

Neuro- Ophthalmology 2019

Diagnostic Errors and Challenges—Avoid the Traps!

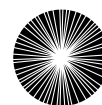
Program Directors

Prem S Subramanian MD PhD and Peter A Quiros MD

**In conjunction with the
North American Neuro-Ophthalmology Society**

Moscone Convention Center
San Francisco, California
Saturday, Oct. 12, 2019

Presented by:
The American Academy of Ophthalmology



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2019 Neuro-Ophthalmology

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Program Director

Peter A Quiros MD

Program Director

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Valerie Biousse MD

Preston C Calvert MD

John J Chen MD PhD

Sophia Mihe Chung MD

Kathleen B Digre MD

Sachin Kedar MD

Andrew G Lee MD

Michael S Lee MD

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Raghu Mudumbai MD

Jason H Peragallo MD

John Pula MD

Mitchell B Strominger MD

Madhura A Tamhankar MD

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Prem S Subramanian MD PhD

2015 Michael S Lee MD

Prem S Subramanian MD PhD

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2019 Neuro-Ophthalmology Subspecialty Day Planning Group

On behalf of the American Academy of Ophthalmology and the North American Neuro-Ophthalmology Society (NANOS), it is our pleasure to welcome you to San Francisco and Neuro-Ophthalmology 2019: Diagnostic Errors and Challenges—Avoid the Traps!



Prem S Subramanian MD PhD
Program Director

GenSight Biologics: S,C
Quark Pharmaceuticals: S
Santhera Pharmaceuticals: S



Peter A Quiros MD
Program Director

Quark Pharmaceuticals: S
Regenera: S

Program Planning Group



Anne S Abel MD
None



Valerie Biousse MD
GenSight: C



John J Chen MD PhD
None



Eric L Berman MD
None



Preston C Calvert MD
None



Sophia Mihe Chung MD
National Eye Institute: S

No photo
available

Kathleen B Digre MD

Elsevier: P
National Eye Institute: S
Springer: P
Part owner on patent pending
on Thin-Filme: P
Springer: P



Michael S Lee MD

Evolvemed: C
National Eye Institute: S
Quark Pharmaceuticals: S
Springer: P
Uptodate: P
Vindico: C



John Pula MD

None



Sachin Kedar MD

EON Reality: P



Collin M McClelland MD

None



Mitchell B Strominger MD

None



Andrew G Lee MD

None



Raghu Mudumbai MD

None

No photo
available

Madhura A Tamhankar MD

Horizon: C

No photo
available

Jason H Peragallo MD

None

2019 Subspecialty Day Advisory Committee

Daniel S Durrie MD, Chair (Refractive Surgery)

AcuFocus, Inc.: C,O
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Alphaeon: O
Avedro: C,L,O
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Julia A Haller MD (Retina)

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Michael S Lee MD (Neuro-Ophthalmology)

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Uptodate: P | Vindico: C

Shahzad I Mian MD (Cornea)

National Eye Institute: S

R Michael Siatkowski MD (Pediatric Ophthalmology)

None

Kuldev Singh MD (Glaucoma)

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Administration: C,S

AAO Staff

Melanie Rafaty

None

Ann L'Estrange

None

Debra Rosencrance

None

Beth Wilson

None

Neuro-Ophthalmology 2019 Contents

	2019 Neuro-Ophthalmology Planning Group	ii
	CME	vi
	Faculty Listing	viii
	How to Use the Audience Interaction Application	xii
	Program Schedule	xiii
Section I:	Vision Loss—Follow That Symptom?	2, 30
Section II:	Bugs and Drugs—Do They Matter?	10, 36
	Are You AT the Table or ON the Menu?	8
Section III:	Double Vision—50/50 Chance to Pick the Right One!	15, 42
Section IV:	Tests Will Give Me The Answer!	20, 46
	Faculty Financial Disclosure	55
	Presenter Index	58

CME Credit

The Academy's CME Mission Statement

The purpose of the American Academy of Ophthalmology's Continuing Medical Education (CME) program is to present ophthalmologists with the highest quality lifelong learning opportunities that promote improvement and change in physician practices, performance, or competence, thus enabling such physicians to maintain or improve the competence and professional performance needed to provide the best possible eye care for their patients.

2019 Neuro-Ophthalmology Subspecialty Day Meeting Learning Objectives

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

- Recognize urgent signs and symptoms in the evaluation of adults with diplopia
- Direct the initial workup of a patient with visual loss from optic neuropathy
- Distinguish the key manifestations of medication-related and infectious neuro-ophthalmic disorders
- Interpret neuro-ophthalmologic diagnostic testing results and identify pitfalls and key findings

2019 Neuro-Ophthalmology Subspecialty Day Meeting Target Audience

The intended audience for this program is comprehensive ophthalmologists.

Teaching at a Live Activity

Teaching instruction courses or delivering a scientific paper or poster is not an *AMA PRA Category 1 Credit™* activity and should not be included when calculating your total *AMA PRA Category 1 Credits™*. Presenters may claim *AMA PRA Category 1 Credits™* through the American Medical Association. To obtain an application form, please contact the AMA at www.ama-assn.org.

Scientific Integrity and Disclosure of Conflicts of Interest

The American Academy of Ophthalmology is committed to ensuring that all CME information is based on the application of research findings and the implementation of evidence-based medicine. It seeks to promote balance, objectivity, and absence of commercial bias in its content. All persons in a position to control the content of this activity must disclose any and all financial interests. The Academy has mechanisms in place to resolve all conflicts of interest prior to an educational activity being delivered to the learners.

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2019 Neuro-Ophthalmology Subspecialty Day CME Credit

The American Academy of Ophthalmology is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide CME for physicians.

The Academy designates this live activity for a maximum of 7 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Attendance Verification for CME Reporting

Before processing your requests for CME credit, the Academy must verify your attendance at AAO 2019 and/or Subspecialty Day. Badges are no longer mailed before the meeting. Picking up your badge onsite will verify your attendance.

Badge Scanning and CME

Getting your badge scanned does not automatically grant CME credit. You still need to record your own educational activities. NOTE: You should claim only the credit commensurate with the extent of your participation in the activity.

CME Credit Reporting

Onsite, report credits earned during Subspecialty Day and/or AAO 2019 at CME Credit Reporting kiosks located in South Lobby, West Lobby, and the Academy Resource Center, West, Booth 7337.

Registrants whose attendance is verified at AAO 2019 receive an email on **Monday, Oct. 14**, with a link and instructions for claiming credit online. Attendees can use this link to report credits until **Wednesday, Oct. 30**.

Starting **Thursday, Nov. 14**, attendees can claim credits online through the Academy's CME web page, aao.org/cme-central.

Academy Members

The CME credit reporting receipt is not a CME transcript. CME transcripts that include credits entered at AAO 2019 will be available to Academy members through the Academy's CME web page beginning **Thursday, Nov. 14**.

The Academy transcript cannot list individual course attendance. It will list only the overall credits claimed for educational activities at Subspecialty Day and/or AAO 2019.

Nonmembers

The American Academy of Ophthalmology provides nonmembers with verification of credits earned and reported for a single Academy-sponsored CME activity. To obtain a printed record of your CME credits, claim them onsite at the CME Credit Reporting kiosks. Nonmembers choosing to claim credits online through the Academy's CME web page after **Thursday, Nov. 14**, will have one opportunity to print a certificate.

Proof of Attendance

The following types of attendance verification are available during AAO 2019 and Subspecialty Day for those who need it for reimbursement or hospital privileges, or for nonmembers who need it to report CME credit:

- CME credit reporting/proof-of-attendance letters
- Onsite registration receipt
- Instruction course and session verification

You must have obtained your proof of attendance at the CME Credit Reporting kiosks onsite, located in South Lobby, West Lobby, and in the Academy Resource Center, West, Booth 7337.

Faculty



Anne S Abel MD
Wayzata, MN



M Tariq Bhatti MD
Rochester, MN



John J Chen MD PhD
Rochester, MN



Ore-Ofeoluwatomi O Adesina MD
Houston, TX



Valerie Biousse MD
Atlanta, GA



Sophia Mihe Chung MD
St Louis, MO



Anthony C Arnold MD
Los Angeles, CA



Gabrielle R Bonhomme MD
Pittsburgh, PA



Kimberly Cockerham MD FACS
Stockton, CA



Eric L Berman MD
Charleston, SC



Mark S Borchert MD
Los Angeles, CA



Fiona E Costello MD
Calgary, AB, Canada



Mays A El-Dairi MD
Durham, NC



Guy V Jirawuthiworavong MD
Torrance, CA



Melissa W Ko MD
Jamesville, NY



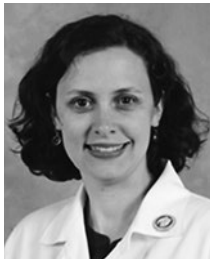
Valerie I Elmalem MD
Roslyn Heights, NY



Randy H Kardon MD PhD
Iowa City, IA



Kevin E Lai MD
Indianapolis, IN



Courtney E Francis MD
Seattle, WA



Sachin Kedar MD
Omaha, NE



Jacqueline A Leavitt MD
Rochester, MN



Lynn K Gordon MD PhD
Los Angeles, CA



Lanning B Kline MD
Birmingham, AL



Andrew G Lee MD
Houston, TX



Michael S Lee MD
Minneapolis, MN



Collin M McClelland MD
Edina, MN



Raghu Mudumbai MD
Seattle, WA



Norah Lincoff MD
Buffalo, NY



Neil R Miller MD
Baltimore MD



Nancy J Newman MD
Atlanta, GA



Grant T Liu MD
Philadelphia, PA



Heather Moss MD PhD
Palo Alto, CA



Paul H Phillips MD
Little Rock, AR



Peter W MacIntosh MD
Chicago, IL



Mark L Moster MD
Philadelphia, PA



Stacy L Pineles MD
Los Angeles, CA



John Pula MD
Chicago, IL



Kenneth S Shindler MD PhD
Philadelphia, PA



Prem S Subramanian MD PhD
Aurora, CO



Peter A Quiros MD
Pasadena, CA



R Michael Siatkowski MD
Oklahoma City, OK



Nicholas J Volpe MD
Chicago, IL



Joseph F Rizzo III MD
Boston, MA



Shira S Simon MD
Chicago, IL



Judith E Warner MD
Salt Lake City, UT



Janet C Rucker MD
New York, NY

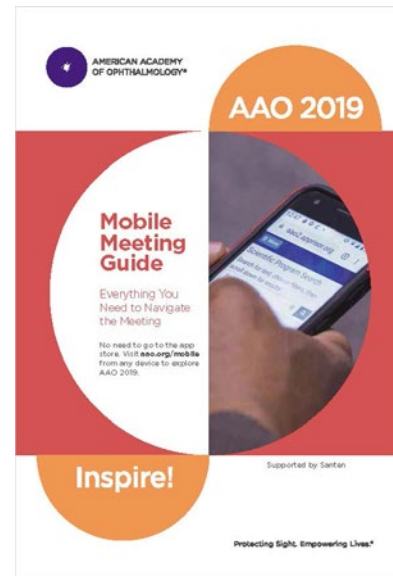


Mitchell B Strominger MD
Reno, NV

Ask a Question and Respond to Polls Live During the Meeting Using the Mobile Meeting Guide

To submit an answer to poll or ask the moderator a question during the meeting, follow the directions below.

- Access at www.aao.org/mobile
- Select Program, Handouts & Evals
- Filter by Meeting – Neuro-Ophthalmology Meeting
- Select Current Session
- Select “Interact with this session (live)” Link to open a new window
- Choose “Answer Poll” or “Ask a Question”



Neuro-Ophthalmology 2019: Diagnostic Errors and Challenges—Avoid the Traps!

In conjunction with the North American Neuro-Ophthalmology Society (NANOS)

SATURDAY, OCT. 12, 2019

7:00 AM CONTINENTAL BREAKFAST

8:00 AM Welcome and Introductions
Prem S Subramanian MD PhD*
Peter A Quiros MD*

Section I: Vision Loss—Follow That Symptom?

Moderators: Sophia Mihe Chung MD* and John Pula MD

Panelists: Lynn K Gordon MD PhD, Andrew G Lee MD, Norah Lincoff MD, and Mark L Moster MD*

8:02 AM	Introduction and Audience Interaction	Sophia Mihe Chung MD*	
8:04 AM	“My Vision Was Blurry and Then Got Better”	Heather Moss MD PhD*	2, 30
8:19 AM	“I’m Having Trouble Driving”	Ore-Ofeoluwatomi O Adesina MD	2, 30
8:34 AM	“My Vision Is Slowly Getting Worse”	Sachin Kedar MD*	3, 31
8:49 AM	Point–Counterpoint: Extensive Lab Workup for All New Cases of Optic Neuritis	Lynn K Gordon, MD, PhD Andrew G Lee MD Norah Lincoff MD Mark L Moster MD*	5
8:59 AM	“I’m Missing Letters When I Read”	Fiona E Costello MD*	6, 32
9:14 AM	“I Can’t See Anything to the Right!”	Courtney E Francis MD	6, 33
9:29 AM	“I Woke Up One Day With Bad Vision”	Mays A El-Dairi MD	7, 33
9:44 AM	Summary and Audience Interaction	Peter A Quiros MD*	
9:47 AM	REFRESHMENT BREAK and AAO 2019 EXHIBITS		

Section II: Bugs and Drugs—Do They Matter?

Moderators: Collin M McClelland MD and Mitchell B Strominger MD

Panelists: Lanning B Kline MD, Neil R Miller MD*, Nicholas J Volpe MD*, and Judith E Warner MD

10:17 AM	Are You AT the Table or ON the Menu?	Prem S Subramanian MD PhD*	8
10:22 AM	Introduction and Audience Interaction	Collin M McClelland MD	
10:24 AM	“I Am On So Many Medicines, and Now I Can’t See!”	Gabrielle R Bonhomme MD	10, 36
10:39 AM	“My Neck Hurts and I’m Cold!”	Michael S Lee MD*	10, 37
10:54 AM	“My Eye Aches, and It’s Blurred When I Read”	Kimberly Cockerham MD FACS*	11, 37
11:09 AM	Point–Counterpoint: NAION Should Be Treated With Medication	Lanning B Kline MD Neil R Miller MD Nicholas J Volpe MD Judith E Warner MD	12

* Indicates that the presenter has financial interest. No asterisk indicates that the presenter has no financial interest.

11:19 AM	“They Told Me My Optic Nerves Are Swollen”	Kevin E Lai MD	13, 38
11:34 AM	“My Vision’s Blurred, and One of My Optic Nerves Is Swollen”	Melissa W Ko MD	13, 40
11:49 AM	Summary and Audience Interaction	Prem S Subramanian MD PhD*	
11:52 AM	LUNCH and AAO 2019 EXHIBITS		

Section III: Double Vision—50/50 Chance to Pick the Right One!

Moderators: Anne S Abel MD and Eric L Berman MD

Panelists: Jacqueline A Leavitt MD, Grant T Liu MD*, Nancy J Newman MD*, and R Michael Siatkowski MD

1:17 PM	Introduction and Audience Interaction	Eric L Berman MD	
1:19 PM	“My Eyelid Droops, and I See Double”	Kenneth S Shindler MD PhD*	15, 42
1:34 PM	“My Eye Bulges, and I See Double”	Paul H Phillips MD	16, 43
1:49 PM	“My Double Vision Comes and Goes”	Stacy L Pineles MD*	16, 43
2:04 PM	Point–Counterpoint: Imaging in Acute Diplopia for Patients Over 50	Jacqueline A Leavitt MD Grant T Liu MD* Nancy J Newman MD* R Michael Siatkowski MD	17
2:14 PM	“My Eye Won’t Close, and I See Double”	Anne S Abel MD	18, 44
2:29 PM	“Everything Is Double and Moving!”	Janet C Rucker MD	18, 44
2:44 PM	“I See Double and Triple Images”	Mark S Borchert MD	19, 45
2:59 PM	Summary and Audience Interaction	Prem S Subramanian MD PhD*	
3:02 PM	REFRESHMENT BREAK and AAO 2019 EXHIBITS		

Section IV: Tests Will Give Me The Answer!

Moderators: John J Chen MD PhD and Raghu Mudumbai MD

Panelists: Anthony C Arnold MD*, Valerie Biousse MD*, Randy H Kardon MD PhD*, and Joseph F Rizzo III MD

3:32 PM	Introduction and Audience Interaction	Raghu Mudumbai MD	
3:34 PM	“My World Is Closing In”	Guy V Jirawuthiworavong MD	20, 46
3:49 PM	“They Told Me I Have Optic Neuritis”	M Tariq Bhatti MD*	21, 47
4:04 PM	“I Can’t See, and the MRI Is Not Normal”	Peter W MacIntosh MD	22, 49
4:19 PM	Point–Counterpoint: OCT Can Predict Visual Outcomes in Patients With Optic Nerve Disorders	Anthony C Arnold MD* Valerie Biousse MD* Randy H Kardon MD PhD* Joseph F Rizzo III MD	24
4:29 PM	“The Doctor Says My Optic Nerves Are Damaged”	Valerie I Elmalem MD	25, 51
4:44 PM	“I Have Pressure in My Head”	Shira S Simon MD*	27, 53
4:59 PM	Summary and Audience Interaction	Prem S Subramanian MD PhD*	
5:03 PM	Closing Remarks	Prem S Subramanian MD PhD* Peter A Quiros MD*	
5:04 PM	Adjourn		

* Indicates that the presenter has financial interest. No asterisk indicates that the presenter has no financial interest.

Case Presentations

Section I: Vision Loss—Follow That Symptom?

“My Vision Was Blurry and Then Got Better”

Heather E Moss MD PhD

CASE PRESENTATION

History and Exam

A 60-year-old man presented for evaluation of transient right-sided vision loss that occurred 2 days previously while at work. He developed rapid loss of vision on the right side to complete darkness, described as “black.” This persisted for over a minute before slowly returning to normal over a minute or two. He attributed the difficulty to the right eye but did not cover each eye individually to confirm this. There were no positive visual symptoms. There was no pain or other neurological symptoms during the episode, preceding it or following it. Vision has been normal since the event.

In the week prior to the episode that led to him seeking care he had 2-3 episodes of right visual blur upon standing. He also reported dimming of right-sided vision upon transitioning from a dark to a light environment.

Past medical history was unremarkable, and he reported having a normal examination with his primary care doctor within the last year. He consumed a glass of wine 2 or 3 times a week and quit smoking tobacco 20 years previously. He took ibuprofen as needed for knee pain and a daily multivitamin.

On examination, BCVA was 20/20 with each eye. He counted fingers in all fields with each eye. Pupils were equal, round, and reactive to light without relative afferent pupillary defect. IOP was 14 in each eye. Slit-lamp examination was remarkable only for rapid tear film breakup and 1+ nuclear sclerosis in both eyes. Dilated posterior segment evaluation was normal, with sharp optic nerve margins, 0.3 cup-to-disc ratio, and healthy rim color in both eyes, and with normal maculae, vessels, and periphery. Cranial nerve examination was unremarkable. Humphrey 24-2 SITA Fast visual field was normal in both eyes, as were OCTs of the optic nerves and maculae.

Clinical Course and Outcome

Patient was referred to the emergency department. ESR, CRP, and routine blood tests were normal. MRI brain did not show acute ischemia in the brain parenchyma. MRA head showed normal intracranial vasculature. MRA neck showed 70% stenosis of the right internal carotid artery.

There was discussion among the medical team regarding the likely perfusional nature of these symptoms and the options of surgical versus medical management of his large vessel atherosclerotic disease. While in the hospital he developed left mouth droop and weakness of the left arm that lasted 15 minutes before resolving. Head CT was normal, and TPA was not administered due to improving symptoms. He under-

went carotid endarterectomy during the hospitalization and was started on aspirin and atorvastatin for secondary stroke prevention.

Following his carotid surgery, he noted a small scotoma in the right eye. Examination reviewed a small retinal hemorrhage, thought to be due to hyperperfusion following carotid repair. His vision normalized over the following weeks. He had no further episode of transient visual loss or left-sided weakness.

“I’m Having Trouble Driving”

Ore-ofe Adesina MD

CASE PRESENTATION

History and Exam

A 52-year-old man noticed the onset of peripheral visual changes 7 months ago in the right eye. This visual change was affecting his driving, and he often did not see the next car when changing lanes. He was evaluated by an optometrist and was found to have ocular findings suspicious for glaucoma with bilateral optic nerve cupping. His IOPs were normal, and he was diagnosed with low-tension glaucoma (LTG). He was started on a prostaglandin analog. His vision continued to decline progressively despite the addition of a second ocular antihypertensive.

The patient was referred for ophthalmic evaluation in the consideration of glaucoma surgery. He has a history of LASIK surgery OU in 1998 without other ocular history. His past medical history is significant for hyperlipidemia. His medications include a cholesterol-lowering agent. His family history is positive for his mother having “severe” glaucoma. He denies any headaches or other systemic symptoms.

On examination, his BCVA is 20/25 OD and 20/30 OS. IOP is 15 OD and 16 OS, with pachymetry of 560 and 558 microns OD and OS, respectively. External examination is unremarkable. Pupil examination is normal without a relative afferent pupillary defect. Ocular motility is full. Anterior segment examination is normal except for early nuclear sclerosis in both eyes. Gonioscopy reveals open angles in both eyes. Color vision is normal OU. Examination of the optic nerves shows slightly asymmetric cup-to-disc ratios of 0.4 OD and 0.6 OS, with mild to moderate pallor of the left neuroretinal rim. The maculae and peripheral retinas are normal OU. Automated perimetry shows a dense temporal defect OD. In the left eye, there is generalized constriction of the visual field with superior nasal sparing. OCT of the retinal nerve fiber layer shows temporal and superior thinning in the left eye and normal thickness in the right eye.

Clinical Course and Outcome

MRI of the brain and orbits with and without gadolinium was obtained and showed a large intrasellar mass extending superiorly and compressing the optic chiasm. Imaging characteristics were consistent with a pituitary adenoma. Endocrinologic workup was unremarkable. He underwent uncomplicated transphenoidal resection of the lesion that proved to be a non-functional pituitary adenoma. Follow-up examination 1 month after surgery showed 20/25 vision OU, with improvement of his visual field defects. He was able to resume driving.

“My Vision Is Slowly Getting Worse”

Sachin Kedar MD

CASE PRESENTATION

History and Exam

A 35-year-old female patient was referred to neuro-ophthalmology for management of progressive vision loss from optic neuritis. She lives in rural Nebraska and works on her family farm. Her past medical history includes gestational diabetes and common migraine. She is not on any prescription medications. She has a family history of migraine and stroke.

Three months prior to presentation, she fell on the ice, twisting her neck in the process. The following morning, she noticed a pressure-like-sensation behind the right eye. A week later, she experienced blurred vision in the right eye. This prompted a visit to the local emergency department, where she had a normal CT head and CT angiogram of head and neck and was discharged without treatment. Her vision in the right eye continued to slowly worsen, and she saw her ophthalmologist a few days later. She was found to have visual acuity of 20/80 right eye and 20/20 left eye and a swollen right optic nerve. Her family doctor admitted her to a local hospital and treated her with 3 days of intravenous steroids followed by a 2-week oral taper. She reports that her vision improved within 1 week. Six weeks later she had recurrence of decreased vision and pressure sensation behind the right eye. A week later, her ophthalmologist recorded visual acuity of 20/100 right eye, 20/20 left eye and a recurrent swollen right optic nerve. Upon presentation to the neuro-ophthalmology clinic 4 days later, she reported continued worsening of vision and retro-orbital discomfort in the right eye. She denies headache, constitutional symptoms, or other neurological symptoms. She denies recent illness or sick contacts. Farm animals are healthy, and she has not had any bites or scratches from them.

On examination, BCVA is 20/400 right eye and 20/20 left eye. She has loss of color vision in the right eye. A large (1.8 log unit) relative afferent pupillary defect (RAPD) is seen in the right eye. There is no ptosis or proptosis on external examination. Ocular motility is full in both eyes. Anterior segment is normal. Funduscopic examination shows clear vitreous. The right optic nerve shows moderate diffuse swelling and tortuous retinal vessels. The left optic nerve is normal in appearance.

Maculae and periphery are normal. Neurological examination is otherwise normal.

Clinical Course and Outcome

Demyelinating optic neuritis heads the list of differentials for a young female patient who presents with acute painful unilateral vision loss from optic neuritis. However, our patient has multiple recurrent episodes and progressive vision loss, warranting further investigations.

Our diagnostic and therapeutic approach to patients with isolated demyelinating optic neuritis is guided by the findings of the Optic Neuritis Treatment Trial (ONTT), a large prospective multicenter study of 448 patients with acute optic neuritis. The ONTT demonstrated the benefits of intravenous corticosteroids with respect to the rate of early visual recovery compared to oral corticosteroids or no treatment, but without differences noted for long-term visual outcomes between the 3 groups. Importantly, ONTT showed that oral corticosteroids increased rates of recurrent optic neuritis compared to no treatment and intravenous corticosteroids. The ONTT did not show benefit of additional laboratory (blood or CSF) investigations in the diagnosis and management of patients with typical optic neuritis (young patient with acute loss of vision, RAPD, and pain with eye movements). Baseline MRI brain, while not useful in the initial diagnosis and management of typical optic neuritis, helped prognosticate risk for future development of multiple sclerosis. The 15-year probability of developing MS was 25% (95% CI, 18%-32%) for patients with no brain lesions on baseline MRI brain compared to 72% (95% CI, 63%-81%) for patients with 1 or more brain lesions on baseline MRI brain.

Patients with atypical features such as (a) NLP vision, (b) optic disc or retinal hemorrhages, (c) severe optic disc swelling, (d) macular exudates, (e) absence of pain, (f) presence of uveitis, (g) bilateral visual loss, and (h) recurrent disease should be evaluated for alternative causes. The differential diagnosis for unilateral optic neuropathy with disc edema is broad and includes various forms of inflammatory optic neuritis (typical demyelinating, atypical relapsing or recurrent, sarcoidosis, optic perineuritis, neuroretinitis), optic nerve infections (syphilis, herpes zoster, tuberculosis), ischemia (anterior ischemic optic neuropathy, diabetic papillopathy), prechiasmatic optic nerve compression (from tumors, enlarged extraocular muscles, arterial aneurysm, vascular ectasia), optic nerve tumors (optic nerve glioma, optic nerve sheath meningioma), infiltration (leukemia, lymphoma), and radiation optic neuropathy. Due to the presence of several atypical features, we obtained imaging studies and blood and CSF studies for infectious, inflammatory, and neoplastic markers.

MRI brain and orbits showed diffuse enhancement and edema throughout the entire intraorbital segment of the right optic nerve. Enhancement of the optic nerve sheath and adjacent orbital tissue was also noted. There were no intracranial lesions. Atypical variants of optic neuritis including neuromyelitis optica (NMO) and myelin-oligodendrocyte glycoprotein (MOG) antibody optic neuritis were suspected radiologically.

NMO, a humorally mediated disease, causes severe demyelinating disease preferentially affecting the optic nerves and spinal cord. A serum IgG autoantibody against the astrocytic water channel aquaporin-4 (AQP-4) acts as a disease marker. Optic neuritis and/or transverse myelitis may be the initial presentation. Compared to typical cases, optic neuritis in NMO is more frequently bilateral and steroid resistant and leads to

severe and persistent vision loss. OCT imaging shows more thinning of the retinal nerve fiber layer compared to typical optic neuritis. MRI imaging shows atypical features such as long segment enhancement and more posterior involvement including optic chiasm, tracts, and the adjacent hypothalamus. Patients with spinal cord involvement have longitudinally extensive lesions involving greater than 3 segment involvement on MRI spine. Unlike typical demyelinating optic neuritis, CSF examination in NMO may show moderate pleocytosis (>50 cells/mm³). Treatment of acute NMO optic neuritis includes high-dose intravenous methylprednisolone over 5 days followed by plasma exchange in cases of refractory vision loss or recurrence. Long-term immunosuppression with rituximab (treatment of choice), mycophenolate, or azathioprine is necessary to reduce increased lesion burden from recurrent disease.

More recently, serum IgG antibodies to the MOG moiety were discovered in a distinct subset of patients presenting with atypical optic neuritis, including patients with seronegative NMO spectrum disorders. MOG-IgG demyelinating disease is characterized by a higher likelihood of bilateral and recurrent optic neuritis, presence of moderate to severe disc edema, and severe vision loss at onset. MRI characteristically shows long optic nerve enhancement with involvement of optic nerve sheath and periorbital tissue. Patients with MOG-IgG disease are highly steroid responsive and often steroid dependent, similar to chronic relapsing inflammatory optic neuritis.

Blood and CSF test battery results were normal. Serum AQP-4 antibody was negative, while MOG-IgG antibody tested using cell-based assay (FACS) was positive at a titer of 1:100.

Patient was treated with 5 days of IV methylprednisolone, followed by oral prednisone (1 mg/kg/day) tapered over 8 weeks. By day 6 of treatment, her vision had improved to 20/20 right eye. At 7 weeks, she developed recurrent optic neuritis (visual acuity 20/200), which was treated with 5 days of IV methylprednisolone (1 g/day) with a slow oral steroid taper over 24 weeks. While waiting for insurance approval of rituximab for chronic immunosuppression, she had a fourth recurrence on oral prednisone 15 mg/day. Following induction of treatment with rituximab, she was bridged with oral prednisone at 20 mg/day for 3 months followed by slow taper. She remains recurrence-free on rituximab after 16 months.

Point-Counterpoint: Extensive Lab Workup for All New Cases of Optic Neuritis

Lynn K Gordon MD PhD, Andrew G Lee MD, Norah Lincoff MD, Mark L Moster MD

NOTES

[illegible]

“I’m Missing Letters When I Read”

Fiona Costello MD

CASE PRESENTATION

History and Exam

History

A 35-year-old female patient reports a grey “splotch” in her left eye, first noted upon morning waking. She describes noting something “off” with her vision for the past 2 weeks. She initially became aware of this problem when she realized that she was “missing letters” on the license plates of cars in front of her during the drive to work. She currently denies pain and/or positive visual phenomena. When she alternately occludes each eye, she localizes the grey spot as being slightly temporal to fixation in her left eye. She presents a hand-drawn version of the visual disturbance.

Prior to this event, she had no ocular history and reports no current comorbidities. She uses no regular medications. She denies experiencing any recent infectious symptoms. Her history is otherwise significant for high caffeine consumption.

Examination

Blood pressure is 120/70 mmHg. Visual acuity is 20/20 in both eyes. Pupils are 5 mm in light and constrict to 3 mm in bright light, with no relative afferent pupillary defect. Color vision measures 10/10 with Hardy Rand and Rittler (HRR) pseudoisochromatic plates in each eye. Visual fields are normal to confrontation, and Humphrey central threshold 30-2 perimetry testing is normal. Amsler grid testing demonstrates a small paracentral scotoma slightly superior to fixation in the left eye, whereas findings in the right eye are normal. Routine fundus examination reveals no abnormalities. Specifically, the optic nerves show no evidence of edema or pallor.

Clinical Course

The near-infrared reflectance imaging of the left eye uncovers a small, wedge-shaped, dark-gray lesion that involves the superotemporal fovea. The spectral domain OCT findings (corresponding to the defect) reveal a subtle hyper-reflective lesion involving the inner nuclear layer.

“I Can’t See Anything to the Right!”

Courtney E Francis MD

CASE PRESENTATION

History and Exam

A 35-year-old woman presents to her ophthalmologist with a complaint of temporal visual field loss in her right eye. She was at work when a cardboard box fell and hit her on the right side of her head. She reported headache and the visual field loss but denied loss of consciousness.

During evaluation of her head injury, head CT is performed and shows a possible sellar mass. She denies any loss of central vision or difficulty with the peripheral vision in her left eye. She notes frequent headaches but denies photopsias, floaters, diplopia, or other eye symptoms.

Her past medical history is significant for migraine and endometriosis requiring hysterectomy. Her medications include eletriptan and estradiol. She denies tobacco use and drinks alcohol occasionally. Her family history is unremarkable.

On examination, her acuity is 20/20 in each eye. Color vision is full in both eyes, and she has no afferent pupillary defect. Her extraocular movements are full. Confrontation visual fields show loss of the temporal visual field on the right and a normal visual field on the left. Her optic nerves are pink without edema or atrophy, and a dilated fundus exam is otherwise unremarkable. The remainder of her ophthalmologic examination is normal. An MRI is ordered, and she is referred for neuro-ophthalmologic evaluation.

Clinical Course and Outcome

Automated visual fields show an incomplete temporal defect in the right eye and a full field in the left eye. Review of the MRI brain reveals a 9x18x9 mm homogeneously enhancing sellar mass, consistent with a pituitary adenoma, just abutting the optic chiasm. OCT shows normal retinal nerve fiber layer thickness in all quadrants in both eyes.

The monocular temporal visual field loss of the right eye in the setting of normal pupils (eg, absence of an ipsilateral afferent pupillary defect) raises concerns for non-organic or functional visual loss. Confrontational and tangent visual field testing at 1 and 2 meters failed to show appropriate expansion of the right temporal field loss. Goldmann visual fields were performed and show temporal depression in the right eye, with crossing isopters, a nonphysiologic response. When the visual field is tested under binocular conditions, the right temporal field defect persists. This confirms the non-organic nature of her visual field defect. Review of her MRI reveals that while there is evidence of a pituitary macroadenoma, there is no evidence of optic nerve or chiasmal compression by the mass.

There are very few organic causes of a unilateral temporal visual field defect. Typically, retrochiasmal lesions give rise to contralateral homonymous visual field defects. However, as the temporal visual field is larger than the nasal field, there is a small area of monocular representation of peripheral temporal vision represented in the anterior 10% of the calcarine fissure. Therefore, an infarct in the anterior parieto-occipital sulcus will

give rise to an isolated contralateral temporal crescent visual field defect. This crescent is found approximately 60-70 degrees temporally; therefore standard 24-2 and 30-2 Humphrey visual fields fail to test this region.

One should be aware of the limitations in standard visual field testing when evaluating patients with far temporal visual field complaints. Additionally, one should identify associated MRI findings in the contralateral anterior parieto-occipital sulcus.

Lesions affecting the chiasm are the most common cause of bilateral temporal visual field loss. Due to crossing of the nasal fibers of the optic nerves, lesions in this region typically preferentially compress these fibers, leading to the classic bitemporal hemianopia. Pituitary adenomas, craniopharyngiomas, and meningiomas are the most common lesions found in the sellar region. One must be careful when evaluating patients with a unilateral complaint, as the fellow eye may have an asymptomatic early temporal field cut. Bilateral visual field testing should always be performed.

A mass compressing the posterior optic nerve or anterior chiasm could lead to a unilateral temporal visual field cut. However, as this is presynaptic and asymmetric, there should be an associated afferent pupillary defect. Long-standing compressive lesions should also lead to optic atrophy, noted on fundus exam and/or OCT scanning.

Optic neuritis can present with any pattern of visual field loss, including temporal field depression. However, as with all unilateral optic neuropathies, there will be an associated afferent pupillary defect.

Traumatic optic neuropathy can occur following blunt head trauma, especially with a blow to the brow. Associated visual acuity and visual field loss are variable but can be as severe as no light perception. Initially the optic nerve appears normal, but there should be an afferent pupillary defect in the setting of unilateral injury. Optic atrophy and progressive retinal nerve fiber layer thinning on OCT occur several weeks after injury.

Patients with acute idiopathic blind spot enlargement (AIBSE) can occasionally present with unilateral temporal visual field loss. AIBSE is a disease of the outer retina, with similarities to multiple evanescent white dot syndrome. Patients typically present with photopsias and may have dyschromatopsia and mildly reduced acuity. The visual field typically shows an enlarged blind spot, as the name suggests, but larger defects can mimic other causes of temporal depression. Exam findings may include uveitis, peripapillary pigmentary changes, and mild disc edema. An afferent pupillary defect is expected with large visual field defects. Multifocal electroretinography should be abnormal in the involved areas. Typically the photopsias resolve, but the visual field defects may persist.

“I Woke Up One Day With Bad Vision”

Mays A El-Dairi MD

CASE PRESENTATION

History and Exam

A 63-year-old woman presents with bilateral painless vision loss for 1 week in the right eye and 3 months in the left eye. She is 2 months post-cataract extraction with multifocal IOL implantation to the left eye. She has a 10 packs/year history of smoking cigarettes and has recently started drinking alcohol more frequently after the death of her husband a year ago. Past medical and surgical histories are unrevealing. Family history is significant for AMD. She denied pain on eye movements, scalp tenderness, jaw claudication, fatigue, weight loss, and symptoms of polymyalgia rheumatica. There was no history of tick bite or cat scratch; she denied recent travels or major illnesses. Her diet is healthy and nonrestrictive, and she denied drinking well water or consuming homemade alcohol. She was recently checked by her primary care physician and is not anemic or diabetic.

On examination, vision was 20/400 in each eye with para-central fixation. Pupils were equal in the light and dark with no relative afferent pupillary defect. She could only identify the control plate on color vision testing OU. Confrontational visual fields were full bilaterally. IOPs were 9 mmHg OD and 12 mmHg OS. The right optic nerve was mildly elevated 360 degrees, with no vessel obscuration or peripapillary hemorrhages; the left optic nerve was pale temporally. The retina and fundus vessels looked normal. Humphrey visual fields showed bilateral cecocentral scotomas.

Impression

Patient has bilateral sequential optic neuropathies with central/cecocentral scotoma pattern of visual field loss (pseudobitemporal fields). This field pattern is usually due to an optic nerve pathology with predilection to the papillomacular bundle.

Clinical Course and Outcome

Workup

- Neuroimaging (MRI brain and orbits with contrast), FTA-Abs was normal. ESR was 2, CRP was 0.3, platelet count was 250,000.
- Genetic testing showed positive LHON-11778 mutation (ND4).
- Baseline ERG was normal.

Management

She was started on idebenone with some improvement in the central vision, although some defects on the visual fields remained. Her optic nerve appearance and OCT remained stable in the left eye; the right optic nerve head pseudoedema resolved and was replaced by pallor over the course of 3 months.

Are You AT the Table or ON the Menu?

Prem S Subramanian MD PhD

Ophthalmology's goal to protect sight and empower lives requires active participation and commitment to advocacy from every ophthalmologist. Contributions to the following three critical funds are a part of that commitment:

- OPHTHPAC®
- Surgical Scope Fund (SSF)
- State Eye PAC

Please join the dedicated community of ophthalmologists who are contributing to protect quality patient eye care for every-body.

The OPHTHPAC Committee is identifying Congressional Advocates in each state to maintain close relationships with federal legislators to advance ophthalmology and patient causes. At Mid-Year Forum 2019, we honored three of those legislators with the Academy's Visionary Award. This served to recognize them for addressing issues important to us and to our patients. The Academy's Secretariat for State Affairs is collaborating closely with state ophthalmology society leaders to protect Surgery by Surgeons at the state level.

Our mission of "protecting sight and empowering lives" requires robust funding of both the Surgical Scope Fund and OPHTHPAC. Each of us has a responsibility to ensure that these funds are strong so that ophthalmology can be represented "at the table."

OPHTHPAC®

OPHTHPAC represents the profession of ophthalmology to the U.S. Congress and operates to protect you and your fellow ophthalmologists from payment cuts, burdensome regulations, scope-of-practice threats, and much more. OPHTHPAC also works to advance our profession by promoting funding for vision research and expanded inclusion of vision in public and private programs—all of which provide better health-care options for your patients. OPHTHPAC is your federal voice in Washington, D.C., and we are very successful in representing your professional needs to the U.S. Congress.

Among OPHTHPAC's most recent victories are the following:

- Securing greater flexibility in the new Medicare Payment System
- Ensuring proper reimbursement of Medicare Part B drugs
- Blocking onerous administrative burdens on contact lens prescribers
- Preserving access to compounded drugs
- Preventing additional cuts to Medicare

However, ophthalmology's federal issues are a continuous battle, and OPHTHPAC is always under pressure to ensure we have strong political connections in place to help protect ophthalmology, its members, and their patients.

The support OPHTHPAC receives from invested U.S. Academy members helps build the federal relationships that advance ophthalmology's agenda on Capitol Hill. These relationships allow us to have a seat at the table with legislators

willing to work on issues important to us and our patients.

We also use these congressional relationships to help shape the rules and regulations being developed by federal agencies. Help strengthen these bonds and ophthalmology's legislative support.

Right now, major transformations are taking place in health care. To ensure that our federal fight and our PAC remain strong, we need the support of every ophthalmologist to better our profession and ensure quality eye care for our patients. Invest with confidence in the strongest PAC working to ensure your success as an ophthalmologist.

Contributions to OPHTHPAC can be made here at AAO 2019, online at www.aao.org/ophthpac, or by texting MDEYE to 41444.

At Mid-Year Forum 2019, the Academy and the North American Neuro-Ophthalmology Society (NANOS) ensured a strong presence of neuro-ophthalmologists to support ophthalmology's priorities. Ophthalmologists visited members of Congress and their key health staff to discuss ophthalmology priorities as part of Congressional Advocacy Day. The NANOS remains a crucial partner with the Academy in its ongoing federal and state advocacy initiatives.

Surgical Scope Fund

The Surgical Scope Fund (SSF) provides grants to state ophthalmology societies to support their efforts to protect patient safety from dangerous optometric surgery proposals. Since its inception, the Surgery by Surgeons campaign and the SSF, in partnership with state ophthalmology societies, have helped 40 state/territorial ophthalmology societies reject optometric scope-of-practice expansions into surgery.

Thanks to the 2019 SSF contributions from ophthalmologists just like you, SSF has had a successful year, preserving patient safety and surgical standards in state legislatures across the country, including six critical wins in Alabama, Texas, Vermont, Wyoming, Maryland, and Iowa. The 2019 battle is far from over, though. For example, Pennsylvania and Massachusetts are under attack, and California and Illinois are facing threats.

If you have not yet made a 2019 SSF contribution, contributions can be made at our booth at AAO 2019 or online at www.aao.org/ssf. If you already have made that 2019 contribution, please go to www.safesurgerycoalition.org to see the impact of your gift.

Dollars from the SSF are critical to building complete cutting-edge political campaigns, including media (TV, radio, and social media), educating and building relationships with legislators, and educating the voting public to contact their legislators. This work helps to secure success in protecting patient safety by defeating optometry's surgical initiatives.

Each of these endeavors is very expensive, and no one state has the critical resources to fight big optometry on their own. Ophthalmologists must join together and donate to the SSF at www.aao.org/ssf to fight for patient safety.

The Secretariat for State Affairs thanks NANOS for joining state ophthalmology societies in already contributing to

Surgical Scope Fund	OPHTHPAC® Fund	State EyePAC
To protect patient safety by defeating optometric scope-of-practice initiatives that threaten patient safety and quality surgical care	Ophthalmology's interests at the federal level Support for candidates for U.S. Congress	Support for candidates for state House, Senate, and governor
Political grassroots activities, government relations, PR and media campaigns No funds may be used for campaign contributions or PACs.	Campaign contributions, legislative education	Campaign contributions, legislative education
Contributions: Unlimited Individual, practice, and organization	Contributions: Limited to \$5,000	Contribution limits vary based on state regulations.
Contributions are 100% confidential.	Contributions above \$200 are on the public record.	Contributions are on the public record depending upon state statutes.

the SSF in 2019, and it looks forward to the society's continued financial support. These ophthalmic organizations complete the necessary SSF support structure for the protection of our patients' sight.

State Eye PAC

It is increasingly important for all ophthalmologists to support their respective State Eye PACs because campaign contributions to legislators at the state level must come from individual ophthalmologists and cannot come from the Academy, OPHTHPAC, or the SSF. The presence of a strong State Eye PAC providing financial support for campaign contributions and legislative education to elect ophthalmology-friendly candidates to the state legislature is critical, as scope-of-practice battles and many regulatory issues are all fought on the state level.

ACTION REQUESTED: Help Ophthalmology Ensure a "Seat at the Table"

Academy SSF contributions are used to support the infrastructure necessary for state legislative/regulatory battles and for public education. State PAC and OPHTHPAC contributions are necessary at the state and federal levels, respectively, to help elect officials who will support the interests of our patients. Contributions to *each* of these three funds are necessary and help us protect sight and empower lives. SSF contributions are completely confidential and may be made with corporate checks or credit cards, unlike PAC contributions, which must be made by individuals and are subject to reporting requirements.

Please respond to your Academy colleagues and be part of the community that contributes to OPHTHPAC, the SSF, and your State Eye PAC. Please be part of the community that ensures ophthalmology has a strong voice in advocating for patients.

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Section II: Bugs and Drugs—Do They Matter?

“I Am On So Many Medications, and Now I Can’t See!”

Gabrielle R Bonhomme MD

CASE PRESENTATION

History and Examination

A 54-year-old man presents urgently reporting progressive, bilateral vision loss of 2 month’s duration. Symptoms are described as a worsening “cloudiness” and patient reports associated biparietal and bilateral retrobulbar pressure, “auricular fullness” and “muffled hearing,” imbalance, and dizziness triggered by head movement. Local eye exam revealed bilateral optic disk edema.

Past medical history reveals heart disease with ventricular tachycardia/fibrillation, premature ventricular contractions with pause, obstructive sleep apnea, hypertension, migraine, erectile dysfunction, and recent admission for catheterization and ablation/cardioversion. Surgical history reveals defibrillator placement and recent insertion of new right atrial lead and single chamber replacement with dual chamber implantable cardioverter defibrillator.

Current medications include amlodipine, amiodarone, atorvastatin, doxazosin, losartan, metoprolol, and sildenafil. He denies any known medication allergies. Family history reveals relatives with glaucoma, hypertension, and heart disease.

On exam, Snellen visual acuity has declined from prior baseline of 20/20 to 20/60 in the right eye, and to count fingers at 1 foot in the left eye, with a left relative afferent pupillary defect. He perceived the control plate only with the right eye and was unable to perceive any Ishihara color plates in the left eye. Ocular motility was full bilaterally, with normal ocular alignment. On dilated ophthalmoscopy, both optic nerves exhibited sectoral, hyperemic disk edema, sectoral pallor, and flame hemorrhages. The remainder of the retinal exam revealed subtle bilateral retinal pigment epithelial changes. Formal visual fields revealed concentric peripheral constriction of the right field. The left field revealed a dense central scotoma and inferior nasal field defect.

Clinical Course and Outcome

Given his bilateral disk edema, blood pressure was checked; it was elevated at 180/109. Given the patient’s hypertension, untreated sleep apnea, concern for giant cell arteritis and potential medication toxicities, his cardiologist was contacted to facilitate workup. Immediate cessation of amiodarone was approved by the cardiologist, and avoidance of sildenafil was recommended. IV methylprednisolone pulse was administered, until ESR, CRP, and CBC were drawn and were normal. As the patient’s defibrillator contraindicated MRI, a CT angiogram of the head and neck and CT head were obtained, and these

excluded intracranial tumor, stroke, sinus thrombosis, and carotid stenosis or dissection. Given concern for elevated intracranial pressure in the setting of headaches and bilateral disk edema, a lumbar puncture was obtained and revealed normal opening pressure of 18 cm H₂O, with bland CSF analysis and inflammatory serologies.

The patient was monitored over the ensuing months, as the disk edema slowly resolved. Subsequent follow-up examination revealed improvement in visual acuity to 20/25 in the right eye and 20/200 in the left eye, with sectoral disk pallor bilaterally. All prior constitutional symptoms described completely resolved immediately after discontinuation of amiodarone and have not reoccurred. Most recent Goldmann perimetry revealed significant improvement in the inferior and peripheral constriction of the right field. The left field exhibits an improved cecocentral relative scotoma and persistent inferior altitudinal defect. OCT revealed global thinning of the retinal nerve fiber layer, ganglion cell, and maculae bilaterally.

“My Neck Hurts and I’m Cold!”

Michael S Lee MD

CASE PRESENTATION

History and Exam

A 77-year-old woman noted intermittent binocular diplopia over the past week. She does not think that it is clearly related to fatigue. She denies a history of childhood strabismus, patching, or strabismus surgery. She has had ptosis of the left upper lid for many years and does not think that it has changed. It seems to be worse with fatigue. Finally, she endorses blurry vision but has not tried covering either eye. Overall, her symptoms do not seem to be getting worse.

Her past ocular history includes cataract surgery in both eyes a few years ago. She has been told that she has a pucker in her left eye. She is a retired teacher who has smoked a pack of cigarettes per day since she was young and rarely drinks alcohol. Her past medical history includes a thyroidectomy for thyroid nodules 45 years ago. She takes levothyroxine, vitamin D, and aspirin. Her family history is noncontributory. On review of systems, she endorses sweats, chills, neck pain, non-productive cough, anorexia, and malaise. She denies weakness, dysphagia, dysarthria, shortness of breath, jaw pain, headache, rash, dysuria, and arthralgias.

Table 1. Examination at Presentation

	Right eye	Left eye
Visual acuity	20/25	20/25
Pupils	Normal	1+ APD
Tonometry	10	13
Color vision	11/11	10/11
SLE	Unremarkable	Unremarkable
Fundus	Normal nerve	Normal nerve
	Normal macula	Normal macula
	Choroidal nevus	

Motility

- Normal saccades/pursuits
- Orthophoric in all gazes

External

- MRD1 = 4 RE, 3 LE
- Normal levator function
- Normal orbicularis strength
- No fatigability
- No lid twitch

Clinical Course and Outcome

A fluorescein angiogram was performed in the office. This demonstrated a large swath of delayed choroidal filling in the left eye, up to almost 90 seconds. This was worrisome for giant cell arteritis (GCA). The patient was immediately admitted for intravenous solumedrol 250 mg every 6 hours. An urgent ESR was 63 mm/hr, CRP was 72 mg/dL, and platelets were 547K. A left temporal artery biopsy showed multinucleated giant cells within the walls of the artery, consistent with temporal arteritis. Despite the rapid administration of high-dose corticosteroids, the patient lost all vision in the left eye on hospital day #2.

“My Eye Aches, and It’s Blurred When I Read (and Garden)”

Kimberly Cockerham MD FACS

CASE PRESENTATION

History and Exam

A 65-year-old woman was referred by her comprehensive ophthalmologist for diagnosis and management in the setting of 4 months of painful, gradually declining vision in her right eye. Her past medical history was significant for a “positive PPD” and pulmonary changes thought to be consistent with tuberculosis; she was diagnosed with TB and treated with ethambutol by a county clinic. She also was taking medications for hyper-

tension and type II diabetes. She denied tobacco and alcohol use, as well as use of other prescribed, legal, or illegal drugs. She had no known drug allergies. She is an avid gardener and works in the gardening section of a large home and garden center, and she reports that her vision and pain worsen after extended exposure to soil. She has no history of cancer, autoimmune disease, or neurologic disease. She has no known family history of hereditary vision loss.

She denies fevers, chills, weight loss, temporal tenderness, jaw claudication, or symptoms of polymyalgia rheumatica. She had seen 5 eye care providers over the last 4 months; the first provider told her to stop the ethambutol, but her visual loss progressed nonetheless. Because of financial considerations and poor insurance coverage, further workup was not obtained (denied by insurance), and when vision declined to 20/400 in the right eye, a noncontrast CT head study was approved and interpreted as being normal.

On examination, her vision was 20/400 OD, with a 3+ relative afferent pupillary defect, pain on eye movement, normal motility, optic nerve pallor, a dense central visual field defect, and extensive nerve fiber loss on OCT OD. Examination of her left eye was normal. She identified 0/11 Ishihara color plates in the right eye and 11/11 in the left eye.

Clinical Course and Outcome

This is a complex case, complicated by the fact that the patient has suboptimal insurance resulting in a limited and misleading workup. Her painful visual loss has a broad differential. The patient is older and her 4-month progression of vision loss and pain is longer than expected for typical demyelinating optic neuritis. The patient is on the younger side for giant cell arteritis, which can produce pain but typically causes acute rather than insidious vision loss. The patient also lacks typical symptoms for this disease. She has a reported handling of peat dust and frequent exposure to regional soil and water, both of which are potential sources of pesticides, fungus, and toxins.

CBC, ESR, CRP, and extensive autoimmune workup was negative. Repeat PPD and serum testing was negative. Chest CT revealed nonspecific scarring without evidence of granulomatous disease or nodules. MRI orbits revealed an enhancing lesion of the orbital apex that was suspicious for inflammation.

Citing family issues, the patient failed to show up for her appointments despite understanding that she had a potentially causative and treatable lesion visualized on the MRI. In addition, she refused to take oral steroids or to go to the infusion center for IV steroids.

Eight weeks later, she returned to clinic with worsened vision and new dysmotility. On examination, her vision was now no light perception OD, and she had a frozen right globe. Her left eye examination remained normal.

The MRI revealed not only an expanded orbital infiltration of the right apex but new involvement of the right cavernous sinus. She was treated with IV corticosteroids followed by oral steroids as an outpatient.

Point-Counterpoint: NAION Should Be Treated With Medication

Lanning B Kline MD, Neil R Miller MD, Nicholas J Volpe MD, Judith E Warner MD

NOTES

“They Told Me My Optic Nerves Are Swollen”

Kevin E Lai MD

CASE PRESENTATION

History and Exam

A 17-year-old female was referred to ophthalmology by her optometrist after being told that she had swollen optic nerves. She reported that 3 weeks previously, she had a rapid onset of pain behind her eyes that progressed to severe frontal headache within 3 days. She noted constant horizontal double vision that resolved with covering either eye. Due to the severe pain, she went to the ER and received a CT head, which was read as normal. She was diagnosed with migraine, and her headache improved after 9 days although eye pain persisted. Her double vision resolved, but she developed constant blurred vision in both eyes that worsened with bending or coughing.

She also described a “whooshing” sound in her ears; it had been present since the onset of her severe headache and did not resolve with her headache. She has not gained or lost any weight recently. She denies any recent travel, illness, or trauma.

She has a past medical history of seasonal allergies and acne. She has no past ocular history. She takes oral cetirizine and minocycline and recently discontinued use of fluticasone nasal spray. She has no allergies. She does not smoke, drink, or use illicit drugs. She denies being sexually active.

On examination, height was 61” (153 cm) and weight was 163 lbs (74 kg). Blood pressure was 118/76 with a pulse of 77. Uncorrected visual acuity was 20/25 in each eye with mild “shadows” of images in each eye that resolved with pinhole. Her BCVA was 20/15 in each eye. Pupils were isocoric, normally reactive, with no relative afferent pupillary defect. Visual fields were full to confrontation in each eye. She saw 14/14 color plates in each eye. Alignment was orthotropic, and motility was full. Intraocular pressures were 16 mmHg in the right eye and 17 mmHg in the left eye.

External and slit-lamp exam were normal. On dilated fundoscopic exam, both optic nerves demonstrated diffuse elevation with nerve fiber layer edema and obscuration of the peripapillary retinal blood vessels, consistent with grade 2 papilledema. The left optic nerve demonstrated a similar appearance. No spontaneous venous pulsations were noted. The macula, peripheral retina, and vitreous were normal.

Automated perimetry demonstrated an enlarged blind spot in each eye. OCT of retinal nerve fiber layer demonstrated thickened nerve fiber layer with buried drusen. Fundus autofluorescence did not demonstrate any optic disc drusen.

Clinical Course and Outcome

The patient had an MRI of the brain with and without contrast as well as an MRV (magnetic resonance venography) of the brain without contrast. The MRI of the brain demonstrated normal sella, optic nerves, and globes. There was no narrowing of the ventricles, and there was no evidence of cerebral venous sinus stenosis or thrombosis. A lumbar puncture demonstrated an opening pressure of 37 cmH₂O. CSF cultures were negative, and glucose, protein, and cell counts were normal. Based

on these findings, we diagnosed her with pseudotumor cerebri with possible secondary causes of minocycline and fluticasone withdrawal.

We started the patient on acetazolamide 500 mg b.i.d. and instructed her to discontinue the minocycline and work on losing 8-16 lbs (3.6-7.2 kg) over the next few months. At her 1-month follow-up visit, she reported that her headaches and eye pain had completely resolved. She still had grade 2 papilledema in each eye, but her transient visual obscurations had resolved and the pulse-synchronous tinnitus was reduced. She still had mildly enlarged blind spots on automated perimetry. We titrated up her dose of acetazolamide to 1000 mg b.i.d., and at her next visit 1 month later she reported a resolution of her symptoms. She had lost approximately 5 lbs and felt like she was back to normal. The enlarged blind spot resolved, but she continued to have grade 1 papilledema in each eye, so we kept her on acetazolamide 1000 mg b.i.d. until her papilledema resolved. She was unable to tolerate doses higher than 1000 mg b.i.d. Over the next 12 months we slowly tapered her off the acetazolamide to ensure that there was no return of her symptoms or the papilledema.

“My Vision’s Blurred, and One of My Optic Nerves Is Swollen”

Melissa Wang Ko MD

CASE PRESENTATION

History and Exam

A 30-year-old man presented overnight to the ED with decreased vision in the right eye. He had a headache for 3 days preceding the vision loss and had noticed increasing blurred vision in the right eye for the last 2 days with associated pain with eye movements. He reported some fatigue for a few weeks prior to his presentation, but denied any other new symptoms.

He had no significant past medical history and did not take any prescription medications. His family history was noncontributory. He reported a history of intravenous drug use.

On examination, his visual acuity was 20/400 OD and 20/20 OS. Color vision was decreased OD with HRR plates. A relative afferent pupillary defect was present OD. Ocular motility was full. Anterior segment was notable for +2 anterior chamber cell and optic nerve swelling OD. Visual field testing revealed an enlarged blind spot OD.

Clinical Course and Outcome

Head CT was normal. MRI brain was unable to be obtained due to retained BB metallic fragments.

Following the noncontrast head CT, a lumbar puncture was obtained. The CSF had a normal opening pressure. The CSF analysis revealed WBC 0, RBC 2, protein 84 (16-46 mg/dL), normal glucose. *Cryptococcus* antigen returned negative.

Blood work was obtained, including CBC (normal), complete metabolic profile (normal), ESR 134 mm/hr, CRP 7.5 (0.1-0.9 mg/dL), ACE level (normal), HIV (pending), Lyme (negative), ANA (negative).

Due to the optic nerve swelling, the patient was started on IV methylprednisolone overnight.

The following morning, a careful general examination revealed a maculopapular rash over most of his body including the soles of his feet and palms of his hands (see Figures 2 and 3). He reported that this started over 6 months prior and he had not think it worth mentioning during initial history taking the previous evening. HIV testing returned positive. Due to the presence of the systemic rash, newly diagnosed HIV status, and history of high-risk behavior, RPR and TPA serology were sent and returned positive. CSF-VDRL returned nonreactive.

He was treated with IV penicillin G (3 million units IV every 4 hours) for 14 days. IV methylprednisolone was given for 3 days, followed by oral prednisone for 5 days with a rapid taper.

Five days into treatment course, his visual acuity improved to 20/40-2 OD, 20/20 OS, with improving color vision OD. Anterior exam showed rare cell OD. Fundus exam demonstrated improving optic nerve edema OD. By the 2-week follow up, his OD visual acuity had returned to 20/20.



Figure 1.



Figure 2.



Figure 3.

Section III: Double Vision—50/50 Chance to Pick the Right One!

“My Eyelid Droops, and I See Double”

Kenneth Shindler MD PhD

CASE PRESENTATION

History and Exam

A 58-year-old white woman presented with a complaint that her left eye had been closed for several days. She thought that her left upper eyelid had some mild drooping for a few days or weeks before it closed, but she was not really sure when that started. At the time of presentation, she could open the lid slightly in the morning, but quickly it would become fully closed and she would be unable to open it. In addition to her eyelid symptoms, she had experienced intermittent double vision for at least several days, more likely a few weeks—but again, she was unsure when this symptom started. The double vision could be vertically or diagonally displaced, changed when she moved her head and refocused, and resolved with one eye closed. Now that her left lid was fully closed, she had no double vision unless she lifted her eyelid.

Her past medical history was significant for hypertension, hyperlipidemia, and hypothyroidism. She was currently taking lisinopril, atorvastatin, levothyroxine (Synthroid), and a multivitamin. She had never smoked, drank alcohol only on rare occasions, and denied recreational drug use. Her family history included migraines on her maternal side. Review of systems was negative for any other symptoms, including no other neurologic symptoms, no headaches, no systemic weakness, no trouble breathing, no trouble swallowing, and no history of head or facial trauma.

On examination her BCVA was 20/20 in each eye. Color vision was full in both eyes. Confrontational visual fields were normal. IOP was 14 in each eye. Slit-lamp examination was normal in both eyes except for mild nuclear sclerotic lens changes. Dilated fundus examination showed normal optic nerves and retina in both eyes. Pupil examination showed mild anisocoria, with the left pupil 0.5 mm larger than the right pupil. This difference was equal in light and dark, with both pupils briskly reactive to light. There was no afferent pupillary defect. Review of old photographs from several years earlier showed a similar mild degree of anisocoria.

External examination showed complete ptosis of the left upper eyelid, without fatigability or a lid twitch. The right upper eyelid came down slightly after manual elevation of the left upper eyelid. Extraocular motility was full in the right eye, but showed slight limitations of elevation and depression of the left eye. Alternate cover testing revealed a 2 prism diopter left hypertropia in primary gaze that increased to 10 diopters in downgaze and converted to an 8 diopter right hypertropia in upgaze; and she had a fairly comitant exotropia of 4 to 6 diopters that increased slightly to 10 diopters in right gaze only.

Clinical Course and Outcome

There was clinical concern for a left CN III palsy, pupil sparing as her anisocoria was equal in light and dark and was long-standing. The patient underwent MRI and MRA of the head on the day of presentation, which showed mild small-vessel ischemic changes with no mass lesions, no strokes, no hemorrhage, and no aneurysm. Views through the orbits showed normal extraocular muscles. A vasculopathic third nerve palsy was suspected, and ocular myasthenia gravis was also considered with anti-acetylcholine receptor antibody testing sent. Despite a history of thyroid disease, thyroid-related orbitopathy was not felt to be the etiology of the diplopia given the presence of profound ptosis, and MRI was also reassuring for no extraocular muscle enlargement.

The patient was seen in follow-up 4 weeks later and again 8 weeks after initial presentation. Examination at both visits again revealed a small left hypertropia that increased in downgaze and converted to a right hypertropia in upgaze, with minor variations in the exact amount of deviation in each gaze. Ptosis remained complete on the left side at each evaluation, although the patient was more cognizant of the eyelid opening better when first awakening each morning. Anti-acetylcholine receptor antibody testing came back negative. Ice testing in the office did not improve ptosis. After failing to improve over several weeks, the patient was sent for repetitive stimulation and single-fiber electromyography testing, which was consistent with myasthenia. Chest CT showed no evidence of a thymoma. The patient was started on pyridostigmine with some improvement in ptosis but bothersome diplopia, and then prednisone was added. Ptosis and diplopia resolved over several months.

“My Eye Bulges, and I See Double”

Paul H Phillips MD

CASE PRESENTATION

History and Exam

A 76-year-old man was referred for evaluation and management of diplopia from thyroid eye disease. He was in his usual state of health until 1 month prior to presentation, when he developed nontender swelling of his left lower lid. Two weeks later he developed intermittent, binocular, vertical diplopia in downgaze. He was evaluated by his local ophthalmologist, who ordered a CT scan of the orbits that showed enlargement of the left inferior rectus muscle and referred the patient for further evaluation and treatment of thyroid-related orbitopathy.

He had mild fatigue for several months but denied weight loss, palpitations, fevers, and night sweats.

Past ocular and medical history were unremarkable; he denied use of alcohol and tobacco and was not taking any medications.

Physical examination showed a visual acuity of 20/20 OU. Confrontational visual fields were full OU. Pupils were equal and reactive, with no relative afferent pupillary defect. External examination showed 1 mm of proptosis of the left globe and mild left lower lid swelling. The lower lid was firm but nontender to palpitation. Ocular motility showed full ductions of the right eye and mild limitation of depression of the left eye. He had a 6 PD left hypertropia in downgaze and was orthotropic in other fields of gaze. Fundus examination showed normal optic discs, macula, and periphery OU. No fundus torsion was appreciated in either eye.

Clinical Course and Outcome

CBC, basic metabolic profile, liver function tests, and thyroid function tests were normal.

Examination of the CT of the orbits with contrast showed a hyperdense enhancing lesion abutting the anterior aspect of the left inferior rectus muscle, which was displaced superiorly. The lesion extended along the left lower anterior orbit and involved the left lower lid. The right orbit was normal.

An orbital biopsy of the lesion showed a diffuse large B-cell lymphoma. He was treated with local radiation and chemotherapy with resolution of the lesion.

“My Double Vision Comes and Goes”

Stacy L Pineles MD

CASE PRESENTATION

History and Exam

A 13-year-old girl presented with intermittent binocular diplopia for 3 months. The diplopia is horizontal and occurs for episodes lasting a few minutes at a time. In between these episodes, she has no problems with her vision. She has no generalized weakness or difficulty swallowing or breathing. She denies recent headaches, altered mental status, or changes in balance.

Her past medical history is significant for a history of a cerebellar medulloblastoma diagnosed and treated 5 years ago with chemotherapy and radiation. Since then, surveillance MRIs have been stable, without any recurrence, as recently as 2 months ago. At this time, she is not taking any medications and social/family history are noncontributory.

On examination her BCVA was 20/20 in the right and 20/20 in the left eye. Color vision was full in both eyes. Pupils were equal and briskly reactive to light, with no afferent pupillary defect. Confrontational visual fields were normal. External examination was normal with no evidence of ptosis or lid retraction. Ocular ductions were full, and initial cover testing was orthotropic in all directions of gaze. Anterior segment and ophthalmoscopic examinations were normal in both eyes, including optic nerves and maculae.

Clinical Course and Outcome

In the clinic, several tests were performed to try to elucidate the cause of her intermittent diplopia. A 30-minute patch test did not change her ocular alignment. There was no fatigue or ptosis on upgaze. A rest test was noncontributory. However, on motility testing after prolonged right gaze (>2 minutes of right gaze), she developed 30 PD of exotropia, which increased in right gaze to approximately 50 PD of exotropia, with limitation to adduction. This resolved after a minute of rest.

Differential considerations included myasthenia gravis, decompensated strabismus, and intermittent exotropia.

Point-Counterpoint: Imaging in Acute Diplopia for Patients Over 50

Jacqueline A Leavitt MD, Grant T Liu MD, Nancy J Newman MD, R Michael Siatkowski MD

NOTES

“My Eye Won’t Close, and I See Double”

Anne S Abel MD

CASE PRESENTATION

History and Exam

A 57-year-old woman with a history of chronic sinusitis, benign paroxysmal positional vertigo (BPPV), and depression presented with worsening double vision for 1 week. Her double vision was constant, horizontal, and associated with a foreign body sensation in her left eye. She described overlapping, horizontal images and denied they were ever separated in space. Sometimes she would even see 3 or more images at a time. Her double vision worsened with occlusion of her right eye and resolved with occlusion of her left eye. She was having difficulty closing her left eye and had been taping it shut at night for the past few days. Colleagues at work noticed the left side of her face was drooping, which prompted her to come in.

She denied fever or chills but had a headache, which she attributed to a sinus infection that was now causing ear stuffiness and pain. She was also suffering from vertigo, nausea, and vomiting, which she attributed to her BPPV. Indeed, she had seen her primary doctor 3 days prior and was diagnosed with a sinus infection. She was prescribed a 10-day course of amoxicillin-clavulanic acid and had started it, without change in her symptoms. CT head without contrast was normal at that time.

On exam, visual acuity was 20/20 right eye and 20/50 left eye. Acuity in the left eye improved to 20/25 with pinhole occlusion. Pupils were symmetric and normal. IOPs were normal. With normal blinks, the left eye did not close well. Slit-lamp exam was remarkable for moderate conjunctival injection with diffuse punctate corneal epithelial erosions in the left eye. Undilated fundus exam was normal bilaterally.

Upon neuro-ophthalmic consultation later that day, visual acuity remained 20/20 right eye and 20/50 left. With pinhole occlusion, her acuity subjectively and objectively improved. Pupils were normal. Color vision was normal. There was a mild abduction deficit in the left eye. The remainder of extraocular motility exam was normal. No nystagmus was seen. Cover testing revealed a small angle esotropia that worsened in left gaze. She had a complete left facial nerve palsy with 8 mm of lagophthalmos in the left eye. She had a good Bell reflex. Facial sensation was intact. She could not hear fingers rubbing near her left eye. Examination of her left ear revealed multiple vesicles on the external ear. Her left external auditory canal was erythematous and swollen, and the left tympanic membrane was not visualized.

Automated visual field testing was normal in the right eye and showed generalized depression in the left eye.

Clinical Course and Outcome

Brain MRI showed mass-like enhancement of the left internal auditory canal and enhancement of the left facial nerve consistent with Ramsay Hunt syndrome but could not rule out schwannoma or a perineural malignant process. She was treated with both valacyclovir 1000 mg t.i.d. and prednisone 60 mg daily for 7 days. She was prescribed artificial tear ointment and a moisture chamber to wear at night for the left eye.

The patient had a protracted clinical course complicated by inpatient hospitalization for severe nausea and vertigo and 3 weeks of subacute rehabilitation. Her facial nerve function was slow to recover despite the prednisone, valacyclovir, and facial nerve stimulation. Repeat MRI 3 months after presentation showed stable mass-like enhancement of the left internal auditory canal and enhancement of the left facial nerve. A platinum weight was placed in her left upper lid, which improved her exposure keratopathy significantly. Facial nerve function continued to slowly improve. She declined repeat neuro-imaging.

“Everything Is Double and Moving!”

Janet C Rucker MD

CASE PRESENTATION

History and Exam

A 35-year-old woman presented to her long-standing strabismus surgeon (pediatric ophthalmologist) reporting oscillopsia at night that started 5 years prior. In addition, she reported progressively worsening constant diplopia and progressive deterioration of balance over a few years.

Ophthalmologic history included strabismus surgery at ages 6 (bilateral medial rectus recessions), 16 (bilateral lateral rectus resections), and 26 (bilateral medial rectus recessions) for a working diagnosis of congenital esotropia. The most recent surgery, at age 26, had alleviated her diplopia, but it had since recurred and prism therapy had been ineffective. With regard to nystagmus history, she was first documented to have had nystagmus without oscillopsia at age 26. Records prior to that time were unavailable, and neither the patient nor her parents were aware of nystagmus prior to initial documentation by the ophthalmologist.

Her pediatric ophthalmologist documented a 3 PD esotropia and “nystagmus increasing with rapid component on gaze to either side” and diagnosed her with recurrent breakdown of a congenital esotropia and manifest latent nystagmus. She had never had neuroimaging.

The patient sought neuro-ophthalmologic consultation for another opinion a year later. On exam, acuity was 20/20 OU. Color vision, pupils, visual fields, and fundus were normal. Eye movement range was full. There was a 10 PD comitant esotropia. She preferred fixation with her right eye. There was right-beat nystagmus in right gaze, left-beat in left gaze, and downbeat in downgaze. Following return to central gaze after sustained left gaze, there were some beats of right-beat nystagmus in central gaze. Smooth pursuit was saccadic in all directions. Gait was steady with a normal base, but she had difficulty with tandem gait.

Clinical Course and Outcome

Additional examination techniques were performed. In right gaze, the right abducting eye was covered. There was no reversal of direction of the right-beating nystagmus. In left gaze, the left abducting eye was covered. There was no reversal of the left-beating nystagmus. With ophthalmoscopy, low amplitude downbeat nystagmus was also seen in central gaze position.

Brain MRI was obtained and revealed a Chiari type 1 malformation extending to the level of C1-2 with inferior pulling and mild prominence of the fourth ventricle. Cerebellar atrophy was also present. There was no syringohydromyelia. She underwent surgical Chiari decompression, with some improvement in balance and the downbeat component of nystagmus at last visit.

“I See Double and Triple Images”

Mark Borchert MD

CASE PRESENTATION

History and Exam

A 65-year-old man with history of diabetes mellitus, hypertension, and hypothyroidism presents with double vision for the past couple of months. He can see 2 people or 2 signs or 2 buildings. This does not resolve with monocular occlusion and occurs intermittently throughout the day, without worsening later in the day. He has no headache, eye pain, or ptosis.

During examination, patient states he sees 2 doctors. The “double” image is the same color and intensity but a few feet over in the room, and it lasts for about 10 seconds. When he is asked to look around the room, he sees another image of the doctor, still full color and intensity on a different wall, again lasting about 10 seconds.

Visual acuity, pupils, and motility are normal. Symptoms do not improve with pinhole. Slit-lamp exam reveals signs of mild ocular surface disease. Fundus exam normal. Visual field test reveals right homonymous hemianopsia. MRI shows either parietal stroke or tumor.

Panel will discuss the difference between illusory and hallucinatory palinopsia, and how to tease this out in a history. It will also focus on how to differentiate between physiologic and pathological after-images.

Section IV: Tests Will Give Me The Answer!

“My World Is Closing In”

Guy V Jirawuthiworavong MD

CASE PRESENTATION

History and Exam

A 44-year-old white female accounting clerk noted blurry, gradual loss of vision in both eyes over a period of 4 months. She wears glasses only for computer work. She saw her optometrist, who was not able to refract her to 20/20 in both eyes. She complained of difficulty seeing at night but denied shimmering lights. She had no headaches or eye pain. Six months after onset, her vision declined to OD 20/40 and OS 20/70. At 7 months, vision declined to OU 20/100, and by 9 months, she was 20/400 OU.

Past medical history was significant for bilateral carpal tunnel syndrome, obesity, and a colon polyp. Past surgical history included appendectomy at age 9 and bilateral arthroscopic knee surgery. Family history was noncontributory. She denied family members needing a white cane or a seeing eye dog. She does not smoke and drinks alcohol occasionally. Review of systems revealed an occasional headache but no numbness or weakness. She denied any history of weight loss, decreased appetite, night sweats, fatigue, skin rashes, cough, shortness of breath, hemoptysis, blood in stool, hematuria, joint pain, or low back pain.

Her medications included a 10-day course of cephalexin, 500 mg tabs 3x a day, for sinusitis, and oral contraception—norethindrone-ethinyl estradiol triphasic (0.5/0.75/1 MG) 35 mcg daily.

On examination, visual acuity was 20/400 OU. Color vision was OD 3.5/14 and OS 3/14. There was no afferent pupillary defect. She had difficulty identifying fingers on peripheral confrontational fields. Her slit-lamp exam was unremarkable. On fundus exam, cup-to-disc ratio was 0.3 OU with no optic disc pallor. The macula showed a loss of foveal reflex. In the peripheral retina there were no bone spicules. Humphrey and Goldmann visual fields showed very severe depression in both eyes, with peripheral ring scotomas. OCT macula showed subfoveal and perifoveal thinning of the outer retina with loss of the ellipsoid zone. Fluorescein angiogram did not show any leakage.

Clinical Course and Outcome

Extensive blood testing for infectious and inflammatory conditions did not reveal any contributory etiologies. MRI brain with and without gadolinium was unremarkable except for some mild right maxillary sinus mucosal thickening. Full-field electroretinogram (ERG) was abnormal, with severely diminished a- and b-waves. Multifocal ERG was ordered but never completed. Antiretinal antibody testing of the patient's serum was sent to a single laboratory, and multiple bands were detected on Western blot, including 23kD, 35kD, 46kD, and 60kD. It is uncertain if confirmatory immunohistochemistry on retinal tissue was also performed. Patient underwent a paraneoplastic workup, which included mammography; CT scan of the chest, abdomen, and pelvis with contrast; and a Pap smear. The chest CT scan indicated the presence of a small-cell lung carcinoma.

The patient underwent 2 cycles, 4 weeks apart, of intravenous methylprednisolone 1000 mg daily for 3 days and subsequent treatment for her underlying cancer. Some improvement was noted on Goldmann visual field. Repeat testing for the specific antiretinal antibody to recoverin was ordered from a different laboratory and was positive. After a long discussion about the risks and benefits of life-long immunotherapy with steroid-sparing agents for her eye condition, the patient elected to continue with watchful observation as she was receiving treatment for her small-cell lung carcinoma. Her visual acuity has remained stable at 20/200 for the last 5 years.

“They Told Me I Have Optic Neuritis”

M Tariq Bhatti MD

CASE PRESENTATION

History and Exam

A 27-year-old woman was referred to the neuro-ophthalmology clinic for evaluation of bilateral optic neuritis. Two months prior, she had a sudden onset of bilateral eye pain. After seeing an optometrist, she was prescribed a steroid-antibiotic eyedrop for bilateral corneal abrasions. She continued to have eye pain in addition to bilateral visual loss, photophobia, dizziness, nausea, and vomiting. She was evaluated in a local emergency room by a neurologist, who noted she could not read the eye chart but otherwise had a normal neurological examination. A cranial and orbital MRI with contrast was normal. Erythrocyte sedimentation rate was 48 mm/hr (normal: < 20 mm/hr), C-reactive protein was 0.7 mg/dL (normal < 0.9 mg/dL), and enzyme-linked immunosorbent assay (ELISA) for neuromyelitis optica (NMO) antibody was 6.9 U/mL (normal: < 3.0 U/mL). She was diagnosed locally with NMO-related optic neuritis and was prescribed 3 days of intravenous methylprednisolone at a dose of 1 gram/day. Following the completion of the steroid therapy, there was mild subjective improvement in vision, but she also reported bright white and blue light throughout the vision with continued eye pain and photosensitivity.

Medical history was notable for allergic rhinitis, reactive airway disease, bipolar disorder, depression, obesity, and polycystic ovarian syndrome. Medications included lamotrigine, desogestrel-ethinyl estradiol, metformin, and montelukast.

In neuro-ophthalmology clinic 8 weeks after onset of symptoms, she appeared to be in no distress, was wearing dark sunglasses, and required assistance from her mother to navigate the hallways. Visual acuity was 20/400 OU. Pupillary examination was normal, with no relative afferent pupillary defect. Color vision was 7/10 OD and 8/10 OS. Stereovision was 40 seconds of arc. Confrontation visual field testing demonstrated peripheral constriction OU. Slit-lamp examination was normal OU, with no intraocular inflammation. IOPs were 12 mmHg OD and 13 mmHg OS. Eye movements were full OU. Dilated fundus examination revealed normal-appearing optic discs with a cup-to-disc ratio of 0.3 OU. The vessels, macula, and peripheral retina were normal OU.

OCT demonstrated normal peripapillary retinal nerve fiber layer and ganglion cell layer-inner plexiform layer thicknesses OU. Automated visual field perimetry could not be performed because of the eye pain and photosensitivity.

Clinical Course and Outcome

Contradictory clinical examination findings of wearing sunglasses, normal stereopsis, and lack of optic disc pallor strongly suggest non-organic visual loss. The normal MRI and OCT strongly argued against optic neuritis. In addition, a cell-based assay using fluorescence-activated cell sorting technique was negative for aquaporin-4 immunoglobulin-G, indicating that the patient did not have NMO and that the low-titer result of the ELISA test was a false positive, that test having a lower specificity than cell-based assays.

“I Can’t See, and the MRI Is Not Normal”

Peter MacIntosh MD

CASE PRESENTATION

History and Exam

A 47-year-old woman was referred for evaluation of slowly progressive and painless vision loss in the left eye for 4 weeks, followed 2 weeks later by the right eye. She thought she needed glasses but could not be refracted better by her optometrist, who referred her to neuro-ophthalmology. Her medications include fish oil, a probiotic, and calcium daily. She had no significant past medical history; family history was notable for her mother losing vision similarly in both eyes at the age of 58 with a “negative workup.” She denied cigarette use, but drank 2 glasses of wine per day. She worked as a financial advisor.

On examination her BCVA was 20/40 in the right and 20/200 (pinhole 20/60) in the left eye. Ishihara color plates were 1/11 in the right eye and 0/11 in the left. Pupils demonstrated a left relative afferent defect. Confrontational visual fields were normal. External examination was normal with no evidence of proptosis, ptosis, or lid retraction. Ocular motility was full in all directions. Anterior segment and ophthalmoscopic examination were normal in both eyes. Dilated exam in the right eye revealed a sharp and nonedematous optic nerve head without pallor. Normal macula, vessels, and periphery. Left optic nerve head was similarly sharp and nonedematous but demonstrated subtle temporal pallor. Normal macula, vessels, and periphery. The Goldmann visual field demonstrated central scotomas worse in the left than in the right eye (Figure 1A and B). OCT of the retinal nerve fiber layer demonstrated temporal thinning in both eyes (Figure 2).

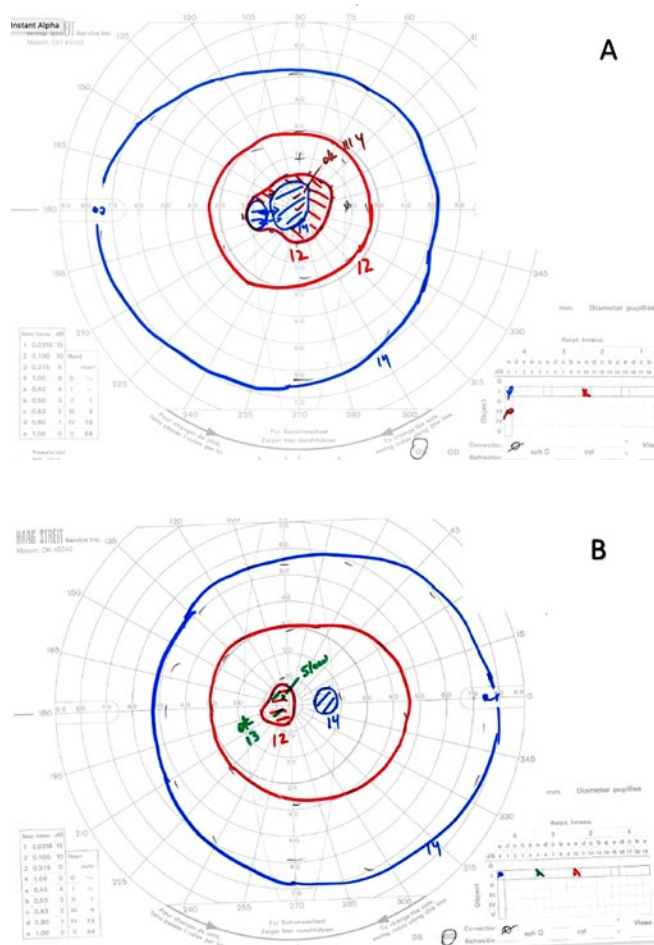


Figure 1. Goldmann visual fields, left (A) and right (B) eyes.

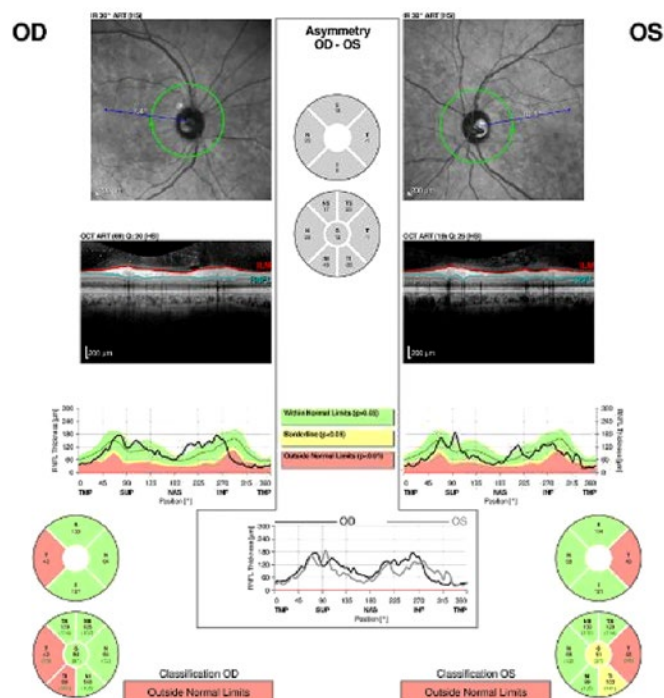
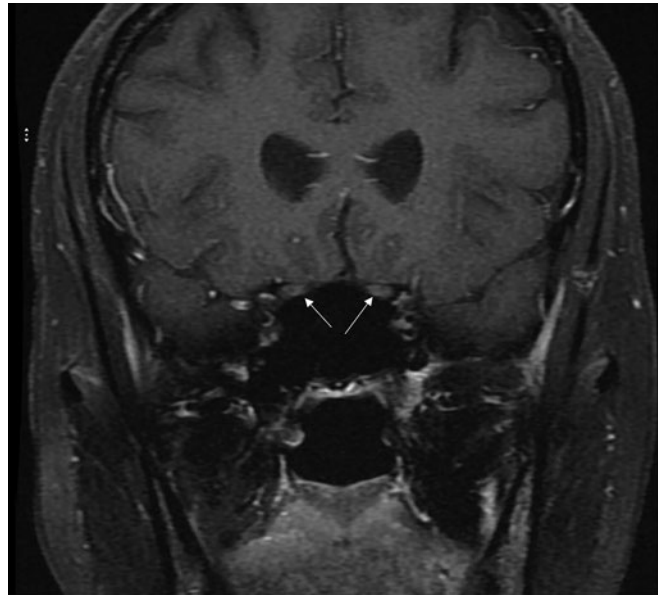


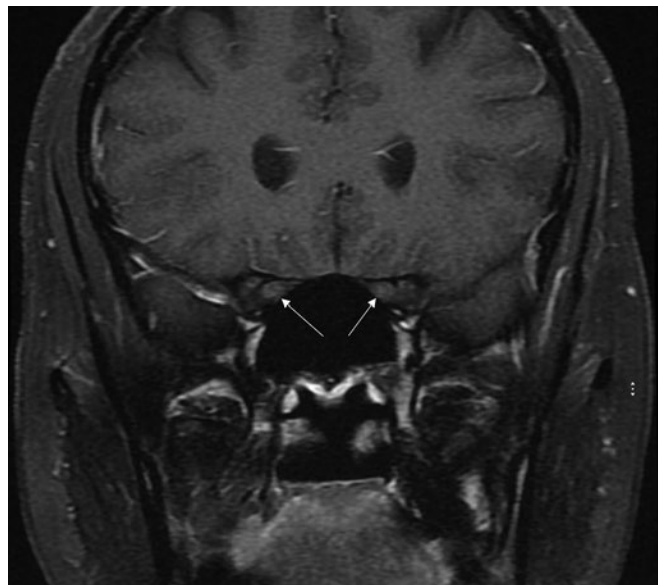
Figure 2. OCT RNFL right and left eyes.

Clinical Course and Outcome

The patient underwent MRI of the brain and orbits with and without gadolinium; results showed subtle enhancement of the bilateral intracranial optic nerves (Figure 3). She was admitted for IV steroids, but there was no improvement of her vision; in fact, on day 2 of IV steroids, her right eye vision deteriorated further to 20/200, again without pain. Her Humphrey visual fields demonstrated bilateral central scotomas (Figure 4).



A



B

Figure 3a and 3b. Coronal T1-weighted MRI Orbits post contrast at presentation.

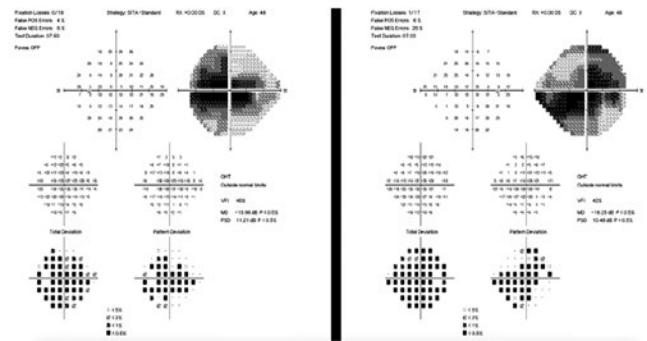


Figure 4. Post-steroid, pre-vision recovery Humphrey visual fields.

Given the family history and the patient's progressive and sequential vision loss, genetic testing for Leber hereditary optic neuropathy (LHON) was ordered and she was empirically treated with idebenone 300 mg, 3 times daily. She was also advised to completely abstain from alcohol and smoking. LHON testing for the most common mutations, 11778, 14484, and 3460, was normal. Further workup showed normal ANCA, ANA, ACE, Lyme, syphilis, AQP4-IgG, MOG-IgG, and dominant optic atrophy genetic testing. Whole mitochondrial genome analysis was pursued and revealed a 10197G>A mutation, which has been described in other conditions with mitochondrial complex I function.^{1,2} She was further counseled to discuss estrogen hormone replacement therapy with her PCP.

Remarkably, after 3 months of follow-up, the patient's visual acuity improved to 20/25 in the right eye and 20/30 in the left, with some improvement in Humphrey visual field (Figure 5).

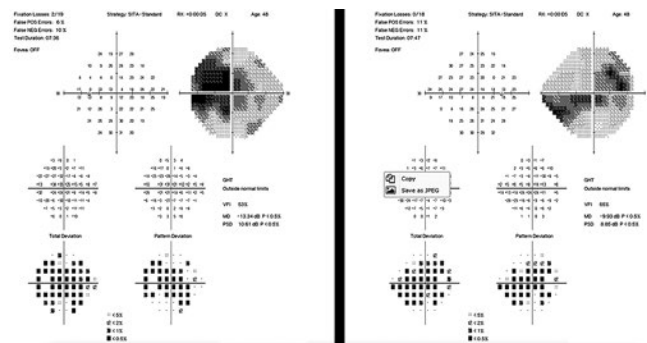


Figure 5. Post-steroid, post-vision recovery Humphrey visual fields.

References

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2. Huang TL, Wang JK, Yoong Pang C, Kung Tsai R. Leber's hereditary optic neuropathy associated with the m.10197G>A mutation. *J Clin Exp Ophthalmol*. 2017; 8(4):4-5.

Point-Counterpoint: OCT Can Predict Visual Outcomes in Patients With Optic Nerve Disorders

Anthony C Arnold MD, Valerie Biousse MD, Randy H Kardon MD PhD, Joseph F Rizzo III MD

NOTES

“The Doctor Says My Optic Nerves Are Damaged”

Normal Vision and Thin RNFL: Now What?

Valerie I Elmalem MD

CASE PRESENTATION

Discussion points: Overall RNFL thinning vs. focal change, correlation of structure and function, factors that affect OCT measurements (disc tilt, refractive error, signal quality), OCT artifacts, normal macular GC-IPL complex in face of abnormal RNFL, is there a “definitive” ON test?

History and Exam

A 56-year-old man presents for evaluation of headache and an abnormal OCT. Past ocular history includes moderate-high myopia and vitreous floaters. Past medical history includes hypertension, hyperlipidemia, and asthma. Current medications include aspirin 81 mg daily, rosuvastatin, fish oil, and valsartan. On examination, visual acuity with correction is 20/20 OU. Refraction is $-4.50 -0.25 \times 70$ OD and $-4.50 -1.25 \times 125$ OS. Color vision is 10/10 Ishihara color plates. Confrontation visual fields are full to finger counting OU. Pupils are equal, round, and reactive, and there is no relative afferent pupillary defect. IOPs are 16 OD and 17 OS. Ocular motility is full OU, and he is orthophoric. There is no nystagmus. Slit-lamp examination shows trace nuclear sclerotic cataracts. Dilated funduscopy examination shows pink, sharp, tilted optic discs with peripapillary atrophy, and cup-to-disc ratio is 0.0 OU (see Figure 1). The macula and periphery are normal.

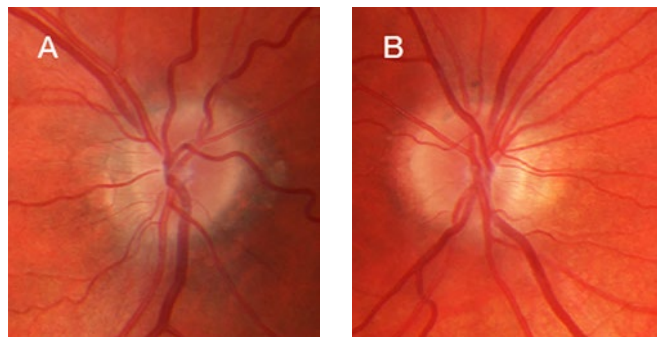


Figure 1. Color optic disc photographs: (A) right optic disc, (B) left optic disc.

Humphrey visual field 24-2 SITA Fast (Figure 2) is reliable and full in the right eye and essentially full with mild inferonasal loss and borderline GHT in the left eye. OCT of the optic disc OD (Figure 3) shows an average retinal nerve fiber layer (RNFL) thickness of 84 microns with decreased superior and nasal measured thickness. The OS shows an average RNFL thickness of 83 microns with decreased measured inferior and nasal thickness. Disc area is 1.28 mm² OD and 1.21 mm² OS. The signal strength is 9/10 OU.

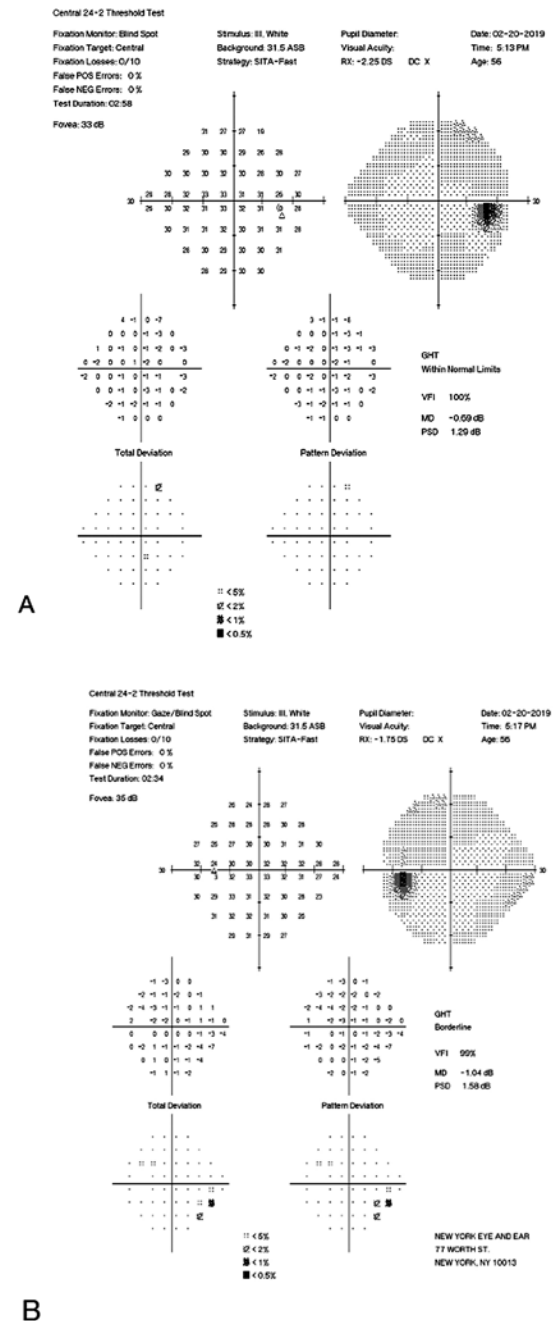


Figure 2. Humphrey visual field: (A) right eye, (B) left eye.

Technician: Operator, Cirrus

Signal Strength: 9/10

9/10

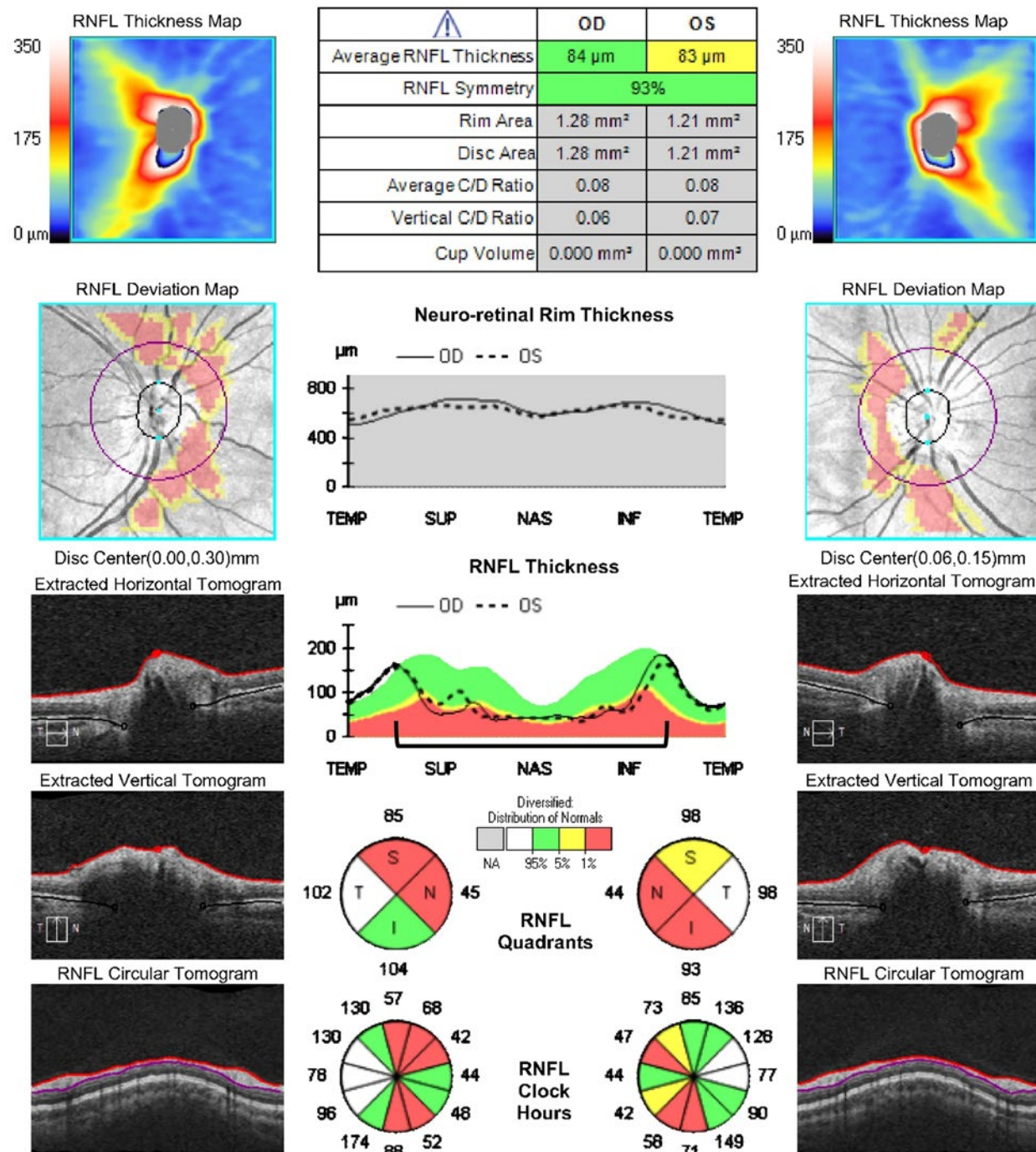
ONH and RNFL OU Analysis: Optic Disc Cube 200x200 **OD** **OS**

Figure 3. OCT of the optic disc.

“I Have Pressure in My Head”

Shira Simon MD

CASE PRESENTATION

History and Exam

A 36-year-old female was referred by her primary care physician for concern of idiopathic intracranial hypertension (IIH) because of worsening headaches along with a finding on her otherwise normal MRI brain of an “empty sella with suspicion for IIH.”

The patient had been having worsening headaches over 3 months. The headaches often started with positive visual phenomena (usually expanding zig-zags) and culminated with a pulsating pain. She has had a few episodes of emesis, photophobia, and phonophobia during the attacks. She had similar headaches as a teenager, which were managed with over-the-counter pain medication. She had been taking 800-mg ibuprofen 3 times daily for the past couple of weeks but reports that her headaches have been worsening. She also reported frequent episodes of blurring in her vision that resolved with blinking and intermittent ringing in her ears.

Her past medical history was significant for depression, anxiety (she is on sertraline), dry eye, and mild recent weight gain (around 5 pounds over the past year). She had a BMI of 29. Her family history was notable for a history of migraine headaches in her mother and maternal aunt and grandmother.

The referring provider’s funduscopic exam showed mildly elevated optic nerves bilaterally. MRI brain showed no abnormalities within the optic nerve or brain other than a partially empty sella. A lumbar puncture (LP) was pursued locally, which showed an opening pressure of 22 cmH₂O and normal CSF constituents (borderline 20-25 cmH₂O, elevated > 25 cmH₂O).

On examination in the neuro-ophthalmology clinic, BCVA was 20/20 in both eyes, IOP was 16 in both eyes, and there was no relative afferent pupillary defect. Color vision was full in both eyes. Ocular motility was full. Anterior segment examination was normal aside from mild blepharitis and dry eye changes. Funduscopic examination demonstrated crowded optic nerve heads with elevated, irregular borders.

Clinical Course and Outcome

Fundus autofluorescence demonstrated multiple areas of hyperautofluorescence characteristic of optic disc drusen. There was no obscuration of the vessels on the disc and no other evidence of disc edema or pallor. Given the essentially normal opening pressure on LP, lack of papilledema on examination, and migrainous features of her headaches, she was diagnosed with migraines and pseudopapilledema from optic disc drusen. Her intermittent blurred vision was due to dry eye. The MRI finding of an empty sella was an incidental finding.

The patient was referred to neurology for headache management. Her symptoms have mostly resolved with propranolol (60 mg daily) as prophylaxis and sumatriptan (50 mg as needed) for more severe episodes. She no longer requires over-the-counter pain medication, and her rebound headaches have resolved. She is using artificial tears regularly and denies any recurrence of blurred vision.

Diagnosis and Teaching Points

Section I: Vision Loss—Follow That Symptom?

“My Vision Was Blurry and Then Got Better”

Heather E Moss MD PhD

DIAGNOSIS AND TEACHING POINTS

Final Diagnosis

This patient had transient vision loss in the right eye due to atherosclerotic stenosis of the right internal carotid artery.

Teaching Points

Though unilateral transient visual loss has a broad differential diagnosis, ischemia is a cause that necessitates emergent evaluation. Isolated monocular or homonymous visual field loss can occur due to ischemia of the ipsilateral eye or contralateral cerebral hemisphere, respectively. Patients often have difficulty determining which event they experience, and making the distinction may not be necessary since both are considered transient ischemic attacks (TIAs).

TIA is a medical emergency because it is a threatened stroke with high short-term risk of symptomatic stroke. Although TIA outcomes following transient visual symptoms tend to be less severe than those following other TIA syndromes, over 1% have a symptomatic cerebral stroke in the next year.¹ In patients with transient monocular vision loss associated with ipsilateral carotid artery stenosis, 8% had another ischemic event over the subsequent 3 years, and 69% of these were brain events.² Between 11% and 18% of individuals with transient monocular vision loss from a presumed ischemic cause have evidence of asymptomatic acute cerebral ischemia (ie, stroke) on MRI.³

TIA is a clinical diagnosis. Workup of suspected TIA includes noninvasive imaging of cervicocephalic vessels, either by magnetic resonance angiography, computed tomography angiography, or carotid ultrasound; electrocardiography with prolonged cardiac rhythm monitoring if initial EKG is normal; echocardiography if no vascular stenosis or cardiac rhythm disturbance has been detected; vascular risk factor evaluation; and consideration of additional specialized testing based on demographics and features of the presentation.⁴ In one study of patients evaluated in a TIA clinic, over 19% of those presenting with transient visual symptoms had a major finding on their evaluation that led to a change in management.¹

Evaluation urgency depends on patient risk. The risk of stroke following TIA is highest in the short term in patients with vascular risk factors, older age, elevated blood pressure, and other features. If presenting under 24 hours from symptom onset, an MRI with diffusion weighted imaging is helpful to identify individuals with concurrent brain ischemia who should be hospitalized both for urgent evaluation of modifiable stroke risk factors and to expedite treatment of stroke should another

event occur. If presenting under 72 hours from symptom onset, hospitalization should be considered if testing for modifiable risk factors cannot be completed as an outpatient in 48 hours, or there is evidence of focal ischemia (on retinal exam or on MRI), or they are a high-risk patient (eg, 60 years of age or older with diabetes and systolic blood pressure above 140 or diastolic blood pressure above 90 per one common risk assessment score, ABCD²).⁴

There is some controversy regarding appropriate management of carotid artery stenosis in patients presenting with transient ipsilateral vision loss. In the pivotal NASCET trial that enrolled patients with stroke or TIA associated with ipsilateral carotid artery stenosis, surgical carotid endarterectomy for patients presenting with ischemic ipsilateral monocular vision loss was associated with higher risk of ipsilateral stroke when stenosis was low grade and no change in risk when stenosis was higher grade compared with medical therapy. This is in contrast to results for patients presenting with brain ischemia, in whom there was a reduction in stroke risk following carotid endarterectomy for those with high-grade carotid stenosis.²

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“I’m Having Trouble Driving”

Ore-ofe Adesina MD

DIAGNOSIS AND TEACHING POINTS

Our patient presented with a pituitary adenoma causing chiasmal compression and optic nerve cupping that was initially misdiagnosed as low-tension glaucoma (LTG). While optic nerve cupping is the hallmark of glaucomatous optic neuropathy, it is not pathognomonic for LTG, as cupping can result from any disease process that causes injury of ganglion cell axons leading to loss and thinning of the neuroretinal rim.

Causes of optic nerve cupping include compressive or infiltrative anterior visual pathway lesions and ischemic (both arteritic and nonarteritic) optic neuropathies, as well as congenital, hereditary, post-traumatic, demyelinating, or toxic optic neuropathies. Nonglaucomatous cupping from causes such as methanol poisoning, vitamin B12 deficiency, or genetic optic neuropathies like Leber hereditary optic neuropathy or dominant optic atrophy usually cause symmetric, bilateral optic neuropathies that typically present with central or cecentral visual fields defects with notable optic atrophy. Clinical features that increase the index of suspicion for nonglaucomatous optic nerve cupping include pallor of the remaining neuroretinal rim, vertically aligned field defects, and other visual fields defects atypical for glaucoma. Marked asymmetry of optic nerve cupping and other signs of asymmetric optic neuropathy should also indicate the possibility of an alternate diagnosis. These findings include a large relative afferent pupillary defect; asymmetric loss of color vision; asymmetric cupping, especially without history of asymmetric IOP elevation; visual acuity less than 20/40; and a patient younger than 50 years of age.

LTG is a form of glaucoma in which damage occurs to the optic nerve without IOPs exceeding the normal range, and this was the diagnosis given to our patient. Because compressive or infiltrative lesions of the optic nerve can cause optic disc cupping and mimic visual field loss from glaucoma, LTG should be a diagnosis of exclusion, and neuroimaging is warranted in any suspicious or atypical presentation. Imaging should preferably be in the form of MRI of the brain and orbits, with and without gadolinium contrast, with fat suppression.

In our case, the patient had all the clinical features leading to atypical presentation for LTG: progressive optic disc cupping and visual field loss in the setting of normal IOP, asymmetry of optic nerve cupping and pallor of the left optic nerve, and unusual visual field defects of generalized depression of the left eye with a temporal hemifield defect in the right eye with bitemporal predominance. The inferonasal defect OS could have been mistaken for glaucomatous damage, especially if the temporal defects were mild early on. This pattern of field loss, however, is consistent with a junctional scotoma due to involvement of the anterior optic chiasm by unilateral compression of the left optic nerve and contralateral crossing nasal fibers. Bitemporal hemianopsias are almost pathognomonic for chiasmal compression and warrant prompt neuroimaging to identify the causative lesion.

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“My Vision Is Slowly Getting Worse”

Sachin Kedar MD

DIAGNOSIS AND TEACHING POINTS

Final Diagnosis

Myelin-oligodendrocyte glycoprotein (MOG)-IgG associated optic neuritis

Teaching Points

Optic neuritis associated with AQP-4 antibody (NMO) and MOG-IgG antibody are distinct clinical entities. It is important to differentiate these entities from the more common demyelinating optic neuritis as the natural history and therapeutic options for these conditions are different. These conditions should be clinically suspected in patients with inflammatory optic neuritis with atypical clinical features and characteristic radiological features on neuroimaging, confirmed with serological testing for the antibodies using a cell-based assay. While high-dose intravenous corticosteroids are used in the acute treatment of optic neuritis in all 3 conditions, NMO and MOG-IgG optic neuritis may need prolonged immunotherapy to prevent recurrence and relapse. Chronic immunosuppression with rituximab, mycophenolate, or azathioprine is used in the management of these conditions.

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“I’m Missing Letters When I Read”

Fiona Costello MD

DIAGNOSIS AND TEACHING POINTS

Diagnosis

Paracentral acute middle maculopathy

Explanation to Audience Response Question

Macular lesions in paracentral acute middle maculopathy (PAMM) are best visualized with near-infrared reflectance imaging; correlating spectral domain OCT (SD-OCT) testing shows hyper-reflective bands at the level of the inner nuclear layer and sparing the outer retina. In contrast, the hyper-reflective band-like lesions seen with acute macular neuroretinopathy develop slightly lower, at the junction of the outer plexiform layer and outer nuclear layer, and may be associated with disruption of the ellipsoid and interdigitation zones acutely (best seen with SD-OCT).

With reference to the other potential responses, the monocular nature of this lesion and the paucity of optic nerve findings localize this problem to the retina. For this reason cranial MRI will offer very little insight into the mechanism of the problem. Humphrey 10-2 perimetry will simply tell you what you already know—the patient has a lesion near fixation affecting vision. Fluorescein angiography is incapable of adequately assessing the morphology or integrity of either the intermediate capillary plexus or the deep capillary plexus in PAMM. In contrast, OCT angiography not only allows noninvasive imaging of the superficial capillary plexus traditionally seen on fluorescein angiography but also captures flow patterns of the deeper capillary plexuses. In fact, recent cases of PAMM imaged using simultaneous en face OCT and OCT angiography have demonstrated preferential disruption of the intermediate capillary plexus and deep capillary plexus structures. Hence, en face OCT and OCT angiography are additional tests that provide useful diagnostic information.

Discussion

Diagnosing PAMM vs. an optic neuropathy

In this case, and with the benefit of hindsight, the patient had clear clinical features arguing against an optic neuropathy, including (to some extent) well-preserved central vision, the pattern of the visual field defect (a pericentral scotoma separated from the blind spot), intact color vision, and lack of a relative afferent pupillary defect. The fundus examination revealed normal-appearing optic nerves. The latter finding would be somewhat equivocal, however, in cases of a retrobulbar optic neuropathy, as pallor of the optic nerve can take weeks to develop in this clinical context.

In 2013, PAMM was described by Saraff and colleagues as a variant of acute macular neuroretinopathy (AMN).¹⁻⁵ The descriptive moniker “PAMM” refers to the appearance and parafoveal location of a causative gray lesion (best visualized with near-infrared reflectance imaging) that manifests clinically as an acute scotoma.^{1,2} The lesions indicative of PAMM/

AMN (best seen with SD-OCT) are thought to reflect focal intraretinal nonperfusion.¹⁻³ Indeed, PAMM is often referred to an “OCT diagnosis” and is characterized by the appearance of a hyper-reflective band involving the middle retinal layers.

Owing to localization of these lesions at the level of the inner nuclear layer, they have been theorized to represent an ischemic insult of the adjacent intermediate and deep capillary plexuses. Type 1 PAMM lesions involve retinal layers above the outer plexiform layer (reflecting superficial or intermediate capillary plexus occlusion), whereas type 2 lesions involve retinal layers below the outer plexiform layer, implicating the deep capillary plexus.³ Recent studies with OCT angiography have shown evidence of capillary nonperfusion in cases of PAMM, correlating with subsequent inner nuclear layer atrophy.³

As an emerging technology, OCT angiography may be a useful adjunct to the multimodal imaging of AMN/PAMM and may enhance visualization of retinal microvasculature perfusion. Going forward, PAMM may be best evaluated with the use of OCT angiography and en face OCT imaging, in concert with microperimetry techniques to “map out” paracentral scotomas.⁵ With this multimodality investigative approach, it may be possible to classify cases of PAMM into clinically distinct subtypes,⁵ but this awaits further study.

Distinguishing PAMM from AMN

Whereas AMN typically affects younger females, PAMM has more frequently been diagnosed among older male patients.² Yet, recent reports have implicated the diagnosis of PAMM among younger women.^{3,4} In the published literature, PAMM occurs with significantly higher frequency than AMN; fewer than 100 AMN cases have been reported since its initial description 40 years ago.²

Like AMN patients, PAMM patients may have a history of exposure to environmental risk factors, such as caffeine consumption or use of other vasopressor agents.^{2,4} Both clinical entities can be heralded by the acute onset of a paracentral scotoma, with no significant funduscopic or angiographic abnormalities. Moreover, cases of AMN and PAMM can be associated with paracentral hyporeflective, well-demarcated, wedge-shaped macular lesions captured by near-infrared reflectance imaging.² While the scotomas experienced in both PAMM and AMN can improve to some extent, visual disturbances may persist even after prolonged follow-up.²

Importantly, as a clinical entity, PAMM has been associated with numerous retinal vascular diseases (including diabetic retinopathy, hypertensive retinopathy, sickle cell retinopathy, Purtscher retinopathy, central retinal vein occlusion, and retinal artery occlusion), whereas systemic disease associations are less robust with AMN.^{2,5} Furthermore, certain medications (amphetamines, caffeine, vasopressors, and oral contraceptives), migraines, severe hypovolemia, orbital compression injury, and/or viral illnesses (antecedent upper respiratory infection or H1N1 influenza vaccination) have all been reported coassociations with PAMM.² In fact, similar to the observation of a cotton wool spot, identification of PAMM lesions should prompt consideration of a distinct differential diagnosis and, by extension, warrant an appropriate systemic workup.²

There is currently no treatment for PAMM, aside from management of associated environmental, vasculopathic, and systemic risk factors, when present.

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"I Can't See Anything to the Right!"

Courtney E Francis MD

FINAL DIAGNOSIS AND TEACHING POINTS

Final Diagnosis

Functional vision loss with nonorganic unilateral temporal visual field depression

Teaching Points

Organic causes of a unilateral temporal visual field cut are rare. Anterior visual pathway lesions will have an associated afferent pupillary defect. While the patient did coincidentally have a suprasellar lesion, there is no impingement on the visual apparatus and thus it does not explain her complaints.

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"I Woke Up One Day With Bad Vision"

Mays A El-Dairi MD

DIAGNOSIS AND TEACHING POINTS

Differential Diagnosis

- I. Ischemic: anterior ischemic optic neuropathy, arteritic (giant cell arteritis, GCA) vs. nonarteritic (NAION)

Although an ischemic cause would be the most likely differential diagnosis in this age group, the pattern of visual field loss is highly unusual. NAION characteristically follows an altitudinal or arcuate pattern of visual field loss, although a cecocentral scotoma can occur. Furthermore, the lack of optic disc edema and peripapillary disc hemorrhages makes the diagnosis of NAION unusual. For age > 50 years, GCA markers should be checked when there are findings of ischemia to the eye/head/face despite lack of symptoms.

- II. Toxic (eg, ethambutol, linezolid, heavy metals, methanol, ethanol, khat)

The pattern of the visual field loss described in toxic optic neuropathy, cecocentral scotomas, is similar to our patient's. However, toxins typically cause a slow, gradual but progressive loss of vision and are associated with optic atrophy. Methanol ingestion, however, presents as acute bilateral simultaneous visual loss in the company of bilateral optic disc edema. Our patient did admit to increased alcohol intake, but she maintained a well-balanced diet. She denied exposure to other potential toxins. Furthermore, she presented with sequential loss of vision with pseudoedema of the optic nerve.

- III. Nutritional

The pattern of the visual field loss described in nutritional deficiency optic neuropathy is also similar to our patient's visual field. Specific vitamin deficiencies associated with optic neuropathies include B12, folate, and B6. Although vitamin deficiencies can occur in the setting of malabsorption (especially for vitamin B12 and folate), one would expect the optic neuropathy to be fairly symmetrical, with both eyes presenting with vision loss at the same time, and the nerve would not be swollen.

- IV. Inflammatory

A. Autoimmune: multiple sclerosis, myelin oligodendrocyte glycoprotein (MOG), neuromyelitis optica (NMO) spectrum disorder, sarcoidosis, other. The lack of associated symptoms in our patient does not rule out an inflammatory optic neuritis. Patients present with unilateral (more common) or bilateral vision loss usually accompanied by eye pain or pain on eye movement. On examination during the acute phase, the nerve is most commonly normal or hyperemic but can also be swollen (33%). Contrast

enhanced brain and orbits MRI is highly sensitive and shows enhancement in the retrobulbar optic nerve about 96% of the time. Optic neuritis in the setting of MOG and NMO antibodies requires more aggressive management, usually requiring long-term immune suppression.

- B. Infectious: syphilis, Lyme, *Bartonella*, *Brucella*, herpes virus, influenza, other. Fortunately, these infections are rare, but all of them have been reported to cause an optic neuritis or neuroretinitis. The patient often reports an antecedent viral prodrome and may have other associated systemic symptoms. MRI will usually show enhancement of the optic nerve, similar to optic neuritis. Serology has good sensitivity but should be ordered based on the history and associated findings.

V. Neoplastic/paraneoplastic

- A. The clinical picture of one swollen nerve and one atrophic nerve should always raise the suspicion for Foster-Kennedy syndrome when one nerve is pale due to direct compression from a frontal lobe tumor and the contralateral optic nerve is swollen due to raised intracranial pressure. Patients usually have signs of high intracranial pressure and often have decreased sense of smell.

A patient with an optic nerve sheath meningioma presents with slow, progressive visual loss associated with optic nerve pallor but may present with a unilaterally swollen optic nerve. However, the patient would be expected to have unilateral findings and symptoms unlike those of our patient.

- B. Paraneoplastic optic neuropathy (eg, collapsin response-mediator protein-5 or autoimmune optic neuropathy/retinopathy): Patients with paraneoplastic optic neuropathy usually present with symmetric indolent visual loss associated with progressive optic atrophy; the nerve is unlikely to be swollen. Workup is typically performed when all other workup is negative and there is progression of the visual decline.

VI. Genetic

The pattern of the visual field loss described in genetic/mitochondrial optic neuropathies is similar to our patient's. The most common genetic diseases affecting the optic nerve are noted.

- A. Leber hereditary optic neuropathy (LHON) is a genetic mitochondrial disorder, passed from a mother to her children. Patients who carry the LHON gene typically have normal vision until they experience subacute, unilateral, painless central scotoma in one eye. A few weeks to months later, a similar presentation and clinical course occur in the fellow eye. The nerve is frequently described to be pseudo-swollen (elevated nerves that do not leak on fluorescein angiogram) in the acute phase and pale later. Although LHON is classically described in teenage boys, it can occur at any age.

- B. Dominant optic atrophy (DOA) can present at any age, but often the patient will be aware of mild decreased vision in their 20s and 30s. Examination reveals bilateral central scotomas and pale optic nerves. DOA can be associated with hearing loss and seizures. Genetic testing is available for 2 subtypes: OPA-1 and OPA-3.

- C. Wolfram disease is also a mitochondrial disease, but it is coded by a nuclear gene, WFS1, with an autosomal dominant pattern of inheritance. It is also called DIDMOAD, an acronym for diabetes insipidus, diabetes mellitus, deafness and optic atrophy. Wolfram disease usually presents with childhood diabetes mellitus type 1 with development of optic atrophy a few years thereafter. Patients may also have sensory neuropathy, renal complications, cognitive disease, and early death.

Teaching Points

- LHON is a genetic mitochondrial disorder with 90%-95% of affected patients carrying 1 of 3 point mutations in the mitochondrial DNA: m.11778G>A, m.14484T>C, and m.3460G>A. It is characterized by bilateral acute or subacute central loss of vision. Many carriers of the gene may be normal until a "stressor" causes the optic neuropathy to be manifest, potentially explaining the wide age range and clinical pattern of visual loss (see below).
- Demographics: While the typical age for presentation is during the second and third decades of life, visual loss can occur at any age. Of individuals carrying the gene, males have about a 50% chance of vision loss, while females have about a 15% risk (ie, males are more likely to manifest the disease than females).
- Exam findings: In 40% of patients, the optic nerves appear to be swollen with telangiectatic vessels but are in fact pseudo-edematous, as fluorescein angiography fails to demonstrate leakage. In the following weeks, the optic nerves become pallid.
- The prognosis for visual recovery is poor, resulting in severe visual impairment affecting the central papillo-macular bundle in the majority of patients.
- Stressors are proposed to be precipitating factors for vision loss. Triggers may include any new illness or metabolic change, nutritional deficiencies, psychological stress, some toxins, some medications (eg, anti-retroviral and anti-mycobacterial drugs), alcohol, and smoking (including inhaling smoke from a fire). The data are conflicting, but the mechanism is proposed to be insufficient ATP production in response to the metabolic demands in the face of a stressor.
- Baseline EKG is warranted due to higher rate of cardiac conduction abnormalities.
- Treatment: Clinical studies have suggested a beneficial trend, albeit not statistically significant, of idebenone, an analogue of ubiquinone, to reduce reactive oxygen species production, with visual improvement. Early treatment appears to provide the greatest benefit. A gene therapy vector is currently being investigated as a potential treatment. Early results support its safety and an encouraging visual trend in patients treated with a single intravitreal injection of the viral vector.

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Section II: Bugs and Drugs—Do They Matter?

“I Am On So Many Medications, and Now I Can’t See!”

Gabrielle R Bonhomme MD

FINAL DIAGNOSIS AND TEACHING POINTS

Final Diagnosis

Amiodarone-associated optic neuropathy (bilateral)

Discussion

Amiodarone remains one of the most widely administered anti-arrhythmic medications and has significantly improved life expectancy and quality of life in patients with ventricular arrhythmia. Amiodarone may be administered IV as a loading dose, then continued in oral form in the post-procedure time interval, often for months to years. Systemic side effects have been well described and include QT prolongation, bradycardia, liver toxicity, ataxia, nausea, dysgeusia, and confusion. Regarding amiodarone’s ocular side effects, corneal verticillata (or vortex keratopathy) is commonly seen, but it usually remains asymptomatic.¹

The first report of amiodarone optic neuropathy was documented in 1987 by Gittinger and Asdourian.² Controversy remains concerning this diagnosis, as the causality of optic neuropathy appears questionable to some, and the pathogenesis of suspected amiodarone-associated optic neuropathy remains nebulous. Several existing theories on the mechanism of nerve injury include lamellar body deposition in the substance of the nerve¹ or in surrounding glial cells,⁴ resulting in slowed axoplasmic flow, nerve ischemia as a subset of nonarteritic [anterior] ischemic optic neuropathy (NAION), or direct neurotoxicity.¹ More recently, Liao et al postulated the induction of apoptosis of RGC-5 cells.³

When evaluating a patient exhibiting features suggestive a clinical diagnosis of amiodarone-associated optic neuropathy, a systemic approach is recommended.⁴ The relationship between amiodarone use and onset of vision loss, the tempo of progression, the presence of typical systemic amiodarone side effects, and documentation of optic nerve dysfunction are primary considerations that will help identify this diagnosis.⁴ Whether the optic neuropathy is unilateral, bilateral, sequential, or simultaneous will also help identify this diagnosis and differentiate it from anterior ischemic optic neuropathy, which is usually unilateral at initial onset.^{2,5} The pattern of visual field defect may vary, including dense central loss, arcuate nerve fiber bundle defects, or altitudinal field loss.¹⁻⁷ Given amiodarone’s insidious effect on vision, the exclusion of other more common etiologies of optic neuropathy, such as giant cell arteritis (GCA), NAION, elevated intracranial pressure, or compressive optic neuropathy, is paramount, and requires ancillary testing and diagnostic

imaging. The absence of a crowded, cupless “disk at risk” may help exclude NAION.⁴ Passman et al reported that 58% of subjects with amiodarone-associated optic neuropathy experienced improved visual acuity after cessation of the medication.⁵ Once suspected, direct communication with the prescribing cardiologist to discuss cessation and continued monitoring of visual function on continued amiodarone should be pursued promptly in order to optimize the patient’s visual potential.

Teaching Points

1. Amiodarone-associated optic neuropathy should be considered in cases of insidious vision loss due to bilateral, simultaneous optic neuropathy, though it may mimic arteritic anterior ischemic optic neuropathy (GCA) in a patient of appropriate demographic.
2. Differentiating suspected amiodarone toxicity from a classic NAION is complicated by the similar optic disk appearance and history of vasculopathic conditions associated with both disorders. Bilateral simultaneous optic neuropathy and insidious (non-acute) onset are key features of amiodarone-associated optic neuropathy, whereas vision loss due to NAION usually is unilateral or sequential, and acute in onset.²
3. Amiodarone-associated optic neuropathy may present as bilateral symmetric optic disk edema, which has a broad differential, including malignant hypertension, compressive lesion, and elevated intracranial pressure that may require a more extensive diagnostic workup.
4. Prompt discontinuation (and / or replacement with an alternative medication) of amiodarone may improve visual function in some cases of optic neuropathy.

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“My Neck Hurts, and I’m Cold!”

Michael S Lee MD

DIAGNOSIS AND TEACHING POINTS

Final Diagnosis

Giant cell arteritis causing posterior ischemic optic neuropathy with choroidal filling delay and intermittent double vision

Teaching Points

1. Among older patients (especially those 70+) with new neurologic signs and symptoms, GCA should be among the differential diagnoses. This patient presented with intermittent double vision. It is important to keep in mind that GCA can cause intermittent diplopia, an isolated cranial nerve palsy, or even what looks like an orbital process. She also has evidence of an optic neuropathy with an afferent pupillary defect and dyschromatopsia. In order to pick this up, one needs to at least check color vision and perform a good pupil check. Visual fields were performed in this patient but were too unreliable in both eyes to be of value.
2. Although we are most familiar with headache, scalp tenderness, and jaw claudication as the most worrisome symptoms of GCA, keep in mind that neck pain, fevers, chills, malaise, anorexia, and nonproductive cough are other, less common ones. The patient may sound like they are sick with some infection, and we need to at least consider that GCA could be at play here.
3. In elderly patients with vision loss from GCA, a fluorescein angiogram may show choroidal filling delay. This is nearly pathognomonic for GCA. If you have a patient with an ischemic optic neuropathy, a fluorescein angiogram may be valuable to rule in a choroidal filling delay. However, the absence of this finding certainly does not exclude the diagnosis of GCA.
4. Finally, it is possible to lose vision from GCA despite rapid initiation of corticosteroids. If this is going to happen, it will do so within the first 5 days of steroid use.

“My Eye Aches, and It’s Blurred When I Read (and Garden)”

Kimberly Cockerham MD FACS

DIAGNOSIS AND TEACHING POINTS

Final Diagnosis

Nonspecific orbital inflammation and Tolosa-Hunt syndrome

International Headache Society (IHS) Diagnostic Criteria

Tolosa Hunt syndrome (THS) is classified under painful cranial neuropathies and other facial pains. The IHS lays down diagnostic criteria for THS that have high sensitivity (approximately 95% to 100%) but low specificity (approximately 50%). They are summarized as follows:

- Unilateral headache
- Includes both of the following:
 - Presence of granulomatous inflammation of the cavernous sinus, superior orbital fissure, or orbit, as seen on MRI or biopsy
 - Palsies of 1 or more of the oculomotor nerves (cranial nerves III, IV, and/or VI) on the same side
- Corroboration of the cause as evidenced by both of the following:
 - Palsies of cranial nerves III, IV, and/or VI have followed headache in 2 weeks or less, or have developed simultaneously with a headache
 - Localization of a headache around the eye on the same side
- Not better explained by any other headache etiology

Teaching Points

Ethambutol, a first-line antituberculous agent, was first reported to result in ocular toxicity in the 1960s. Vision loss is typically bilateral and often painless, with a central/cecocentral pattern resulting in early visual acuity and color vision loss. Automated visual fields may also exhibit a bitemporal hemianopia type pattern in addition to central vision loss. The toxicity has been characterized as dose (> 15 mg/kg/day) and duration (> 3 months) related and somewhat reversible upon prompt discontinuation of ethambutol. However, the course of the ocular toxicity can be unpredictable, and permanent severe visual loss may occur. All patients treated with ethambutol should undergo regularly scheduled vision screening every 1-2 months.

Pain can be a red herring in many types of vision loss but should not be dismissed, especially when it persists and localizes to the side of the visual deficit. Similarly, only a minority of patients taking ethambutol will develop ethambutol toxicity, and the unilateral, progressive vision loss in this patient should make drug toxicity a less likely consideration. Compounding the difficulties in this case was the patient’s lack of adequate insurance coverage to allow her to obtain recommended laboratory and neuroimaging studies early in her disease course. She

also did not have a primary care physician who could potentially coordinate and advocate for her care.

Like all testing, neuroimaging studies must be both ordered *and* interpreted correctly to assist in diagnosis. In this case, a CT head without contrast was inadequate to visualize the apical orbital lesion, and an orbital study should have been considered. Even an experienced neuroradiologist may miss a subtle lesion if an inadequate history is provided, and like all busy physicians, a radiologist may overlook an important finding. Thus, if you order an imaging study and suspect that pathology should be present but receive a report that the study was normal, do not hesitate to review the images yourself with either the original radiologist or another colleague with expertise.

The differential diagnosis of progressive visual loss and pain in a 65-year-old white woman includes the following:

1. Giant cell arteritis
2. Trigeminal neuralgia
3. Referred pain from inflammation of the orbit, sinus, or cavernous sinus process
4. Ocular disorders such as narrow-angle glaucoma, corneal diseases, intraocular tumors, dry eye, and optic neuropathies can all cause pain in association with visual blurring.

As noted above, pain can be a distractor or a clue to the cause of the visual loss.

1. Giant cell arteritis is most common in white patients of both genders over the age of 70. Temporal tenderness, jaw claudication, and eye pain can be the initial presentation or occur in combination with visual loss. Elevation of the ESR and CRP, anemia, and thrombocytosis are characteristic. Oral and/or IV steroids are indicated, and temporal artery biopsy is performed for pathologic confirmation.
2. The classic presentation for trigeminal neuralgia produces episodic, severe, unilateral facial pain accompanied by sensory loss and numbness. Eye pain can occur if the ophthalmic division of the trigeminal is involved. In trigeminal neuralgia the eyes are affected least and last. The facial and/or eye pain tends to worsen with time. Visual loss is not part of the presentation.
3. Inflammation and malignant processes can cause pain and/or visual loss. Appropriate history, examination, and appropriate neuroimaging are essential.
4. Ocular causes for pain and visual blurring: a complete eye examination including ancillary testing is essential to exclude any ocular source for the vision alteration and pain.

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“They Told Me My Optic Nerves Are Swollen”

Kevin E Lai MD

DIAGNOSIS AND TEACHING POINTS

Diagnosis

Pseudotumor cerebri

Discussion

The terms “pseudotumor cerebri (PTC)” and “idiopathic intracranial hypertension (IIH)” are often used interchangeably, but they cannot be used as a shortcut in the process of working up and treating a patient with headaches and suspected optic nerve edema. It is appropriate to consider the diagnosis of IIH in young, overweight females who present with headaches and optic nerve edema, but such patients also may have an identifiable, secondary cause of elevated intracranial pressure. Just as not all optic nerve edema is papilledema, not all patients who fit the demographics and clinical findings of IIH have an idiopathic process.

Friedman et al (2013) provided a useful framework that we use in classifying and diagnosing pseudotumor cerebri.¹ “Pseudotumor cerebri syndrome” is the umbrella term that encompasses all forms of increased intracranial pressure that cannot be attributed to a mass, hydrocephalus, or meningeal process. It is divided into primary and secondary pseudotumor cerebri syndrome: idiopathic intracranial hypertension (IIH) falls under the category of primary pseudotumor cerebri syndrome in this schema. This framework then allows us to classify the various secondary causes of pseudotumor cerebri, such as cerebral venous thrombosis, medication-associated intracranial hypertension, and intracranial hypertension associated with systemic diseases such as anemia, renal failure, and sleep apnea. As Friedman et al put it: “‘Idiopathic intracranial hypertension from a secondary cause’ is an oxymoron.”

In this case of a young obese female with a history and exam findings consistent with intracranial hypertension, the ophthalmologist may fall into the trap of ignoring the full medical history and workup in favor of treating the patient empirically for IIH, thus missing the secondary cause for the intracranial hypertension.

The Modified Dandy criteria remain the standard for diagnosis of IIH²:

1. Only symptoms consistent with intracranial hypertension or papilledema

2. Only clinical findings specific to intracranial hypertension or papilledema
3. Elevated intracranial pressure ≥ 25 cmH₂O in the lateral decubitus position
4. Normal CSF composition
5. No evidence of hydrocephalus, mass, structural, or vascular lesion on MRI or contrast-enhanced CT for typical patients, MRI and MRV for all others
6. No other causes of intracranial hypertension identified

A systematic approach to the history, exam, and workup for the patient with suspected IIH is essential. Beyond the history of present illness, care should be taken to review the patient's past medical history, diet and supplement history, and medication list. Anemia,³ renal transplantation,⁴ and obstructive sleep apnea⁵ all have been implicated in increased intracranial pressure. Withdrawal from chronic steroid use,⁶ use of tetracycline derivatives,⁷⁻¹⁰ excess vitamin A ingestion and more commonly vitamin A derivatives (isotretinoin, all-trans-retinoic acid) use,¹¹⁻¹² and synthetic growth hormone administration¹³ also may induce intracranial hypertension, with many other medications and conditions reported.¹⁴⁻¹⁶

Because acne medications (specifically minocycline and vitamin A derivatives such as isotretinoin¹⁷) are used commonly in young adolescents, all patients should be queried about the use of oral or topic medications for skin conditions. Patients may not report these medications because they consider them cosmetic or trivial. Likewise, a history of leukemia may be important to know given the use of all-trans-retinoic acid in the treatment of acute promyelocytic leukemia.¹²

Another potential pitfall is assuming that the presence of optic disc drusen excludes intracranial hypertension. Various ancillary tests may help differentiate optic disc drusen or other forms of pseudopapilledema from true optic nerve edema, including autofluorescence,¹⁸ fluorescein angiography,¹⁹⁻²⁰ B-scan ultrasound,²¹⁻²² and spectral domain OCT.²³⁻²⁵ However, papilledema and optic nerve drusen can be present concurrently, and so some patients with optic disc drusen or other forms of pseudopapilledema should be counseled that they may still need to undergo further workup for increased intracranial pressure.²⁶

All of the diagnostic testing for elevated intracranial pressure is essential for diagnosis of pseudotumor cerebri/IIH¹, which is comprised of the following:

1. Neuroimaging (contrast-enhanced CT or MRI of the brain in typical cases, with MRV of the brain unless contraindicated²⁷)
2. Lumbar puncture with opening pressure, performed in the lateral decubitus position
3. Cerebrospinal fluid (CSF) studies, which in typical cases includes cell count, glucose, and protein and may include other tests such as gram stain, fungal and/or bacterial cultures, viral PCR, Lyme PCR, FTA-ABS, cytology, or other tests depending on the clinical presentation

Proceeding with treatment for presumed IIH prior to completion of the workup may result in missing potentially life-threatening or sight-threatening conditions, such as meningitis, malignancies, or cerebral venous thrombosis. Initiating acetazolamide or other pressure-lowering medications prior to lumbar puncture may result in falsely low opening pressures. Because the intracranial pressure may vary widely from one moment to the next, it is possible for the opening pressure to be

measured as less than 25 cmH₂O despite having clinical findings and symptoms consistent with intracranial hypertension; in those cases pseudotumor cerebri is not definite but may be classified as probable in the appropriate clinical situation.²⁸ Pressure readings may also be spuriously elevated when the patient coughs, strains, or holds his or her breath during the procedure. The procedure report may also erroneously report a "high" opening pressure that is < 25 cmH₂O.

Treatment of any underlying condition must be concurrent with the treatment of the intracranial hypertension. For medication-associated pseudotumor cerebri, discontinuation of the offending agent is important and may be sufficient to induce disease remission. Anticoagulation and management by a neurologist may be necessary for cerebral venous thrombosis. Surgical intervention in pseudotumor cerebri is reserved for severe or progressive visual loss in the setting of medication failure.

Teaching Points

- Idiopathic intracranial hypertension (IIH) is a diagnosis of exclusion. All other causes of intracranial hypertension must be ruled out before a diagnosis of IIH can be established. IIH cannot be diagnosed by history and presence of papilledema alone, nor can it be diagnosed after an incomplete workup.
- A focused medical history targeted at dietary, supplement, and medication history as well as specific medical conditions is essential to the workup of patients with suspected IIH. Systemic conditions such as anemia, history of renal transplantation, and obstructive sleep apnea are associated with increased intracranial pressure, and medications for acne (tetracyclines and vitamin A derivatives), withdrawal from chronic steroid use, synthetic growth hormone, and other vitamin A derivatives have also been implicated in intracranial hypertension.
- Brain imaging and a lumbar puncture with opening pressure and CSF studies are required in the workup of IIH. IIH is diagnosed only after all of these studies have been performed and are noted to be normal.
- Patients with pseudopapilledema can also have true papilledema and increased intracranial pressure. The presence of optic disc drusen on ancillary testing does not exclude the possibility of concomitant papilledema.
- Treatment for pseudotumor cerebri should be directed at any underlying cause as well as treating the intracranial hypertension.

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“My Vision’s Blurred, and One of My Optic Nerves Is Swollen”

Melissa Wang Ko MD

DIAGNOSIS AND TEACHING POINTS

Final Diagnosis

Syphilitic optic neuropathy. The early differential diagnosis included sarcoidosis, optic neuritis due to possible demyelinating condition, and optic neuritis due to systemic lupus erythematosus.

Discussion

The Centers for Disease Control and Prevention (CDC) in 2015 issued a clinical advisory regarding ocular syphilis as there had been an increase in reports; the CDC received reports of more than 200 cases in 2014-2015, which was attributed to high-risk unprotected sexual behavior with multiple partners.

Clinical manifestations of ocular syphilis can occur at any stage of syphilis and involve any eye structure, but manifestations can include anterior or posterior uveitis, optic neuropathy, and retinal vasculitis. There can be patchy, diffuse neuroretinitis with areas of hemorrhage. Optic nerve involvement may be unilateral or bilateral and can present as a perineuritis or anterior or retrobulbar optic neuritis. The perineuritis of ocular syphilis is typically asymptomatic. The visual loss of syphilitic optic neuropathy can range from mild to severe (as in our case). When the presentation is an anterior optic neuritis, as it was with our case, there is nothing characteristic on ophthalmic exam that can easily distinguish it from nonsyphilitic optic neuritis. However, the patient’s history of intravenous drug use and maculopapular rash were features suggesting a potential infectious etiology.

Both a nontreponemal (RPR, VDRL, TRUST) and a treponemal-specific serological test (FTA-ABS, MHA-TP, TPPA, TPA-EIA) should be obtained to secure the diagnosis. While treponemal tests typically remain positive after infection, nontreponemal assay titers decrease following adequate treatment and return to nonreactive over time. Thus, if a patient has a past history of treated syphilis and is reinfected, the treponemal-

specific studies would not be helpful, but a new positive non-treponemal test would indicate the new infection.

If there are ocular manifestations of syphilis, patients should be evaluated for neurosyphilis via lumbar puncture. CSF is the only way to definitively diagnose neurosyphilis; typical findings include an elevated WBC and protein. CSF-VDRL has high specificity but low sensitivity for neurosyphilis, meaning it can lead to few false positives but more false negatives (CSF-VDRL can be negative in over 70% of patients with neurosyphilis). If the CSF-VDRL is negative but your clinical suspicion remains high for neurosyphilis, a CSF-FTA-ABS test can be obtained, which has higher sensitivity than CSF-VDRL with fewer false negative results.

Regarding treatment, if there is evidence of ocular syphilis, this should be treated with the same regimen as neurosyphilis (either IV penicillin G 3 for 10-14 days or IM penicillin G with probenecid daily for 10-14 days). Those with concurrent HIV infection receive the same regimen but should have closer monitoring due to higher risk for treatment failure. Those newly diagnosed with HIV should also start on antiretroviral therapy.

There was active discussion the following day on our team regarding the decision to treat empirically with IV methylprednisolone in the setting of an active infection. While some members spoke against this decision, others felt that the severity and degree of vision loss and the nonspecific ocular signs justified this overnight decision. There are reports that early steroid initiation can prevent a Jarisch-Herxheimer reaction but result in worsening ocular symptoms. No clinical trials exist comparing the benefit and timing of treatment with and without steroids. There are 2 case series of HIV-positive patients with ocular syphilis (20 patients total), and there was no difference in clinical or visual outcomes between those who received steroids with penicillin (10 patients) and those who received penicillin alone. The benefits of concurrent steroid use are unknown at this time.

It can take 3-6 months after infection to develop an acquired immunity, but because this immunity is incomplete, re-exposure to syphilis can lead to reinfection. HIV-positive patients may relapse even with high-dose penicillin treatment; thus close monitoring concurrently with infectious disease is recommended in the first 1-2 years following therapy.

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Section III: Double Vision—50/50 Chance to Pick the Right One!

“My Eyelid Droops, and I See Double”

Kenneth Shindler MD PhD

DIAGNOSIS AND TEACHING POINTS

Final Diagnosis

Ocular myasthenia gravis

Teaching Points

Myasthenia gravis (reviewed by Gilhus et al, 2019) commonly presents with isolated ocular findings including ptosis and limited ocular motility.¹ The presentation can mimic a pupil-sparing third nerve palsy, as well as fourth nerve palsies, sixth nerve palsies, intranuclear ophthalmoplegia, and other supranuclear nerve palsies.²

When the pattern suggests a third nerve palsy, noninvasive imaging is recommended, although this topic has been controversial. In the past, it has been suggested that pupil-sparing third nerve palsies, which are likely to be vasculopathic and unlikely due to an aneurysm, be watched over a period of time to assess for eventual pupil involvement,³ in part because of limited quality of noninvasive testing and the inherent risks of conventional. The increased availability and quality of noninvasive imaging has led to some reports recommending such imaging for all new cranial nerve palsies,⁴ including pupil-sparing third nerve palsies. Either CT- or MR-angiography can be considered. While neither can be expected to identify 100% of posterior communicating artery aneurysms, the sensitivity of each test is high, and ultimately the decision of which one to order should be based on the expertise and comfort level of the radiologist who will be reading the study.⁵

In the case presented, some features were atypical or unclear for a diagnosis of third nerve palsy, which could have led to consideration of other diagnoses. Also several typical findings of myasthenia were not present or hard to discern based on the patient's findings. This patient had complete ptosis with only mild ocular dysmotility, which is atypical for third nerve palsies but certainly possible. The patient's anisocoria also made the evaluation more complicated, as myasthenia itself does not affect the pupil, while third nerve palsies often do, with a larger pupil on the side of the palsy as in this case. There was reasonable evidence, however, that this anisocoria was physiologic and not related to the ptosis and diplopia, since the anisocoria did not vary in light versus dark and was noted to be present several years earlier on photographs.

Some of the testing and clinical evaluation was equivocal in terms of being able to discern between third nerve palsy and myasthenia. Curtaining was noted, with the right eyelid dropping mildly after lifting the left eyelid, but while this sign is often looked for in myasthenia, it is nonspecific and can be seen other asymmetric etiologies for ptosis,⁶ including third nerve palsy. Furthermore, the presence of complete ptosis of the left upper eyelid made it difficult to detect eyelid fatigability or a lid twitch, since the lid would not open at all to look for these signs. With complete ptosis, ice test could potentially still lead to improvement and suggest the diagnosis, but in this case the eyelid was likely too weak by the time the patient was being examined to improve after resting with ice.

Both time and ancillary testing are frequently needed to secure the diagnosis of myasthenia. Antibody testing is often negative in isolated ocular myasthenia,⁷ as seen in this case. Often time is needed either to see a change in the pattern of ptosis or ocular misalignment in order to suggest a diagnosis of myasthenia or, as in this case, to see whether a suspected vasculopathic cranial nerve palsy fails to improve, raising suspicion for other etiologies, including myasthenia. Electrophysiologic testing with repetitive stimulation or single-fiber electromyography may ultimately be needed to confirm the diagnosis of myasthenia.⁷

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“My Eye Bulges, and I See Double”

Paul H Phillips MD

DIAGNOSIS AND TEACHING POINTS

Diagnosis

Diffuse large B-cell lymphoma

Discussion and Teaching Points

This patient presented with mild proptosis and diplopia and was initially thought to have an enlarged left inferior rectus muscle. He was referred with the misdiagnosis of thyroid-related orbitopathy (TRO). Indeed, TRO is the most common cause of acquired proptosis and extraocular muscle enlargement.¹ TRO is an autoimmune disease that affects women 5-6 times more frequently than men. Cigarette smokers are at increased risk to develop the disease. Common findings of TRO include proptosis, lid retraction, diplopia, extraocular muscle restriction, and enlarged extraocular muscles with sparing of the tendons on imaging. Many patients will have or develop hyperthyroidism either prior to, concurrent with, or following the ocular findings. However, about 10% of patients may remain euthyroid. Patients with typical findings and clinical course do not require biopsy confirmation.

This patient had several findings that were not consistent with TRO. He had no lid retraction, a common sign of TRO. Inferior rectus muscle restriction from TRO would cause limited upgaze with a left hypotropia as well as left fundus extorsion. However, he had limited downgaze with a left hypertropia, presumably from inferior rectus paresis or mechanical displacement of the inferior rectus muscle by the inferior orbital mass. Fundus torsion was normal. Finally, he had firmness to palpation of the left lower lid. Patients with TRO may have lid edema but typically do not have firmness to palpation of the lids.

These atypical findings for TRO required imaging of the orbits. Indeed, orbital imaging showed an inferior orbital mass that was abutting and displacing the inferior rectus muscle. The presence of a mass mandated biopsy, which resulted in the diagnosis of diffuse large B-cell lymphoma.

The majority of orbital lymphomas are of B-cell origin.² Histological subtypes include extranodal marginal zone B-cell lymphoma (59%), diffuse large B-cell lymphoma (23%), follicular lymphoma (9%), and mantle cell lymphoma (5%). Orbital lymphoma primarily affects elderly patients, with 70% of patients with diffuse large B-cell lymphoma (DLBCL) > 50 years of age.^{2,3} There is an even gender distribution among patients with DLBCL. Ocular manifestations are unilateral in 90% and include proptosis, limited ocular motility, diplopia, swelling, pain, ptosis, chemosis, and lid edema. Systemic symptoms such as fever, night sweats, and weight loss occur in 8% of patients. Symptoms progress over weeks to months.

Diagnosis of orbital lymphoma requires a biopsy of the lesion identified on neuroimaging. Staging of the disease includes full-body positron emission tomography, computed tomography or magnetic resonance imaging, and a bone mar-

row biopsy. The histological subtype of lymphoma is the most important factor for prognosis.⁴ Treatment includes partial surgical excision, external radiotherapy, and chemotherapy.³

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“My Double Vision Comes and Goes”

Stacy L Pineles MD

DIAGNOSIS AND TEACHING POINTS

Final Diagnosis

Ocular neuromyotonia

Teaching Points

Ocular neuromyotonia is a rare motility disorder characterized by episodic diplopia and strabismus due to involuntary, tonic extraocular muscle contraction and delayed relaxation from brief repetitive firing of an ocular motor nerve. The paroxysms may occur spontaneously or be triggered by sustained gaze in the direction of the affected muscle.¹ Treatment with membrane-stabilizing agents such as carbamazepine and gabapentin is frequently limited by pharmacological intolerance, recurrence upon discontinuation, or a failed therapeutic response.^{2,3} Spontaneous resolution is uncommon.³⁻⁷ Ocular neuromyotonia is a result of excessive conduction of cranial nerve innervation to an extraocular muscle. Demyelinated or compacted axons are thought to be the locus at which ephaptic neural transmission occurs, creating a short circuit for lateral spread and amplification of neural activity.¹

The initial step in the evaluation of intermittent strabismus is characterizing the strabismus. In cases of neuromyotonia, the patient may be orthotropic on initial examination. Similarly, intermittent strabismus such as intermittent exotropia and intermittent small vertical deviations may be fused on initial examination. In order to determine whether a patient is fusing an intermittent deviation, a 30-minute patch test can be performed to adequately dissociate a patient's fusion and manifest their strabismus. If intermittent strabismus is not the etiology in cases such as this one, then myasthenia gravis should also be considered.

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“My Eye Won’t Close, and I See Double”

Anne Abel MD

DIAGNOSIS AND TEACHING POINTS

Final Diagnosis

Ipsilateral sixth and seventh nerve palsy secondary to Ramsay Hunt syndrome

Teaching Points

In patients with facial nerve palsy (FNP), there are two important distinctions to make quickly: (1) Is the FNP central or peripheral? And (2) Is the FNP isolated? Due to bilateral upper motor neuron innervation of the upper facial muscles, frontalis and orbicularis strength are spared in a central FNP. Therefore, isolated lower facial paralysis with preservation of brow elevation and forced eyelid closure is concerning for a central cortical process like stroke or tumor. Conversely, complete unilateral facial paralysis of the upper and lower face is consistent with a peripheral FNP involving structures at the level of the pons (nuclear), cerebellopontine angle, and/or elsewhere along the course of the facial nerve.

The most common causes of peripheral FNP are Bell palsy, Ramsay Hunt syndrome, and trauma. Bell palsy is an idiopathic diagnosis of exclusion and typically has a good prognosis. The etiology remains unclear, but leading hypotheses include herpes simplex infection and compression from perineural edema, as the facial nerve courses through the temporal bone. In the absence of atypical symptoms, laboratory tests and neuroimaging are typically not done for Bell palsy unless there is no clinical improvement after 3 weeks. Infectious and neoplastic causes should be strongly considered at that time. Screening for Lyme

disease should be performed in endemic areas, and testing for sarcoidosis is indicated in recurrent or bilateral cases.

Ramsay Hunt syndrome is a peripheral FNP caused by varicella zoster infection. The classic Ramsay Hunt triad is FNP with ipsilateral otalgia and vertigo. Ipsilateral hearing loss also is common. Ipsilateral sixth nerve palsy is uncommon in Ramsay Hunt syndrome but has been reported. In the absence of a vesicular rash, peripheral FNP associated with vertigo, hearing loss, or sixth nerve palsy is suggestive of an intrinsic pontine or cerebellopontine angle lesion, and these patients must undergo MRI brain with contrast unless medically contraindicated.

The importance of a careful sensorimotor and cranial nerve exam in FNP cannot be over emphasized. Bell palsy is a mononeuropathy. Impairment of additional cranial nerve function should prompt early neuroimaging.

Sensorimotor and cranial nerve exam are equally important in patients with monocular diplopia. As ophthalmologists, we are often relieved when a “double vision” consult is a patient with monocular diplopia, as this is a refractive problem localizing to the tear film, cornea, or lens. However, we cannot rely on the history alone. This patient’s exposure keratopathy blurred her left eye enough that she did not notice her binocular diplopia from her left sixth nerve palsy. In FNP, the ophthalmologist is often consulted to protect the cornea, but we must also confirm the diagnosis and rule out additional cranial nerve involvement so a more sinister diagnosis is not missed.

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“Everything Is Double and Moving!”

Janet C Rucker MD

DIAGNOSIS AND TEACHING POINTS

Final Diagnosis

Chiari I malformation with cerebellar eye findings, including gaze-evoked nystagmus in right and left gaze, downbeat nystagmus in central and downgaze, rebound right-beat nystagmus in central gaze, saccadic smooth pursuit, and mild gait ataxia.

The comitant esotropia could represent a congenital esotropia, though a component of a cerebellar esotropia is also possible.

Teaching Points

1. Nystagmus: Congenital vs. acquired

The main challenges when faced with a patient who has nystagmus are to adequately characterize and localize the nystagmus

and to differentiate the acquired from the congenital forms. This latter task is not always as easy as it might seem, especially with manifest latent nystagmus and especially in the face of a long-standing esodeviation of the eyes.

The age of onset of nystagmus might seem a good indicator to differentiate congenital from acquired nystagmus. Classic forms of congenital nystagmus—such as infantile nystagmus syndrome, which is typically predominantly horizontal pendular nystagmus—are noted in infancy, making diagnosis straightforward. Classic latent nystagmus—in which there is no nystagmus when both eyes are open and fixating, and nystagmus beating away from a covered eye is unmasked by monocular cover—does not have acquired mimics. The absence or presence of oscillopsia, a subjective sense of visual motion, is also generally helpful in differentiating congenital from acquired forms of nystagmus, as it is typically absent in congenital forms.

2. Nystagmus patterns: Manifest latent vs. posterior fossa acquired lesion

The difficulty in differentiating congenital from acquired nystagmus arises with manifest latent nystagmus, which does mimic cerebellar forms of nystagmus and can develop later than infancy and can even cause oscillopsia in dim lighting conditions.

With manifest latent nystagmus there is typically an underlying congenital esodeviation of the eyes, and the patient fixates with one eye only when both eyes are open. The nystagmus beats toward the open, fixating eye and toward the abducting eye in lateral gaze. However, if the open, fixating eye (or the abducting eye in lateral gaze) is covered, thereby forcing fixation with the opposite eye, the nystagmus will reverse direction. Though vertical components of nystagmus are not typical of manifest latent nystagmus, upbeat nystagmus accompanying otherwise typical manifest latent nystagmus has been reported.

Nystagmus features strongly suggesting cerebellar dysfunction include (1) gaze-evoked nystagmus that does not reverse direction if the abducting eye is covered, as occurred in our patient (in other words, right-beating nystagmus in right gaze, left-beating in left gaze, upbeating in upgaze) and (2) downbeat nystagmus, which is present by definition in central gaze and often enhanced in downgaze and was also seen in our patient. Further, the presence of rebound nystagmus (in our patient, right-beating nystagmus in central gaze after sustained left gaze) is strongly suggestive of posterior fossa pathology.

3. Nystagmus: The “company it keeps”

As always in neurological disorders, diagnosis is heavily dependent on whether or not additional symptoms and signs are present. In other words, a symptom must be interpreted in terms of the neurological company it keeps. In our patient, difficulty with tandem gait explained her subjective symptom of progressive imbalance and also strongly suggested a posterior fossa lesion.

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“I See Double and Triple Images”

Mark Borchert MD

DIAGNOSIS AND TEACHING POINTS

Final Diagnosis

Palinopsia

Teaching Points

CNS causes for diplopia or polyopia should be considered when the diplopia is transient, not dependent on direction of gaze, involves only certain objects within the visual field, or is unchanged under binocular and monocular viewing with each eye.

Section IV: Tests Will Give Me The Answer!

“My World Is Closing In”

Guy V Jirawuthiworavong MD

DIAGNOSIS AND TEACHING POINTS

Final Diagnosis

Cancer-associated retinopathy

Teaching Points

In summary, this patient presented with bilateral, progressive visual loss over months with decreased color vision, severely depressed visual fields, OCT macula with outer retinal thinning, positive antiretinal antibodies, unremarkable MRI of the brain with gadolinium, and a systemic cancer workup positive for small-cell lung carcinoma. The diagnosis is a paraneoplastic autoimmune retinopathy (pAIR) from cancer-associated retinopathy (CAR).

A broad differential diagnosis of gradual, bilateral visual loss with OCT retinal changes includes the following:

1. Vitreoretinal interface disorders (epiretinal membrane, vitreomacular traction)
2. Dry AMD
3. Macular edema
 - a. Diabetic macular edema
 - b. Systemic medications (thiazolidinediones, fingolimod, tamoxifen, taxanes, niacin, interferon)
 - c. Uveitic cystoid macular edema (CME)
 - d. Ocular medications (prostaglandin analogs)
 - e. Post-surgery (Irvine-Gass syndrome (post-cataract extraction CME)
4. Infectious (toxoplasmosis, presumed ocular histoplasmosis syndrome, tubercular serpiginous-like choroidopathy)
5. Inflammatory (sarcoidosis, Vogt-Koyanagi-Harada syndrome, posterior scleritis)
6. Retinal degeneration
 - a. Retinitis pigmentosa (RP) and allied disorders (rod-cone dystrophy, RP syndromes)
 - b. Macular dystrophy (cone-rod dystrophy, Best disease, Stargardt disease)
7. Toxicity (hydroxychloroquine, chloroquine, thioridazine, chlorpromazine, quinine)
8. Macular telangiectasia
9. White dot syndromes (serpiginous chorioretinopathy, acute zonal occult outer retinopathy [AZOOR])
10. Nutritional, vitamin A deficiency
11. Autoimmune retinopathy (AIR)
 - a. Paraneoplastic (pAIR): (i) CAR, (ii) melanoma-associated retinopathy (MAR)
 - b. Non-paraneoplastic (npAIR): (i) anti-recoverin autoimmune retinopathy, (ii) with antiretinal antibodies of unknown significance
12. Radiation-induced retinopathy

The lack of optic nerve pallor and subtle retinal findings narrow the differential diagnosis to a retinal etiology in this case. OCT of the macula showed thinning of the outer retina, but there was no vitreomacular traction, intraretinal fluid, or subretinal fluid. The thinning of the outer retina can be seen with conditions such as dry macular degeneration, RP, macular dystrophy, white dot syndrome (serpiginous chorioretinopathy, AZOOR), vitamin A deficiency, or AIR (CAR, MAR, npAIR). The severely contracted visual fields with only subtle fundus abnormalities suggested a retinal dystrophy or AIR. AIR was more likely given the rapid decline in the patient's vision. She was not on hydroxychloroquine or other medications that could mimic this presentation.

CAR, MAR, and npAIR often cause attenuated vasculature, but patients can sometimes have no frank retinal findings on fundus examination. OCT will typically show loss or mottling of the ellipsoid zone (photoreceptors), but occasionally will show no abnormalities and only be detected on electroretinography (ERG). MAR patients usually present with a preceding diagnosis of melanoma. Underlying cancer screening and the presence of antiretinal antibodies against retinal proteins and retinal tissue can help differentiate CAR, MAR, and npAIR. This patient's serum initially detected the presence of multiple antiretinal antibodies of unknown significance. Her systemic cancer workup revealed the presence of small-cell lung carcinoma. Repeat testing for antirecoverin antiretinal antibody was positive. Current literature recommends confirmation of the presence of antiretinal antibodies from 2 different laboratories that utilize both Western blotting and confirmatory immunohistochemistry. The treatment for CAR is to treat the underlying cancer. There is currently no standard of care for the treatment of npAIR.

Paraneoplastic autoimmune retinopathy (CAR and MAR) is a rare idiopathic disorder that affects adults. The condition remains poorly understood as the pathophysiological mechanism of the disease remains to be elucidated. Patients complain of gradual loss of vision over months, often accompanied by photopsias and decreased night vision. They often present with visual fields similar to patients with RP, with a ring scotoma that later progresses into tunnel visual fields which worsen at a faster rate than inherited retinopathies. This condition typically affects both eyes and tends to be symmetric in presentation. Central vision and color vision is often affected later in the disease, and there is minimal to no relative afferent pupillary defect. Patients present insidiously over several months, often without any visible retinal changes on funduscopy at presentation. The rarity of the condition and the lack of ophthalmoscopic findings make the diagnosis quite elusive for the clinician. The optic nerve can have mild waxy pallorous changes with attenuated vasculature as the disease progresses. The condition is diagnosed by history and retinal exam and confirmed

with visual field testing, fluorescein angiogram, fundus autofluorescence, OCT, ERG, mfERG, and positive antiretinal antibody testing that is found associated with an underlying malignancy.

CAR is most commonly associated with small-cell lung carcinoma, followed by the female gynecological and breast cancers. Other solid tumor cancers as well as hematological cancers have been reported in association with CAR. MAR is found in association with cutaneous malignant melanoma. CAR and MAR are excluded diagnostically by the absence of any underlying systemic cancer upon screening. The first antiretinal antibody described associated with CAR was the antirecoverin antibody. Recoverin is an important photoreceptor protein involved in the light transduction cascade. However, the exact pathophysiological mechanism by which the antirecoverin antibody causes such retinal degeneration still remains to be determined. In addition, many other antiretinal antibodies associated with CAR have been identified, such as enolase. There is even less knowledge concerning the pathogenicity of these other antiretinal antibodies. In regard to MAR, the antiretinal antibodies are shown to bind to bipolar cells on immunohistochemical staining of retinal tissue, suggesting that the bipolar cells are most affected in MAR patients, which is supported by the b-wave being predominantly affected on ERG.

Of note, antirecoverin antibodies as well as many other antiretinal antibodies have been found in nonparaneoplastic retinopathy patients. There continues to be much controversy about the utility of the presence of antiretinal antibodies, in particular the non-antirecoverin protein bands found on serum testing in Western blots. Many normal patients can have antiretinal antibodies present in their serum. By recent consensus (2016), antiretinal antibody detection should be done on Western blot and confirmed on immunohistochemistry. However, interpretation of positive antiretinal antibody results must be made in the context of the patient. Patients with CAR, MAR, or npAIR should show abnormalities on objective tests of the retina, such as OCT, ERG, or mfERG. If these tests are normal, an alternative cause of the vision loss should be considered.

The optimal treatment for CAR and MAR remains unclear. Responses to various therapeutic interventions, such as immunosuppression, have been anecdotal and variable in CAR and MAR. Even after the oncologist has adequately treated the underlying malignancy, vision often remains severely compromised. Controversies about the ocular management of CAR and MAR remain.

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“They Told Me I Have Optic Neuritis”

M Tariq Bhatti MD

DIAGNOSIS AND TEACHING POINTS

Final Diagnosis

False positive ELISA neuromyelitis optica (NMO) antibody, non-organic visual loss, and idiopathic eye pain

Teaching Points

In this patient, the lack of objective clinical findings, absence of optic nerve enhancement on MRI, normal OCT, normal stereopsis, and the sunglasses sign strongly support the diagnosis of non-organic visual loss.^{1,2}

Optic neuritis is a clinical diagnosis that is supported with paraclinical testing such as MRI, OCT, and serology. Acute inflammatory demyelinating optic neuritis typically presents with acute to subacute, unilateral visual loss associated with eye pain exacerbated by eye movements. The eye pain often resolves within several days to a couple of weeks from the onset of visual loss. Persistent eye pain is not characteristic of optic neuritis. Vision can be preserved (but often with loss of color vision), or it can be profoundly affected to the level of no light perception. In unilateral or bilateral asymmetric cases there is a relative afferent pupillary defect. In approximately one-third of cases there is mild optic disc edema.

Because most patients with optic neuritis have very good visual recovery, it can be challenging to make the diagnosis if the patient is seen several weeks to months after the episode of visual loss. Stunkel et al found that 60% of patients referred to a university-based practice for optic neuritis had an alternative diagnosis.³ Therefore, it is incumbent upon the clinician to perform a detailed history and examination without confirmation bias in order to establish the clinical diagnosis of optic neuritis and avoid performing unnecessary serological testing.

The vast majority of patients with optic neuritis are left with a “footprint” of their attack—in particular, optic disc pallor and OCT changes. Optic disc pallor sets in approximately 4 to 6 weeks after the onset of symptoms. In terms of the OCT, peripapillary retinal nerve fiber layer thickness and in particular

ganglion cell layer–inner plexiform layer thickness are reduced approximately 4 to 8 weeks after a bout of optic neuritis.^{4,5}

Optic neuritis should not be considered simply in terms of a dichotomy etiology of either idiopathic or multiple sclerosis (MS) related. Other inflammatory, infectious, toxic, metabolic, and hereditary conditions should be considered in the differential diagnosis, particularly in atypical cases of optic neuritis. Clinical characteristics of atypical optic neuritis include absence of pain, severe optic disc edema with hemorrhages, retinal pathology (eg, hemorrhage, subretinal fluid, cotton wool spots, retinitis), intraocular inflammation, simultaneous bilateral visual loss, persistent visual loss, recurrent visual loss, and steroid dependence. MRI findings of bilateral optic nerve enhancement, long-segment optic nerve enhancement (> 18 mm), and chiasmal involvement should prompt a workup for non-MS related optic neuritis.

A panel of international experts developed the following diagnostic criteria for NMO spectrum disorder (NMOSD):⁶

- I. Positive AQP4-IgG
 - A. At least 1 core clinical characteristic (see below)
 - B. Exclusion of alternative diagnoses
- II. Negative or Unknown AQP4-IgG
 - A. At least 2 core clinical characteristics (see below) occurring as a result of 1 or more clinical attacks and all of the following:
 1. At least 1 core clinical characteristic must be optic neuritis, acute myelitis with longitudinally extensive transverse myelitis (LETM), or area postrema syndrome.
 2. Dissemination in space (2 or more different core clinical characteristics; see below)
 3. Fulfillment of additional MRI requirements
 - a. Optic neuritis: Brain MRI showing normal findings or only nonspecific white matter lesions or optic nerve MRI with T2-hyperintense lesion or T1-weighted gadolinium-enhancing lesion extending greater than half the optic nerve length or involving optic chiasm
 - b. Acute myelitis: Requires associated intramedullary MRI lesion extending ≥ 3 contiguous segments (LETM) or ≥ 3 contiguous segments of focal spinal cord atrophy in patients with history compatible with acute myelitis
 - c. Area postrema syndrome: Requires associated dorsal medulla/area postrema lesions
 - d. Acute brainstem syndrome: Requires associated periependymal brainstem lesions
 - B. Exclusion of alternative diagnoses

III. Core Clinical Characteristics

- A. Optic neuritis
- B. Acute myelitis
- C. Area postrema syndrome: episode of otherwise unexplained hiccups or nausea and vomiting
- D. Acute brainstem syndrome
- E. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
- F. Symptomatic cerebral syndrome with NMOSD-typical brain lesions

AQP4-IgG is a very important component of the diagnostic criteria, and a positive test requires only 1 core clinical characteristic such as optic neuritis to make the diagnosis of NMOSD. In 2004, Lennon et al first recognized AQP4-IgG as a biomarker for NMOSD. Indirect immunofluorescence assay was used to detect the antibody and was found to have a sensitivity of 73% and a specificity of 91%.⁷ However, since that time, cell-based assays have been developed for AQP4-IgG that are more specific and sensitive than antibody-based assays such as indirect immunofluorescence and ELISA.⁸ For this reason, performing a cell-based assay for the detection of AQP4-IgG is strongly recommended. It should be noted that serum AQP4-IgG is more sensitive than cerebrospinal AQP4-IgG.⁹

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“I Can’t See, and the MRI Is Not Normal”

Peter MacIntosh MD

DIAGNOSIS AND TEACHING POINTS

Final Diagnosis

Leber hereditary optic neuropathy

Teaching Points

Leber hereditary optic neuropathy (LHON) is a mitochondrial optic neuropathy that presents with painless, sequential, subacute vision loss. The sequential vision loss with central scotomas on visual field testing was very helpful in making the diagnosis of LHON. The family history of affected mother was also helpful diagnostically, since the mitochondrial DNA mutation in LHON is inherited solely from the mother.

Clinically, the optic nerve head may be normal acutely, or it may demonstrate circumpapillary telangiectatic microangiopathy and pseudoedema that can aid in making the diagnosis in the acute setting. The MRI may be completely normal, or it may demonstrate optic nerve enhancement and chiasmal enlargement, though the pathophysiology of these MRI changes is not yet understood.¹⁻⁴ The presence of contrast enhancement of the optic nerve may be confusing as it suggests optic neuritis, leading to treatment with IV steroids and an expectation of rapid visual improvement. However, lack of improvement and an atypical history for optic neuritis, as in this case, should raise suspicion for an alternate diagnosis.

Although typically a condition of young men, LHON tends to present at a later age in women when compared to men. A protective role of estrogen has been postulated as an explanation for both the male preponderance of LHON and the delayed onset in affected females;⁵ hence the recommendation to this patient to initiate estrogen hormone therapy after discussion with her PCP. Mitochondrial mutations at positions 11778, 14484, and 3460 account for about 95% of LHON cases,⁶ and the rate of visual recovery is highest for the 14484 mutation.⁷ The remainder of cases, like this case, are made up of other novel mutations, which can be determined by requesting full mitochondrial genome sequencing. There is little published literature on the rate of visual recovery for the mutation our patient had; however, over 3 months, she did demonstrate significant recovery of central vision, though her visual field remained abnormal. It is unknown if this improvement was spontaneous or related to idebenone therapy, start of estrogen hormone therapy, or some combination of the three.

Many other conditions may present with optic nerve enhancement and/or enlargement. The most common is optic neuritis from various etiologies, including idiopathic, sarcoidosis, and demyelination from multiple sclerosis (MS) and neuromyelitis optica. Optic neuritis can typically be differentiated

from LHON clinically by the presence of pain with eye movements and acute vision loss. These patients require whole brain MRI with contrast to evaluate for lesions suggestive of MS as the underlying etiology, as well as possibly lumbar puncture and CSF analysis to evaluate for oligoclonal bands. MRI of the orbits is not required to make the diagnosis of optic neuritis, but on MRI, an optic nerve lesion will enhance with contrast when active and demonstrate T2 hyperintensity. Neuromyelitis optica (NMO) may also present with optic neuritis, but it is more likely to be bilateral than in MS. NMO is distinct from MS in that the MRI is often not diagnostic of MS and longitudinal spinal cord lesions are more common. Furthermore, recovery of vision in NMO is often poor, and treatment is different than it is with MS. Aquaporin 4 antibody (NMO ab) and anti-myelin oligodendrocyte glycoprotein (MOG) testing may also be helpful.

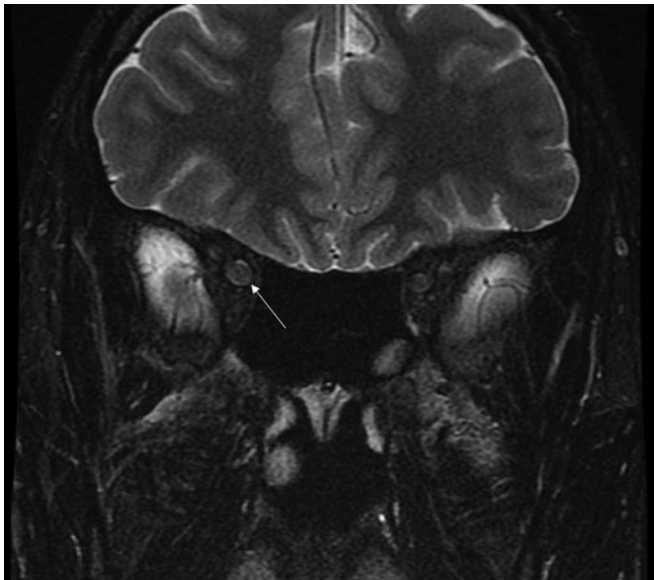
In sarcoid optic neuritis, the presentation may be protean.^{8,9} Some present similar to idiopathic optic neuritis, while others may have optic nerve head or subretinal granulomas, or a swollen nerve due to optic nerve or optic nerve sheath infiltration with or without optic nerve head edema.¹⁰ Sarcoidosis is a known cause of optic perineuritis, which appears as enhancement of the optic nerve sheath around an unenhancing optic nerve. Radiographically, this finding may be confused with optic nerve sheath meningioma (ONSM, discussed later), but the presence of pain and rapid vision loss in optic perineuritis should help exclude ONSM.

Tumors of the optic nerve are another important differential for optic nerve enhancement and enlargement which include glioma and nerve sheath meningioma. Primary optic nerve gliomas come in 2 forms: (1) juvenile, benign, pilocytic astrocytoma and (2) rare, malignant glioblastoma of adulthood.

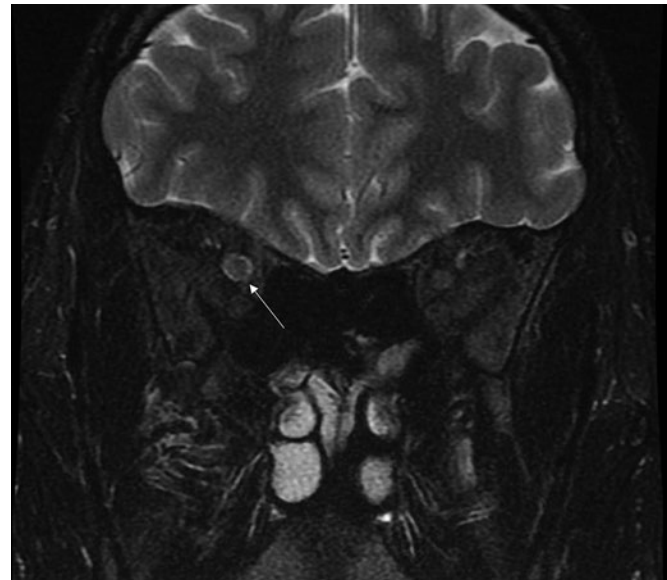
Benign juvenile optic nerve glioma presents with slowly progressive, painless vision loss and proptosis. The disc may be swollen or pale. Visual field defects are usually of the central or cecentral type, but if the chiasm is involved, bitemporal hemianopia may be present also. Most patients present before 10 years of age, and importantly, about 25% also have neurofibromatosis type I (NF1).

Malignant optic nerve glioblastoma, on the other hand, occurs in middle-aged adults and presents with vision loss, headache, and pain with eye movements, similar to an inflammatory conditions such as optic neuritis. Often disc edema is present with signs of venous stasis retinopathy. Vision loss may progress rapidly within weeks. Radiation and chemotherapy are the mainstays of treatment.

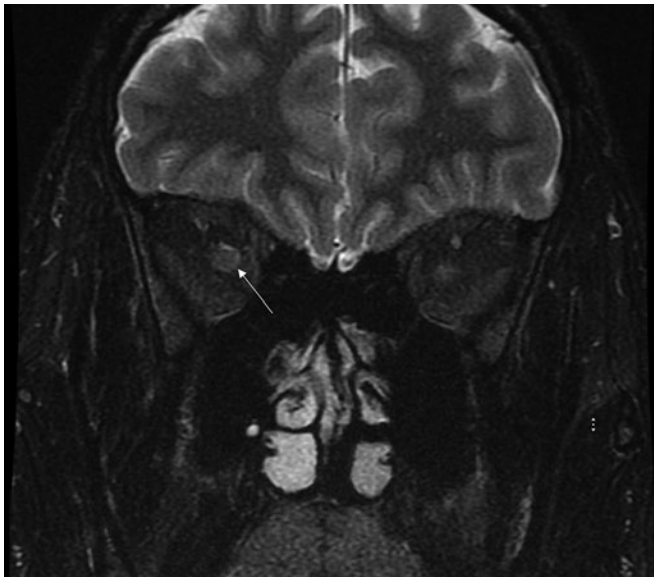
The diagnosis of optic nerve glioma is clinical and radiographic. The workup includes MRI of the orbits without and with gadolinium. MRI is preferred to CT as it better evaluates for intracranial extension.^{11,12} Typically, the MRI will reveal fusiform enlargement, kinking, and enhancement of the optic nerve, with the T2-weighted axial MRI demonstrating high signal intensity with a central linear core of lower signal intensity (Figure 1).^{12,13} About 50% may already display chiasmal involvement. Biopsy is almost never needed, especially in the setting of NF1.



A



B



C

Figure 1. Coronal T2-weighted MRI Orbits optic nerve glioma.

ONSM may also present with progressive, painless vision loss with optic nerve enlargement. These tumors occur primarily in middle-aged women and are usually unilateral, though bilateral cases may be seen in neurofibromatosis type II (NF2).^{14,15} In contrast to optic nerve glioma, ONSM in children is rare and more likely associated with a more malignant tumor and NF2.¹⁶ Radiographically, ONSM appears as fusiform enlargement but without kinking of the optic nerve. In axial plane cuts, ONSM may appear as “tram tracking” with enhancement of the sheath tumor around the normal optic nerve.

Although not required for the diagnosis of all of these conditions, neuroimaging is a very helpful adjunctive test. The use of gadolinium is often helpful to demonstrate contrast enhancement and, in the case of MS or NMO, to indicate active disease. Ultimately, it is often a combination of the clinical history, exam, and imaging findings that will guide the physician to the correct diagnosis.

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“The Doctor Says My Optic Nerves Are Damaged”

Normal Vision and Thin RNFL: Now What?

Valerie I Elmaleh MD

DIAGNOSIS AND TEACHING POINTS

Diagnosis

This patient has small, crowded, tilted optic discs with peripapillary atrophy and moderate to high myopia. The disc area is small, at 1.28 mm² OD and 1.21 mm² OS, when compared to the average disc area as measured by OCT in the white population, which is 2.10 to 2.35 mm². More precise histologic measurement of the optic disc reveals the mean disc size across populations to be between 2.57 mm² and 2.81 mm².¹

Discussion

Measurement of the disc area can be influenced by refractive error leading to altered magnification effect requiring several correction factors.¹ Interpretation of OCT can be difficult in

high myopes due to these magnification effects because the OCT detects a smaller disc area, with apparent retinal nerve fiber layer (RNFL) thinning.^{2,3} In addition to magnification effects, myopes often have anomalously temporally displaced RNFL bundles that follow the superior and inferior arcades. This causes the peaks of thickness measurements on the circular scan to be more widely spread apart on the TSNIT plot, resulting in thinning of the superior and inferior RNFL thicknesses compared to emmetropes (see black bracket in Figure 2A, p. 25).^{2,3} These factors result in artifactual RNFL thinning, also occasional referred to as “red disease.”

The 5-line raster images of OCT enhanced depth imaging (EDI) (see Figure 4) show a steeply tilted disc bilaterally compared to the normal tilt in (Figure 4.C).⁴ All of these factors contributed to the “abnormal” measurements seen on OCT in our patient.

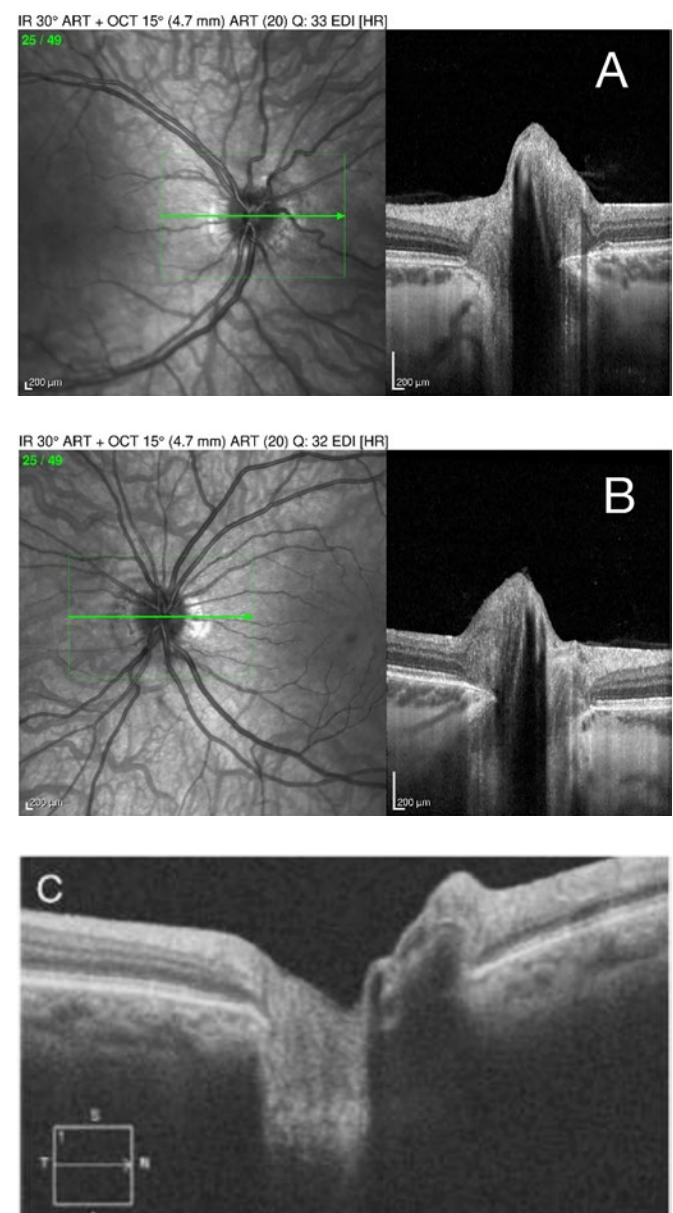


Figure 4. Five-line raster enhanced depth imaging OCT of the optic disc showing the angle of tilt: (A) right optic disc from our patient, (B) left optic disc from our patient, (C) normal optic disc tilt. Adapted from reference 4.

Several factors can contribute to an abnormal OCT of the optic nerve with normal (or near normal) visual fields:

I. Anatomic Factors

- A. Tilted optic disc (as described above):³ Bruch membrane opening (BMO). Minimum rim width (BMO-MRW) analysis may provide higher specificity than the peripapillary RNFL in tilted discs independent of refractive error.⁵
- B. Refractive error, which results in altered magnification and artifactual thinning of the RNFL: high myopia (with longer axial length).³ For myopic patients, analysis of the 3-dimensional neuroretinal rim thickness (2% false positive) is more accurate than peripapillary RNFL (27% false positive).⁶ In addition, high myopes often have anomalously displaced vessels and superior and inferior RNFL bundles that can cause the appearance of superior and inferior thinning of the RNFL compared to emmetropes.
- C. Congenital optic pit: This is a defect in the lamina cribrosa, which may displace the nerve fibers, resulting in arcuate defects or enlargement of the blind spot on visual fields. If there is associated serous macular detachment, there may be a central scotoma. The disc is of normal to slightly enlarged size, and the pit is usually located temporally. Patients with optic pits have preserved visual function until a serous macular detachment occurs in childhood or later in life as vitreous liquifies. OCT may display artifacts or RNFL thinning in the region of the optic pit. If a membrane is present on the pit, it can be protective against serous macular detachment.^{7,8}
- D. Large disc: The peripapillary RNFL distribution is nasalized, and the vessels emerge vertically rather than temporally on the disc, which creates an artifact.^{3,9}
- E. Small disc/optic nerve hypoplasia³: The visual function can vary widely in optic nerve hypoplasia but can be normal in some cases. A double ring sign may be present. On OCT, there is thinning of the nasal > temporal RNFL with associated thinning of the ganglion cell-inner plexiform layer (GC-IPL). Macular OCT demonstrates foveal hypoplasia in clinically affected eyes with visual disturbance.¹⁰
- F. Optic disc drusen: There can be artifacts in the automatic linear tracing of the RNFL by OCT which can result in artifactual thinning of the RNFL despite the disc appearing elevated. EDI-OCT can show changes consistent with drusen, even if not apparent on B-scan ultrasound or fundus autofluorescence.
- G. Prior papilledema with gliosis: The gliotic RNFL can result in falsely high or low measured thickness on OCT, and the patient may have a nearly full visual field despite having clinical optic nerve pallor. The GC-IPL analysis will be helpful in showing atrophy in the setting of active or resolved papill-

edema. In cases of severe papilledema, the edema can extend to the macula with subretinal fluid, leaving the ellipsoid layer slightly disrupted once the subretinal fluid regresses.

In a study by Kim et al in 2015, factors that were significantly associated with false positive OCT RNFL and ganglion cell analysis (GCA) map included longer axial length, smaller disc area, smaller average cup-to-disc ratio, and larger fovea-disc angle (tilted disc).² In this study, the rate of false positive on the RNFL map was about 30%; and on the GCA map, about 40%. A later study did not find the GCA map false positive rate to be as high.¹¹ The superior quadrant was associated with the highest frequency of false positive on the RNFL and GCA.²

II. Mild Damage to the Optic Nerve

- A. Early glaucoma (pre-perimetric): One must carefully look at the ganglion cell complex analysis to assess for any pattern of loss, as well as focal thinning of the RNFL along with an associated, contiguous notch in the disc seen clinically.^{8,9} The visual field may still appear normal in early glaucoma, as it may not be sensitive enough to detect very subtle pre-perimetric changes.
- B. Healed optic neuritis: After optic neuritis, there will typically be thinning of the RNFL and GC-IPL on OCT even if the patient recovered vision with a normal Snellen high-contrast visual acuity and visual field. Low-contrast visual acuity is more sensitive in detecting subtle damage to the vision than Snellen acuity and standard visual field testing.
- C. Old traumatic and compressive optic neuropathy with recovery of vision: Findings in traumatic optic neuropathy and treated compressive optic neuropathy can be similar to those in healed optic neuritis, with thinning of the RNFL and GC-IPL on OCT despite excellent clinical recovery.

III. OCT Image Acquisition Artifacts

- A. The infrared image and the linear tracing on the RNFL circular tomogram must be carefully inspected. If the linear tracing of the RNFL layer seems off, one can repeat the scan or make manual corrections to allow for more accurate measurements.
- B. The signal quality of 7/10 or higher will improve the accuracy of the OCT. Some patients may need to be dilated to improve signal quality.

When making a decision regarding the clinical relevance of an abnormal OCT, it is important to place the OCT in the context of the clinical examination findings, including high-contrast visual acuity, color vision, low-contrast acuity, visual field, size, appearance of the optic disc and any associated anatomic variations, and the refraction with shorter or longer axial length. One must also carefully inspect the OCT RNFL and GC-IPL analysis in search of artifacts or false positives.

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"I Have Pressure in My Head"

Shira Simon MD

DIAGNOSIS AND TEACHING POINTS

Final Diagnosis

Migraine headaches, pseudopapilledema, and an incidental empty sella

Teaching Points

The global prevalence of primary headaches is around 50%, and tension type headaches may have a lifetime prevalence of almost 80%, while migraine has a prevalence of 15%. Headache is one of the most frequent presenting complaints in the ER, and rates of neuroimaging for headaches in the ER can be upwards of 70%. While an empty sella can be a sign of raised intracranial pressure (ICP), which is seen in approximately 90% of patients with idiopathic intracranial hypertension (IIH), it can also be seen in normal individuals, with rates in the literature ranging from 5% to 30+%; these statistics will likely only increase as neuroradiologists continue to evaluate for this. Given these probabilities, it is not uncommon for a patient with primary headaches without raised ICP to have an incidentally found empty sella on imaging. For these two incredibly common and ubiquitous conditions, it is prudent to have a systematic plan in place to discern the etiology and help target treatment.

The modified Dandy criteria provide helpful guidelines for making a diagnosis of IIH. These include signs and symptoms of IIH, no neurologic deficits aside from VI nerve palsy, normal neuroimaging (no mass, thrombus, hydrocephalus, or otherwise) aside from findings known to be associated with chronic increased ICP, increased cerebral spinal fluid opening pressure on lumbar puncture (LP > 25 cmH₂O) with otherwise normal CSF constituents, and no other etiology of intracranial hypertension.

Worsening headaches were the most common symptom (84% of participants) identified in the IIH Treatment Trial (IIHTT). Other symptoms included transient visual obscurations (68%), back pain (53%), pulse synchronous tinnitus (52%), vision loss (32%), and diplopia (20%). Asking about these symptoms can help in determining whether there is symptomatic elevated ICP.

There are noninvasive ways on clinical examination to evaluate for elevated ICP. The most obvious and specific method is to evaluate for optic nerve edema. However, optic disc drusen (pseudopapilledema) can confound this type of scenario, as drusen may mimic or mask mild disc edema. Autofluorescence and echography can be helpful in identifying optic disc drusen.

There is also a rare entity called "IIH without papilledema" wherein patients can have raised ICP and headaches without any disc edema. In both of the aforementioned cases, an elevated opening pressure on LP can suggest IIH if there are also indirect signs of raised ICP on neuroimaging. It is important to note that LP opening pressures can be variable, and therefore caution must be made in labeling a patient with IIH based on an isolated elevated opening pressure alone if there is no papilledema. In a retrospective review of referrals at a tertiary

medical center in Atlanta, 39.5% of patients referred for IIH were found to have been incorrectly diagnosed.

Evaluation of the optic nerves for the presence of spontaneous venous pulsations (SVPs) can also be used to help distinguish between normal and raised ICP states. The caliber of the retinal vein can vary with differences between IOP and cerebral spinal fluid pressure as the retinal vein crosses the lamina cribrosa. This is typically visualized with direct ophthalmoscopy. Near infrared videography has recently been explored as an alternative for evaluation. However, there are limitations to this approach: 10% of normal patients do not exhibit SVPs, and fluctuations in ICP may make SVPs at times visible even in the setting of raised ICP.

Other methods to noninvasively detect raised ICP include venous ophthalmodynamometry (utilizing central retinal vein pressure as a proxy for ICP), OCT to evaluate for deflection of the peripapillary Bruch membrane, ultrasonography to evaluate the optic nerve sheath diameter (> 5 mm is suggestive of raised ICP), and scanning laser tomography to evaluate optic nerve height. Otic approaches also exist, including evaluating for negative displacement of the tympanic membrane, finding decreased amplitudes on ocular vestibular evoked myogenic potentials, and more. None of these noninvasive indirect measures of ICP are perfect in identifying raised ICP.

Radiographic signs can suggest elevated ICP. Most relevant to this case is an empty sella. This is presumed to result from subarachnoid and arachnoid space cerebrospinal fluid entering the sella turcica and flattening the pituitary gland, so that it lines the floor and walls of the sella. Chronically raised ICP in the setting of IIH not only flattens the pituitary gland but also leads to remodeling of the sella turcica with enlargement of the sella, which contributes to the appearance of an empty sella. An empty sella can also occur from a primary, often congenital, cause wherein the diaphragma sellae—covering of the sphenoid bone—is deficient or absent. Endocrinopathies such as growth hormone deficiency and hypogonadotropism could be associated with this. An empty sella can also be due to a secondary cause, such as a history of pituitary damage (from apoplexy or Sheehan syndrome), previous surgery or radiation, trauma, history of infection, or hormonal change (eg, from menopause). Lastly, most relevant to this case, it can be idiopathic and seen in normal individuals.

There can be other helpful radiographic signs of elevated ICP, in addition to an empty sella. In 2013 Friedman et al described radiographic criteria for the suggestion of IIH in the absence of disc edema and a VI nerve palsy. Three of the following 4 findings on imaging were considered integral to this diagnosis: an empty sella, posterior globe flattening, distention of the perioptic subarachnoid space, and transverse venous sinus stenosis. Bidot et al described other common features found in patients with long-standing IIH, including optic nerve head protrusion, tortuosity of the optic nerve, cerebellar tonsillar herniation, and meningoceles.

In cases of persistent headaches without papilledema, patients should work with their primary care physician (with or without the assistance of a neurologist) to find the optimal treatment plan. While nonsteroidal anti-inflammatory agents may help, patients should be cautioned that rebound headaches

can occur after taking these medications for more than a few days each week. A variety of other medications can be explored, depending on the underlying etiology. IIH patients can be treated with acetazolamide or topiramate, acute headaches may benefit from agents like acetaminophen, and migraines may need prophylactic treatment such as tricyclic antidepressants and beta blockers, among others. Smoking cessation, regular exercise, and other healthy habits should also be encouraged.

The ophthalmologist plays an important role in some cases of headache, such as this one, where it is unclear if raised ICP could be contributing to the headaches. By evaluating for disc edema, spontaneous venous pulsations, cranial nerve palsies, and other signs of elevated ICP, an ophthalmologist can help confirm or rule out papilledema. In this case, this integral role helped determine that this patient does not fulfill the criteria for IIH but still facilitated appropriate treatment for dry eye symptoms and headaches.

While IIH is generally not a difficult diagnosis to make, there are many factors that can complicate the picture—mild or no disc edema, optic disc drusen, borderline elevated opening pressures on LP, other radiographic findings astute neuroradiologists point out, and a patient endorsing recent weight gain and worsening headaches, among others. In case of doubt, neuro-ophthalmology can help confirm the appropriate diagnosis and identify the right course of action.

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Ore-Ofeoluwatomi O Adesina MD

None

Anthony C Arnold MD

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Eric L Berman MD

None

M Tariq Bhatti MD

Receptos: C

Valerie Biousse MD

GenSight: C

Gabrielle R Bonhomme MD

None

Mark S Borchert MD

None

John J Chen MD PhD

None

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Mays A El-Dairi MD

None

Valerie I Elmalem MD

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None

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Heather Moss MD PhD

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Mark L Moster MD

Gensight: S,C

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Raghu Mudumbai MD

None

Nancy J Newman MD

Gensight: C,S

National Eye Institute: S

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Stacy L Pineles MD

Fitz Frames: C

John Pula MD

None

Peter A Quiros MDQuark Pharmaceuticals: S
Regenera: S**Joseph F Rizzo III MD**

None

Janet C Rucker MD

None

Kenneth S Shindler MD PhDFM Kirby Foundation: S
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None

Shira S Simon MD

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Presenter Index

Abel, Anne S 18, 44
Adesina, Ore-Ofeoluwatomi O 2, 30
Arnold*, Anthony C 24
Bhatti*, M Tariq 21, 47
Biousse*, Valerie 24
Bonhomme, Gabrielle R 10, 36
Borchert*, Mark S 19, 45
Cockerham*, Kimberly 11, 37
Costello*, Fiona E 6, 32
El-Dairi, Mays A 7, 33
Elmalem, Valerie I 25, 51
Francis, Courtney E 6, 33
Gordon, Lynn K 5
Jirawuthiworavong, Guy V 20, 46
Kardon*, Randy H 24
Kedar*, Sachin 3, 31
Kline, Lanning B 12
Ko, Melissa W 13, 40
Lai, Kevin E 13, 38
Leavitt, Jacqueline A 17
Lee, Andrew G 5
Lee*, Michael S 10, 37
Lincoff, Norah 5
Liu*, Grant T 17
MacIntosh, Peter W 22, 49
Miller*, Neil R 12
Moss*, Heather 2, 30
Moster*, Mark L 5
Newman*, Nancy J 17
Phillips, Paul H 16, 43
Pineles*, Stacy L 16, 43
Rizzo, Joseph F 24
Rucker, Janet C 18, 44
Shindler*, Kenneth S 15, 42
Siatkowski, R Michael 17
Simon*, Shira S 27, 53
Subramanian*, Prem S 8
Volpe*, Nicholas J 12
Warner, Judith E 12