasal is a highly selective cholinergic agonist approved to treat dry eyes. Perfluorohexyloctane forms a monolayer at the air-liquid interface of the tear film which can be expected to reduce evaporation. Cyclosporin is now available in multiple formulations. The recent outbreak of contaminated eye drop related infections was due to resistant Pseudomonas contamination in multi-dose bottles of tears that were lacking preservative, in violation of FDA rules. There is, however, safe packaging for multidose preservative-free tears.

SUMMARY
Brief overview of the potential benefits and harms of newer topical medications, including oxymetazoline, phentolamine, pilocarpine, cenegermin, varenicline nasal, and perfluorohexyloctane, with evidence. Pearls about artificial tears and

blepharitis treatments.

CME ANSWERS

1. E
2. A
3. B

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WILL DEVICES HELP ME?

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LEARNING OBJECTIVES

1. The attendee will appreciate the range of technologies that are being used in attempts to restore vision.
2. The attendee will develop a sense of which types of therapeutic approaches might be relevant for blindness caused by lesions at different locations along the afferent visual pathway
3. The attendee will develop a perspective of how to guide patients who seek guidance on considering the various forms of visual rehabilitative approaches.

CME QUESTIONS

1. Blindness caused by neural injury can be improved by (choose all that apply):
   A. gene therapy
   B. prosthetic therapy
   C. perceptual training
   D. light therapy
   E. all of the above

2. Which therapeutic approach has been most successful?
   A. gene therapy
   B. prosthetic therapy
   C. perceptual training
   D. light therapy
   E. no single response is appropriate

3. Which therapeutic approach has the greatest potential to treat a wide range of blinding conditions?
   A. gene therapy
   B. prosthetic therapy
   C. perceptual training
   D. light therapy

4. Should patients be counseled to pursue one of the forms of treatment discussed in this review?
   A. patients should be counseled to understand whatever approach is being considered
   B. patients should be discouraged from pursuing any of these forms of therapy given their experimental nature
   C. patients should be advised to consider pursuing any of these forms of therapy
   D. A and C

KEYWORDS

1. Visual Restoration
2. Neuroplasticity
3. Visual prosthetics
4. Genetic therapy

Blindness is a serious disability that reduces independence and the potential for gainful employment (N.B. 2/3 of our blind citizens are unemployed), and increases the risk for obesity, depression and mortality. Blindness is projected to impact 3.5% of the United States population (i.e. 1 in 28 individuals) over age 45 by the year 2030[1-4], thus making it one of the more significant medical disabilities. Accounting for lost wages, supportive services and increased co-morbidities, the annual cost of blindness in the United States is a staggering $16.5 billion per year.[5] In the industrialized world, blindness

is usually caused by untreatable neural disease for which few therapies have provided any meaningful restoration of visual function. This summary addresses a variety of technical approaches to either restore some vision or improve visual function.

Neural forms of blindness are exceptionally challenging to treat as putative therapies must convey detailed and topographically organized visual information to the brain to provide hope for improved vision. Both biological approaches (i.e. stem cells; transplantation of retinal neurons; genetic and epigenetic therapies) and engineered devices provide potential opportunities for visual restoration, and each approach has benefits and disadvantages. The benefits of the biological approaches will be briefly reviewed before addressing the potential advantages of engineered physical devices, which is the prime focus of this review.

Biological Strategies for Visual Restoration

A wide variety of biological strategies have been used for visual restoration, but the most compelling to date has been targeted genetic therapies. In brief, single "point" mutation genetic defects that cause blindness are prime targets for genetic therapy, which is given via an adeno-associated virus (AAV) vector delivered into the vitreous or subretinal space. The initial studies were directed toward treatment of Leber Congenital Amaurosis (due to mutation in the RPE 65 gene) but are now being expanded to other forms of outer retinal disease. The first patient who received the FDA-approved drug for this condition, Luxturna, was a 13 year-old boy who had been severely blind, but over months to years post treatment (in 2018) he developed the ability to ride a bike and even walk in dark, unfamiliar environments which had been especially difficult for him to do before treatment. CRISPR technology is now also being used to treat some forms of genetic blindness.[6]

Optogenetic therapy in which genetic transfection is performed (via an AAV injection to deliver opsin proteins to selected retinal neurons that survive a retinal degeneration) has been used with some improvement in vision in a single patient (in 2021).[7.] The reported improvement allowed the patient to recognize large test objects that had not been possible before treatment. The optogenetic approach may require use of specialized glasses to deliver higher levels of light of a specific wavelength that maximally incites the transfected opsin protein. The optogenetic approach has the advantage over genetic insertion to replace mutated proteins (as described above) in that retinal neuronal classes that are not as susceptible to degeneration from outer retinal diseases (e.g. retinal ganglion cells) can be targeted. Optogenetic "switches" also make it possible to activate or inhibit neuronal firing, which theoretically can enable a type of "ON" and "OFF" functionality that is inherent in normal retinal output.

Remarkably, genetic approaches have demonstrated significantly improved visual function even for patients born with severe *congenital* blindness, which had previously been considered to be less amenable to therapeutic intervention. There remains some uncertainty about the durability of genetic or optogenetic therapy and whether subsequent treatments might be needed in some patients.

Engineered Strategies for Visual Restoration - "Devices"

Traditional approaches to visual restoration involved used of special lenses to provide an optical benefit to improve visual function. These approaches are still routinely used, but they cannot restore vision as they can only enhance visual function for whatever level of vision remains.

This description focuses on head-mounted, desk-top and implantable devices that incorporate technologies designed to help the visually-impaired. These categories of devices are designed to improve visual "function", meaning improved ability to perform daily tasks even without measurable improvement in traditional measures of visual function, like central acuity.

Head-Mounted Devices. A wide variety of head-mounted devices have been developed to provide assistance to visually-impaired patients. Such devices generally provide input via auditory or tactile input to in essence bypass the visual channel (i.e. "sensory substitution"). The rapid development of sophisticated software programs has provided significant capabilities for the blind. In particular, optical character recognition (OCR) programs that convert text (of almost any font) into computer-generated voice are especially useful for the blind. OCR technology can be used to scan images, photographs or documents, or to recognize items on a shelf in a grocery store, street signs and traffic lights.[8] The information is transferred to the user in real-time thus assisting with tasks such an open navigation in unfamiliar environments. Numerous such devices are available commercially, with a range of prices, with the more expensive devices (e.g. OrCam MyEye, Israel) offering greater ease of use and functionality for roughly $5,000. Attempts are also being made to have such devices provide navigational guidance cues to the blind, but this is a much more demanding task that has yet to provide sufficient benefit.

Implantable Devices. Prosthetic devices that deliver electrical stimulation to activate the visual pathway distal to a degenerated site have been explored for the retina (including supra-choroidal, sub-retinal and epi-retinal placement); optic nerve; lateral geniculate body and visual cortices (both primary and higher associative). Presently, only retinal and cortical devices are active in clinical trials. Many companies have formed but most have been disbanded, some due to slow scientific progress but several due to commercial headwinds. The early focus of retinal devices on retinitis pigmentosa, which affects a very small segment of the population, constrained the potential for profit, which by the nature of device development also imposed a relatively long time for potential return-on-investment.

The only surviving *retinal* device in the U.S. is now marketed by Science Corporation (Alameda, California) which purchased the retinal technology and device concept from Pixium, which had been performing clinical tests based on the photodiode-based technology developed at Stanford University. (Science Corporation also is developing an optogenetic strategy for visual restoration.) The commercial plan for the Science Corporation device, which is implanted subretinally, is to treat the much larger population of patients with age-related macular degeneration (ARMD). The most successful outcomes for this device delivered 20/420 vision to some ARMD patients[9]. A similar photodiode-based device from is being developed by Iridium (Taiwan), which has the additional benefit of wireless, pixel-level control.

The second active clinical trial in the United States is being conducted with a wireless visual c*ortical* implant (consisting of 16 or more "pods", each with 4 electrodes) under the direction of Phil Troyk (at the Illinois Institute of Technology).[10.] This group has recently implanted their second patient. The psychophysical results have not been released publicly but they have been generally been positive (as will be discussed).

The visual prosthetic field seems poised at an inflection point, offering hope of 20/200 or better vision, potentially freeing the “legally-blind” of that stigma and offering meaningful improvements in quality-of-life.

Devices to Enhance Vision or Visual Function Through Training or "Wizard" guidance.

A wide range of external (i.e. non implantable) devices to help the visually-impaired have been developed over the last two decades.[11]

One such device - "Be My Eyes" is being developed by a Danish company to provide remote viewing and guidance assistance from a sighted human volunteer to a visually-impaired person who wears glasses with an embedded camera. When assistance is needed, a user electronically notifies a registered human assistant (i.e. someone who has signed up on the company "app") who then provides real-time guidance to the blind person by viewing imagery captured by the head-mounted camera. Over 8 million individuals across more than 150 countries have signed up to provide guidance for more than 700,000 users (according to the company website). The company seeks to "do everything" to make their services "free to the blind".

Some devices have been developed to "train" the visual system to improve function by tapping into the potential of neuroplasticity. A FDA-approved head-mounted device made by Luminopia is designed to treat amblyopia by delivering dichoptic imagery to each eye, with the less good eye receiving enhanced (spatial or temporal) visual input (including by streaming preferred TV shows).[12] Treatment is given for one hour per day for six days in a week, and purportedly demonstrates improvement in vision as early as 4 weeks. Some other attempts at training the afferent visual pathway have failed outright (as did the NovaVision approach and device.[13])

This failure of some perceptual training concepts does not negate the possibility of improved afferent visual function with training, as K. Huxlin (University of Rochester, NY) has demonstrated.[14,15] Her laboratory was the first to study the potential for visual improvement post stroke using various methods of perceptual training that have included attentional manipulations, cross-modal cues, virtual reality and transcranial electrical stimulation. Even with these efforts and prolonged training (up to six months), the benefits are generally modest and are not necessarily durable. An ongoing clinical trial (ClinicalTrials.gov # NCT04798924) is collecting additional data on the outcomes of such training to establish the degree functional benefits can be derived.

Other approaches, including "light therapy" (sometimes referred to as "syntonic phototherapy" that delivers controlled intensity of specific wavelengths of light) have been advertised as means to improve vision[16], but also to treat everything from chronic pain, to arthritis, to seasonal affecting disorders and gum disease.

Summary. Each of the above categories of treatment options offers the potential for improved visual "function" potentiall for amblyopia, early-onset blindness (i.e. retinal degenerations), or stroke. Implantable devices, especially at the level of the cortex, offers the potential for treatment of the largest range of blinding conditions. Roadmaps to guide the development of better retinal devices are becoming more clear with accrued experience across the field.[17] The technological improvements in the prosthetic field have been quite impressive, but a better understanding of the underlying neuroscientific consequences of blindness is critical to better guide the development of the technology.[18]

CME ANSWERS

1. **A, B, C**
2. **E**
3. **D**
4. **A**

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Neuro-Ophthalmology Problems from Childhood to Adulthood [2.0 CME]

Moderators: Melinda Chang, MD & Jason Peragallo, MD

Many pediatric neuro-ophthalmologic conditions persist as patients age, and considerations in adulthood may differ from childhood. In this session, we will discuss the diagnosis, management, and complications of optic pathway gliomas, cerebral/ cortical visual impairment (CVI), congenital optic neuropathies, and amblyopia in various stages of life.

Upon completion of this session, participants should be able to:

(1) List the endocrinopathies that are associated with optic nerve hypoplasia and the age range at which endocrine testing is indicated.

(2) Describe the differences between cerebral/cortical visual impairment (CVI) in children and cortical blindness in adults.

(3) Discuss the potential advantages of binocular treatments for amblyopia.

Introduction, *Melinda Chang, MD & Jason Peragallo, MD*
Optic Pathways Gliomas, *Robert Avery, DO*
Cortical Visual impairment, *Gena Heidary, MD, PhD*
Optic Nerve Hypoplasia + Inherited Optic Neuropathies, *Mark Borchert, MD*
Amblyopia, *Eric D. Gaier, MD, PhD*

OPTIC PATHWAY GLIOMAS IN CHILDREN VERSUS ADULTS

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LEARNING OBJECTIVES

1. List the different age of onset between children and adult optic pathway gliomas.
2. Describe the differences and similarities of tumor pathology between children and adults that manifest optic pathway gliomas.
3. Explain the frequency of Ophthalmologic evaluations in patients with optic pathway gliomas.

CME QUESTIONS

1. Which is the most common pathology for optic pathway gliomas or any visual pathway tumor?
   A. Craniopharyngioma
   B. Rathke cleft cyst
   C. Juvenile pilocytic astrocytoma, WHO grade 1
   D. FGFR receptor positive melanoma

2. Adults presenting with a biopsy proven low grade glioma of the visual pathway have the following change of their tumor converting to a high grade glioma:
   A. 2%
   B. 30%
   C. 80%
   D. 90%

3. For NF1-OPGs actively undergoing treatment with chemotherapy, the recommended frequency of eye exams is:
   A. Every 3 months
   B. Every 12 months
   C. Not necessary as they are undergoing treatment.
   D. Every 4 week.

KEY WORDS

1. Neurofibromatosis type 1
2. Juvenile pilocytic astrocytoma
3. Optic pathway glioma

OVERVIEW

Optic pathway gliomas (OPGs) are low grade gliomas that are located anywhere along the optic nerves, chiasm or optic tracts.[1] OPGs can be isolated to one or more of these structures. An overwhelming majority of OPGs are juvenile pilocytic astrocytoma that are labeled WHO grade 1 tumors.[2] Typical histologic features include the Rosenthal fiber. Less commonly, OPGs can be grade II such as oligodendroglioma, pleomorphic xanthoastrocytoma, and pilomyxoid astrocytoma.

The presenting signs/symptoms are similar across ages and are most typically visual acuity loss, visual field loss, color vision loss and optic atrophy.[1] OPGs isolated to the optic nerve and pushing on the globe may manifest as proptosis, pulsatile exophthalmos or even as ocular motor deficits.

Low grade gliomas in adults are quite rare and account for less than 1% of brain tumors. Low grade gliomas along the visual pathway in adults are even loss common. While the overall survival of low grade gliomas is quite high in adulthood (>90% over 5 years), they all require active surveillance as conversion from a low grade into a high grade glioma (i.e., glioblastoma, WHO grade 4) is believed to be nearly 30% in adulthood.[3] Even if the original biopsy confirms a WHO grade 1 low grade glioma, suspicion for malignant transformation should be high in cases refractory to therapy or with rapid growth. Adults can present with OPGs in nearly any decade of life. Vision loss ranges from mild to no light perception.

Low grade gliomas are the most common brain tumors in children and adolescents—accounting for over 20% of intracranial masses. In total, OPGs account for 5% or 1 in 20 brain tumors. In children with Neurofibromatosis type 1 (NF1), approximately 15-20% will develop an OPG.[4] Children with NF1 are also predisposed to developing low grade gliomas outside of the anterior visual pathway. Interestingly, less than 50% of OPGs associated with NF1 require treatment as the OPG does not cause vision loss or any other significant ophthalmic deficit. On the other hand, OPGs not associated with NF1 frequently cause vision loss and require treatment.

Once the initial diagnosis of an OPG has been made, children should undergo comprehensive eye exams that include quantitative visual acuity testing every 3 months for the first year.[5] If the visual exam is stable and there are no concerning tumor features on MRI, then the frequency of exams can be reduced to every 6 months.[1] If a child is undergoing treatment for their OPG, they should be examined every 3 months to help determine treatment response or failure. Once they have completed therapy, examinations every 3 month for the first year is recommended. Since NF1-OPGs are less frequently treated, even less commonly after age 8 years, examination intervals can extend to annually after three years of stability or age 8—whichever occurs later.[5]

Quantitative visual acuity testing and when possible, quantitative visual field testing, are the essential elements of the ophthalmic exam in children with OPGs. New deficits from tumor progression can present as isolated visual acuity loss, isolated visual field loss or even both visual acuity and visual field loss concurrently. A two-line loss of visual acuity (i.e., 0.2 logMAR) is considered significant and beyond normal variation in a child who is able to fully cooperate.[6] As with all exams, the contributions of color vision testing and refractive error should also be considered when determining a change in visual acuity. Other ancillary tests such as visual evoked potentials and optical coherence tomography have been used, but are not considered standard of care or primary endpoints in clinical trials.[6]

Reasons to treat OPGs are complex and should always be made in collaboration with a neuro-oncologist experienced in caring for these tumors. A comprehensive discussion of the nuances to treating OPGs is beyond the scope of this presentation. A more detailed discussion of treatment decisions for NF1-OPG can be found in de Blank et al.[4] As mentioned, a 0.2 logMAR worsening in visual acuity or a reliable decline in visual field are frequently utilized in the decision to initiate treatment. While tumor changes visualized on MRI are not closely associated with changes in vision, on occasion progressive tumor growth alone may be an indication to consider treatment. In children with monocular vision as a result of their tumor or other etiologies, the threshold to initiate treatment may be lower—especially in younger children who cannot cooperate.

First line treatment for OPGs is typically Carboplatin and Vincristine or Vinblastine monotherapy. Ongoing clinical trials are comparing first line therapies to MEK-inhibitors.[2] For treatment refractory OPGs, radiation therapy has been used, but should be avoided in children with NF1 due to the risk of secondary radiation side effects.

In summary, there are significant differences between OPGs in adults and children. OPGs in adult are rare and tend to be most often isolated to the optic nerve and carry a significant risk of malignant transformation. OPGs in children are relatively common, impact multiple locations throughout the anterior visual pathway and rarely experience malignant transformation.

CME ANSWERS

1. **C**
2. **B**
3. **A**

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CEREBRAL/CORTICAL VISUAL IMPAIRMENT (CVI) FROM CHILDHOOD TO ADULTHOOD

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LEARNING OBJECTIVES

1. The attendee will become familiar with a recently developed consensus definition of CVI.
2. The attendee will recognize at risk children through an evaluation of the demographic profile of children with CVI, and will become familiar with novel assessment tools which are used to facilitate in identification and diagnosis of CVI.
3. The attendee will gain exposure to the current understanding of the natural history of CVI in an effort to inform best practices for supporting children with this diagnosis from adolescence to early adulthood through services and accommodations.

CME QUESTIONS

1. Which of the following etiologies are associated with the development of CVI?
   A. Hypoxic ischemic encephalopathy
   B. Posterior reversible encephalopathy syndrome (PRES)
   C. Periventricular leukomalacia
   D. Choices A and C
   E. All of the Above
   F.None of the Above

2. A diagnosis of CVI may be established in spite of normal neuroimaging.
   A. True
   B. False

3. Subnormal visual acuity is a required criterion for the diagnosis of CVI.
   A. True
   B. False

KEYWORDS

1. Cerebral/cortical visual impairment
2. CVI
3. functional vision assessment

Case Presentation

A 27-year-old woman with a history of prematurity with periventricular leukomalacia and a diagnosis of CVI. The case presentation will review the management of her condition from childhood through adulthood.

Defining CVI

In 2023, an interdisciplinary CVI Workshop led by Dr. Melinda Chang and Dr. Lotfi Merabet was convened at the NIH to examine the state of the art understanding of CVI and inform the preparation of an upcoming NIH-led national registry for CVI. Through this meeting, a consensus definition of CVI was developed. The definition considers that CVI represents brain based visual impairment characterized by afferent dysfunction which exceeds but may be comorbid with ocular conditions. Although the injury which results in CVI occurs during visual development, often the condition is unrecognized until later. CVI is distinct from other brain based disorders of language, cognitive function, or social function.[1]

Who is at Risk?

CVI is a leading cause of significant visual impairment in children in developed countries, and therefore it is critical for an increased awareness of children who may be at risk. Diagnoses which are commonly associated with CVI include a

history of perinatal hypoxia, periventricular leukomalacia in a preterm infant, inherited genetic conditions, head injury/trauma, hydrocephalus, perinatal encephalitis/meningitis, and CNS malformations.[2] Further, children with CVI may have other neurologic comorbidities such as cerebral palsy, cognitive delay, seizure disorder, and hearing loss which exacerbate the impact of brain based visual impairment and also complicate establishing the diagnosis of CVI in a timely manner.[2,3]

Spectrum of Function

Visual acuity may range from profoundly impaired to within the normal range, but with higher order visual perceptual difficulties. The clinical profile of the child who presents later during childhood may be more likely to have not been recognized early because of good visual acuity and the higher order processing issues become apparent during school age. Children with periventricular leukomalacia and a history of prematurity have been described to have this clinical profile.[4]

Assessment Tools

There are numerous tools which have been developed to assess for CVI, but no standardized approach exists. Many of these assessment tools, such as the CVI-Range are inventories of behavioral characteristics associated with CVI such as difficulty with visual complexity, inability to sustain visual attention, difficulty with visuomotor planning, and difficulty with visual memory. Recent efforts have focused on the validation of these existing tools for clinical research.[5] Further, tools which facilitate in evaluation of children with higher order processing deficits but good visual acuity such as HVFQI-51 are also being implemented.[6]

Services and Accommodations

The ophthalmologist's role is to recognize CVI and initiate the age-appropriate treatment. This includes comprehensive ophthalmic care (ex. refraction, management of strabismus, documentation of visual field loss), and appropriate referrals to low vision, functional visual assessment, teacher of visual impairment, orientation and mobility specialist, and registration with State Services. When transitioning from childhood to adulthood, the role of the eye care provider shifts to ensure that there is appropriate support and infrastructure, but active management by neuro-ophthalmology is not required.

CME ANSWERS

1. **D**
2. **A**
3. **B**

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APPROACH TO CONGENITAL OPTIC NEUROPATHIES

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LEARNING OBJECTIVES

1. The attendee will be able to identify the major congenital disc anomalies by appearance.
2. The attendee will know which congenital disc anomalies are associated with systemic or other ocular problems and which need to be evaluated for other problems based on the age at presentation.
3. The attendee will know which optic disc anomalies may be hereditary and the appropriate genetic work up for each based on the clinical features and age of each patient.

CME QUESTIONS

1. A young woman with bilateral optic nerve hypoplasia consults you for family planning prior to getting pregnant. Should genetic testing be done
   A. Yes
   B. No

2. Hypopituitarism in optic nerve hypoplasia
   A. Is nearly always present in infancy
   B. may evolve up until puberty
   C. occurs in 20% of patients
   D. Is usually associated with absent septum pellucidum

3. In the absence of family history, genetic work up is indicated in adult with bilateral coloboma for family planning purposes
   A. True
   B. False

KEYWORDS

1. optic nerve hypoplasia
2. congenital optic atrophy
3. coloboma
4. genetics

HIGHLIGHTS

Congenital optic neuropathies commonly encountered by neuro-ophthalmologists include optic nerve hypoplasia (ONH), coloboma, morning glory syndrome (MGS), peripapillary staphyloma, and "funky anomalies" or abnormal appearing optic nerves that do not fit one of the above categories. ONH is associated with endocrinopathies in 80% of children diagnosed in infancy, and endocrine workup is indicated to identify and treat hypopituitarism. Untreated cortisol or thyroid deficiency may have severe or fatal consequences. ONH is also associated with structural brain abnormalities, and neuroimaging is primarily indicated to anticipate developmental disorders that occur in association with these brain malformations. Colobomas of the optic nerve may be bilateral and associated with colobomas of other ocular structures; targeted exome sequencing may be considered in these cases. MGS has been associated with moyamoya syndrome, and peripapillary staphyloma (and possibly MGS) have been associated with basal encephaloceles. Neuroimaging may be indicated in these two conditions. Excavated optic atrophy may occur in premature children with periventricular leukomalacia or hydrocephalus. Neuroimaging is indicated in children with excavated optic atrophy without a history of CNS disease, or in children with non-excavated optic atrophy. Teenagers and adults with newly diagnosed congenital optic neuropathies may not necessarily require the full work-up described above, since they are past the age when certain complications typically become evident (for example, hypopituitarism associated with ONH manifests at or prior to

puberty). Considerations for genetic testing in teenagers and adults with congenital optic neuropathies may depend individual circumstances, such as anticipation of future children.

SUMMARY

1. Anomalous optic discs

1.1 Optic nerve hypoplasia (ONH)

Optic nerve hypoplasia is the most common congenital optic nerve anomaly causing blindness. Its estimated incidence is 1/ 7-10,000 live births. ONH is characterized by a small optic disc that may or may not be pale. Estimation of optic disc size may be difficult with indirect ophthalmoscopy, especially in the face of refractive errors that impact magnification. Estimation of relative size based on distance to the fovea or blood vessel diameter may help in borderline cases. This is best done with direct ophthalmoscopy or fundus photography. Often the putative scleral canal surrounding the small optic disc can be distinguished as a hypo- or hyper-pigmented "double ring." This is not always present and can also be seen with normal optic nerves associated with myopia.

Optic nerve hypoplasia is commonly associated with hypothalamic dysfunction. 80% of children diagnosed in infancy develop hypopituitarism within the first 5 years of life.[i] The most common pituitary problem is growth hormone deficiency, but children with this problem may grow normally until age 6 years, so it is frequently not detected unless there is associated hypoglycemia.

Central hypothyroidism is the second most common pituitary problem, occurring in 40% of children. Failure to diagnose this problem before three years of age can lead to significant developmental delay. Central hypothyroidism cannot be diagnosed with newborn thyroid screening programs.[ii] [iii]

Sudden death is a well-described, but uncommon, consequence of undiagnosed or under-treated adrenal insufficiency.[iv] ACTH deficiency develops in 20 % of children with ONH.

Beyond 5 years of age, evolving hypopituitarism usually manifests as delayed or precocious puberty. Other less treatable hypothalamic problems are unfortunately common. These include dysregulation of hunger and thirst, body temperature instability, hypothalamic obesity, and sleep/wake dysrhythmias.

Anatomic abnormalities of the hypothalamus are rarely seen on MRI scans of children with ONH. Histologically, some hypothalamic nuclei are missing, but white matter tracts transverse those regions of missing nuclei.[v] But MRI frequently detects disorganized cerebral cortex and white matter, which are common findings in children with ONH. Historically neuroimaging focused on the corpus callosum and the septum pellucidum, the absence of which was thought to confer risk for hypopituitarism and the syndrome of "septo-optic dysplasia." It is now recognized that hypoplasia of the corpus callosum, as well as other major cortical malformations (polymicrogyria, white matter hypoplasia, cortical heterotopia, schizencephaly) confer high risk for developmental delay and/or seizures, but no increased risk for hypopituitarism.[vi] Absence of the septum pellucidum has no associated risks. Thus, MRI is indicated for anticipation of developmental problems, but not for hypopituitarism.

All young children with ONH need to be monitored for cortisol and thyroid insufficiency, since failure to diagnose or treat these conditions could have severe or fatal consequences. These should be tested semi-annually until age 3 years and annually thereafter until age 6 years. Growth needs to be monitored, and growth deceleration needs to be evaluated with provocative growth hormone testing.

There are no known genetic variants that cause ONH. Several variants have been associated with ONH, but few of these have been found in multiple cases.[vii] Many of the reported cases have been misdiagnosed or diagnosed by MRI scans alone. (Small optic nerves on MRI are not specific for ONH.) Although numerous siblings, even identical twins, have been reported with ONH, there have been no definite cases of multigenerational transmission. Exome sequencing for cases of ONH is not recommended.

1.2 Coloboma

Colobomas involving the optic disc result in an inferior nasal defect that often extends onto the adjacent retina. Remote chorioretinal or iris colobomas are not uncommonly seen in the same eye due to spared regions of fetal fissure defects. Rarely, the defect results in complete splitting of the disc resulting in the appearance of a duplicated optic disc.

The majority of colobomas are isolated and unilateral. Most hereditary cases are bilateral, although they may be very asymmetric. The parents of a child with newly diagnosed bilateral coloboma without a family history should be evaluated for occult colobomas in the retinal periphery. A de-novo mutation should be considered in bilateral cases with no affected family members. Targeted exome sequencing could be considered in such cases. The most common affected genes and their associations are: *PAX2* (renal coloboma syndrome); *CHD7* (CHARGE syndrome); *FOXE3* (hearing loss; cognitive delay); *BCOR* (congenital cataracts, glaucoma); *ALDH1A3* (autism, cognitive delay); *EPHA2* (congenital cataracts); and *PAX6* (aniridia, microphthalmia). However, the yield from exome sequencing is low in cases without syndromic problems or other congenital eye anomalies. This is the case even with a strong family history.[viii]

1.3 Morning glory syndrome (MGS)

The morning glory optic disc anomaly has a characteristic funnel appearance like that of the morning glory flower. The central funnel is filled with gliotic appearing dysplastic retina that has been dragged into the funnel. There is associated dragging of the peripapillary retinal vessels. The anomaly is nearly always unilateral and appears to be caused by dysgenesis of the lamina cribrosa.[ix], [x] Frequently there is smooth muscle found at the base of the funnel that may or may not be causing the dragging of retinal tissue into the funnel. Often there is a slow rhythmic posterior-anterior movement of the central gliotic retinal tissue that may be seen on ophthalmoscopy. There may be progressive vison loss along with worsened dragging of retinal tissue. There is no known genetic cause of morning glory syndrome, but it is associated with vascular anomalies of the anterior cerebral circulation from agenesis of A1 segments to bilateral carotid stenosis resembling Moya-Moya disease in 45% of cases.[xi] This has led some investigators to recommend MRA or catheter angiogram of the brain for all children with MGS. There is a paucity of cases that have suffered stroke associated with MGS, though a recent neurosurgical study suggested that half of affected patients have evidence of progression on serial scans.[xii] Spontaneous resolution of carotid stenosis in MGS has also been reported.[xiii]

1.4 Peripapillary staphyloma

In contrast to MGS, peripapillary staphyloma is caused by thinning and ectasia of the peripapillary sclera. This may similarly cause funnel-shaped retrodisplacement of the optic disc that is commonly confused with MGS. However, in contrast to MGS, a normal optic disc can be seen at the base of the ectasia. This results in mild dragging of the peripapillary retinal vessels, also like MGS. This is also nearly always unilateral and not due to a known genetic variant. Vision may be preserved if the staphyloma does not involve the macula, though there is nearly always associated amblyopia due to unilateral high myopia. Amblyopia may be prevented with contact lens treatment if detected early.

Peripapillary staphyloma may be associated with basal encephalocele. Such an association has also been reported in MGS, raising the question as to whether peripapillary staphyloma and MGS represent a spectrum of disease. However, Moya moya disease has not been reported with peripapillary staphyloma, and most of the reports of basal encephalocele associated with MGS have posterior staphyloma when the fundus photographs are reviewed. The associated prevalence is uncommon, but unknown. Routine neuroimaging is controversial in the absence of other signs, such as hypertelorism.

1.5 Funky anomalies

Numerous unique variations in optic disc appearance have been described. These generally have no systemic or genetic implications. These include sectoral optic nerve hypoplasia, hamartomas, pits and vascular anomalies.

2. Excavated optic atrophy

Optic atrophy occurring late in gestation, such as that associated with hydrocephalus or periventricular leukomalacia, commonly presents with a large excavated optic cup and thin optic rim, reminiscent of glaucomatous optic atrophy. The reason for this presentation is unknown. The underlying cause is usually obvious and, in the absence of high intraocular pressure or buphthalmia, does not need further work up. If there is no history CNS disease, an MRI of the brain should be obtained. But first, it should be distinguished from physiologic cupping or megalopapilla, which have healthy optic rims and no adverse consequences.

3. Non-excavated Optic atrophy

Typical optic atrophy in a newborn or young child needs evaluation. In the absence of a known etiology all cases should be evaluated with neuroimaging regardless of laterality. Tumors of the chiasm or hypothalamus may be present at birth, or

shortly thereafter. Optic atrophy in infancy may be caused by anything that causes optic atrophy in older children including occult head trauma, toxic and nutritional deficiencies and hereditary optic neuropathies. History and examination should be used to direct the work up.

4. How to approach an adult with congenital optic nerve anomaly

In cases of teenagers or adults with newly diagnosed congenital disc anomalies, the question of further work-up depends on the risk for associated problems. For instance, in the case of optic nerve hypoplasia, since hypopituitarism always manifests by the time of puberty, endocrine work up is not indicated. Since the vascular anomalies associated with MGS are congenital, MRA is probably not going to be useful for an adult with newly diagnosed MGS.

On the other hand, genetic testing may be useful in adults with syndromic or complex colobomas who anticipate having children.

CME ANSWERS

1. **B**
2. **B. (May evolve up until puberty)**
3. **A**

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"AMBLYOPIA FROM CHILDHOOD TO ADULTHOOD"

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LEARNING OBJECTIVES

The attendee will be able to:

1. Understand the neurobiology of amblyopia and the critical period.
2. Describe diagnostic and management approaches for the older patient with amblyopia.
3. Appreciate spontaneous recovery of and emerging therapies for amblyopia in older patients.

CME QUESTIONS

1. Which of the following is true?
   A. Strabismus acquired in adulthood can cause amblyopia.
   B. Adults with amblyopia can never have binocular dipoplia because of interocular suppression.
   C. Amblyopia is a form of optic neuropathy and can be diagnosed in adulthood using OCT.
   D. Children aged 13-17 with newly diagnosed amblyopia should be treated.
   E. New digital therapies for amblyopia have been shown to be ineffective in adults.

2. True or false: Adult patients with residual anisometropic amblyopia can improve visual acuity in the amblyopic eye through wearing glasses that corrects the amblyopic eye.
   A. True
   B. False

3. Which of the following statements concerning spontaneous recovery from amblyopia in adulthood is FALSE?
   A. Recovery associated with fellow eye visual loss is common.
   B. Recovery associated with fellow eye visual loss is clinically meaningful.
   C. Younger adults tend to have greater amblyopic eye visual acuity gains after fellow eye visual loss.
   D. Adults with greater fellow eye visual acuity loss tend to have greater amblyopic eye visual acuity gains.
   E. None of the above (all are true)

KEYWORDS

1. Amblyopia
2. Critical period
3. Neuroplasticity
4. Anisometropia
5. Strabismus

HIGHLIGHTS

- Closure of the critical period of neuroplasticity precludes meaningful recovery from amblyopia in older individuals, but several lines of evidence from animal models to humans serve to challenge this dogma.
- Diagnosis of amblyopia in adulthood in the absence of a clear history relies on diagnosing an amblyogenic condition (if still present), identifying visual deficit features consistent with amblyopia, and excluding other causes of visual loss.
- Older individuals prescribed their best optical correction commonly improve visual acuity in the amblyopic eye.
- Adults with amblyopia who suffer vision-limiting injury or disease (such as NAION) affecting the better-seeing, fellow eye frequently gain lines of visual acuity in the amblyopic eye.
- New therapies for amblyopia, enabled by advancements in digital technology, offer hope to treat individuals with amblyopia who do not respond to traditional therapies.
- Pharmacologic modulation and activity-driven engagement of neuromodulatory systems to enhance or rejuvenate plasticity are promising approaches to facilitate recovery in older individuals.

SUMMARY

Amblyopia results from abnormal visual experience during a critical period of visual development that ends around age 8. So called amblyogenic drivers include strabismus, anisometropia, and pathologies that occlude the visual axis (such as cataract). The visual deficit of amblyopia is characteristically susceptible to visual crowding. The neurobiologic changes in visual cortex that mark critical period closure serve to limit neuroplasticity that would otherwise allow for recovery.[1] If not treated in childhood, visual deficits incurred during this time are widely considered permanent and recalcitrant to reversal, though treatment is recommended for newly diagnosed individuals up to age 17.[2]

Despite this dogma, extensive evidence supports the potential to effectively treat amblyopia in older individuals. One example is improvement in best-corrected visual acuity with prescription of optimal correction for the amblyopic eye.[3] Another example is a widely reported observation in adults with amblyopia who gain lines of visual acuity in the amblyopic eye after vision limiting disease or injury to their better-seeing, fellow eye (such as NAION).[4,5] Pharmacologic retinal silencing has recently garnered exciting pre-clinical supporting evidence by reversal of monocular amblyopic deficits in animals aged beyond critical period closure.[6] These phenomena, along with molecular targets revealed through basic neuroscience, provide a roadmap by which amblyopia may one day be treated in adulthood.[7]

New avenues for amblyopia treatment in older individuals are under active investigation. Development and growing availability of digital technologies that separate and allow for differential manipulation of the image channels for each eye have enabled advancements in amblyopia therapy, now approved and available for prescription in children.[8,9] Their efficacy in older individuals is anecdotal. Neuromodulatory systems shown to enhance or rejuvenate plasticity can be harnessed through challenging or engaging tasks (as in “perceptual learning”) or directly modulated through pharmacology.[10] These approaches have been tested in pilot studies that show promising results.

CME ANSWER

1. **D**
2. **A**
3. **E**

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