North American Neuro-Ophthalmology Society

36th Annual Meeting

March 6-11, 2010 • JW Starr Pass Marriott Resort & Spa, Tucson, AZ

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Welcome to the JW Starr Pass Marriott Resort & Spa
Tucson, AZ

North American Neuro-Ophthalmology Society

36th Annual Meeting

March 6-11, 2010

Sponsored by: The North American Neuro-Ophthalmology Society

MISSION STATEMENT

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

TARGET AUDIENCE

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

POLICY ON COMMERCIAL SUPPORT AND FACULTY DISCLOSURE

The North American Neuro-Ophthalmology Society maintains a policy on the use of commercial support which ensures that all educational activities sponsored by NANOS provide in-depth presentations that are fair, independent, and scientifically rigorous. To this end, all speakers and planners are required to complete a "Disclosure Form". This information is included in this syllabus (see pages 8 - 11) and/or may be supplemented by announcements by moderators.

DISCLOSURE OF UNLABELED/UNAPPROVED USES

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

ACCREDITATION

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

CREDIT DESIGNATION

The North American Neuro-Ophthalmology Society designates this educational activity for a maximum of 34 *AMA PRA Category 1 Credits™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

NANOS

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NANOS is a 501 (c) (3) non-profit organization - Tax ID: 85-0342069

NANOS CME MISSION STATEMENT

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

To this end, the Society sponsors an annual scientific meeting which is its main CME (continuing medical education) activity. Recent advances in the structure and function of the nervous and visual systems as they pertain to neuro-ophthalmology, its pathology, new therapies, and new diagnostic and therapeutic technology comprise the major focus of the annual scientific meeting and its CME content. In addition, the Society supports joint sponsorship with other respected and recognized medical organizations that comply with the ACCME Essential Areas and their Elements.

Members of the Society, physicians, fellows, and resident physicians comprise the meeting participants and target audience for our CME program. They are predominantly neuro-ophthalmologists, neurologists, and ophthalmologists but also include physicians and scientists from other disciplines and specialties.

The annual scientific meeting of NANOS includes the following types of activities: symposium topics of current interest, special lectures, reports of original research presented at both platform and poster sessions, and reports of special committees assigned to evaluate and report to the membership on specific problems and controversial issues.

The NANOS annual scientific meeting features advances and best practices in neuro-ophthalmology, so that as a result attendees can incorporate them into their medical practices. The scope of the meeting includes: enhancing our diagnostic skills by discussion of challenging cases, promoting evidence-based treatments and avoiding ineffective treatments, and using new diagnostic tools and techniques. Participants should learn the results of ongoing basic and clinical research in neuro-ophthalmology. NANOS uses member surveys, program evaluations (both during and after the meeting), meetings of its Scientific Program Committee, Education Committee, and Board of Directors, and other appropriate means to assess the effectiveness whether the program achieved these outcomes and discuss the knowledge gaps that exist in the field of neuro-ophthalmology that should be addressed in future educational activities.

The NANOS Board of Directors, Scientific Program Committee, Education Committee, and CME Committee review and assess the educational gaps and content and participant critiques of the annual NANOS CME program and general membership comments and suggestions to ensure that all educational objectives are achieved.

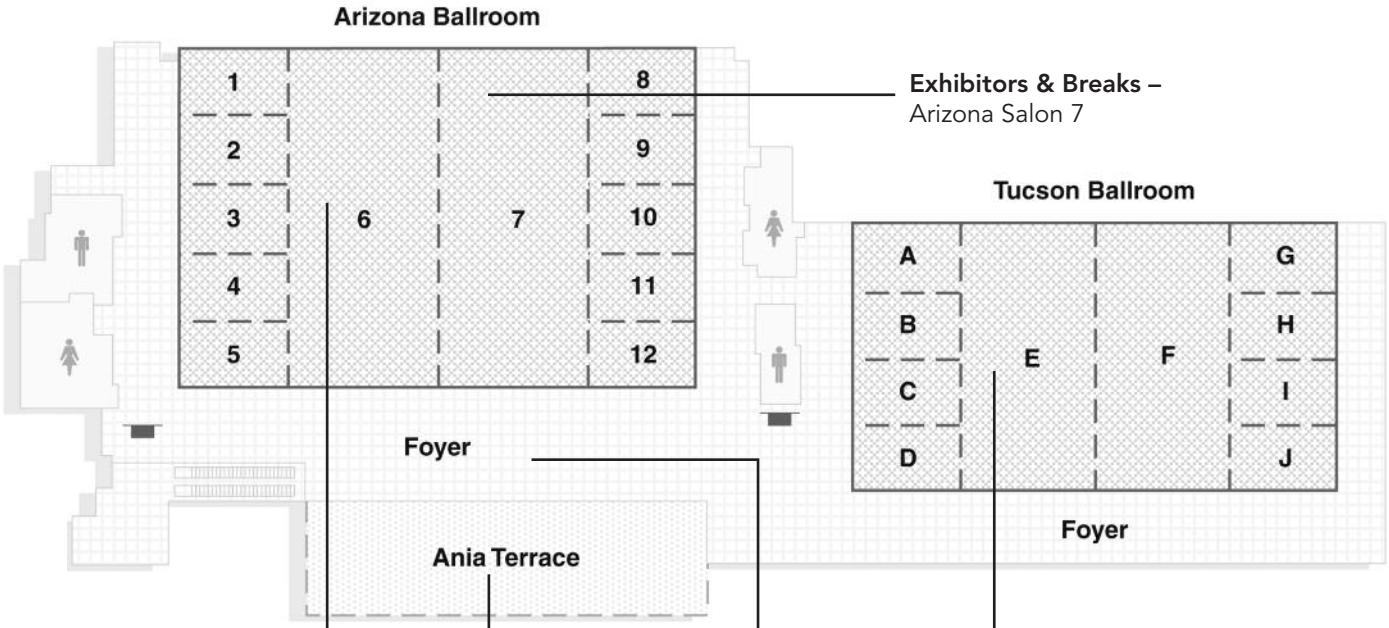
Adopted by the NANOS CME Subcommittee October 11, 2005

Adopted by the NANOS Board of Directors October 15, 2005

Reviewed and Approved by the NANOS Board of Directors February 10, 2007

Updated by the NANOS CME Subcommittee and NANOS Board of Directors January 9, 2009

JW STARR PASS MARRIOTT RESORT & SPA FLOOR PLAN



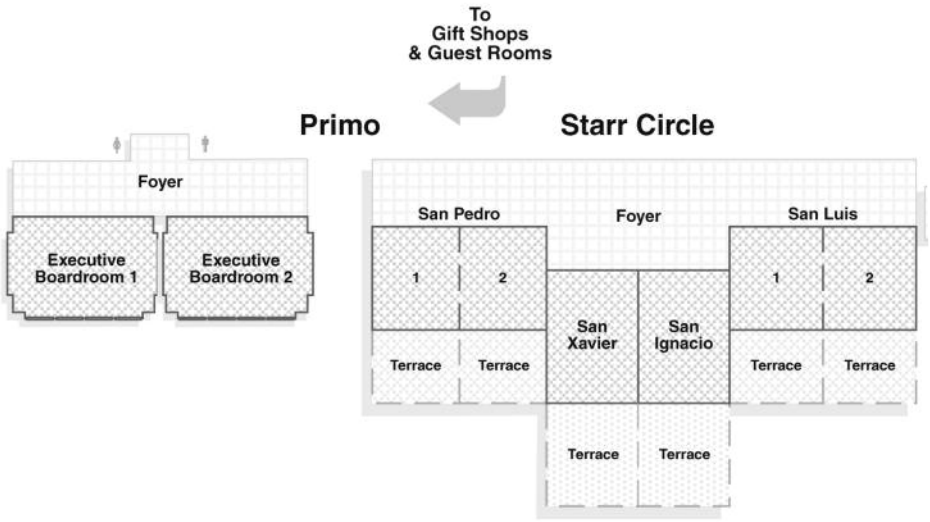
Exhibitors & Breaks –
Arizona Salon 7

NANOS General Session –
Arizona Salons 1-6

Opening Reception –
Ania Terrace

Poster Session –
Tucson Salons A-E

NANOS Registration Desk –
Arizona Ballroom Foyer



Spouse/Guest Hospitality Suite –
Signature Grill
(not shown on floorplan)

NANOS 2010 SPEAKERS AND MODERATORS

Laura Balcer, MD, MSCE
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NANOS would like to thank the following Supporters and Exhibitors for their financial support of these activities:

2010 Supporters (as of 2-5-10)

Pfizer

Pfizer has contributed $25,000

Teva Neurosciences

Teva Neurosciences has contributed $25,000

2010 Exhibitors (as of 2-5-10)

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CME ACTIVITES FACULTY DISCLOSURE STATEMENTS

The North American Neuro-Ophthalmology Society is required by the Accreditation Council for CME to make available to participants of this conference the following information regarding presenters' relationships to industry. Presentations must be unbiased, scientifically rigorous and include a balanced view of therapeutic options. Faculty must disclose (see below) relevant financial relationships with any commercial supporter and with the manufacturers of products or competing products discussed in their presentation. Faculty must disclose to the audience unlabeled or unapproved uses of products or technology in their presentations.

Disclosure information for Poster Presentations is listed in this syllabus at the end of each abstract.

FULL NAME	COMMERCIAL INTEREST	COMPENSATION TYPE/REASON
Madhu Agarwal, MD	None	
Robert Avery, DO	None	
Laura Balcer, MD, MSCE	Biogen-Idec, Novartis	Honorarium/consulting
Jeffrey Bennett, MD, PhD	EMD Serono, Teva, Biogen Idec	Research grant/consultant/honorarium
Gabrielle R. Bonhomme, MD	None	
Michael Brodsky, MD	None	
Michael Burdon, MB, BS	None	
Joseph Chacko, MD	None	
Jane Chan, MD	Biogen, Sanofi-Aventis, Pfizer	Horarium/grant
Manokaraananthan Chandrakumar, MD	None	
Yanjun Chen, MD	None	
Sophia Chung, MD	QLT, Inc., Pfizer Ohthalmics	Consulting fees/study monies/Pt recruitment/administrative
Kimberly Cockerham, MD	Allergan, Galderma, Renovo, Activatek, El Camine ASC	Honorarium/consultant/seat panel/shareholder/surgeon owner
Shelley Cross, MD	None	
Kathleen Digre, MD	None	
Raymond Douglas, MD, PhD	None	
Eric Eggenberger, DO, MSEpi	Biogen, Teva, Serono, Bayer	Honorarium/grant/research
Valerie Elmalem, MD	None	
Steven Feldon, MD	B & L, Boehringer Ingelheim, Pfizer, Teva	Research PI/site investigator
Michael Fisher, MD	None	
Rod Foroozan, MD	None	
Mohammad Fouladvand, MD	Chestnut Medical	Consulting fee/independent contractor
Courtney Francis, MD	None	
Steven Galetta, MD	Biogen Idec, Teva	Honorarium/consulting
Caterina Giannini, MD, PhD	None	
Nitza Goldenberg-Cohen, MD	None	
Thomas R. Hedges, III, MD	None	
Jeong-Min Hwang, MD	None	
Randy Kardon, MD, PhD	Lundbeck Pharmaceuticals, Department of Veterans Affairs, Department of Defense, National Institute of Health, Visuals Unlimited	Consulting/research/royalty
Aki Kawasaki, MD, MER	Bayer Spa	Honorarium for membership of advisory panel
John Keltner, MD	None	
Claudia Krispel, MD	None	
Jeanne Le Ber	None	
Nancy Lombardo	None	
Patrick H. Luetmer, MD	None	

CME ACTIVITES FACULTY DISCLOSURE STATEMENTS, continued

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Paul Phillips, MD	None	
Stacy Pineles, MD	None	
Sashank Prasad, MD	None	
Amy Pruitt, MD	Teva, American Academy of Neurology, Imclone (spouse)	Investigator funding/honorarium/stock sold
Valerie Purvin, MD	Bayer - ED Drug Panel	Honorarium/consulting
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Joel Schuman, MD	Alcon Laboratories, Optovue, Vindico, Carl Zeiss Meditec, Merck & Co., National Eye Institute, SOLX, SLACK, Inc., Inspire Pharmaceuticals, Inc., Bioptigen	Lecture fees/consulting/patents/royalty/grant
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Rebecca Stacy, MD, PhD	None	
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Valerie Touitou, MD	None	
Jonathan Trobe, MD	None	
Michael Vaphiades, DO	None	
Agnes Wong, MD	None	
Brian R. Younge, MD		
Patrick Yu-Wai-Man, MD	None	

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FULL NAME	COMMERCIAL INTEREST	COMPENSATION TYPE/REASON
Marie Acierno, MD	None	
Adeela Alizai, MD	None	
Anthony Arnold, MD	Pfizer, Honorarium for NAION Study Meeting	
Susan Benes, MD	Pfizer, Lundbeck	Research Support/Honorarium/Speaker's Bureau
Valerie Biousse, MD	None	
Mark Borchert, MD	None	
Swaraj Bose, MD	None	
Preston Calvert, MD	None	
Thomas Carlow, MD	None	
Pamela Chavis, MD	Lundbeck Pharmaceuticals	Honorarium
Wayne Cornblath, MD	None	
Fiona Costello, MD, FRCP	None	
Ivy Dreizin, MD	Will discuss Melatonin and Bright Light for Circadian Re-entertainment	
Ed FitzGibbon, MD	None	
Deborah Friedman, MD	None	
Larry Frohman, MD	None	
Karl Golnik, MD	None	
Lynn Gordon, MD, PhD	None	
Thomas Hwang, MD, PhD	None	
Janine Johnston, MD, FRCP	None	
Michael Lee, MD	Pfizer,Teva Neuroscience,Quark Pharmaceuticals	Research funds/Multicentered study
Andrew Lee, MD	None	
Leah Levi, MD, MBBS	None	
Y. Joyce Liao, MD, PhD	None	
Luis Mejico, MD	None	
Mark Moster, MD	Biogen	Honorarium/Speaker
Anil Patel, MD, FRCS(C), FACS	None	
Howard Pomeranz, MD	None	
Peter Quiros, MD	None	
Lyn Sedwick, MD	None	
Prem Subramanian, MD, PhD	Eisai America, Inc., Pfizer, Inc., Teva Pharmaceuticals	Consulting fee/Research Support
Roger Turbin, MD	None	
Nicholas Volpe, MD	None	
Judith Warner, MD	None	

FRANK B. WALSH AND PLATFORM DISCLOSURE STATEMENTS

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The following individuals are presenting during the Frank B. Walsh Session and/or Platform Presentation Session.

FULL NAME	COMMERCIAL INTEREST	COMPENSATION TYPE/REASON
Robert Avery, DO	None	
Michael Burdon, MB, BS, MRCP, FRCOPH	None	
Fiona Costello, MD, FRCP	None	
Emma Davies	None	
Michael J. Fisher, MD	None	
Mohammad Fouladvand, MD	Chestnut Medical	Consulting fee
Nitza Goldenberg-Cohen, MD	None	
Jeong-Min Hwang, MD	None	
Randy Kardon, PhD	Lundbeck Pharmaceuticals, Department of Veterans Affairs, Department of Defense, National Institute of Health, Visuals Unlimited	Lundbeck: Consultant compensation; Dept. of Veteran Affairs: grant for salary and research support; Dept. of Defense: grant for salary and research support; NIH: grant for salary and research support; Visuals Unlimited: Royalty, author
John Keltner, MD	None	
Claudia Krispel, MD	None	
Grant T. Liu, MD	None	
Raymond Magauran, MD	None	
Stacy Pineles, MD	None	
Michael Salman, PhD, MRCP	None	
Matthew Thurtell, MD	None	
Valerie Touitou, MD	None	
Patrick Yu-Wai-Man, MD	None	
Gabrielle Bonhomme, MD	None	
Joseph Chacko, MD	None	
Yanjun Chen	None	
Sophia Chung, MD	QLT Inc.; Pfizer Ophthalmics	Consultant (spouse)/patient recruitment/administrative
Valerie I. Elmalem, MD	None	
Courtney Francis, MD	None	
John Guy, MD	None	
Jacqueline Leavitt, MD	None	
Louise Mawn, MD	None	
Heather E. Moss	None	
Sarkis Nazarian, MD	None	
Steven Newman, MD	None	
Joshua Pasol, MD	None	
Paul Phillips, MD	None	
Sashank Prasad, MD	None	
Barry Skarf, MD, PhD	Pfizer	Investigator (no personal remuneration)
Rebecca Stacy, MD	None	
Madhura Tamhankar, MD	None	
Michael S. Vaphiades, D.O.	None	
Manokaraananthan Chandrakumar, BSC	None	
Timothy McCulley, MD	None	

North American Neuro-Ophthalmology Society

36th Annual Meeting

March 6-11, 2010 • JW Starr Pass Marriott Resort & Spa, Tucson, AZ

Educational Program Schedule

SATURDAY, MARCH 6

		LOCATION
12:00 p.m. – 5:00 p.m.	Board Meeting	San Pedro 2
2:00 p.m. – 8:30 p.m.	Registration	Arizona Ballroom Foyer
5:00 p.m. – 7:00 p.m.	NORDIC Reception	San Pedro 1
7:00 p.m. – 8:30 p.m.	Opening Reception (all are welcome)	Ania Terrace

SUNDAY, MARCH 7

6:30 a.m. – 5:30 p.m.	Registration	Arizona Ballroom Foyer
6:30 a.m. – 7:45 a.m.	Continental Breakfast	Arizona Salon 7
6:30 a.m. – 12:30 p.m.	Exhibit Hall Open	Arizona Salon 7
8:30 a.m. – 10:30 a.m.	Spouse/Guest Hospitality Suite	Signature Grill
7:45 a.m. – 5:00 p.m.	**FRANK B. WALSH SESSION [6.75 CME]** *Chair: Brian R. Younge, MD* *Neuropathologist: Caterina Giannini, MD, PhD* *Neuroradiologist: Patrick H. Luetmer, MD*	Arizona Salons 1–6
5:15 p.m. – 5:45 p.m.	Frank B. Walsh Committee Meeting	San Ignacio
5:30 p.m. – 6:30 p.m.	Resident/Student Program and Reception	Arizona Salons 10–12
6:30 p.m. – 8:00 p.m.	JNO Editorial Dinner	Signature Grill
Evening	Dinner on your own	

FRANK B. WALSH SESSION [6.75 HRS CME]

Session I

Moderators: Michael C. Brodsky, M.D., & Gabrielle R. Bonhomme, M.D.

Session II

Moderators: Ivy J. Dreizin, M.D., & Susan Pepin, M.D.

FRANK B. WALSH SESSION [6.75 HRS CME], continued

Session III
Moderators: Jacqueline A. Leavitt, M.D., & Brian R. Younge, M.D.

Session IV
Moderators: Marian Rubenfeld, M.D., Ph.D., & Jane W. Chan, M.D.

Something Wicked This Way Comes

Michael Vaphiades, Shelly Gupta, Cheryl Palmer
University of Alabama at Birmingham, Birmingham, Alabama, United States

HISTORY & EXAM:
A 63 year-old Caucasian woman with a 10 year history of hearing loss presented with a progressive decline in vision over the last 2 years. History was significant for previously treated tuberculosis. She denied tobacco, alcohol, or drug use. At the time of initial vision loss (2 years ago), she was found to have a swollen optic nerve OS, followed 2 weeks later with optic nerve swelling OD. Her vision continued to worsen and a fat suppressed cranial and orbital MRI scan was read as normal without evidence of optic nerve enhancement. However, on repeat MR imaging 9 months later, marked bilateral optic nerve enhancement was seen. A fat suppressed cranial and orbital MRI 3 months later, confirmed this finding.

The patient was treated with high does corticosteroids, without improvement. On laboratory evaluation, a CBC, Lyme, Cat Scratch, syphilis testing, toxoplasmosis, HIV, Brucellosis, Rocky Mountain spotted fever were all unremarkable. ANA 1:40. A lumbar puncture showed 10 WBC, glucose of 73 (40-70), protein of 34, and negative cryptococcal antibody, no AFB and no oligoclonal bands. Cytology was negative for malignancy, but showed small mature appearing lymphocytes. CT of the chest and gallium scans was negative. Erythrocyte sedimentation rate was 10 and CRP was 0.22 (0.0-4.9 mg/L). Bilateral temporal artery biopsies showed no evidence of arteritis.

On examination, vitals were normal. Visual acuity was light perception OD and no light perception OS. Color vision was absent OU, visual fields severely constricted OU, and pupils measured 7 mm OU with minimal reactivity OD, no reactivity OS, and an RAPD OS. Muscle balance testing revealed a 40 prism diopter XT, ductions full. No proptosis noted. Trigeminal and facial nerves were intact bilaterally. On slit lamp exam, anterior segment and intraocular pressures were normal. Posterior exam was normal except for optic nerve atrophy OU.

FINANCIAL DISCLOSURE: NONE

Something Wicked This Way Comes
Answer

FINAL DIAGNOSIS:
Bilateral infiltrative optic neuropathy secondary to Neurosarcoidosis

SUMMARY OF CASE INCLUDING PATHOLOGY:
Findings were concerning for sarcoidosis, bilateral optic nerve sheath meningiomas, or neuromyelitis optica (NMO). A trial of corticosteroids was repeated without improvement. Leber's, CRMP-5, ACE, and NMO testing were normal. Repeat MRI of the brain and orbits showed bilateral optic nerve thickening with abnormal enhancement throughout their course. Enhancement was also noted in bilateral third and fifth cranial nerves. There was bilateral enhancement of internal auditory canals suggestive of seventh and eighth cranial nerve involvement. The brain parenchyma and remaining leptomeninges demonstrated no abnormal enhancement. No mass lesion was present.

After review by the institution's tumor board, optic nerve biopsy for definitive diagnosis was performed. Biopsy of the left optic nerve showed numerous well-formed granulomas with abundant polyclonal chronic inflammation. Inflammation consisted of lymphocytes and plasma cells which appeared reactive. Scattered multinucleated giant cells were seen in the granulomas, but no necrosis was present. Gram, GMS, and AFB stains were all negative. Biopsy confirmed sarcoidosis and the patient was started on intravenous cyclophosphamide.

Sarcoidosis is an inflammatory condition of unknown etiology. Approximately 5% of patients with systemic sarcoidosis develop central nervous system involvement, (neurosarcoidosis) (1). Very few patients present with neurosarcoidosis without involvement of other organs. CNS sarcoid manifestations include headache, meningitis, stroke, seizure, transverse myelitis, peripheral neuropathy, pituitary or hypothalamus involvement, and myelopathy (2, 3). The most common presentation is cranial nerve abnormalities, with the facial nerve most commonly involved followed by the optic nerve (1, 4). Optic nerve sarcoidosis may be isolated to the nerve, chiasm, sheath, or a combination (5). Clinical presentation includes papilledema, papillitis, retrobulbar neuritis, mass, and optic atrophy. Optic nerve findings can mimic a meningioma, idiopathic orbital inflammation, leptomeningeal spread of tumor, optic neuritis, or optic glioma (5).

Without systemic findings, a diagnosis of neurosarcoidosis can prove challenging. MR imaging is sensitive yet nonspecific as in our case. Isolated optic nerve sarcoid is rare with few reported cases. During the few weeks that we had evaluated this patient, her symptoms had quickly worsened and a diagnosis needed to be made. Biopsy of the optic nerve is always undertaken with trepidation but proved the correct decision.

KEY WORDS: optic nerve, deafness, MRI, temporal artery biopsy, hearing loss

REFERENCES:
1. Kellinghaus S, Schilling M, Ludemann P. Neurosarcoidosis: Clinical experience and diagnostic pitfalls. Eur Neurol 51:84-88, 2004.
2. Ng KL, McDermott N, Romanowski CAJ, Jackson A. Neurosarcoidosis masquerading as glioma of the optic chiasm in a child. Postgrad Med J 71:265-268, 1995.
3. Stern BJ, Krumholz A, Johns C, et al. Sarcoidosis and its neurological manifestations. Arch Neurol 42:909-917, 1985.
4. Jennings JW, Rojiani AM, Brem SS, Murtagh FR. Necrotizing neurosarcoidosis masquerading as a left optic nerve meningioma: Case Report. Am J Neuroradiol 23:660-662, 2002.
5. Pollock JM, Greiner FG, Crowder JB, Crowder JW, et al. Neurosarcoidosis mimicking a malignant optic glioma. J Neuro-Ophthalmol 28:214-216.2008.

Painful Pseudo Optic Neuritis

John Guy, Norman Schatz
Bascom Palmer Eye Institute, Miami,Fl, United States

HISTORY & EXAM:
A 65 year-old gentleman complained of painful visual loss in his right eye for 8 days. Examination showed visual acuity was 20/300 OD and 20/25 OS. Visual fields showed a dense superior altitudinal defect in the right eye. Pupils showed a right afferent defect. Ophthalmoscopy revealed normal optic nerve heads. MRI revealed enhancement of the right optic nerve sheath and mild ethmoid sinusitis as well as a few hyperintense foci on the flair images of the brain. After 3 days of IV Solu-Medrol 1000mg per day the pain persisted requiring Percocet. The patient was discharged on Ceftin 500 mg BID and prednisone 60 mg/day for 11 days. Endoscopic ENT sinus surgery was normal.

Two weeks after admission visual acuity dropped to no light perception. There were no other changes in the examination. A repeat MRI continued to show enhancement of the right optic nerve sheath as well as now ill-defined enhancement at the orbital apex. The patient underwent extensive blood work, a lumbar puncture; CT scans of the chest abdomen and pelvis. These tests were normal. Pain control now required continuous infusions of dilaudid. On the day of surgery the patient was noted to have ptosis and ophthalmoplegia. This was not present the night before. The patient underwent exploration of the right orbit and a small biopsy of the optic nerve and sheath. Histopathology of the orbital biopsy failed to reveal any abnormality even on silver stain for mycotic organisms. The optic nerve biopsy revealed cystic spaces within the nerve.

FINANCIAL DISCLOSURE: NONE

Painful Pseudo Optic Neuritis
Answer

FINAL DIAGNOSIS:
Gram-negative optic neuritis

SUMMARY OF CASE INCLUDING PATHOLOGY:
PPD staining revealed the absence of axonal material in the cystic spaces. Myelin staining was normal showing no demyelination. The severe pain persisted. He was placed empirically on antifungal agents. Again there was no improvement in pain, visual loss or ophthalmoplegia. Another procedure was performed. A frontal craniotomy revealed an ill-defined infiltration of the clinoid tuberculum sella and dura. Frozen sections revealed polymorphonuclear leukocytes. Gram Stain revealed gram-negative organisms. The next day cultures grew Pseudomonas aeruginosa. After craniotomy he was started on meropenem 1 g IV q.8 hours. Within days the pain ceased. He no longer required narcotic pain control. Ophthalmoplegia improved, but vision remained no light perception. After 6 weeks lid movement and extraocular motility were normal. There was no pain however the patient developed lung abscess even while on meropenem.

The pain and visual loss suggested either an inflammatory, neoplastic or fungal process. At no time was the eye or orbit red and ophthalmoplegia developed only on the morning prior to surgery approximately 6 weeks after the onset of visual loss. The cultured pseudomonas aeruginosa was sensitive to Ceftin that we started on his first admission for IV Solu-Medrol, due to the presence of ethmoid sinusitis. However, the patient had stopped the Ceftin of his own volition after discharge. Whether it would have stopped the progression of visual loss is unclear. Pseudomonas aeruginosa infection involving the optic nerve in the absence of signs of orbital cellulitis is unusual. The optic nerve histopathologic findings of cystic spaces with normal myelination that were devoid of axonal material is consistent with optic nerve transection.

KEY WORDS: Optic Neuritis, Infectious

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Japanese Nodles

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HISTORY & EXAM:
An 11 year-old African American girl had diplopia, fever and abdominal pain. Four weeks prior, she presented with fever, vaginal ulcers and discharge and was given antibiotics. Two days later, she developed an oral ulcer. The ulcers were cultured for HSV and she was begun on acyclovir. HSV PCR was negative. Fevers continued and she developed abdominal pain, headache, chills, decreased appetite, and weakness of gait. CXR and KUB were negative. EBV and influenza testing were negative for acute infection. ESR and CRP were mildly elevated and later normalized. Nine days after symptom onset, she had persistent fever, abdominal pain, myalgias, nausea, vomiting, diarrhea, and dehydration. Vaginal and oral ulcers had resolved/improved. Laboratory testing revealed low WBC, low hemoglobin/hematocrit, normal platelets, high LDH, normal uric acid; HSV serology, gonococcal and chlamidial cultures, RPR, HIV, CMV PCRand culture, Trichomonas, bacterial vaginosis wet prep, ANCA, ANA, C3/C4, and Coomb's test were negative. Blood and urine cultures were negative x 3. Ophthalmology consultation revealed a normal examination (no uveitis).

She developed drowsiness, recurrent vaginal ulcers with discharge, chest pain with chest wall tenderness, and loose stools. MRI abdomen/pelvis was normal. Workup for inflammatory bowel disease was initiated. Video capsule endoscopy showed mild inflammation and ulcerations. Endoscopy showed esophagitis, duodenitis, chronic inactive gastritis, and focal active colitis in the cecum. PPD was negative. Peripheral smear showed non-specific red blood cells abnormalities with no signs of leukemia or lymphoma.

About 4 weeks after symptom onset, she developed intermittent binocular diplopia, dizziness, progressive somnolence, confusion, and moaning. She had 10-15 PD esotropia and partial right abduction deficit, with gaze-evoked horizontal nystagmus. Other cranial nerves were unremarkable. She developed gait ataxia but no dysmetria. She had normal strength, tone and DTRs. Brain MRI was postponed for several days (the video endoscopy capsule had not yet been passed). Head CT with contrast was normal.

FINANCIAL DISCLOSURE: NONE

Japanese Nodles
Answer

FINAL DIAGNOSIS:
Kikuchi-Fujimoto Disease with brainstem encephalitis

SUMMARY OF CASE INCLUDING PATHOLOGY:
Full body PET CT showed abnormal lymphadenopathy in multiple regions in the body (bilateral cervical, axillary, inguinal, pelvic, and porta hepatis), all measuring less than 1 cm. Differential diagnosis included infection and lymphoma.

Brain MRI with contrast showed T2-hyperintensity in bilateral hypothalami (left greater than right), periaqueductal region of the midbrain, pons surrounding the upper 4^{th} ventricle, and medulla oblongata (left greater than right). The right lower ventral pons was also affected, adjacent to the root entry zone of the right sixth nerve. All lesions were T1-hypointense and did not enhance. Differential diagnosis included Neuro-Behçet's, demyelinating disease, or vasculitis.

The final diagnosis was histiocytic necrotizing lymphadenitis (Kikuchi-Fujimoto disease). Her fevers and mental status improved spontaneously. She was treated with intravenous steroids; sixth nerve palsy and diplopia resolved, as did her other neurologic and systemic symptoms.

Her presentation was initially very suggestive of Neuro-Behçet's or Systemic Lupus Erythematosis. There was no uveitis or retinal vasculitis on eye examination. Gastrointestinal symptoms ensued and endoscopy was thought to be consistent with Crohn's disease. Occult malignancy was considered when WBC count and hemoglobin/hematocrit became low. Mental status deteriorated and signs localizing to the brainstem suggested Neuro-Behçet's versus ADEM. Cervical lymph node biopsy was necessary to make the correct diagnosis.

KEY WORDS: fever of unknown origin, diplopia, sixth nerve palsy, nystagmus, brainstem encephalitis

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Brainstem Botanicals

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HISTORY & EXAM:
A 46 year-old white gentleman c/o vertical double vision x 1 year. It was intermittent at first but became constant x 5 months. He had associated headaches. An optometrist had tried prisms without help. The patient also had some imbalance attributed to the diplopia. He had lost 30 lbs over the past 2 years. No fevers. PMH included hypertension and increased cholesterol on meds. POH of LASIK ou. Social history was significant for smoking 2 ppd x 25 years and heavy EtOH use on the weekends. Family history included brain cancer in his father.

Exam included blood pressure of 140/80. Vision was 20/20 ou. Color vision was 10/10 ou. External exam revealed upper lid retraction ou. Pupils were 5 mm ou with a poor light reaction. No RAPD. There was, however, a brisk near response ou. He could not look up and had downbeat nystagmus, especially in right, left, and downgaze. He assumed a 15 degree chin-up position. Convergence retraction nystagmus was noted. A mild left hypertropia was measured in primary gaze. Mild gait ataxia was documented. The rest of his exam was normal including pink, sharp optic discs ou.

The constellation of upper lid retraction (Collier's sign), upgaze palsy, convergence retraction nystagmus, light-near dissociation, and skew deviation led to a diagnosis of dorsal midbrain syndrome. MRI of brain was ordered.

FINANCIAL DISCLOSURE: NONE

Brainstem Botanicals
Answer

FINAL DIAGNOSIS
Germinoma with extensive lymphocytic infiltration

SUMMARY OF CASE INCLUDING PATHOLOGY:
MRI brain was read as bilateral abnormalities involving the paramedian nucleus of the thalamus and the tectal area of midbrain and pons. Atrophy of the mammillary bodies was noted. The ddx at this point included thiamine deficiency, glioma, and MS. Thiamine supplementation helped modestly. CSF exam revealed: WBC 5 (87% lymphs), RBC 1, Protein 46, Glucose 65, No malignant cells, VDRL nonreactive, IgG index 0.76 (nl 0.28-0.66), and oligoclonal bands present. Neurosurgery felt neoplasm was unlikely. The patient was treated with IV ceftriaxone x 2 wks which appeared to help symptoms. Doxycycline po was then begun. An extensive work-up for viral, bacterial, fungal, inflammatory, and paraneoplastic meningoencephalitis was carried out and was negative. Intestinal biopsy was negative for Whipple's disease. Trials of prednisone and fluconazole were used without improvement. The patient's symptoms remained stable.

The MRI was repeated 10 months later and showed enhancing lesion of medial thalami, periaqueductal gray matter of the tectum, and extends into the pons anterior to the 4th ventricle producing moderate to severe obstructive hydrocephalus. VP shunt and brain biopsy was then carried out in the "pineal area" but showed only nonspecific inflammation. Repeat lumbar punctures disclosed increasing lymphocytes and protein, but no malignant cells.

MRI was again repeated 6 months later. It was read as shunt tube placement with return of ventricular system to normal. The enhancement involving the pontine brainstem is stable but there has been significant progression in size of lesion in the midbrain and peduncles. Brain biopsy was repeated and finally disclosed a germinoma with extensive lymphocytic infiltration. Immunohistochemically, the tumor was negative for PLAP and occasionally positive for OCT4 which confirmed a germinoma.

The patient was treated with radiation. 7 months later, exam showed 20/25 vision out and additional bilateral INO and downgaze palsy.

MRI lesions did not look like tumor, therefore brain biopsy was delayed. Multiple lumbar punctures failed to disclose malignant cells, which propagated the false assumption of chronic encephalitis.

The subjective improvement of patient on antibiotics steered us towards Whipple's disease even though intestinal biopsy proved negative.

The finding of oligoclonal bands/high IgG index also swayed us towards an immunological problem (MS) or infection (encephalitis) even though these findings can occur with a neoplasm.

KEY WORDS: germinoma, dorsal midbrain syndrome, diplopia, lid retraction

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Could be Just Another Case of MS?

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HISTORY & EXAM:
The patient is a 48 year-old white female who complains of decreased vision in both eyes for the past one year. She also complains of significant pain in both eyes that worsens with eye movements over the last month. The patient has noted worsening, constant headaches over the same period of time but denies nausea, vomiting, or diplopia. When asked, she does admit to her vision "blacking out" for a few seconds in both eyes when she moves from supine to standing.

Past medical history includes hypertension on valsartan, acid reflux, headaches, anemia, and bladder problems. The patient underwent hysterectomy in 1996. There is a family history of leukemia in her father. The patient denies any tobacco, alcohol, or drug use.

On examination, blood pressure is 160/88. Corrected visual acuity is 20/20 in each eye. Color vision is 11/11 in each eye using Ishihara plates. External exam reveals mild proptosis bilaterally with Hertel measurements of 18 OU on a base of 93. She also has xanthelasmae of lower lids OU and upper lid OS. Motility is limited mildly in right, left, and upgaze OU (-1) without diplopia. Confrontational visual fields are full OU. Pupils are 6 mm OU and react briskly to light OU. No RAPD. Slit lamp examination of anterior segment is unremarkable. Tonometry is 18 OU. Dilated fundus examination reveals grade 2 disc edema OU without obscuration of blood vessels. There is mild obscuration of nerve fiber layer at the nasal disc margin OU. The discs are pink. Vessels, maculae, and periphery are within normal limits.

A diagnostic procedure was then performed.

FINANCIAL DISCLOSURE: NONE

Could be Just Another Case of MS?
Answer

FINAL DIAGNOSIS:
Ormond's Disease or multifocal fibrosclerosis

SUMMARY OF CASE INCLUDING PATHOLOGY:
An MRI of brain without and with contrast was performed. The brain revealed no mass. She had some periventricular white matter disease. There was chronic appearing sphenoid sinus disease. Of interest, bilateral orbits had intraconal soft tissue signal. There was low signal on T1 weighted imaging and moderate signal on T2. It did enhance and was visible on post-gadolinium fat sat images.

The differential diagnosis included sarcoid, Wegener's, thyroid eye disease, orbital pseudotumor, TB, lymphoma, neurofibromas, and meningiomas. Lab work-up included normal values for ACE, ANA, c-ANCA, p-ANCA, T4, and TSH. Sed rate/CRP were elevated at 44 and 59.2 respectively. Lysozyme was high at 25 (nl 9-17), and RF was elevated at 33 (nl 0-14). Lumbar puncture was performed. Opening pressure was normal at 14 cm H2O. All CSF studies were unremarkable.

An anterior orbitotomy was then performed OS to biopsy the abnormal intraconal tissue. The biopsy specimen was almost completely sclerotic (dense fibrous connective tissue) with only a sparse, chronic inflammatory infiltrate, mostly lymphocytes. CD68 and CD45 markers were used to identify macrophages and lymphocytes, respectively.

Interestingly, the patient had undergone a retroperitoneal needle biopsy earlier in the year which had also shown fibrosis with a polymorphous inflammatory cell infiltrate. She had undergone stenting from kidneys to bladder due to the retroperitoneal fibrosis. (Withheld information)

The features were most consistent with a bilateral, idiopathic, sclerosing orbital pseudotumor with history of retroperitoneal fibrosis. The diagnosis was Ormond's Disease or multifocal fibrosclerosis. Prednisone 80 mg daily was started with some subjective improvement. Exam has been stable. Rheumatology has been consulted to begin a steroid-sparing agent.

Ormond's disease or multifocal fibrosclerosis is a rare, idiopathic disorder which can be characterized by fibrous lesions at multiple sites, including retroperitoneal fibrosis, Reidel's thyroiditis, sclerosing cholangitis, mediastinal fibrosis, as well as orbital involvement.

The dilemma in this case occurred after seeing the abnormal MRI orbital findings. The question arose whether to biopsy the abnormal orbital tissue or treat first with prednisone. The prednisone treatment may resolve the orbital findings thereby saving the patient an invasive procedure. I think the correct protocol was carried out here. Getting the biopsy documented exactly what we were treating. This is paramount since the patient may need chronic steroids or a steroid-sparing agent.

KEY WORDS: Proptosis, Ocular pain, Disc edema, Magnetic resonance imaging

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A Bitter-Sweet Diagnosis

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HISTORY & EXAM:
A 49 year-old, healthy male presented to the retina service with a foreign body sensation, flashes, and floaters OS. His vision was 20/20 OD and 20/25 OS with anterior and vitreous cell OS. The left optic disc was swollen and hyperemic and fluorescein angiography demonstrated both disc leakage and perifoveal vasculitis. The patient had an extensive negative work-up for systemic disease. He was treated with prednisone and topical prednisolone. Two months later the patient's ocular inflammation had resolved, but the left disc remained swollen. He was then referred for a neuro-ophthalmic evaluation. Vision was then 20/20 OU with intact color vision, but he had a left relative afferent papillary defect (APD) and an enlarged blind spot OS on visual field testing. An MRI showed scattered T2 hyperintensities in the subcortical white matter.

His prednisone taper was continued but his intraocular inflammation recurred and he was started on mycophenolate mofetil. Two months later he had a recurrence of symptoms OU, with 20/20 vision OD and 20/25 vision OS, no discernible APD, and full visual fields. Examination revealed panuveitis in the right eye along with new bilateral optic disc swelling. Repeat MRI demonstrated slightly increased signal intensity in the right optic nerve (Figure 2) and stable white matter subcortical lesions. Over the course of the next 8 months he had several episodes of recurrent ocular inflammation OU as his medications were adjusted. A lumbar puncture demonstrated an opening pressure of 22cm H20 and an elevated protein of 110 mg/dl. Two weeks later he presented to the emergency ward with floaters OU, arthralgias, fever, chills, and a rash.

FINANCIAL DISCLOSURE: NONE

A Bitter-Sweet Diagnosis
Answer

FINAL DIAGNOSIS:
Papillitis associated with neuro-Sweet's syndrome

SUMMARY OF CASE INCLUDING PATHOLOGY:
The patient's temperature was 102°F, and his white blood cell count was 17 th/cmm with 85% neutrophils. A repeat lumbar puncture showed elevated protein of 72 mg/dl. A repeat MRI was stable. Eye examination revealed bilateral panuveitis (without hypopion) and swollen optic nerves OU. The patient had a nontender pustular rash on both arms and hands, but no genital or oral ulcers. A skin biopsy showed a neutrophilic and granulomatous inflammation in the reticular dermis without vasculitis but with papillary dermal edema. Immunohistochemical stains for bacteria and fungi were negative. These findings were consistent with Sweet's syndrome.

Sweet's syndrome is characterized by bilateral, usually tender, plaques on the limbs and is often accompanied by fever, neutrophilic leukocytosis, and malaise (1). It has been associated with conjunctivitis, episcleritis, and iritis, but posterior and optic nerve inflammation such as with our patient is unusual (2, 3). Involvement of the central nervous system has been associated with Sweet's syndrome in the rare variant "neuro-Sweet's" and can be accompanied by nonspecific signal abnormalities on MRI (4).

Our patient was treated with methylprednisolone after an infectious etiology was ruled out. His symptoms improved and he was discharged on prednisone. Sweet's syndrome can be associated with rheumatologic disease and underlying malignancies (3). Our patient had a negative cancer screen including colonoscopy as well as normal chest, abdominal, and pelvic CT. Further rheumatological work-up revealed no new abnormalities. His ocular inflammation recurred while on prednisone and he then began infliximab. At last examination his vision was 20/20 OD and 20/40 OS with macular edema OS and mild disc margin blurring OU, but no intraocular inflammation.

This patient's optic nerve edema, which persisted despite resolution of uveitis, may be related to neuro-Sweet's syndrome. Another consideration was neuro-Behçet's, which can have a similar clinical presentation to neuro-Sweet's (2) and may even coexist (5). All patients with Sweet's syndrome must be evaluated for underlying malignancies or rheumatological disease, which may yet emerge in our patient with time and further work-up.

KEY WORDS: Disc edema, Autoimmune disease, vitritis, afferent pupillary defect

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Childish Nerve

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HISTORY & EXAM:
A 75 year-old man had sudden onset of loss of vision in his right eye on September 1st 2008. He presented to an outside facility and was noted to have a count fingers vision and a swollen right optic nerve with disc hemorrhages. He was diagnosed with a NAION. On subsequent office visits at the outside facility his vision deteriorated to NLP vision in the right eye.

The patient presented to our institute on January 21st 2009. He denied any headache, muscle aches, jaw claudication, or loss of appetite. On examination the vision in the right eye was NLP and the left eye was 20/25 with correction. There was a right afferent pupillary defect. The right optic nerve appeared swollen superiorly with pallor temporally and telangectatic vessels nasally. The left optic nerve appeared normal with a full field. Photos, FA and OCT were performed.

Laboratory testing showed an ESR of 38 and a CRP of 1.72. Oral steroids were started and a temporal artery biopsy was performed which was negative for arteritis. An MRI of the orbits was obtained which showed enlargement and enhancement of the optic nerve extending from the intraorbital portion of the optic nerve to the pre-chiasmal portion of the optic nerve. More laboratory testing was performed as well as a diagnostic procedure.

FINANCIAL DISCLOSURE: NONE

Childish Nerve
Answer

FINAL DIAGNOSIS:
Acute loss of vision due to pilocytic astrocytoma of the optic nerve with progressive loss of vision

SUMMARY OF CASE INCLUDING PATHOLOGY:
After obtaining the MRI, the patient underwent a series of laboratory studies. The patient deferred a spinal tap. The rest of the blood tests including a repeat ESR and CRP, ANCA, NMO-IgG, ANA, ACE, RPR, and double stranded DNA were negative.

Serial MRI's were obtained which showed progression of the nerve enhancement and involvement of the chiasm. Due to changes in the visual field in the left eye, he then agreed to proceed with a biopsy.
A biopsy was performed and intraoperative photos were obtained. Identified was an abnormally enlarged right optic nerve and chiasm with mass effect on the ipsilateral carotid artery. The biopsy revealed Rosenthal fibers and fibrillary cells which were consistent with the diagnosis of optic nerve pilocytic astrocytoma.

This man initially presented with an AION-like picture with sudden onset of loss of vision. However, there was progressive loss of vision to no light perception and the swollen disc appearance months later required further investigation. Patients with no light perception vision should have complete evaluation for inflammatory, compressive or infiltrative causes.

KEY WORDS: pilocytic astrocytoma, optic nerve, adult, AION

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I am Allergic to what…

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HISTORY & EXAM:
A 57 year-old gentleman presented with stepwise vision loss in one eye over 24 hours. He woke up from a nap with decreased vision in the temporal visual field in the right eye, which progressed to "graying out of his entire visual field" within a few hours; the next morning, the vision in the right eye was completely lost. He had no ocular pain, headache, jaw claudication or generalized malaise. He was recovering from a perforated gastric ulcer, for which he was treated conservatively two weeks prior to the vision loss.

His past medical history included chronic obstructive lung disease, for which he was treated with Mometasone, Fluticasone-Salmeterol, Montelukast, Tiotropium and low dose Prednisone (discontinued for 2 weeks due to gastric ulcer). He was also taking Omeprazole for gastric ulcer. He smoked until 2 years prior.

His exam revealed a well nourished and pleasant man with normal vital signs. The systemic exam was remarkable for mild bibasilar crackles in both bases with normal lung expansion. The ocular exam revealed visual acuity of NLP in the right eye and 20/20 in the left eye; there was >3.0 log unit RAPD on the right. Ocular motility was full. Intraocular pressure was 14 mmHg in the right eye and 13 mmHg in the left eye. Slit-lamp examination was normal. He had pallid edema of the right optic nerve head with a patch of retinal whitening temporal to the optic disc. The left optic disc appeared normal and had a small cup.

The lab studies revealed ESR 35 mm/hr, CRP 18.4 mg/dl, white blood cell 22400/mm^3, red blood cell 4.66 × 10^6/mm^3, hemoglobin 14.4 g/dl, hematocrit 44%, platelet 184000/mm^3. Chemistry panel and anti-neutrophil cytoplasmic antibody (ANCA) were within normal limits. MRI showed no enhancement of the optic nerve.

FINANCIAL DISCLOSURE: NONE

I am Allergic to what…
Answer

FINAL DIAGNOSIS:
Churg-Strauss syndrome

SUMMARY OF CASE INCLUDING PATHOLOGY:
Temporal artery biopsy was performed, after fluorescein retinal angiography showed patchy choroidal hypoperfusion consistent with arteritic anterior ischemic optic neuropathy (AION). The pathology of the temporal artery biopsy revealed inflammatory and granulomatous infiltrate in the perivascular connective tissue consisting of a mixture of lymphocytes, plasma cells and abundant eosinophils. Systemic hypereosinophilia (21%) was noticed subsequently. Transbronchial biopsy of the lung showed prominent number of eosinophils in the infiltrating area consistent with eosinophilic pneumonitis. The diagnosis of Churg-Strauss syndrome was made based on the constellation of eosinophilia, asthma, pulmonary infiltrates and systemic vasculitis.

The patient was given high dose corticosteroids as well as adjunctive immunosuppression therapy with Methotrexate. His vision stabilized at light perception in the right eye and 20/20 in the left eye. Pulmonary infiltrate as well as coughing completely resolved.

Churg-Strauss syndrome (CSS) is a systemic vasculitic syndrome characterized by asthma, eosinophilia, sinus involvement, pulmonary infiltrate, neuropathy and extravascular esinophilia (Masi 1990). Pathological features include esinophilic vasculitis and extravascular granulomas (Lie 1990). There have been few reports of CSS with vision loss secondary to non-giant cell granulomatous vasculitis in temporal artery. Weinstein et al. (1983) reported a 61 year old man with sudden loss of vision in one eye, and recurrent amaurosis fugax with retinal infarcts in the other eye. Alberts et al. (1994) described a 76 year old lady with vision loss that improved with steroid therapy. Conn (1982) reported a case of 49 year old lady with vision loss associated with primary biliary cirrhosis and polychondritis. The presentation of our patient was different from the other cases in the absence of systemic symptoms, such as fever, weight loss, malaise, or other major organ involvements, the dramatic changes that are more likely to render aggressive investigation.

The patient presented with arteritic AION with atypical features. The association of arteritic AION with seemingly common chronic lung disease prompted identification of a single unifying pathology, rendered appropriate therapy that led to resolution of the systemic symptoms and prevented further deterioration of the vision. It is imperative to search for systemic vasculitides in a young patient who presents with arteritic AION, even when there is paucity of systemic symptoms.

KEY WORDS: Vision loss, Disc edema, Ischemic optic neuropathy, Vasculitides, Temporal artery biopsy

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What's in a Name?

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HISTORY & EXAM:
A 36 year-old woman presented with headaches, double vision worse in left gaze, and numbness of the left forehead and cheek. Visual acuity, color vision and computerized static perimetry were normal. There was 1mm of anisocoria (left larger than right) with brisk reaction OU and no ptosis. She had an 8 diopter esotropia in primary gaze that increased in left gaze. MRI of the orbits revealed a T1 isointense, T2 isointense, homogenously enhancing extra-axial mass in the left middle cranial fossa involving the left cavernous sinus. Partial resection of the mass was performed. Pathology was felt to be nonspecific and non-diagnostic. Post-operative MRI of the brain revealed additional small, meningeal masses in the right posterior fossa, left frontal region and left occipital region. Chest CT and spinal fluid analysis were unrevealing. She was evaluated by the pulmonary and neuro-oncology services. A second biopsy was recommended. However, the patient's symptoms had resolved following the surgery and post-operative steroid taper, so she declined.

Two years later, she presented with left eye blurriness and pain in the left cheek and chin developing over 3 months. MRI of the brain demonstrated enlargement of all the meningeal masses and segmental dural enhancement. MRI of the spine did not reveal additional abnormalities. Repeat partial resection of the left cavernous sinus mass was performed. Post operatively visual acuity was 20/20 OD, CF at 4' OS with impaired color perception and central scotoma OS. There was a left afferent pupillary defect without anisocoria. Ductions were full OD, with limited supraduction (75%) and adduction (90%) OS. Abduction, infraduction and intorsion were preserved OS. There was a complete left ptosis. There was decreased sensation in V1, V2, and V3 on the left.

FINANCIAL DISCLOSURE: NONE

What's in a Name?
Answer

FINAL DIAGNOSIS:
Multifocal inflammatory myofibroblastic tumor of the central nervous system

SUMMARY OF CASE INCLUDING PATHOLOGY:
This is the case of a middle aged woman with enlarging intra-cranial masses with possible steroid responsiveness presenting as cranial neuropathies. Differential diagnosis based on imaging characteristics of the multiple intra-dural, extra-axial masses included lymphoma, sarcoid, meningioma and meningeal metastatic disease.

Microscopic examination of both biopsy specimens demonstrated dura (solid black arrows) with an attached mass of fibrosis and mixed inflammatory infiltrates composed of mature T and B lymphocytes (solid red arrow), macrophages (open red arrows) and plasma cells (open black arrows) with entrapped nerve roots (yellow arrows). There were no granulomas. Stains for micro-organisms were negative. Flow cytometry did not reveal a monoclonal population. This is consistent with inflammatory myofibroblastic tumor (IMT) of the central nervous system.

IMT is characterized by mature inflammation without evidence of clonality and is a pathological umbrella term that encompasses diverse presentations of space occupying inflammatory lesions including inflammatory pseudotumor and plasma-cell granuloma regardless of location. Multiple lesions are rare. An alternative diagnosis is a rare nodular presentation of idiopathic hypertrophic pachymeningitis. The classification of rare entities including mass occupying pseudotumors and meningeal inflammation such as hypertrophic pachymeningitis (IHP) as variations along a spectrum of idiopathic inflammation rather than as distinct processes is important for understanding the natural history and response to therapy.

Treatment response to steroids, steroid sparing immunomodulatory agents, radiation and surgery has been documented for both IMT and IHP. Following her second biopsy, our patient was treated with a prolonged course of steroids. Steroids were weaned following initiation of mycophenelate. Her symptoms, clinical exam and repeat imaging have improved.

The initial work up led to resection of a cavernous sinus mass with a non-diagnostic biopsy. This distracted from consideration of primary or secondary inflammatory etiologies with steroid responsiveness. The subsequent presentation of multiple mass lesions is a particularly rare manifestation of a spectrum of idiopathic inflammatory disorders of the CNS.

KEY WORDS: Intracranial tumors, Inflammatory pseudotumor, Idiopathic hypertrophic pachymeningitis

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Let's Put It Under High Mag

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HISTORY & EXAM:
A 56 year-old male presented with acute onset of droopy left eyelid and double vision associated with headaches. He otherwise felt well. He had known type II diabetes for 5 years and was followed for hyperlipidemia. Four years earlier he had lower extremity pain and numbness that was attributed to diabetes and resolved with medications. Six months prior to presentation he was diagnosed with a Bell's palsy on the right side that spontaneously resolved. One month before his current symptoms he had left facial weakness that improved with acyclovir and corticosteroids.

Visual acuity was 20/20 in each eye with normal color vision. The right pupil was 2 mm and briskly reactive to light. The left pupil was 7 mm and fixed. There was complete left ptosis with adduction, elevation and depression deficits. Left superior oblique and lateral rectus function was intact. Right eye motility was normal. Fundus examination was normal bilaterally. He was strong except for weak finger extension. Cold sensation was decreased below the elbow and thighs. Vibration sensation was markedly impaired on the toes. Reflexes everywhere were normal except ankle reflexes were depressed bilaterally.

An MRI/ MRA of the brain were normal. A cerebral angiogram was normal. MRI of the spine showed intense enhancement of the cauda equina nerve roots from L2-L5. A CAT scan of the chest, abdomen and pelvis and a whole body PET scan were negative for malignancy and sarcoidosis. The CSF protein was elevated (148 mg/dl, normal: 15-55 mg/dl) with no cells. Laboratory tests including CBC, ESR, RPR, ANCA, ANA, Lyme antibodies, Hepatitis B, Hepatitis C and HIV were negative. Serum cryoglobulins were undetectable. Electromyography showed markedly reduced and absent sensory amplitudes in the upper and lower limbs. Motor responses were absent from the feet. Motor velocities were subnormal in the arm and leg. Distal motor latencies were markedly prolonged.

A diagnostic test was performed.

FINANCIAL DISCLOSURE: NONE

Let's Put It Under High Mag
Answer

FINAL DIAGNOSIS:
Anti-MAG IgM antibody-mediated neuropathy

SUMMARY OF CASE INCLUDING PATHOLOGY:
Serum protein electrophoresis showed a monoclonal IgM spike (470 mg/dl, normal: 40-270). An ELISA test detected a high-titer of IgM myelin associated glycoprotein (MAG) antibody (16,525 [units], normal: < 1000 TU) suggesting anti-MAG antibody mediated demyelination as a cause of peripheral neuropathy in our patient. Urine protein electrophoresis was negative for Bence-Jones protein. The patient was initially treated with prednisone and diplopia improved. Limb weakness, numbness and imbalance progressed. Prednisone was tapered and Rituximab was initiated. There was a complete resolution of the third nerve palsy at 3 month follow-up except for a 1 mm of anisocoria and a substantial improvement of gait, improved sensations and strength of limbs following Rituximab therapy.

Chronic acquired demyelinating neuropathies are uncommon, compared to axonal neuropathies. The most frequently encountered is chronic inflammatory demyelinating polyneuropathy (CIDP), an idiopathic autoimmune disorder that typically causes more weakness and loss of reflexes than axonal neuropathies, and a greater degree of nerve conduction slowing. Facial nerve involvement is not uncommon with CIDP, but involvement of other cranial nerves is rare (1). The antibodies responsible for demyelination in most patients with CIDP are unknown. Serum studies that reveal presence of paraprotein most commonly IgM, with no associated hematological disorder is found in 10% of patients and is referred to as monoclonal gammopathy of undetermined significance (MGUS) (2). The IgM antibodies may be directed against MAG and sulfoglucuronyl paragloboside (SGPG), which are elements of periaxonal myelin in peripheral nerves. The interaction leads to segmental demyelination. Neuropathy associated with anti-MAG antibodies differs from classical CIDP in its clinical, electrophysiological and pathological features (3). Patients with anti-MAG CIDP are older, the clinical course is more slowly progressive without relapses and remissions, and sensory neuropathy is more prominent. Anti-MAG neuropathy tends to be poorly responsive to immunomodulatory therapies. Cranial nerve involvement is extremely rare in anti-MAG neuropathy. A distinctive electrophysiologic feature of anti-MAG neuropathy is markedly increased distal latencies indicating, slowed motor conduction along more proximal long nerve segments.

Our literature review revealed 2 patients with facial palsy with anti-MAG neuropathy (3, 4) and one patient who had bilateral oculomotor nerve palsies, anti-MAG neuropathy and B-cell lymphoma (5). To the best of our knowledge complete pupil-involving third nerve palsy has not been described previously as a manifestation of “benign” anti-MAG associated peripheral neuropathy.

In conclusion anti-MAG neuropathy is rare, but must be considered when evaluating an undiagnosed cranial neuropathy, especially if there is clinical evidence of a more generalized peripheral nerve disorder.

Our patient presented with an acute-onset of pupil-involving third nerve palsy, suggesting intracranial compression by a posterior communicating artery aneurysm. With negative MRI, of the brain and cerebral angiogram, the initial impression was that the cranial neuropathies and distal sensory loss were the consequence of diabetes. MRI enhancement of the cauda equina suggested inflammatory etiologies such as sarcoidosis, and carcinomatous meningitis but the remainder of the work up to establish these etiologies was negative. The detection of IgM paraprotein led to further work-up to rule out myeloma and other lymphoproliferative disorders. Electrodiagnostic testing indicated an acquired demyelinating neuropathy, possibly anti-MAG. Detection of high titer of anti-MAG antibody in the absence of a systemic disorder secured the diagnosis.

KEY WORDS: oculomotor nerve, Magnetic resonance imaging

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Under Pressure

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HISTORY & EXAM:
An 81 year-old Hispanic female with a past medical history of diabetes, hypertension and hypercholesterolemia was referred by an outside ophthalmologist for evaluation of “disc edema.” The patient reports longstanding poor vision of an unclear length of time. She was treated with topical pressure-lowering drops for several years for low-tension glaucoma. Despite well-controlled pressures, she continued to have worsening visual acuity and visual fields and self-discontinued the eye drops. Her past ocular history is otherwise significant for bilateral cataract extractions with intraocular lens implants.

On exam, best-corrected visual acuity is 20/300 OD, 20/70 OS. Color vision is 2/12 OD, 1/12 OS Ishihara color plates. Pupils are irregular with physiologic anisocoria, reactive without rAPD. Brightness sense is decreased in the right eye. Anterior segment exam is unremarkable except for posterior chamber intraocular lenses; intraocular pressure is 17 mm Hg OD, 13 mm Hg OS. Ocular motility is full. Automated 30-2 Humphrey visual fields show peripheral constriction OD, with a central defect OS. Fundus exam reveals a hyperemic disc with optociliary shunt vessels OD and diffuse pallor OS. MRI of the brain and orbits revealed no mass lesion.

A diagnostic procedure was performed.

FINANCIAL DISCLOSURE: NONE

Under Pressure
Answer

FINAL DIAGNOSIS:
Paget's disease of bone with bilateral optic canal stenosis and compressive optic neuropathies

SUMMARY OF CASE INCLUDING PATHOLOGY:
She was diagnosed with bilateral optic neuropathy (OD>OS). Her acuity and dyschromatopsia were not consistent with glaucoma. Given the history of likely slowly progressive or longstanding vision loss and the appearance of her nerves with pallor OS and optociliary shunt vessels OD, she was initially thought to have a Foster Kennedy syndrome. She underwent MRI of the brain and orbits with gadolinium enhancement looking for a meningioma. The MRI revealed calvarial thickening and heterogeneous bone marrow signal and enhancement representing Paget's disease vs. hyperostosis frontalis interna. No meningioma or other mass lesion was identified. She underwent further imaging with a CT of the orbits with and without contrast, which was diagnostic of Paget's disease of bone and additionally showed marked narrowing of the optic canals bilaterally.

Further endocrinologic work-up revealed normal serum alkaline phosphatase, calcium and phosphate levels and no other skeletal symptoms or abnormalities. Her Paget's disease was determined to be indolent and not active. Her vision remained stable and so no further intervention was made.

The patient's clinical presentation was not consistent with low-tension glaucoma. Differential diagnosis included a mass such as a meningioma causing a Foster Kennedy syndrome and bilateral ischemic optic neuropathies causing a pseudo-Foster Kennedy syndrome. The patient was a poor historian and did not have a clear time course of the vision loss. She had no other symptoms of Paget's disease. Canal narrowing was not reported on the MRI but was seen on the CT scan.

KEY WORDS: Paget's disease of bone, Compressive optic neuropathy, Low-tension glaucoma

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Dodge Dusted

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HISTORY & EXAM:
59 year-old man with refractory acute myelogenous leukemia (AML) was triaged into clinic with red eyes. His eye irritation began when dust blew in his eyes after starting his vintage car a week earlier. He also developed sinusitis congestion and complained of clear nasal discharge. A subconjunctival hemorrhage OD had been diagnosed 5 days prior to his clinic presentation. The redness had spread to the left eye and the eyes became very swollen. He had 8-9/10 pain and could not open the right lid. His vision had dropped 20/70 OD and 20/80 OS. Visual fields were full to confrontation. His pupils were reactive and without a relative afferent defect. He had significantly reduced extraocular movement (EOM) in all directions OD and mildly limited EOM OS. There was moderate resistance to retropulsion and proptosis OD > OS. Cranial nerve V was intact bilaterally. The conjunctiva was hemorrhagic and chemotic OD > OS. Anterior segment, intraocular pressure and dilated fundus exam were normal. The patient was alert and oriented.

He was admitted for further evaluation. Magnetic resonance imaging showed bilateral orbital enhancement with mild tenting of the right globe. There was moderate paranasal sinus disease and intracranial dural enhancement along the floor of the anterior cranial fossa on the right.

Biopsy was scheduled but platelets were <10. Platelets were transfused. Less than 24 hours later, he was CF OD, and bare HM OS, with rapidly progressive proptosis and bilateral complete ptosis. Tonopen intraocular pressure was 15 OD and 50 OS. A biopsy was performed.

FINANCIAL DISCLOSURE: NONE

Dodge Dusted
Answer

FINAL DIAGNOSIS:
Microsporidia

SUMMARY OF CASE INCLUDING PATHOLOGY:
59 year-old with acute myelogenous leukemia and rapidly progressive bilateral orbital process. Surgical findings were concerning for invasive fungal infection and based on the constellation of findings voriconazole as well as broad spectrum antibiotics were started. Nasopharyngoscopy and rigid rhinoscopy showed no masses, drainage, or areas of necrosis; there was a slight moth-eaten appearance in the anterior portion of the left inferior turbinate. Within 24 hours of starting the intravenous medication, his vision returned, proptosis, and EOM improved.

Surgical pathology returned with diagnosis of ulcerated and necrotizing conjunctivitis, negative for viral cytopathic effect, negative for leukemic blasts. A few degenerated tiny forms suggestive of yeast (e.g.torulopsis) were present in one small focus of exudate on both PAS and GMS stains; however, this is not definitive. Acid fast bacilli stain is negative for organisms. Tissue gram stain (phenol green) is negative. Immunohistochemical studies for HSV-1, HSV-2, and CMV are negative.

Patient's visual status improved with return of vision and resolution of all orbital signs but after finishing his 7 day empiric course of voriconazole, his eye pain returned. Repeat MRI showed improved orbital findings but new dural enhancement. Further investigation was requested and 22 days after surgical biopsy, electron microscopy showed structures consistent with microsporidia.

Post-operative day 23 he was re-admitted with fever, pneumonia and mental status changes. Broad spectrum antibiotics were started as well as Albendazole and Fumidil B eye drops for ocular microsporidiosis. Post-operative day 31 he was restarted on voriconazole and then discharged home the following day. He developed bilateral ear pain and hearing loss. Post-operative day 44, he developed severe mental status changes and was re-admitted. Albendazole was restarted as were broad spectrum antibiotics. Patient became minimally responsive and expired post-operative day 49.

The dilemma of the clinical presentation included the initial diagnosis of subconjunctival hemorrhage, very low platelets limiting surgical intervention, and the decision to stop the empiric voriconazole after 7 days. Ultimately the patient's immunocompromised state led to his demise from this disseminated parasite.

To our knowledge, after extensive review of the literature, this is the first reported case of orbital Microsporidia. Microsporidia are spore forming intracellular parasites known to cause keratoconjunctivitis in immunocompromised hosts and stromal keratitis in immunocompetent hosts.1-3 Ocular infection is thought to arise from direct inoculation of the conjunctiva.1 A patient with AML and microsporidial endophthalmitis has been reported.4 There is one case report of presumed intracranial Microsporidia.5 Our AML related case had bilateral severe orbital involvement and intracranial involvement with biopsy proven Microsporidia. After initial favorable response to medical treatment, our patient developed progressive neurological compromise and ultimately died. Medical treatment for microsporidia is challenging as there may be species specific response to topical and systemic agents.1

KEY WORDS: Orbit, Complications of cancer, Infection, Proptosis, Vision Loss

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Stuffy Nose

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HISTORY & EXAM:
A 36 year-old AAF presented with a 6 month history of progressive visual loss OD and bilateral proptosis. Her past medical history was significant only for chronic rhinosinusitis with nasal polyps. Sinus surgery had been recommended to her many years previously but she declined. Her review of systems was positive for severe headache, anosmia, bloody nose, and inability to breathe through her nose for years. Her medical history was negative and she was not on medications. She underwent neuro-imaging that prompted multiple consultations. Ophthalmological examination demonstrated CF 2' OD and 20/20 OS. She had a dense APD, bilateral proptosis, bilateral elevation and abduction deficits, and corresponding optic nerve pallor OD. Perimetry revealed only a nasal crescent of field remaining OD and a normal field OS. Nasal polyps were evident on anterior rhinoscopy.

FINANCIAL DISCLOSURE: NONE

Stuffy Nose
Answer

FINAL DIAGNOSIS:
Chronic sinusitis and inflammatory pseudopolyp

SUMMARY OF CASE INCLUDING PATHOLOGY:
CT and MRI showed complete opacification with expansion of the paranasal sinuses filled with a high-density material with extensive destruction of the skull base and sphenoid sinus. The optic canal on the right was completed eroded with extension of the lesion into the apex. Expansion of the ethmoid air cells with erosion of the medial walls of the maxillary sinuses, orbital walls, clivus, and pterygoid plates was also noted. The process extended into the inferotemporal fossa, pterygoid plate region, posterior nasopharynx and anterior, middle, and posterior cranial fossae with evidence of mass effect on the brainstem. The patient underwent image-guided endoscopic sinus surgery to debulk her nasal polyps, widely open her sinuses and to determine the nature of the erosive process involving the sphenoid sinuses and skull base. At operation, extensive nasal polyps and inspissated debris were encountered in multiple sinuses. Mucoceles were decompressed and removed. Large regions of skull base erosion with obvious intracranial pulsations were seen. No cerebrospinal fluid leaks were identified and there were no complications. Final pathologic diagnosis was chronic rhinosinusitis with inflammatory polyps. There was no evidence of malignancy or presence of fungi.

This patient refused sinus surgery years ago and was again reluctant to pursue further evaluation and surgery. When warned of the potential life-threatening situation, she finally agreed to have surgical debridement. Surgery was critical to rule out underlying malignancy, fungal rhinosinusitis, and to debride and decompress the impacted material. Extreme caution was exercised in the face of distorted anatomy and demineralized bone. Visual loss occurred in the right eye and was imminent in the left eye.

KEY WORDS: nasal polyposis, chronic rhinosinusitis, visual loss, skull base erosion, neuro-imaging

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Up In Orbit: A 51 Year-Old Woman with Monocular Visual Loss and Adduction Deficit

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HISTORY & EXAM:
A 51 year-old woman presented with 6 months of subacute vision loss in the left eye. Examination revealed 20/40 acuity OS, visual field constriction, and a left APD. Brain MRI revealed an enhancing mass within the left orbit (shown below). She then experienced rapid vision loss of the left eye accompanied by severe headache and eye pain, nausea, and vomiting. Examination revealed HM acuity and severe loss of color vision OS, a mydriatic (but reactive) left pupil, and a left adduction deficit with 15pd XT. Spinal fluid evaluation was normal. Body CT scan revealed multiple pulmonary nodules. Bronchoscopy revealed lymphocytosis and elevated CD4/CD8 ratio, suggesting probable sarcoidosis (although no granulomas were present). With corticosteroid treatment, the acuity OS promptly improved to 20/50 (with persistent color vision impairment and left APD). Oral corticosteroids were weaned over 9 months, with a stable acuity of 20/40 OS. After 16 months of a stable course without treatment, she developed bronchitis and worsening vision. Examination revealed acuity 20/70 OS. Corticosteroids were resumed, but vision continued to decline rapidly, to 20/200. Brain MRI was repeated and showed persistence of the enhancing left orbital mass.

A diagnostic procedure was performed.

FINANCIAL DISCLOSURE: NONE

Up In Orbit: A 51 Year-Old Woman with Monocular Visual Loss and Adduction Deficit

Answer

FINAL DIAGNOSIS:
Schwannoma, arising from the inferior division of the left oculomotor nerve, causing compressive optic neuropathy

SUMMARY OF CASE INCLUDING PATHOLOGY:
The patient presented initially with left optic neuropathy and concomitant partial left third nerve palsy, suggesting an orbital apex syndrome that was confirmed by MR imaging. Sarcoidosis was suspected given the results of chest CT and bronchoalveolar lavage, and treatment with steroids yielded dramatic improvement. However, after 16 months of observation without change, visual loss recurred, and corticosteroids produced no improvement. A lateral orbitotomy was performed to biopsy the lesion. A discrete lobulated mass was identified arising from the inferior division of the oculomotor nerve, causing inferolateral compression of the optic nerve. Histological analysis revealed spindle cell neoplasm with neural features (+S100 staining), consistent with schwannoma. A subtotal resection was performed.

One month post-operatively, acuity OS improved from 20/200 to 20/60, accompanied by mydriasis and partial adduction, elevation, and depression deficits. At four months following surgery, acuity OS improved to 20/25 with near-complete resolution of third nerve palsy. At 16 months, acuity OS was 20/20, with residual left APD and mild temporal pallor.

The main differential diagnosis for an orbital apex syndrome in this case included inflammatory and neoplastic processes. An inflammatory lesion (such as sarcoidosis or orbital pseudotumor) was a strong consideration, given the evidence of systemic sarcoidosis and the dramatic clinical response to corticosteroids. However, once visual loss eventually recurred and failed to respond to corticosteroids, the diagnosis was questioned. Orbitotomy and biopsy revealed a schwannoma, arising from the oculomotor nerve and causing optic nerve compression. In retrospect, the finding of possible pulmonary sarcoidosis may have been a “red herring.”

Oculomotor nerve schwannoma is relatively rare (1, 4). Histopathologic studies of more common varieties often demonstrate the presence of an inflammatory infiltrate (5), suggesting an intriguing explanation for our patient’s initial improvement with corticosteroids. Alternatively, her rapidly declining vision may have been precipitated by acute intratumoral hemorrhage and vasogenic edema.

KEY WORDS: Orbital apex syndrome, Sarcoidosis, Inflammation, Schwannoma

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Something to Sink Your Teeth Into…

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HISTORY & EXAM:
21 year-old Kuwaiti male presents with previous diagnosis of cerebral palsy, hypertension and nystagmus. He was born at 37 weeks via normal spontaneous vaginal delivery with a birth weight of 2800grams. Parents describe nystagmus starting at 2 weeks of life. He is globally developmentally delayed, minimal walking starting at 3 years old and he was not verbal until 4 years-old. He is the oldest of three siblings, all with similar presentations. There is no known consanguinity within the family.

On ophthalmic exam, visual acuity in right eye was 20/100 and left eye was 20/50. Refraction shows high myopia and astigmatism in both eyes. Krimsky testing demonstrates a 45 prism diopter right exotropia in the distance and 15 prism diopter right exotropia at near. He exhibits latent nystagmus with both a dissociated horizontal and dissociated vertical deviation. Hypometric saccades and head thrusts were seen. Slit lamp exam showed a normal anterior segment exam. Posterior segment exam shows an optic nerve with normal margins and color, cup to disc ratio of 0.1 in both eyes. The mid-peripheral retina exhibits an extensive bone-spicule pigmentary degeneration.

Neurologic testing shows an independent, wide based ataxia. Rapid alternating movements were slow and irregular. Finger-nose-finger testing was impaired. Mild distal motor weakness was seen. Normal sensation and normal deep tendon reflexes. No rigidity or spasticity of extremities was noted.

FINANCIAL DISCLOSURE: NONE

Something to Sink Your Teeth Into…
Answer

FINAL DIAGNOSIS:
Joubert syndrome

SUMMARY OF CASE INCLUDING PATHOLOGY:
Laboratory testing shows chronic renal failure with creatinine 3.4.

MRI of the brain shows focal atrophy-encephalomalacia of anterior-superior cerebellar vermis with a “molar tooth” sign. Mild anomalous, “bat-wing-shaped” fourth ventricle. Partially empty sella.

Renal ultrasound was performed and showed increased echogenicity consistent with medial renal disease. A renal biopsy was performed and showed interstitial fibrosis and tubular atrophy, glomerulomegaly compatible with nephronophthisis.

The combination of cerebellar ataxia, hypometric saccades, pigmentary retinopathy, nephronophthisis and “molar tooth” sign on MRI lead to the clinical diagnosis of Joubert Syndrome.

Discussion:
Joubert syndrome (cerebellooculorenal syndrome) is a rare autosomal recessive neurologic disease. It is neurologically characterized by hypoplasia in the midline of the cerebellum, specifically the superior cerebellar peduncle. It is most commonly diagnosed by clinical exam but it is radiographically confirmed. Patients with Joubert syndrome universally have cerebellar ataxia and global developmental delay. They commonly presents in infancy with ataxia and global developmental delay. Infants classically have episodic hypernea.

Two broad categories of the syndrome have been described including those with retinopathy (type A) and those without retinopathy (type B).

Neuroophthalmic features may include multiple types of nystagmus including see-saw, latent, pendular or jerk. Hypometric saccades with head thrusts are common amongst many patients with Joubert syndrome. Pigmentary retinopathy and retinal colobomas have been noted in a few reported patients. The retinopathy associated with Joubert syndrome appears to be a subtype of retinitis pigmentosa. Affected individuals can present with a variety of different types of strabismus including esotropia, exotropia or orthotropia.

Nine different genetic tests can be performed to help confirm the diagnosis; however, the sensitivity of such tests is yet to be determined. Overall, the diagnosis remains a combination of clinical findings and neuroimaging. Early and prompt diagnosis is necessary to prevent long term damage from chronic kidney disease and other sequelae common with this condition.

This clinical presentation was difficult given the patient’s age at presentation. Knowledge of this syndrome and careful examination of this child at a younger age may have allowed a proper diagnosis. Earlier diagnosis may have prevented some complications from untreated severe chronic kidney disease and provided his family a better understanding of his disease process.

KEY WORDS: Developmental and congenital anomalies, Nystagmus and disorders of ocular stability, Saccades, Magnetic resonance imaging, Retina

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My Music Did Go with the Flow

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HISTORY & EXAM:
A 53 year-old male violinist presented with a five day history of progressive, painless loss of vision in both eyes. He denied headaches, diplopia, transient visual obscurations or other neurological symptoms. He was vegetarian, in good health, and denied systemic disease.

A retina specialist thought he had bilateral papilledema and sent him for neuro-ophthalmology consultation. Examination showed that the best corrected visual acuity was 20/200 in the right eye and 20/40 in the left eye. The pupils were equal and reactive to light and there was a questionable right relative afferent pupillary defect. Confrontation visual field testing showed that he could count fingers in all quadrants of both eyes. Goldmann perimetry of the right eye, showed a moderately dense central scotoma, an enlarged blind spot, and slightly constricted peripheral isopters. In the left eye, Goldmann perimetry showed minimal constriction of the isopters superotemporally. With the Amsler grid, the patient noted distortion and waviness of lines superotemporally, O.S. The patient was able to identify 12 out of 15 Ishihara plates with the right eye, by fixating eccentrically with his nasal field. He identified all 15 color plates with his left eye. Extraocular movements were full and his slit-lamp examination was unremarkable. Intraocular pressures were within normal limits.

Examination of the ocular fundi revealed that both optic discs were edematous, elevated and surrounded by multiple flame-shaped hemorrhages that radiated from the optic discs and obliterated the disc margins. Small exudates and scattered dot and blot hemorrhages were present surrounding both optic discs; no substantial hemorrhage was noted along the retinal vascular arcades outside the immediate peripapillary area. In both eyes, the retinal venules appeared distended and engorged, with boxcarring of the blood column. There were serious macular detachments in both eyes. There were no abnormalities in the retinal periphery of either eye.

FINANCIAL DISCLOSURE: NONE

My Music Did Go With the Flow
Answer

FINAL DIAGNOSIS:
Multiple Myeloma presenting with bilateral central retinal vein occlusions secondary to hyperviscosity syndrome

SUMMARY OF CASE INCLUDING PATHOLOGY:
The patient was admitted to the hospital for additional evaluation. Laboratory tests showed mild pancytopenia (WBC 3.1 K/microliter, Hgb 9.7 g/dL, platelets 135 K/microliter), high serum protein, low serum albumin, and high LDH. Vitamin B12, folate and iron levels were normal. CT of the head without contrast did not show any acute abnormality. MRI, MRA and MRV of the brain without contrast, revealed a poorly-defined heterogeneous infiltrate involving the clivus, suggesting a possible malignancy. A whole body bone scan was then obtained and showed multiple areas of uptake involving ribs, bilaterally, the right scapula, and left femur. A metastatic bone survey revealed vague lucencies throughout the skull consistent with multiple myeloma. Serum electrophoresis with immunofixation revealed a large IgA lambda monoclonal protein in the beta region. The patient's serum viscosity was elevated at 7.24 centipoise (cps). A bone marrow biopsy established the diagnosis, showing diffuse infiltration by monoclonal plasmacytic cells precursors (CD38+, CD56+, and cytoplasmic lambda +). The patient underwent two courses of plasmapheresis in addition to treatment with lenalidomide, allopurinol, zoledronic acid and dexamethasone.

One month later, the visual acuity was 20/25 in both eyes, with significant absorption of the retinal hemorrhages and amelioration in the appearance of the retinal vasculature. Serous detachment in both maculae was still present. At six months, the patient's visual acuity was 20/20 in both eyes with resolution of the retinal hemorrhages and normalization of the caliber of the retinal venules. There was no macular edema or serous detachment although there were residual hard exudates and minimal elevation of the optic discs, nasally. The patient has now undergone an autologous bone marrow transplant and is doing well.

- Bilateral Disc Swelling and visual loss was initially considered to be Papilledema.
- MRI showed infiltration of the clivus, suggesting a malignancy, possibly multiple myeloma.
- Further laboratory evaluation revealed hyperviscosity syndrome and a large IgA lambda monoclonal protein, confirming the diagnosis.
- The clinical findings of disc swelling, retinal hemorrhage and serous macular detachment were a result venous congestion resulting from the hyperviscosity syndrome caused by multiple myeloma.
- Only 2 such cases have been described previously in the literature (1, 2).

KEY WORDS: Bilateral Optic Nerve Swelling, Peripapillary Hemorrhage, Central Vein Occlusion, Hyperviscosity Syndrome, Multiple Myeloma

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Curtains

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HISTORY & EXAM:
A 51 year-old man was referred for evaluation of bilateral ptosis, diplopia, and headache.

The patient was feeling well until 3 months prior to evaluation when he had mild holocranial headaches, photophobia, fatigue, loss of appetite and low grade fevers.

The symptoms were unchanged until 3 weeks prior to presentation when he had gradual onset of upper lid ptosis OU, intermittent diplopia on side gaze and increased severity of his headaches. His ptosis had progressed such that he had to manually lift his upper lids in order to function.

Past medical history was remarkable for chronic back pain and rheumatic fever as a child. Medications included Ibuprofen for headaches and Naproxen for back pain. He denied use of tobacco, alcohol and other recreational drugs.

On the day of evaluation, he was alert, oriented X 3, and afebrile.

He had a best corrected visual acuity of 20/20 with full confrontation visual fields OU.

External examination showed bilateral upper lid ptosis with a marginal reflex distance of 0.5 mm OD and 1.5 mm OS. His levator function was 10 mm OD and 11 mm OS. There was no Cogan lid twitch or variability throughout the examination.

Pupils were 3 mm, briskly reactive with no relative afferent pupillary defect.

Ocular motility showed moderate elevation deficits OU and mild bilateral adduction deficits, OD>OS with adduction lag OU during horizontal saccades. He had a 6 prism diopter exophoria at distance and a 12 prism diopter exophoria at near.

Slit lamp, fundoscopic examination, facial sensation and CN VII function were normal.

Blood tests including complete blood count, electrolytes, ESR, CRP, and HIV serology were unremarkable. Chest X-ray was normal.

MRI of the brain with gadolinium showed enhancing lesions in the periaqueductal region and the interpeduncular cistern extending towards the surface of the cerebral peduncles.

FINANCIAL DISCLOSURE: NONE

Curtains
Answer

FINAL DIAGNOSIS:
Cryptococcal meningitis

SUMMARY OF CASE INCLUDING PATHOLOGY:
Lumbar puncture showed an opening pressure of 23 cm H_2O. White blood cells were 464/uL, 72 % lymphocytes, with no red blood cells. Protein was 140 mg/dL and glucose was 40 mg/dL. Cytology showed reactive lymphocytes with no signs of malignancy.

Cerebrospinal fluid tests including gram stain, bacterial cultures, AFB-culture, VDRL, angiotensin converting enzyme, oligoclonal bands, myelin basic protein, PCR for Epstein Bar virus and Herpes Simplex virus were all unremarkable.

Cerebrospinal fluid was positive for cryptococcal antigen with a titer of 1:2 and fungal cultures grew Cryptococcus neoformans. Serum testing showed cryptococcal antigen with a titer of 1:8.

The patient was treated with intravenous liposomal amphotericin and oral flucytosine with gradual improvement of his symptoms and neurological signs.

Cryptococcal meningitis often occurs in immunocompromised patients. Neuro-ophthalmic findings are frequent and include papilledema, optic disc atrophy, and cranial nerve VI palsies.[1,2]

Internuclear ophthalmoplegia and cranial nerve III palsies are rare but have been described.[1-5]

Our case represents the first reported patient with cryptococcal meningitis to present with bilateral, severe ptosis.

His findings are consistent with bilateral cranial nerve III palsies, internuclear ophthalmoplegia and possibly a nuclear ptosis.

The slight asymmetry of his upper lid ptosis favors bilateral cranial nerve III palsy as opposed to a nuclear ptosis.

Neuro-ophthalmic findings have been attributed to elevated intracranial pressure, direct invasion of the organism, and arteritis.[3,4]

Our patient's findings likely result from the lesions noted on neuroimaging as the localization is consistent with our patient's findings and he had mildly elevated intracranial pressure with no papilledema.

Our patient is unique as he was a healthy man with no immunosuppressive disease who presented with bilateral ptosis and bilateral adduction/elevation deficits from cryptococcal meningitis.

Our patient is unique as he was a healthy man with no immunosuppressive disease who presented with bilateral ptosis and bilateral adduction/elevation deficits from cryptococcal meningitis.

KEY WORDS: ptosis, diplopia, ocular motor nerve, internuclear ophthalmoplegia, meningitis

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The Gift that Keeps Giving

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HISTORY & EXAM:
In January 2005 a 55 year old gentleman was referred for a 6 month history of double vision and reduced acuity. The double vision was relieved by covering either eye. He was initially treated with prism glasses by his local optometrist. On examination visual acuity was 20/30- on the right and 20/20 on the left. There was no definite APD. Automated static perimetry was unremarkable. His pupils were 4 mm on the right and 3.5mm on the left reactive without APD. He had marked limitation in elevation on the right side with moderate limitation in depression. He had 3mm of right ptosis. His funduscopic examination was unremarkable.

His medical history however was remarkable. In 1997 he began to have problems with nose bleeds and underwent an otolaryngologic evaluation and subsequent endoscopic biopsy which showed “cancer”. He reportedly had sinonasal vault adenocarcinoma. He underwent preoperative radiation therapy with 50 Gy in 28 sessions followed by a craniofacial resection. Pathology failed to reveal any active tumor with evidence of chronic inflammation and fibrosis.

A CT scan done when the patient first began to complain of double vision (12/04) was read as normal. He had an MRI scan in February which was also said show only post operative changes. In May of 2005 he returned with a one month h/o complete visual loss OD. He was NLP and 20/25 with a greater than 1.8 log unit right APD. He also now had complete ptosis on the right side, complete ophthalmoplegia, loss of V1, but no evidence of proptosis. A CT scan was obtained which showed increased density in the area of the medial orbital apex and an MRI showed a soft tissue mass. An attempt at fine needle aspiration biopsy was unremarkable and the patient underwent endoscopy and biopsy.

FINANCIAL DISCLOSURE: NONE

The Gift that Keeps Giving
Answer

FINAL DIAGNOSIS:
Mucormycosis in a low grade radiation induced fibrosarcoma

SUMMARY OF CASE INCLUDING PATHOLOGY:
Endoscopy (6/05) demonstrated a mucopyocele and culture grew out staph alcalginis facelis and enterococcus treated with Ketek. He had persistent pain in the area of the face and orbit and had no recovery of vision or motility. Neurontin (later switched to Tegretol) was administered for chronic pain. In September 2005 was discharged to local follow-up. In December of 2005 he was started on steroids but every time the steroids were tapered in February of 2006 his fever returned and he developed mental status changes. In March of 2006 he was referred back to our facility with marked mental status problems and evidence of hydrocephalus. He was treated with a ventriculostomy. Visual acuity was NLP OD and 3 pt OS with persistent complete ophthalmoplegia OD. An MRI scan showed progression of soft tissue mass in the orbital apex but also involvement of right frontal white matter. A repeat endoscopy at this point demonstrated evidence of fungus. Because of the extensive soft tissue changes a frontal orbitotomy was performed and a biopsy this time showed evidence of a fibrosarcoma and invasive mucormycosis. The patient was treated with palliative care and died in July of 2005.

Radiation induced tumors are uncommon except in the setting of retinoblastoma with gene defects (much higher incidence). The lag time to development may be as much as 10-30 years. Reported radiation induced tumors have included meningiomas, gliomas, neurofibromas, ependymomas, and variants of sarcomas. In this case it was difficult to separate atypia due to chronic inflammation from a low grade sarcoma. Mucor in an otherwise immune competent host is unusual. The use of steroids here probably put him at greater risk. The sudden and complete loss of vision suggests that the mucor may well have been present (and indolent) at the time of the first biopsy.

1) Radiation can cause secondary tumors even in absence of genetic predisposition..
2) Radiation induced tumors may be indolent and difficult to diagnose.
3) Areas of previous radiation may be a higher risk for secondary infection with bacteria and fungus.
4) Repeat biopsies may be necessary if the findings don't match the imaging and clinical situation.

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Lightning Never Strikes Twice

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HISTORY & EXAM:
The patient is a 40 year-old man who initially presented with a chief complaint of bilateral floaters and blurred vision worsening over the past few months.

Medical history reveals Barrett's esophagus, with recent biopsy revealing a small focus of dysplastic cells of signet cell adenocarcinoma endoscopically resected with clear margins, after presenting to his internist with heartburn. He reports a remote history of pleural effusion and unexplained thrombocytopenia in his 20s. Current medications include Zantac, Prilosec, and Klonopin. Review of systems reveals severe fatigue, night sweats, arthralgias, and a 25 pound, unexplained weight loss. Family history reveals history of ALS in his mother. His wife is recently deceased due to lymphoma. He has four children, denies smoking, occasionally drinks alcohol, and exercises regularly.

On initial examination, his visual acuity refracts to 20/20 in each eye, with normal color perception by Ishihara testing. Intraocular pressure was 12 in the right eye and 13 in the left. There is no afferent papillary defect. Formal visual fields revealed bilaterally enlarged blind spots. Anterior segment exam revealed bilateral conjunctival injection. Dilated examination revealed bilateral 2+ vitreous cell, and bilateral disk edema.

Subsequent MRI of the brain and orbits was unremarkable, without evidence of optic nerve enhancement or parenchymal lesion. Lumbar puncture revealed slightly elevated opening pressure of 21 cm H_2O, with no evidence of WBC, bacteria, or malignant cells. Fungal and anaerobic CSF cultures were negative. Serologic workup for infectious neuroretinitis, inflammatory, and autoimmune disorders was unrevealing. PPD was normal. Sedimentation rate was elevated at 17 (0-15), and CRP was elevated at 9 (<0.74). WBC was elevated at 11, with elevated neutrophils (78).

FINANCIAL DISCLOSURE: NONE

Lightning Never Strikes Twice
Answer

FINAL DIAGNOSIS:
Given his recurrent epigastric pain, his gastroenterologist and surgeon obtained another esophageal, duodenal, and colonic biopsies, which revealed chronic signs of inflammation, with PAS filled macrophages, without evidence of dysplasia. Subsequent PCR was positive for T. Whipplei.

SUMMARY OF CASE INCLUDING PATHOLOGY:
Given his history of remote pleural effusion, papilledema, elevated WBC, and lymphadenopathy, a PET scan was obtained, and revealed increased uptake in noted in the neck, bilateral axillae, chest, abdomen, and pelvis, as well as diffusely hypermetabolic splenomegaly suggestive of lymphoma. Axillary lymph node biopsy was obtained for tissue diagnosis, and revealed follicular hyperplasia, paracortical expansion, and aggregates of epithelioid histocytes with an apparent follicular location. Flow cytometry demonstrates heterogenous T-cells and polytypic B-cells.

At this point, he reports worsening symptoms of floaters, gastritis, and noticed a small, nonmobile, nontender 3-4 cm mass of the neck. Dilated fundoscopy reveals worsened bilateral disk edema, and several areas of subretinal hypopigmented lesions. He was referred to the Retina Service. Fluorescein angiogram revealed late leakage of both nerves, focal areas of choroidal staining, and bilateral macular edema, without signs of vasculitis. The Retinologist recommended oral Prednisone treatment, followed by sub-Tenon's steroid injections for presumed sarcoidosis. His disk edema, macular edema, and vitritis improved with several courses of sub-Tenon steroid injections.

Given the ongoing concern for lymphoma, his neck mass was excised, and revealed a lipoma. A second lumbar puncture was obtained, and did not reveal evidence of malignant cells. In order to obtain a tissue diagnosis, another diagnostic procedure was performed.

He was started on antibiotic treatment, with ceftriaxone 2 grams IV, followed by oral Bactrim for one year. His epigastric pain, arthralgias, and ocular inflammation slowly resolved. Subsequent biopsy 1.5 years after initiation of treatment did not reveal any evidence of T. Whipplei.

KEY WORDS: disk edema, vitritis, floaters, uveitis, lymphadenopathy

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Lymphing Along

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HISTORY & EXAM:
A 54 year-old female with a history of bilateral lung transplantation in 2005 for complications of acute respiratory distress syndrome, which followed aspiration pneumonia, presented in June 2007 with multiple symptoms including blurred vision, mild confusion, diffuse weakness and shortness of breath. One year following transplant she experienced mild rejection further complicated by Aspergillus infection. Past ocular history was significant for bilateral cataract extractions and left corneal transplant for toxic anterior segment syndrome. Medications included prednisone, mycophenolic acid, alendronate sodium, tacrolimus, epoetin alfa, valganciclovir Hcl, voriconazole, trimethoprim and sulfamethoxazole, repaglinide and warfarin among others.

On examination, visual acuity was 20/400 OD and 20/50 OS with no relative afferent pupillary defect, mild bilateral optic atrophy and bilateral visual field defects. The remainder of the ophthalmic examination including extraocular motility was unremarkable. Other significant findings included increased reflexes throughout, shuffling gait and a positive Romberg sign. She was slow to respond but otherwise her mental status was intact.

Initial serologic evaluation (CBC, peripheral smear, RPR, VDRL, HIV, CMV, ACE, EB virus, toxoplasma, carcinoembryonic AG) was non-contributory. MRI demonstrated edema and enhancement centered within the hypothalamus, tracking posterior along the optic tracts into the basal ganglia bilaterally. Numerous foci of T2 hyperintensity within the cerebral hemispheres, most prominently at the gray-white matter junction, and pons were seen. Lumbar puncture (LP) was notable for a protein of 315. Testing of the CSF for multiple infectious agents, cytology and flow cytometry was negative.

Symptoms worsened despite broad spectrum antimicrobial coverage, decadron trial, treatment for tuberculosis and plasmapheresis. Following a prolonged seizure she had persistent alternated mental status. Hematocrit and platelets dropped and renal failure developed. CSF protein increased to 899; other CSF measures remained unremarkable. Brain biopsy demonstrated miningothelial hyperplasia and necrotic tissue. She expired July, 2007 and an autopsy was performed.

FINANCIAL DISCLOSURE: NONE

Lymphing Along
Answer

FINAL DIAGNOSIS:
Thrombotic microangiopathy related to calcineurin inhibitor toxicity

SUMMARY OF CASE INCLUDING PATHOLOGY:
Microscopic findings included numerous fibrin thrombi within capillaries and small caliber arterials and acute infarcts involving the hypothalami, frontal lobes, temporal lobes and the pituitary stalk. Similar findings were seen in the kidneys. These findings of thrombotic microangiopathy are consistent with calcineurin inhibitor toxicity.

Thrombotic microangiopathy (TMA) is a well described complication of organ transplant. It is characterized by intravascular platelet aggregation and thrombosis. It is recognized side effect of calcineurin inhibitor therapy. TMA has been described following lung transplantation with an incidence of roughly 5%. It is most common in post transplant patients using calcineurin inhibitors. Other offending medications include cyclosporine and sirolimus. Although, pathogenisis is yet to be fully established, it is clear that endothelial injury with platelet aggregation is pivotal. The mainstay of therapy is discontinuation of the offending medication. Plasmaphoresis has been felt to be beneficial in selected cases.

Tacrolimus discontinuation and plasmaphoresis were unsuccessful in our patient, underscoring the seriousness of this disorder.

This case presented numerous difficulties. The history of aspergillus infection raised suspicion of fungal infection. Immune suppression raised suspicion to lymphoproliferative and other infectious diseases. Moreover, MRI findings in thrombotic microangiopathy are non-specific. Brain biopsy was non-diagnostic related to the location of the biopsy: the selected area was too necrotic for identification of the specific etiology, delaying identification of the correct diagnosis.

KEY WORDS: angiopathy, transplant, optic tract, calcineurin inhibitor

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