### SATURDAY, FEBRUARY 9, 2013

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<td>12:00 p.m. – 8:30 p.m.</td>
<td>Registration</td>
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<td>12:00 p.m. – 5:00 p.m.</td>
<td>NANOS Board Meeting</td>
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<td>1:00 p.m. – 4:00 p.m.</td>
<td>Clinical Trials 101 [3 CME]</td>
<td>Magpie AB</td>
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<td>6:30 p.m. – 8:00 p.m.</td>
<td>Opening Reception (all are welcome)</td>
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**Presenters:** Benjamin Frishberg MD, Deborah Friedman, MD and Ann Stoutenburg, CCRC

**Description:** This course is designed for all clinicians who are interested in participating in multicenter clinical trials. We will discuss the value of clinical research, basics concepts of study design to consider when deciding whether proposed trial has scientific merit, the responsibilities of becoming a site investigator and the concept of equipoise. Participants will learn about the infrastructure needed for a successful clinical trial site, protection of research subjects, budgeting and contracting. The course is directed toward practicing physicians in academic medicine and private practice, as well as trainees, with limited or no background/experience in clinical research.

At the conclusion of this program, participants should be able to: 1) Analyze a study protocol prior to participation in a trial; 2) Describe the importance of clinical equipoise as a site investigator; 3) List the responsibilities of being a site investigator; 4) Define the basic elements of a clinical site budget; 5) Understand IRB requirements and the contracts process; and 6) Determine the infrastructure needed to be a successful site.

*This course is designed to procure the following desirable physician attributes: Employ evidence-based practice; work in interdisciplinary teams*

### SUNDAY, FEBRUARY 10, 2013

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<td>6:30 a.m. – 3:30 p.m.</td>
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FRANK B. WALSH SESSION [7.25 CME]  Ballrooms 2-3

Chair: Valérie Biousse, MD  
Neuroradiologist: Pat Hudgins, MD  
Neuropathologist: Daniel J. Brat, MD, PhD  
Expert Panel: Steven Galetta, MD, Andrew Lee, MD, Neil Miller, MD

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

The format is a clinicopathologic conference. Clinical cases will be presented by neuro-ophthalmologists with comments by a neuroradiologist, neuropathologist and other selected experts. Necropsy, surgical pathology, and neuroimaging will help illuminate clinical points. Cases will be discussed from clinical, anatomic, radiologic and pathologic aspects with emphasis on diagnosis, pathophysiology and management. Audience participation is encouraged.

At the conclusion of this program, participants should be able to: 1) Recognize the varied presentations of neuro-ophthalmic disease; 2) Correlate the anatomic localization and histopathologic appearance with the clinical presentations; 3) Effectively use radiologic procedures in diagnosis; 4) Recognize both the value and limitations of neuropathology; and 5) Discuss newly described diseases and their connection to neuro-ophthalmology.

This course is designed to procure the following desirable physician attributes: Medical knowledge; work in interdisciplinary teams.

11:50 a.m. – 1:10 p.m.  Lunch  Ballroom 1
12:00 p.m. – 1:00 p.m.  Membership Retention and Recruitment Committee Meeting  Superior A
5:15 p.m. – 5:45 p.m.  Frank B. Walsh Committee Meeting  Superior A
5:15 p.m. – 5:45 p.m.  Fellowship Directors Meeting  Superior B
5:45 p.m. – 6:15 p.m.  Professional Standards (Fellowship) Committee Meeting  Superior B
5:30 p.m. – 6:30 p.m.  Student/Resident/Fellow Program and Reception  Wasatch

Evening  Dinner on your own
Frank B. Walsh Session I

Moderators: Beau Bruce, MD & Paul H. Phillips, MD

8:00 a.m. - 8:20 a.m.  
**Golden Grapes**
Heather E. Moss, MD, PhD

8:20 a.m. - 8:40 a.m.  
**Ain’t No Sunshine When You Are Gone!**
Veeral S. Shah, MD, PhD

8:40 a.m. - 9:00 a.m.  
**Some Orbital Confusion**
Steven A. Newman, MD

9:00 a.m. - 9:20 a.m.  
**A Wolf in Bear’s Clothing**
Peter W. MacIntosh, MD

9:20 a.m. - 9:40 a.m.  
**No Rhabdo?**
Mark R. Melson, MD

9:40 a.m. - 10:10 a.m.  
**Coffee Break**

Frank B. Walsh Session II

Moderators: Sachin Kedar, MD & Janet C. Rucker, MD

10:10 a.m. - 10:30 a.m.  
**Behind the Curtain**
Marc H. Levin, MD, PhD

10:30 a.m. - 10:50 a.m.  
**Deaf and Dizzy. Have We Been Susacked?**
Jorge C. Kattah, MD

10:50 a.m. - 11:10 a.m.  
**It’s All in Your Head**
William L. Hills, MD

11:10 a.m. - 11:30 a.m.  
**Is it Naughty or Nice?**
Daniel Gold, DO

11:30 a.m. - 11:50 a.m.  
**A Difficult Bug to Swallow**
Kenneth Lao, MD

11:50 a.m. - 1:10 p.m.  
**Lunch**
### Frank B. Walsh Session III

**Moderators:** M. Tariq Bhatti, MD & Matthew J. Thurtell, MBBS, FRACP

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<td>Philip M Skidd, MD</td>
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<td>Vivek Patel, MD</td>
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<td>Spots, Spots Everywhere, And Not A Spot To See</td>
<td>Sarkis M. Nazarian, MD</td>
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### Frank B. Walsh Session IV

**Moderators:** Mark R. Melson, MD & Gregory P. Van Stavern, MD

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Golden Grapes

Heather E. Moss1, Sean Zivin2, Amy Lin1,3, Vinay Aakalu1, Senad Osmanovic1, Omar Al Heeti4, Stockton Mayer1, Mahesh Patel1

1University of Illinois at Chicago/ Department of Ophthalmology and Visual Sciences Chicago, IL, USA, 2University of Illinois at Chicago/ Department of Radiology Chicago, IL, USA, 3University of Illinois at Chicago/ Department of Pathology Chicago, IL, USA, 4University of Illinois at Chicago/ Department of Medicine Chicago, IL, USA

History & Exam

A 71 year-old African American woman presented with a painful right retrobulbar optic neuropathy and weight loss. ESR was 74. She was treated with steroids. Temporal artery biopsy did not show arteritis. Nine days later, while on a steroid taper, she developed fevers, worsening right eye vision, ptosis, partial ophthalmoplegia and pain. Past medical history was remarkable for nasal septoplasty one month prior, urinary tract infection three weeks prior, hypertension, bladder cancer and diabetes complicated by retinopathy. Neuro-ophthalmic evaluation included visual acuity of NLP OD and 20/30 OS. Pupils were equal. Motility in the right eye was limited to small incyclotorsional and horizontal movements. On the right there was complete ptosis, 2mm proptosis, trace conjunctival injection and no periorbital edema. Sensation was diminished in the right V1 and V2 regions. There was 360 degree optic disc elevation with peripapillary hemorrhages and cotton wool spots on the right. Left ophthalmic and complete neurological evaluations were otherwise normal. Otorhinolaryngology evaluation including sinus endoscopy was unremarkable. MRI revealed diffuse enlargement and enhancement of the right optic nerve sheath and diffusion restriction of the right optic nerve. There were no acute intracranial or perinasal sinus abnormalities. Serum testing, including serial blood cultures, ANA, ANCA, ACE, HIV, quantiferon TB gold, toxoplasma and Bartonella serologies, was unrevealing. CSF analysis showed 2261 WBC/μL (74% PMN, cytology without malignant cells), glucose 126mg/dL, protein 198mg/dL, and negative culture. Antimicrobial agents were started. Steroid taper was completed. Repeat spinal tap had normal opening pressure, and CSF with 480 WBC/μL (43% PMN, no malignant cells), protein 80mg/dL, glucose 74mg/dL, and negative infectious studies for Lyme, syphilis, HSV, VZV, and toxoplasma. Right optic nerve elevation progressed and she developed vitritis and vitreous hemorrhage. MRI and B-scan showed subchoroidal collection. A procedure was performed.

Financial Disclosures: Dr. Moss received funding from NIH grant number K12 EY021475. No other authors had disclosures.
Golden Grapes

Answer

Final Diagnosis
*Staphylococcus aureus* abscess of right optic nerve, chiasm and choroid

Summary of Case
Biopsy of the optic nerve sheath was pursued due to progression despite medical management. During surgery no orbital inflammation was noted. Upon incision of the optic nerve sheath purulent material came forth. Gram stain showed gram-positive cocci in clusters. Cultures grew methicillin-sensitive *Staphylococcus aureus*. Anaerobic, fungal, viral and acid fast cultures were negative. She subsequently developed temporal field loss in the left eye. MRI showed extension of enhancement and diffusion restriction into the optic chiasm diagnostic of abscess(1). The right eye was enucleated to remove infected material. Gross examination showed thickening of the optic nerve and peripapillary retina with focal choroidal thickening, vitreous opacities, and adhesions of orbital soft tissue to the globe. Microscopic examination showed neutrophilic infiltrate with cell debris in the optic nerve, peripapillary retina, vitreous and choroid. A choroidal infiltrate consisted primarily of polyclonal plasma cells and reactive lymphocytes. There were no findings of neoplasm or granulomatous inflammation. The patient has been treated with long term antibiotics. Her vision has remained stable and MRI has improved. Though bacterial infections of the orbital apex, orbit and brain are well described and a case of *S. aureus* retinal abscess has been reported(2), this case of optic nerve/chiasm abscess is unique in the modern literature to our knowledge. The causative agent, *S. aureus*, is an aerobic bacterium that is carried by 20-80% of the population primarily in the nares(3). In a retrospective study of 163 patients with brain abscesses it was the causative agent in 21%, following streptococci(35%) and unidentified(27%)(4). An unidentified source of the abscess(as was the case in our patient) was common in this study, occurring in 19% of patients. The only more common sources were post-operative and sinusitis. In our patient, the host factor of immunosuppression due to diabetes likely contributed to infection establishment and progression.

Struggle/Dilemma of the Clinical Presentation Description
Diagnosis was challenging as bacterial infection was thought less likely than inflammatory or viral perineuritis, or fungal orbital apex syndrome as the inciting event. Management was initially challenging due to lack of diagnosis. Additional steroid therapy and anticoagulation for possible cavernous sinus thrombosis were considered. Management was challenging after diagnosis due to progression despite appropriate antibiotics. Surgical evacuation of infected orbital material and alteration of antibiotics to optimize CNS penetration were implemented with resultant stabilization.

Keywords: Optic Nerve, Optic chiasm, Abscess, Neuro-imaging

References
Ain't No Sunshine When You are Gone!

Veeral S. Shah1, Linda Sternau2, Michelle Felicella2, Sanders Dubovy1, Chris Alabiad1, Norman J. Schatz1, Byron L. Lam1

1Bascom Palmer Eye Institute / University of Miami, Miami, FL, USA. 2Memorial Regional Hospital/Neurosurgery Division Hollywood, FL, USA

History & Exam
An 18 year-old Latin American female presented with progressive visual loss OD over 6 weeks. She initially had blurry vision and photophobia OD with a central scotoma OD on HVF testing. At that time, examination revealed a right swollen optic nerve with retinal hemorrhages. She was otherwise healthy, and denied any eye pain, neurological deficits, trauma medications, tobacco, alcohol, or drug use. A fat suppressed orbital MRI scan showed evidence of optic nerve enhancement OD. On laboratory evaluation, CBC, Lyme, Cat Scratch, syphilis, toxoplasmosis, HIV, and NMO IgG testing were all unremarkable. Infectious, autoimmune and paraneoplastic laboratory workup was unrevealing, except for elevated Epstein-Barr Virus IgG. Lumbar puncture showed an opening pressure of 13 cm water, protein of 25, glucose of 67, and 1 WBC. Cytology was negative for malignancy. With the presumed diagnosis of optic neuritis, she was treated with high doses IV steroids without improvement. Her isolated visual symptom led to multiple unrevealing consultations, as her visual acuity continue to decline. At this time a second opinion was sought at our service. Visual acuity was no light perception OD with an amaurotic pupil and 20/20 OS. Color vision was 12/14 and visual fields were full in the OS. Anterior segments and intraocular pressures were normal. Funduscopy revealed neovascularization of the right optic disc with punctate hemorrhages, sclerotic retinal arteries, and retinal venous stasis. The remainder of the ophthalmic and neurologic exam was normal. Repeated MRI of the orbits demonstrated right optic nerve sheath thickening and diffuse enhancement of the nerve extending into the optic canal to 3 mm before the chiasm. The patient underwent exploration of the right orbit and a biopsy of the optic nerve/sheath was performed. Histopathology of the optic nerve/sheath biopsy failed to reveal any abnormality and showed chronic inflammatory changes. A subsequent procedure was performed.

Financial Disclosures: The authors had no disclosures.
Final Diagnosis
Malignant Glioma optic nerve pathway (a pediatric case of Malignant Glioma of “Adulthood”)

Summary of Case
The initial biopsy of the right optic nerve and sheath demonstrated chronic inflammatory infiltrates and marked fibrocellular changes. The right optic nerve diffusely stained positive for CD45. However there was no gross, microscopic, or immunohistochemical evidence of meningioma or other tumors. Although the initial biopsy was unrevealing, the patient’s clinical course and repeated orbital MRI scan supported a diagnosis of infiltrative process. The subsequent procedure was a frontal-orbital craniotomy with unroofing of the right optic canal and right optic nerve resection yielding intracanalicular and intracranial portions of the nerve (see Figure, short edited video will be shown in presentation). 1) Intracanalicular right optic nerve specimen showed dense fibrovascular tissue with macrophage infiltrates. 2) Intracranial portion of the right optic nerve specimen revealed large pleomorphic and hyperchromatic atypical cells infiltrating the nerve. Sectioned tissue underwent immunostaining for GFAP, Ki67, Olig 2, and IDH1. These atypical cells were strongly GFAP positive, but were negative for Olig and IDH1. The Ki67 index of the posterior margin of the tissue was 4-5%. These results were consistent with Anaplastic Astrocytoma WHO Grade III. Malignant Glioma of “Adulthood” is a rare malignant astrocytoma of the anterior visual system that leads to rapidly progressive vision loss, neurological deficits, and poor survival 4. Rapid monocular vision loss, early mimicking of optic neuritis, the development of a retinal artery/vein occlusion, and eventually blindness characterizes this neuro-ophthalmic syndrome1. Malignant gliomas of the optic nerve aggressively spreads to involve the fellow eye in 4-6 weeks, rendering complete blindness, and ultimately, leading to terminal intracranial infiltration3. Malignant gliomas of optic nerve typically occur in middle-aged men1. This case is noteworthy due to the young age of the patient and the undefined clinical course. This patient was managed aggressively with surgical resection of the pre-chiasmal tumor, and treated post-operatively with Temozolomide and stereotactic radiotherapy treatment.

Struggle/Dilemma of the Clinical Presentation Description
This is one of the youngest reported cases of malignant glioma of “adulthood”. Given the patient’s age, this case illustrates the difficulty in identifying a rare disease that masquerades as a common optic neuritis. The first optic nerve biopsy failed to provide a diagnosis. The clinical progression and imaging prompted a subsequent excisional biopsy that established the diagnosis of anaplastic astrocytoma. Finally, the management and treatment of malignant glioma is not defined in pediatric cases.

Keywords: Malignant Glioma of Adulthood, Optic Neuritis, Anaplastic astrocytoma, Temozolomide, Central Vein/Artery occlusion

References
History & Exam
In April 2012, a 64 year old gentleman was referred for progressive horizontal diplopia. Acuity was 20/25. 24-2 demonstrated moderate diffuse depression OD > OS, and some arcuate VF changes OS. Palpebral fissures were 13 and 10 with an upper lid range of 15 and 12. Hertels 28/19 with some resistance to retropulsion. There was no APD, but definite limitation in elevation > abduction, adduction, and depression OD with 100 seconds stereopsis. Applanation tensions were 16 and 12. OCT demonstrated minimal thinning of NFL superiorly and nasally, but symmetric OU. CT scan (A,B) demonstrated R orbital pathology. In September 2006 he had been referred for a second opinion regarding a 5 year history of intermittent swelling around the right orbit, worsening over 7 months associated with double vision, and proptosis (C,D). This had initially responded to steroids for presumed orbital inflammatory disease. In September acuity was 20/20 and 20/25 with superior arcuate OS. Hertels were 26/22 with moderate resistance to retropulsion, no APD and limitation in elevation and abduction OD. OCT showed minimal thickening OD, and slight thinning OS. Because of the atypical nature (absent pain) he was tapered off steroids, (E,F,G) and an orbital biopsy was performed. The biopsy was read as showing areas of sclerosis and subtle inflammatory infiltrate felt compatible with the diagnosis of sclerosing idiopathic orbital inflammatory disease (R,S). In June 2007 he returned with an enhancing soft tissue mass involving the right buccal space with invasion of the right hemimandible (H,J). FNAB 7 open biopsy showed lymphocytes (37% CD 19, 31% CD 19+kappa, 6% CD19+lambda) (T,U,V,W). This kappa light chain restricted B cell population was felt compatible with lymphoma, and the patient was treated with chlorambucil for “marginal zone lymphoma with plasmacytic differentiation” with no evidence of progression and no new symptoms. An additional test was performed.

Financial Disclosures: The authors had no disclosures.
Some Orbital Confusion

Final Diagnosis
Persistent and recurrent low grade B cell lymphoma (marginal zone) demonstrated by gene rearrangement studies.

Summary of Case
In spite of 2 years without treatment his clinical examination had not changed. One month later acuity remained 20/25 bilaterally, with no APD, no change in VF, but persistent limitation in elevation and depression on the right, and 10mm of residual proptosis. Review of the original orbital pathology failed to confirm malignancy and a repeat orbital biopsy was planned. PCR for IGH rearrangement done on the initial 2006 specimen demonstrated evidence of clonal immunoglobulin heavy chain gene rearrangement consistent with the presence of a clonal B-cell lymphoma. His entire picture was thus felt compatible with an extremely indolent low grade marginal B-cell lymphoma and plans were made for treatment with Rituximab. While ocular and adnexal lymphoma makes up only 1% of B-cell lymphomas it is the most common primary malignancy in the orbit. Flow cytometry and immunohistochemistry are usually adequate to make the diagnosis but when there is scarce lymphocytic infiltration and significant reactive expression the diagnosis may be difficult. PCR based gene rearrangement analysis offers an additional tool in identifying malignant involvement. When confined to the orbit these lesions may respond to local radiation therapy. Systemic involvement may occur at any time in 25 to 50%. As these lesions may disseminate years or even decades later continued surveillance is advised. Recent use of biologic agents expands our treatment armamentarium.

Struggle/Dilemma of the Clinical Presentation Description
What to do with a patient who presents with evidence of orbital pathology (over 11 years) but relatively mild signs and symptoms 6 years after an orbital biopsy demonstrated “sclerosing orbital inflammatory disease” who in the interim had an additional lesion in the jaw that demonstrated low grade lymphoma treated for 2 years with chlorambucil? The patient is minimally symptomatic. Do we need another biopsy for treatment?

Keywords: Orbit, Marginal zone Lymphoma, IGH-PCR, Immunohistochemistry

References

A Wolf in Bear's Clothing

Peter W. MacIntosh¹, Agatha Bogard², Pete Setabutr¹, Heather E. Moss¹

¹University of Illinois, Department of Ophthalmology and Visual Sciences, Chicago, IL, USA.
²University of Illinois, Department of Pathology, Chicago, IL, USA

History & Exam

An eleven-month-old African-American girl with medical history of reactive airway disease developed a bump and bags under both eyes which her mother attributed to minor trauma. There were no signs of systemic illness. A week later, her mother noticed more prominent right eye edema and a new bump behind the right ear with crusting and tearing of the right eye. She was evaluated at an ED where she was diagnosed with conjunctivitis and treated with oral amoxicillin and gentamicin eye drops. There was no improvement, and over two weeks the bilateral periorbital edema progressed and she developed rhinorrhea and fevers. On exam, the patient averted to light and fixated and followed with either eye. Pupils were equal, round and reactive to light, but difficult to assess for rAPD due to lid edema and patient squeezing. Extraocular movements appeared full. There were no involuntary eye movements. There was a right hypertropia with resistance to retropulsion. Intraocular pressures were soft to palpation in both eyes. There was 2+ right lid edema and ptosis and trace left lid edema and ptosis (External Photo). The remainder of the anterior ophthalmic exam was unremarkable. Limited dilated funduscopic exam appeared normal in both eyes. Abdominal exam revealed a right-sided mass. Neurological and systemic exams were otherwise normal. Complete blood count and basic metabolic profile were normal. Urine catecholamines were negative. CT examination of the orbits revealed bilateral orbital and paranasal sinus masses with spiculations, calcifications and osseous destruction (Radiology Image 1). MRI studies confirmed multiple T1 and T2 hypointense extra-axial masses of the calvarium, skull base and bones of the face, particularly involving the orbits, which enhanced with contrast and were slightly diffusion restricted (Radiology Images 2-6). CT of the abdomen demonstrated right adrenal and rib masses (Radiology Images 7-9). A diagnostic procedure was performed.

Financial Disclosures: The authors had no disclosures.
A Wolf in Bear’s Clothing

Final Diagnosis
Myeloid Sarcoma

Summary of Case
A right inferior orbitotomy was done for tissue diagnosis. Histological analysis of the tumor mass showed sheets of poorly differentiated, infiltrative cells with moderate eosinophilic to amphophilic cytoplasm, large nuclei and prominent nucleoli (Pathology Images 1-2). Immunophenotyping by flow cytometry showed expression of CD4, CD43, CD45RO, CD68, CD99, lysozyme, and myeloperoxidase (Pathology Image 3), diagnostic of myeloid sarcoma (MS). Bone marrow aspirate confirmed acute myeloid leukemia (AML) (Pathology Images 4-5), while CSF analysis did not show malignant cells. Genetic analysis showed rearrangement of the mixed lineage leukemia (MLL) gene (Pathology Images 6-7). Peripheral blood smear showed rare atypical circulating cells equivocal for AML. MS is a rare extramedullary complication of acute leukemia consisting of a solid tumor proliferation of myeloid blasts that can involve any part of the body including head, body cavities and subcutaneous tissue. It is most common in children under 10 years of age with primitive AML.1, 2 Most of these children are of African, Asian, South Pacific and Latin American decent.3 Although rare, AML can present with orbital involvement in the form of MS before diagnosis of the underlying leukemia.1,4 In such cases, the subsequent development of leukemia usually occurs within 5-12 months. A recent study by Johnston et al found that orbital MS patients had significantly higher overall survival than central nervous system (CNS) MS and patient with non CNS MS.5 Leukemia represents 2-6% of orbital tumors in children, but eleven percent of children with proptosis will have some form of acute leukemia.1 CT and MRI are important for distinguishing neoplasms from hematomas or abscess, but cannot distinguish granulocytic neoplasms from other tumors. Tissue diagnosis is often necessary. Leukemia is strongly suggested by the presence of elevated WBC and peripheral and medullar blasts, though these were not present in our patient.1

Struggle/Dilemma of the Clinical Presentation Description
The initial presentation was confused by the emergency department for conjunctivitis and cellulitis. Subsequent presentation and imaging were classic for metastatic neuroblastoma. Lymphoma and leukemia were initially felt to be unlikely by the hematology/oncology team due to tumor location, normal CBC and no hepatosplenomegaly. These data lead to a strong bias for neuroblastoma as the likely diagnosis and it was the focus of her initial work up. Biopsy confirmed the true diagnosis.

Keywords: Myeloid sarcoma, Abdominal mass, Orbital tumor, Child

References
No Rhabdo?

Mark R. Melson

Vanderbilt University School of Medicine, Nashville, TN, USA

History & Exam
A 5 year-old girl presented for evaluation of a right orbital mass displacing the globe superiorly. She had a 5 week history of swelling around her right eye. Her pediatrician diagnosed a blocked tear duct and referred her to an ophthalmologist. She failed empiric treatment for orbital cellulitis and was subsequently referred to an orbital surgeon elsewhere. A computed tomography scan by the orbital surgeon revealed a mass in the right orbit. The patient’s family was told that she had cancer and needed urgent treatment. In the week prior to seeing us, her family began giving the child commercially-marketed supplements for cancer treatment. The patient complained of swelling around the right eye, mild discomfort along the right inferior orbital rim, and intermittent, binocular horizontal diplopia. Her past medical and ocular history were unremarkable. She was adopted at age 7 months and there was no known history of pre- or perinatal problems. She was home-schooled and enjoyed playing outdoors. There were no known sick contacts and she had no preceding illness. Her visual acuity was 20/40 OD and 20/20 OS. On the right, there was limitation of infraduction and abduction, 3 mm of relative proptosis, mild periorbital edema and superior displacement of the globe. There was no relative afferent pupillary defect. The anterior segment and funduscopic examination were unremarkable. Her CT scan showed an ill-defined mass in the inferior right orbit which appeared to encase the inferior rectus and invade through the orbital floor into the maxillary sinus. MRI of the orbits showed a “large, enhancing, ill-defined mass arising from the inferior rectus muscle...invades right maxillary and right ethmoid sinuses...abuts posterior wall the globe and inferior optical nerve sheath...most likely represents rhabdomyosarcoma.” Anterior orbitotomy with biopsy was performed.

Financial Disclosures: The author had no disclosures.
Final Diagnosis
Orbital zygomycosis in an immunocompetent child

Summary of Case
Intraoperatively, the orbital mass was firm and white. There was invasion through the orbital floor. Intraoperative frozen-section pathology consultation noted “moderately cellular spindle cell lesion with mixed inflammatory infiltrate.” She was discharged home pending final pathologic diagnosis. The pediatric oncology service was contacted about meeting the patient once final pathology was known. On post-operative day 3, her parents reported increased swelling and chemosis around the eye. On the same day, the final pathology from the initial biopsy showed granulomatous infiltration with fibrosis and fungal elements identified consistent with zygomycosis. She immediately returned to the hospital where she was admitted with a plan for surgical debulking by both otolaryngology and oculoplastic surgery. Surgery proceeded without complication and an orbital catheter was placed for direct orbital and sinus irrigation with antifungal medication. Amphotericin B was started both intravenously and intraorbitally, though the orbital catheter was dislodged on post-op day #2. Evaluation for immunosuppression was completed and revealed no evidence of systemic immunosuppression. Posaconazole therapy was added and the patient was discharged home after 10 days once it was clear that her disease was not clinically progressing. Cultures from her surgical debulking never grew any organism. She subsequently received outpatient amphotericin B IV therapy for 3 months and oral posaconazole for a total of 15 months, over which time her examination normalized and radiographic evidence of disease resolved. Orbital zygomycosis in immunocompetent patients, especially children, is a rare cause of an orbital mass mimicking cellulitis. Management includes surgical debulking, long-term antifungal medication, and evaluation for immune suppression. Emerging organisms such as Apophysomyces elegans may make these presentations more common in the future.

Struggle/Dilemma of the Clinical Presentation Description
Rapid onset of orbital swelling in this age group mimicking orbital cellulitis is classic for rhabdomyosarcoma. Our patient's imaging was concerning for a destructive tumor and the family had already been told the child had cancer. Frozen section pathology was not conclusive enough for final diagnosis and culture was not obtained at the initial biopsy. The final diagnosis was unexpected and there are no clear guidelines for management, especially in immunocompetent patients such as ours.

Keywords: Orbit, Infection, Zygomycosis, Pediatric

References
History & Exam
A 55 year-old man presented with 6 weeks of intermittent left upper eyelid drooping and blurring of vision, worse later in the day. There was no significant past medical history, no smoking history, nor any systemic symptoms. On examination there was 2 mm of left upper eyelid ptosis with associated fatiguability and Cogan’s lid twitch. The remainder of his examination was normal. Acetylcholine receptor (AchR) antibody positivity and abnormal single fiber electromyelography confirmed the diagnosis of myasthenia gravis. The patient’s symptoms were easily controlled with pyridostigmine. CT imaging of the chest excluded a thymoma, but revealed numerous lung nodules and mediastinal adenopathy that suggested metastatic disease. Subsequent abdominal imaging demonstrated a large mass within the left kidney presumed to be primary renal cell carcinoma. A radical nephrectomy was performed. The renal mass was composed of an atypical lymphoplasmacytic infiltrate with only scattered IgG4 positive cells within a fibrotic background. There were no evidence of lymphoma or other malignancy. Additional biopsies of paraspinal adenopathy, lung masses, and subcutaneous scalp nodules showed similar inflammatory changes. Symptoms of ocular myasthenia were initially controlled for two years on pyridostigmine but then recurred.

Financial Disclosures: The authors had no disclosures.
Behind the Curtain

Final Diagnosis
Systemic inflammatory pseudotumor recurred. Subsequently, bilateral orbital inflammation, left lacrimal enlargement, diffuse subcutaneous masses, lung nodule growth, and hemolytic anemia all evolved on moderate doses of prednisone, plus trials of mycophenolate mofetil, cyclosporine, lenalidomide, and thalidomide. All signs and symptoms resolved upon starting bimonthly rituximab infusions, while continuing moderate doses of corticosteroids. The patient no longer required pyridostigmine to prevent myasthenic symptoms. Presumed autoimmune glomerulonephritis eventually developed, and the frequency of rituximab was increased to monthly with improvement in the patient’s kidney function. Eight years after initial presentation, he remains free of all ocular and systemic symptoms on monthly rituximab and 15 mg daily prednisone.

Summary of Case
Our patient had aggressive systemic inflammatory pseudotumor presenting initially as ocular myasthenia gravis. The standard chest imaging following the diagnosis of myasthenia enabled recognition of diffuse inflammation several years before other systemic signs and symptoms became apparent. Pathology from numerous biopsies ruled out lymphoma or other malignancies. Despite the prominent fibrotic background, the lesions did not meet current criteria to be considered the IgG4-related sclerosing form of inflammatory pseudotumor. Throughout the patient’s course, the AChR blocking antibody titer correlated with his overall systemic inflammatory state. The titer at the initial presentation of isolated ocular myasthenia gravis was 6.6 μm/L. It peaked two years later at 11.9 μm/L, coincident with the recurrence of ptosis and diplopia, as well as the evolution of diverse signs of systemic autoimmunity, including orbital inflammatory syndrome, inflammatory scalp masses, and autoimmune hemolytic anemia. The antibody titer decreased markedly (and ranged from 1.2 to 1.7 μm/L), and all clinical signs of systemic autoimmunity resolved, upon initiating bimonthly rituximab. The switch to monthly rituximab, prompted by the appearance of autoimmune glomerulonephritis, led to complete disappearance of detectable AchR antibody.

Struggle/Dilemma of the Clinical Presentation Description
Despite extensive active systemic pseudotumor, this patient initially manifested with ocular myasthenia gravis. There was considerable debate as to whether this patient had lymphoma or a reactive lymphoproliferative disorder, and regarding the best treatment for his associated myasthenia gravis. Extensive analysis supported a reactive inflammatory condition. After failure of multiple immunosuppressive agents, his myasthenia and systemic pseudotumor responded to rituximab, which has emerged as an effective agent in many cases of refractory myasthenia gravis.

Keywords: Diplopia, Ptosis, Myasthenia gravis, Autoimmune diseases

References
Deaf and Dizzy. Have We Been Susacked?

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History & Exam
A 60 year old man had an acute myelopathy in December 2010, with normal neuroimaging and spinal fluid (CSF). Although etiology was undetermined, improvement followed steroid therapy with persistent albeit moderate paraparesis. SSA was positive. On May 2, 2012, we first saw him for an acute vestibular syndrome (AVS) with unsteadiness, nausea, vomiting and decreased hearing. He is diabetic, has arterial hypertension, and was taking losartan, metformin, clopidogrel, and atorvastatin but was not on ototoxic or vasodilators medications. Examination at presentation showed left axial lateropulsion, a right beat, horizontal, unidirectional nystagmus in primary, right and up gaze, and a positive left horizontal head impulse test (h-HIT). The h-HIT device measured 0.49 (abnormal) left and 0.89 (normal) right gains Overt, corrective saccades were observed with horizontal left head accelerations; without skew deviation. He had left ear deafness and decreased sensori-neural hearing loss in the right without facial weakness. He had lower extremity pyramidal tract signs. Eye examination showed normal visual acuity, color vision and visual fields by confrontation, right optic nerve surface drusen, a normal left optic nerve, bilaterally normal macula, peripheral retina and branch retinal arteries, normo-reactive pupils without APD, and normal biomicroscopy without uveitis. A cerebello-pontine angle pre- and post- contrast MRI showed discrete restricted diffusion in the left centrum semiovale. CSF showed elevated protein (131 mg/dl,) but was otherwise normal with negative cytology. Two weeks later, he developed an encephalopathy, dysphasia and visual hallucinations. A repeat brain MRI, showed numerous, small bi-hemispheric and corpus callosum areas of restricted diffusion. Cerebral angiography was normal. EEG showed no seizures. Laboratory tests showed unremarkable SPEP, ESR CRP, ANA, ANCA, hypercoagulability, renal, and hepatic function tests. Muscle biopsy was normal. At this point, a diagnostic procedure was performed.

Financial Disclosures: The authors had no disclosures.
Deaf and Dizzy. Have We Been Susacked?

Answer

Final Diagnosis
Intravascular Lymphoma  Teaching Points  Intravascular Lymphomatosis (IL) is an uncommon microangiopathy that causes microinfarcts involving the cochlea, vestibular labyrinth, and the brain. Its clinical phenotype and MRI findings overlap with Susac’s syndrome. AION has been the most common neuroophthalmic manifestation. IL may also mimic VKH syndrome. No retinal arteriolar compromise has been reported to our knowledge IL may respond to treatment with Rituximab, Methotrexate and CHOP as provided to this patient.

Summary of Case
The diagnostic procedure performed in this case was a cerebral biopsy, which established the diagnosis of intravascular lymphoma. Like syphilis and sarcoidosis, intravascular lymphoma has been called the oncologist’s ‘great imitator’, due to the variety of CNS symptoms which can develop. In our patient, further work up included a normal bone marrow biopsy, normal chest and abdomen CT yielding no evidence of systemic lymphoma. Treatment with Methotrexate, Rituximab, and CHOP for an advanced lymphoma is currently in progress. The clinical phenotype in our case is best approached as a “cochleo-encephalopathy syndrome”. The association of acute, unilateral cochleo-vestibular loss, acute sensori-neural hearing impairment in the fellow ear, visual blurring and hallucinations, dysphasia, confusion and incontinence were the essential manifestations. MRI showed multiple, acute “microinfarcts” involving several vascular territories. Angiographic sparing of large and mid-size arteries, suggests a microangiopathy, targeting pre-capillary arterioles with a lumen of <100 mM. Both Susac’s and Sjogren’s syndrome were considered prior to tissue diagnosis, however there was no ancillary evidence for these diagnoses. It is unclear if the spinal cord syndrome 17 months earlier was related to his current diagnosis.

Struggle/Dilemma of the Clinical Presentation Description
This “microangiopathy” etiology was challenging. Negative serum antibodies, normal angiography and CSF, excluded most vasculitis. We depended completely on the clinical phenotype and MRI results. Empiric steroids provided only brief improvement. Stereotactic brain biopsy was the last resource. Intravascular Lymphoma should be included as a “microangiopathy” affecting arterioles with <100 Microns diameter. Susac’s syndrome (SS) was first considered given the overlapping clinical phenotype and neuroimaging. Retinal microangiopathy may be absent in early SS.

Keywords: Intravascular Lymphoma, Cerebral Microangiopathy, Deafness, Acute Vestibular Syndrome, Encephalopathy

References
It's All in Your Head

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History & Exam
A 45-year-old woman with a history of migraine headaches with visual aura presented after an atypical visual aura of 3 days duration without headache. A brain MRI (04/26/2011) revealed multiple intra- and extra-axial enhancing masses including brain parenchyma, pituitary infundibulum and corpus callosum. Medical history: migraine headache with visual aura since age 27 and upper airway resistance syndrome. Left leg and hip weakness/pain since 2009, attributed to fall on icy stairs. Social history: director regional medical imaging center, rare alcohol, never smoked. Travel: lived first 2.5 yrs in Japan, extensive travel Europe and Asia. No new animal exposures. Neuro-ophthalmic examination found of 20/20 right eye and 20/30 left eye. Color vision 10/10 right, 7/10 left without RAPD. Anterior and posterior segments were normal without optic atrophy. Kinetic visual fields demonstrated an incomplete right homonymous hemianopsia. CSF analysis including flow cytometry was negative for malignant cells, oligoclonal bands, VDRL, angiotensin converting enzyme, acid fast stains, mycobacterium tuberculosis complex PCR, Lyme IgG/IgM western blot, Borrelia DNA PCR and cryptococcus antibodies. IgG synthesis rate normal. Serum RPR and HIV 1, 2 antibodies negative. Needle biopsy on 05/23/11 revealed “granulomatous cerebritis” and oral prednisone initiated. Repeat MRI of the brain 07/05/11 found no change in lesion size, but subtle improvement in surrounding vasogenic edema. Tertiary center pathology review concluded the pathology was non-specific and did not concur with granulomatous disease. CT chest and abdomen 09/19/11 did not find evidence of hilar or mediastinal lymphadenopathy or interstitial lung disease. Repeat neuro-ophthalmic exams found slowly decreasing visual acuity left eye, and worsening right homonymous hemianopsia, evolution of right “bow tie atrophy” and left optic disc pallor. Patient’s vision and left hemiparesis continued to worsen. Steroids were slowly tapered in anticipation of open craniotomy and resection of the more superficial mass. A definitive procedure was performed.

Financial Disclosures: The authors had no disclosures.
Final Diagnosis
Isolated intracranial Erdheim-Chester disease presenting as an atypical migraine visual aura without headache

Summary of Case
Resection of superficial lesion was performed on 11/29/11. Immunohistochemical examination found lipid laden histiocytes equivocal for S100, positive for CD68 and CD163 arranged in sheets of inflammation with collagen deposition. The large histiocytic cells were CD1a negative and Factor XIIIa positive. Touton giant cells were identified without evidence of emperiplois. Microbial DNA PCR was negative. No acid fast bacilli, mycobacterium tuberculosis complex or Mycobacterium avium complex DNA were detected. There were no non-caseating sarcoidal granulomas. Pathology consultation from UCSF felt the histiocyte population was S-100 positive, however, NIH/NCI did not. Nonetheless, both agreed that pathology was consistent with Erdheim-Chester disease (ECD). Search for extra-cranial involvement included CT of chest and abdomen, trans-thoracic echocardiogram, long bone x-rays and whole body PET scan, which were unremarkable. Surveillance MRI January and May 2012 found decreasing size of enhancing intracranial lesions without treatment. Repeat visual fields have remained stable and neurologic examination found improved left lower extremity strength. ECD is a non-Langerhans cell histiocytosis (NLCH) proliferative disorder characterized by infiltration of various tissues by foamy histiocytes surrounded by fibrosis of unknown etiology.1,2 There is a strong male predominance and a mean age at diagnosis of 55 yrs.1 Osteosclerosis of the long bones with pain is common. Other organs involved are skin, lungs, heart, and kidneys. Retroperitoneal and orbital lesions reported.2 Central nervous system (CNS) involvement can be seen in up to 50% of affected patients.1 Immunohistochemistry is necessary to differentiate from other NLCH. Presentation typically consists of cerebellar and pyramidal syndromes.2 CNS MR imaging has revealed intra and extra-axial lesions, including ependymal enhancement, brainstem lesions, thickening of the pituitary stalk, cavernous sinus, sellar and hypothalamic lesions.3 Treatment is controversial and has included high dose interferon alpha, steroids, biphosphonates, and cytotoxic agents with variable results.4 Isolated intracranial ECD has been reported twice previously.2,5

Struggle/Dilemma of the Clinical Presentation Description
Needle biopsy of a brain lesion was reported as “granulomatous cerebritis”. Serum and CSF studies did not elucidate an etiology. Without significant response to steroids, a craniotomy and superficial lesion resection performed. Pathology found a predominant histiocytosis. Non-Langerhans cell histiocytosis includes several diseases with overlapping clinicopathologic characteristics. Lack of complete immunohistochemical analysis on initial needle biopsy, extra-cranial involvement and disease progression posed a diagnostic conundrum, resulting in delay of diagnosis.

Keywords: Erdheim-Chester Disease, Histiocytosis, Non-Langerhans Cell, Intracranial, Visual fields, Migraine visual aura

References
Is it Naughty or Nice?

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History & Exam
A 19-year-old woman presented with 4 days of rapidly progressive vision loss in both eyes associated with pain on eye movements. She was a foreign exchange student from Singapore, but had been in the U.S. for 7 months. A subjective fever and cold symptoms were noted 3 weeks prior, and she had experienced transient visual obscurations for 2 weeks. Visual acuity was 20/400 OD and CF at 1 foot OS with dyschromatopsia, left RAPD and bilateral severe optic disc swelling with hemorrhages. An MRI of the brain and orbits revealed large multifocal ring-enhancing lesions with surrounding vasogenic edema centered around the gray-white junction, and bilateral optic nerve enhancement. Neurologic examination was unremarkable except for an odd affect. Lumbar puncture showed an opening pressure of 15.5 cm H20, with elevated protein. CSF myelin basic protein was elevated, but testing for CSF OCB, IgG index, cytology, JC virus, Lyme, bacterial/fungal cultures were normal. Serum studies including SPEP, HIV, ACE, ANCA, SS-A/B, ESR, cryptococcus, Lyme, ANA, and PPD were normal. A transthoracic echocardiogram, CT chest/abdomen/pelvis, and MRI of the spine were normal. Progressive deterioration of vision to HM OD and LP OS within 24 hours of admission in addition to an inconclusive work-up prompted a diagnostic procedure.

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Is it Naughty or Nice?

Final Diagnosis
Acute fulminant MS (Marburg disease)

Summary of Case
Intravenous methylprednisolone (1 g daily) was administered for 7 days with significant improvement in visual function, and she was discharged on a prednisone taper. At 3 weeks, exam showed visual acuity of 20/25 OD, 20/40 OS, with mild disc swelling and a small paracentral scotoma OS. Given large multifocal ring-enhancing lesions and enhancing optic nerves on MRI, work-up was initiated to rule out neoplastic, infectious and inflammatory etiologies. The patient’s young age, acute onset of symptoms, lack of prominent neurologic signs or symptoms (relative to the size of the lesions), normal CT chest/abdomen/pelvis, and normal CSF cytology made a neoplastic process unlikely. Normal white blood counts (blood and CSF), and the absence of systemic illness or immunocompromised state made an infectious etiology less likely. The presence of bilateral optic neuritis along with tumefactive-appearing MRI lesions raised suspicion for a demyelinating or inflammatory etiology. Because of atypical features, profound visual deterioration and lack of a unifying diagnosis, brain biopsy was performed. Neuropathology showed vast areas of confluent demyelination, marked histiocytic infiltrates, perivascular lymphocytic cuffs, and numerous Creutzfeldt cells – suggestive of acute fulminant MS (Marburg variant). Although our case shares similarities with acute disseminated encephalomyelitis (ADEM – eg, age, preceding viral illness, multifocal ring-enhancing lesions, bilateral optic neuritis), neuropathology did not show multifocal inflammation and demyelination centered around venous structures, which would be expected in ADEM. Furthermore, the deep gray matter and spinal cord are commonly affected in ADEM. She did not meet diagnostic criteria for traditional MS (despite similarities to tumefactive MS) because of the (so far) monophasic course and absence of prior neurologic symptoms. Most reported cases of the Marburg variant are rapidly progressive despite treatment, invariably leading to demise (with few exceptions) within weeks to months. It would seem that our patient represents a relatively benign case of “fulminant” MS.

Struggle/Dilemma of the Clinical Presentation Description
The presence of severe optic disc edema with hemorrhages and ring-enhancing lesions on MRI was concerning for a neoplastic, infectious, or inflammatory/demyelinating etiology. Rapid vision loss and diagnostic uncertainty prompted a brain biopsy. Whether her preceding illness induced demyelination or whether her presentation represented the first attack of MS remains to be seen given what has so far been a monophasic process. Immunomodulatory therapies were debated and ultimately glatiramer acetate was initiated.

Keywords: Anterior optic neuritis, Ring-enhancing lesions, Fulminant MS

References

A Difficult Bug To Swallow

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History & Exam

A 54 year-old white male presented to the emergency room with a one month history of progressive binocular diplopia and a one week history of painless loss of vision in his left eye. He denied ocular pain, headaches, previous episodes of vision loss or diplopia, and had no history of trauma. Past medical history included non-insulin dependent diabetes mellitus, hypertension, and a right ventricular thrombus. Examination revealed visual acuities of 20/25 in his right eye and no light perception in his left eye. Pupil exam revealed a 3mm pupil on the right that reacted briskly to light and accommodation without an afferent pupillary defect. The left pupil was 5mm and did not react to light or accommodation and had an afferent pupillary defect. His intraocular pressures were normal. Confrontation visual fields and ocular motility were normal in the right eye. The left eye had complete ophthalmoplegia and mild proptosis. Both optic nerves were flat and pink with cup-disc ratios of 0.2 bilaterally. Cranial nerve testing revealed decreased sensation over the first division of the trigeminal nerve on the left. MRI with contrast of the brain and orbits revealed an infiltrative mass within the apex of the left orbit with extension to the cavernous sinus. The posterior extent of the left optic nerve showed evidence of infiltration by the lesion with coinciding edema. The adjacent sinuses had mild inflammation with mucosal edema. Laboratory data revealed a normal white-blood-cell count and platelet count but the hemoglobin was 7.8, INR was 3.6 secondary to Coumadin, and CRP was 2.8mg/dL. Further diagnostic studies revealed weakly positive ANA (titer of 40), negative ANCA, negative RF, a negative HIV test, and a negative PPD skin test. Blood cultures were negative but Aspergillus versicolor was isolated from a swab of the patient’s nasal cavity.

Financial Disclosures: The authors had no disclosures.
A Difficult Bug To Swallow

Final Diagnosis
Esophageal Adenocarcinoma with metastasis to the left orbital apex

Summary of Case
A whole body CT and PET scan revealed metastatic disease with enhancement at the left orbital apex, numerous lung nodules, numerous lymph nodes within the chest, mediastinum, axilla, and pelvis, enhancement of the spleen, the right adrenal gland, and numerous musculoskeletal lesions including the spine. Following the imaging studies and discussion with the oncologist the patient elected for conservative treatment. He passed away within 2 weeks of presentation without knowledge of the location of the primary cancer. An autopsy was performed that revealed poorly-differentiated adenocarcinoma with signet ring features within the patient’s esophagus and within all metastatic lesions. There was no evidence of Aspergillus infection in the orbital apex and it is felt this was normal flora that was isolated from the nasal swab. Metastatic disease is a rare cause of orbital apex syndrome. More commonly infectious, inflammatory, or local neoplastic processes are the culprit. The most common malignant tumors to metastasize to the orbital apex are cancers of the breast, lung, or kidney, and malignant melanoma\(^1,2\). Adenocarcinoma of the esophagus is the most common type of esophageal carcinoma in the United States. At the time of diagnosis it is not uncommon for it to have spread locally or to have metastasized to distant locations. The most common metastatic locations in order of frequency include regional lymph nodes, liver, lung, bone, adrenal glands, and peritoneum\(^3\). Metastasis involving the orbital apex is extremely rare and it is even more rare for this to be the presenting sign and symptom of the disease.

Struggle/Dilemma of the Clinical Presentation Description
The primary struggle was determining how to treat the patient on presentation. He was diabetic with a history of systemic thrombosis and positive Aspergillus cultures from the nasal cavity that had an infiltrative process involving the left orbital apex. Metastasis was considered but it was not suspected that metastatic esophageal adenocarcinoma was the cause of his orbital apex syndrome. Furthermore, it is unusual for ocular symptoms to be the presenting findings of metastatic disease.

Keywords: Orbital Apex, Metastatic Disease, Ophthalmoplegia

References
**History & Exam**
An 84-year-old woman who noted a headache for 2 weeks and a one day history visual loss OS. Medical history includes hypertension and hyperlipidemia. There is no jaw claudication, scalp tenderness, weight loss, fever, or chills. Examination showed a normal blood pressure and heart rate. Visual acuity is 20/30 OD and no light perception OS. Color vision is 4 of 8 OD and 0 of 8 plates OS. Confrontational fields are full in the right and non-plottable OS. Pupils measure 7mm in each eye with 2+reactivity in the right and no reactivity in the left with greater than 1.2 Log RAPD OD. She has decreased temporal artery upstroke bilaterally. Prednisone 80 mg daily and doxycycline 100 mg b.i.d prescribed for presumed GCA. CBC showed WBC 14.5 (4-10.5), platelets 445 (140-415), creatinine 1.36 (0.57-1.00), CRP 12.1 (0-4.9), RPR NR, ESR 62. A diagnostic procedure performed.

**Financial Disclosures:** The authors had no disclosures.
Final Diagnosis
Sphenoid sinus mucocele induced optic neuropathy (methicillin resistant staphylococcus aureus)

Summary of Case
An 84-year-old woman with headache, acute visual loss and elevated ESR and CRP. A left temporal artery biopsy showed only atherosclerotic changes, no evidence GCA. MRI showed a left sphenoid sinus mucocele compressing the optic nerve and endoscopic sinus surgery revealed pus surrounding the left optic nerve and destroying optic canal. Culture showed abundant methicillin resistant staphylococcus aureus. She was prescribed clindamycin and sulfamethoxazole/trimethoprim as well as high-dose steroids. Remarkably the post-operative vision improved from NLP to 20/25 OS.

Struggle/Dilemma of the Clinical Presentation Description
All the information of the case leads one to consider GCA, yet in light of the negative TA biopsy, one could have biopsied the fellow temporal artery or obtained neuroimaging. We did the latter which revealed the answer, a very unusual cause of optic neuropathy.

Keywords: Optic nerve, Headaches, Giant cell arteritis, Magnetic resonance imaging, Sphenoid sinusitis

References
Diabetes Does Not Explain It All

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History & Exam
A 62 year-old male referred for a six month history of progressive, painless, vision loss. He was initially seen by his local ophthalmologist, who informed him that his vision loss was “not correctable with glasses.” He was then referred to a retina specialist, followed by a neuro-ophthalmology consultation where he had reduced visual acuity and dyschromatopsia bilaterally. He was also found to have pale optic nerves, and a right homonymous hemianopsia. Further evaluation by an outside neurologist, found loss of vibratory sensation to the ankles, and a positive Romberg sign, initial laboratory studies failed to reveal a unifying diagnosis. Due to progressive vision loss and the abnormal imaging he was referred to us. The patient’s medical history was significant for systemic hypertension, type II diabetes mellitus, hypercholesteremia, anxiety and depression. He was taking lisinopril, pioglitazone, glipizide, simvastatin, fluoxetine, and clonazepam. He was a retired business owner, with no history of smoking and rarely drank alcohol. His family history was significant for progressive supranuclear palsy and late onset schizophrenia in his mother; his father died of a stroke. On our examination his, best corrected visual acuity was 20/40 OU, and he was able to identify 2/8 color plates OU. Pupils were normal without an RAPD. Humphrey visual fields showed a fairly congruous right homonymous hemianopsia. The optic nerves were pale with an enlarged cup-to-disc ratio of 0.7 OU. A brain MRI showed global atrophy of the cerebrum, cerebellum, brainstem, upper cervical cord, with extensive confluent periventricular and subcortical disease, without enhancement. On further questioning, he revealed a history of erectile dysfunction and bladder urgency dating back at least ten years. He then developed progressive difficulties with gait, and balance. He denied cognitive deterioration and attributed any slowing in his cognition to normal aging.

Financial Disclosures: The authors had no disclosures.
Diabetes Does Not Explain It All

Answer

Final Diagnosis
Adult polyglucosan body disease (APBD)

Summary of Case
The patient was referred for further evaluation of vision loss and unsteady gait. Neuro-psychological testing found moderate difficulties in memory and executive function. Based on the history of a bladder and erectile dysfunction, sensory neuropathy and neuro-imaging demonstrating atrophy with characteristics of a leukodystrophy, further diagnostic testing was performed. Genetic testing for the glycogen branching enzyme 1 (GBE1) detected a heterozygous mutation, and a functional enzymatic activity assay confirmed dysfunction of glycogen branching enzyme 1. He was enrolled in a clinical trial of trihetanoin, an odd-carbon fatty acids, that is theorized to provide substrate to the citric acid cycle thereby correcting the underlying energy deficit caused by the enzyme abnormality. APBD is a progressive disorder characterized by a neurogenic bladder, progressive gait disorder, sensory loss in the lower extremities, and cognitive decline. However, vision loss with optic atrophy has been rarely associated with APBD. Imaging with MRI typically shows medullary and spinal atrophy, with hyperintense white matter abnormalities. The disease typically present in the 4th or 5th decade. There is pathologic accumulation of intracellular polyglucosan bodies in cells of peripheral nerves and central nervous system. It is also hypothesized that decreased glycogen degradation leads to energy deficit and further dysfunction. Almost a third of the known cases of APBD are heterozygous with an assumed additional, but unidentified, second mutation.

Struggle/Dilemma of the Clinical Presentation Description
The initial symptoms of erectile dysfunction, neurogenic bladder, and peripheral neuropathy were attributed to his history of diabetes mellitus. When the patient developed progressive vision loss, with dyschromatopsia, optic atrophy, and exam findings to suggest a more diffuse process, imaging was obtained. The MRI showed both spinocerebellar atrophy and changes suggestive of a leukodystrophy. Given the progressive nature of this process, particularly the visual signs and symptoms, further investigation was necessary to establish the diagnosis.

Keywords: Adult polyglucosan body disease, Glycogen branching enzyme 1, Optic atrophy

References
Double vision?... Give your head a shake

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History & Exam

**HISTORY:** 54 year old gentlemen referred with diplopia. CC: 3 month history of constant binocular oblique diplopia with mild worsening, progressive disequilibrium, and a wide based gait. No vertigo, loss of coordination, loss of vision or oscilipsia, hearing loss, or tinnitus. PMhx: No history of cancer, hypothyroidism, GI malabsorption or anemia. Occupational history: Food service industry. Diet: Normal Non smoker, non drinker, no illicit drug use. ROS : negative FHx: Negative for spinocerebellar ataxias. Bladder cancer in mother. No meds. **On Exam at presentation:** VA 20/20 OU. Afferent neuro-op exam normal. EOM: +2 left inferior oblique overaction, -1 under action of Left superior oblique. 16LHt on primary gaze, 18 LHt on right gaze and 23LHt on Left head tilt. No subjective torsion but fundus exam shows marked excylotorsion of right eye, mild incyclo of left. No change in deviation upon lying supine. Nystagmus -- primary: high frequency low amplitude right beating and torsional nystagmus. Right gaze: right beating nystagmus, occasional torsional beats. Upbeat nystagmus on upgaze. Left beating in left gaze. Occasional rightward beats on downgaze, with no downbeat nystagmus. Smooth pursuit and saccades well calibrated. Horizontal head shaking showed reproducible right beating nystagmus sustained for 15 sec. Cerebellar exam: Mildly wide based gait -Tandem gait: difficult however no fall preference to one side or other. No appendicular ataxia **Interim examinations:** MRI and CSF analysis normal. Extensive bloodwork was performed. CT neck, abdomen, pelvis negative. Scrotal ultrasound suggestive of right testicular malignancy. Right orchiectomy performed, revealed regressed testicular CA **On exam 7 months later:** Stable vertical diplopia due to skew deviation. Horizontal head shaking now produced upbeat nystagmus. MRI shows vermal atrophy .Overall stabilization of progressive course.

Financial Disclosures: The authors had no disclosures.
Final Diagnosis
Paraneoplastic cerebellar degeneration in association with CRMP-5 antibodies and testicular cancer.

Summary of Case
54-year old man with sub-acute progressive cerebellar disease. Clinical testing suggested left vestibulocerebellar dysfunction vs. irritative right brain stem lesion, presenting with a right beating nystagmus, ataxia, and left hypertropia. Enhanced posterior fossa MRI showed an absence of structural lesion. Blood work included B12, vitamin E, and TSH of which all were normal. CSF with cytology normal. Paraneoplastic syndrome was quickly entertained. Auto-antibody testing revealed CRMP-5 positivity. CT chest, abdomen and pelvis normal. A scrotal ultrasound revealed 2 suspicious lesions in the right testicle. Complete orchietomy was performed and pathology showed characteristic features of a regressed testicular cancer. Treated with IVIG with relative disease stability, with mild progression of cerebellar syndrome. Repeat whole body imaging was negative. Over several months, horizontal head shaking nystagmus, although initially right beating, evolved into upbeat nystagmus following horizontal shaking indicative of central cross coupling as part of his peripheral to central progression. Optic neuropathy is the predominant neuro-ophthalmologic presentation; however, has been described in association with PCD. CRMP-5 is most commonly described in association with small cell lung cancer, and thymoma, and one previous report of testicular CA presenting with limbic encephalitis and choreiform dyskinesias. To our knowledge, our case represents the first to report PCD in association with testicular cancer and CRMP-5 autoantibodies. Although precise differentiation between a left fourth nerve palsy and cerebellar-origin skew deviation was difficult due to conflicting clinical findings, objective excyclotorsion of the lower eye and incyclotorsion of the higher eye was documented, making skew more plausible, in particular given the associated vestibulocerebellar findings.

Struggle/Dilemma of the Clinical Presentation Description
Dysmotility c/w fourth nerve palsy; however, given ataxia, localizing forms of nystagmus, direction of fundus torsion, and vestibulocerebellar dysfunction, skew deviation was more likely. Initial imaging read as normal –vermal atrophy? Patient systemically well with neg. ROS and no history of cancer. CRMP-5 positivity revealed, but uncommon in PCD. Discovery of malignancy required consideration of organ systems beyond the usual suspects associated with CRMP-5 and PCD. U/S suggested testicular CA, but pathology non-confirmatory for active malignancy, but laden with scar suggestive of regressed cancer.

Keywords: Paraneoplastic, Cerebellum, CRMP-5, Nystagmus, Diplopia

References
History & Exam
A 40-year old woman, neurologically normal until age 31, presented with progressive paraparesis over several years. She underwent neurological evaluation at age 32 (neuroimaging, serologies, lumbar puncture, muscle biopsy) with no resultant diagnosis (records unavailable). She required a wheelchair by age 36 and gradually developed slurred speech, cognitive decline, and worsened motor function. Simultaneous with neurologic evaluation, she was undergoing dermatologic evaluation for generalized hyperpigmentation with hypopigmented macules. Family history was notable for 2 younger brothers with similar skin findings. The elder of the two developed parkinsonism in his late 30’s and the younger, progressive paraparesis 2 years after spinal AVM embolization. Neurological examination revealed pseudobulbar affect, perseveration, hypophonia, dysarthric speech, proximal greater than distal and leg greater than arm weakness, decreased vibratory and pinprick sensation in legs, hyporeflexia with upgoing toes, frontal lobe reflexes, upper extremity dysmetria, and hypotonia. Acuity was 20/25 OD and 20/30 OS. Color vision (Ishihara) was control only OD and 2/14 OS. Contrast sensitivity (Peli-Robson) was reduced (line 4 OD, 5 OS). There was no APD. Optic discs were mildly pale temporally. Goldmann field revealed complete central vision loss to small isopters. Ocular motor exam was normal except for hypermetric saccades.

Financial Disclosures: The authors had no disclosures.
Clues Hidden in the Skin

Final Diagnosis
Chediak-Higashi Syndrome (with an adult-onset neurodegenerative phenotype).

Summary of Case
The patient had multifocal neurological illness with optic nerve, spinocerebellar, extrapyramidal, and neuromuscular involvement. Brain MRI showed cortical atrophy. Cervical spine MRI was normal. EMG revealed axonal polyneuropathy. Electroretinogram was normal. Skin biopsy showed lymphocyte intracellular inclusions and amyloid deposition. Lymphocyte panel revealed low natural killer cell activity. Light microscopy of hair shaft showed pigmentary clumping. Normal labs included CK, cryoglobulins, HTLV-1 and 2, SCA 1-3 and 6, OPA-1. VEP was extinguished (age 43). Genetic testing diagnosed Chediak-Higashi Syndrome (CHS). SNP array showed no loss of heterozygosity, suggesting no close parental relationship. Sequencing of the entire coding region of LYST identified homozygosity for a novel six base pair in-frame deletion in exon 43, predicting the loss of asparagine and threonine residues from the LYST protein product. The proband was also heterozygous for an intronic sequence variant distal to the deletion. Homozygosity was confirmed in both affected brothers and both parents. Unaffected brothers were confirmed heterozygotes. Mutations in LYST, a ubiquitously expressed gene concerned with lysosomal trafficking, cause CHS. It is an autosomal recessive disorder characterized by childhood-onset immune dysfunction and hemophagocytic syndrome, partial oculocutaneous albinism and other pigmentary abnormalities, and neurologic dysfunction. Amyloidosis, as in this case, is reported in CHS and may contribute to the neurodegenerative process. Rare CHS patients, such as ours, present with absent or subclinical immunological abnormalities, but develop progressive neurodegenerative disease in early adulthood. Oculocutaneous albinism is characteristic, but was absent in our patient and in other reported cases. There is one case of visual dysfunction in CHS with an extinguished ERG. To our knowledge, optic nerve involvement has not been reported in CHS. Vision loss progressed over two years, with acuity at age 43 of 20/80 OD and 20/100 OS with complete loss of color vision. Both homozygous brothers had bilateral optic nerve involvement.

Struggle/Dilemma of the Clinical Presentation Description
Diagnosis of multifocal neurological disorders is difficult, even when patients present with classic disease manifestations. When usual causes of spinocerebellar degeneration were excluded, diagnostic efforts shifted towards peroxisomal and mitochondrial disorders, especially OPA-1, given reports in Brain of multifocal neurological involvement. The diagnosis of CHS was facilitated by the skin abnormalities, despite the challenges posed by the novel mutation, the absence of immunological dysfunction, and the presence of atypical manifestations such as optic nerve involvement.

Keywords: Chediak-Higashi Syndrome, Optic Neuropathy, Parkinsonism, Spinocerebellar degeneration

References
History & Exam

A 58-year old man presented to the Eye Clinic at his local Hospital after his private Ophthalmologist found bilateral optic nerve edema as the cause of his sudden, painless binocular vision loss. He had noted an erythematous rash that started on his back, spread centrifugally into his extremities, sparing his palms and soles, a couple of weeks before his vision declined. He had concurrent headache, fever, and generalized malaise. The rash had been diagnosed as a heat rash due to exposure to extreme heat while working on his farm. He was treated with a corticosteroid injection at a local Emergency Department, and the rash started to clear after a few days. He was also treated with glaucoma medications by his private Ophthalmologist for elevated intraocular pressures. Past medical history revealed hypertension and hyperlipidemia. He was a farmer, and did not smoke, consume alcohol, or use drugs. He was admitted to his local Hospital, where he was treated with intravenous methylprednisolone for suspicion of bilateral optic neuritis. Brain CT and MRI were read as normal. A lumbar puncture was performed, which had normal opening pressure, slightly elevated protein (100 mg/dL); 50 RBC/hpf; and 13 WBC/hpf, 90% lymphocytic. He had no improvement on corticosteroid pulse. He was empirically treated with different meds after diagnostic lab studies were obtained. Glaucoma eyedrops were discontinued. His exam revealed best corrected visual acuities of 20/100-OU, constricted visual fields, color plates 3/14 OD and 5/14 OS. He had no RAPD. Intraocular pressures were normal. Both optic nerves were elevated and congested. His empiric medication was continued. Over the ensuing months, his optic nerve swelling resolved, revealing optic atrophy. His visual field constriction improved. His best corrected acuities were 20/40 OD and 20/100 OS three months after onset of symptoms.

Financial Disclosures: The authors had no disclosures.
Final Diagnosis
Optic neuropathy due to Rocky Mountain Spotted Fever

Summary of Case
Additional history revealed that the patient had suffered a tick bite about two weeks prior to the onset of his rash. Based on this information and the rash, patient was started on doxycycline and Rocky Mountain Spotted Fever (RMSF) titers were obtained; IgG by EIA was positive; confirmation by IFA was positive at 1:64 dilution. A week later, RMSF IgG IFA titer was positive at 1:256 dilution. Laboratory studies to rule out NMO (Neuromyelitis Optica), vasculitis, lupus, sarcoidosis, toxoplasmosis, syphilis, Brucellosis, Ehrlichiosis, etc. were all negative. Diagnosis of RMSF was made. The patient was treated with doxycycline 100 mg orally every 12 hours for 60 days. RMSF is a disease caused by *R. rickettsii*, an obligate intracellular coccobacillus spread by a tick vector. It manifests after a mean incubation period of 7 days with the triad of high fever, myalgia, and headache. Gastrointestinal manifestations are common. A centripetal rash starts in the wrists and ankles by days 3-7, and characteristically also spreads centrifugally to the palms and soles. It frequently can lead to CNS manifestations, including encephalitis, deafness, stroke-like syndromes, and encephalopathy. Ocular manifestations include conjunctivitis, anterior uveitis, retinal vasculitis, hemorrhages, and arterial occlusions. About 1.5% of reported cases have involved swelling of the optic nerves. A case report of macular star figure has been reported. Case reports generally are not favorable for good recovery of vision after optic nerve involvement. Prior to the antibiotic era, it was a highly lethal disease, but it responds to tetracycline, doxycycline, and chloramphenicol.

Struggle/Dilemma of the Clinical Presentation Description
The initial presentation with a centrifugal rash, sparing the palms and soles, is not typical for RMSF, which usually starts in the wrists and ankles and spreads to the palms and soles, then centripetally toward the trunk. The history of tick exposure was not obtained by the first clinicians who evaluated this patient, leading to an erroneous diagnosis of an allergic rash.

Keywords: Optic nerve vasculitis, Optic neuropathy, Rocky Mountain Spotted Fever

References

History & Exam
A cocaine-abusing 51 year-old man complained in May 2012 of left eye decreased vision and pain for several months. We found no abnormalities of the right eye or its adnexa. There was a ruptured left globe with a mass protruding between the eyelids. Neurologic examination disclosed left hypesthesia of all three trigeminal divisions, left facial weakness, left neurosensory hearing loss, and left sternocleidomastoid and trapezius weakness. Two years earlier, he had had persistent hearing loss in the left ear attributed elsewhere to infection. One year later, he developed left facial weakness diagnosed as Bell’s palsy, treated with corticosteroids without recovery. A few months later, he became hoarse and had difficulty swallowing. Left vocal cord paralysis was diagnosed. He underwent 3 esophageal dilatations without improvement in swallowing. A complete blood count showed a hemoglobin of 7.9. Serum protein electrophoresis, folate, B12, thyroid, BUN, creatinine, and paraneoplastic panel were normal or negative. Head MRI demonstrated an enhancing soft tissue mass extending from the left nasopharynx to the left middle and posterior cranial fossae. Chest CT showed multiple pulmonary nodules, a liver nodule, and a paravertebral cervical mass. Lumbar puncture showed only a slightly elevated protein. Paravertebral mass biopsy showed blood only. Bone marrow biopsy was negative. In May 2012, our partial exenteration of the left orbit showed chronic inflammation and scleral necrosis. The specimen grew Staphylococcus and streptococcus species so he was treated with amoxicillin-clavulanate. He was noncompliant and returned with left socket pain. Examination disclosed maggots and pus. The infection was obliterated with intravenous vancomycin and piperacillin-tazobactam. Dedicated orbital/skull base MRI in June 2012 redemonstrated the nasopharyngeal/intracranial mass without growth. CT chest showed multiple partially cavitary nodules. A left nasopharyngeal biopsy showed chronic inflammation. An additional procedure was performed.

Financial Disclosures: The authors had no disclosures.
Final Diagnosis
Granulomatosis with polyangiitis (Wegener's granulomatosis)

Summary of Case
Bronchoscopy yielded a transbronchial specimen showing necrotizing granulomatous inflammation including distinctive granulomatous microsabscesses. Stains for fungal and AFB organisms were negative. Several days later, ANCA and proteinase 3 antibody were positive. The diagnosis is granulomatosis with polyangiitis (GPA), previously known as Wegener’s granulomatosis. It caused scleritis and secondary globe rupture, the nasopharyngeal/intracranial mass with mononeuritis multiplex (cranial nerves 7-11), and lung lesions. He was treated with prednisone 60 mg daily and rituximab 1 gram every 2 weeks for 2 doses. One month later, proteinase 3 antibody index was negative and chest CT showed interval decrease in the multiple mass-like opacities. Dedicated skull base and neck CT re-demonstrated the nasopharyngeal/intracranial mass relatively unchanged. The diagnosis of GPA appears obvious in retrospect! But there were many confounding factors in this case. The patient was cachectic because of cocaine abuse and difficulty swallowing. The nasopharyngeal/intracranial mass was large and eroding bone, suggesting neoplasm. Although GPA can cause this, intracranial lesions are rare and one of this size is extremely rare (1). The cavitary lung lesions certainly occur in GPA, but because of the cranial findings, neoplasm and infection were the primary considerations. The ruptured globe, which in retrospect probably resulted from scleritis, was superinfected and scarred, making the diagnosis of GPA difficult. The nasopharyngeal biopsy was interpreted as chronic inflammation, although in retrospect it did show small zones of “dirty” necrosis. Nasopharyngeal biopsies in GPA are known to be often falsely negative (2, 3). Even the bronchoscopic biopsy was not classic for GPA, missing a convincing vasculitis.

Struggle/Dilemma of the Clinical Presentation Description
The lessons from this case are that a pathologic disease of GPA may be hard to make. But confronted with a ruptured globe, together with multiple lung nodules and chronic nasopharyngeal and meningeal-based masses, GPA should be a top consideration and repeated biopsies may be necessary. Moreover, had the clinicians not been preoccupied with presumptions of neoplasm and infection, they would earlier have ordered the highly specific and relatively sensitive blood tests--ANCA and PR3!

References
Occam’s Razor or Gamma Knife?

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History & Exam
A 53 year-old female presented to the ER with ptosis in right eye and double vision. Medical history included hypertension, end-stage renal disease on hemodialysis, and an episode of anterior uveitis in the right eye 10 years earlier. She was diagnosed with a right 3rd and 6th nerve palsy. She was not evaluated by an ophthalmologist. MRI of the brain without gadolinium showed an enlarged pituitary gland with a 13mm focal mass invading the right cavernous sinus without involvement of the optic chiasm. Prolactin level was 402 ng/mL. ACTH, GH, TSH, and cortisol were within normal limits. She was treated 2 days later with gamma knife radiosurgery consisting of 20 Gy to the tumor while maintaining a dose of less than 6 Gy to the optic nerves and chiasma. She was started on bromocriptine. 6 months later, she still had a residual right 3rd and 6th nerve palsy. MRI without gadolinium showed mild interval decrease in size if the mass. 4 months later, she presented to our institution with pain in the right eye and headache. Visual acuity was 20/25 OU. Pupils were equal with no afferent defect. She had a large angle esotropia and no abduction OU consistent with complete bilateral sixth nerve palsies. Anterior segment and fundus examination were within normal limits. Automated visual fields were unreliable but within normal limits. MRI again demonstrated residual tumor in the right cavernous sinus with no optic nerve or chiasmal involvement. Prolactin level remained elevated at 336 ng/mL.

Financial Disclosures: The authors had no disclosures.
Occam's Razor or Gamma Knife?

Answer

Final Diagnosis
Wegener’s Granulomatosis Masquerading as a Prolactinoma

Summary of Case
The patient was lost to follow-up for six months. She then presented again with pain and visual loss in the right eye. Visual acuity had decreased to 20/400 OD. Repeat MRI showed increased size of the mass and new involvement of the right pre-chiasmal optic nerve. A fronto-orbital craniotomy and decompression of the mass was performed. Pathology revealed fibrous tissue with an extensive inflammatory infiltrate, including granulomas, histiocytes, and scattered giant cells, along with perivascular inflammation and necrosis. The results were consistent with a diagnosis of Wegener’s granulomatosis (WG). Upon further questioning, the patient revealed a history of a kidney biopsy showing WG over 12 years prior as the cause for her end-stage renal disease. She was placed on oral prednisone due to an adverse reaction to rituximab. Compliance and follow-up remain poor. Visual acuity at the last follow-up was 20/50 OD with an unchanged motility exam. WG is a systemic, necrotizing, granulomatous vasculitis of unknown etiology, first described in 1939 [1]. Diffuse small and medium size vessel involvement in WG classically leads to upper and lower respiratory tract, and kidney involvement. Central nervous system involvement has been reported in approximately 22-54% of cases of WG [2]. Most commonly this involves peripheral neuropathy resulting from vasculitis affecting the small vessels. Pituitary involvement is extremely rare, and the exact mechanism is unknown. When it does occur, it usually leads to central diabetes insipidus with loss of the normal hyperintense signal in the posterior pituitary. However, we are not aware of any similar reports of WG mimicking a pituitary prolactinoma [2,3].

Struggle/Dilemma of the Clinical Presentation Description
The mass behaved like a prolactinoma, and was treated with gamma knife--was this premature? Are the bilateral VI palsies now a complication? Even if we had known the results of the previous kidney biopsy, would anyone have followed Occam’s Razor and suspected something as rare as Wegener’s granulomatosis involving the pituitary? Would a gadolinium enhanced study have helped?

Keywords: Wegener’s Granulomatosis, Prolactinoma, Headaches, Magnetic resonance imaging, Intracranial tumors

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Admissions Ad Nauseum: A Cryptic Case of Chiasmopathy

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History & Exam
A 38 year old healthy female presented with blurred vision. Her ophthalmologist found acuities of 20/200 OD and 20/50 OS, a central scotoma OD and a temporal hemianopia OS. Neurological examination was normal. MRI revealed patchy leptomeningeal enhancement. VEP, SSEP, BAEP were all unrevealing. ANA was elevated at 1:320. Lumbar puncture (LP) had elevated opening pressure of 31 cm of water, WBC 34, protein of 231, glucose <10 and positive oligoclonal bands. Fungal, bacterial, mycobacterial cultures, cytology and flow cytometry were negative. A second LP was similar. Our neuro-ophthalmology service found acuities of 20/200 OD and 20/30 OS, dyschromatopsia OD, a right relative afferent pupillary defect, trace temporal disc pallor OU and a generally depressed field OD and temporal hemianopsia OS consistent with a junctional scotoma. MRI demonstrated diffuse leptomeningeal enhancement within the brainstem, optic chiasm, infundibulum, pituitary gland, prepontine cistern and cranial nerves VI-VIII bilaterally. Chest CT was negative. PET scan showed increased uptake in a supraclavicular node, which was normal on biopsy. RPR, Lyme, HIV, ANA, dsDNA and ACE were negative. Bone marrow biopsy showed no malignancy. A trans-sphenoidal biopsy showed normal pituitary tissue and dura. She was treated with IV methylprednisolone for 3 days and vision improved to 20/30 OU then discharged on 60mg prednisone daily only to returned two days later with headache and visual acuity of light perception OD and 20/400 OS with visual field constriction OD>OS. Secondary to hyponatremia she experienced a generalized tonic clonic seizure. After 1 gram of IV methylprednisolone daily and sodium repletion, for three days, acuities returned to 20/50 OD and 20/30 OS. Vision declined two more times with oral prednisone taper, and improved with 1 gram IV methylprednisolone bolus. MRI showed persistent peri-chiasmatic and perineural enhancement and new hydrocephalus, a third LP was performed.

Financial Disclosures: The authors had no disclosures.
Admissions Ad Nauseum: A Cryptic Case of Chiasmopathy

Final Diagnosis
Cryptococcal neoformans var grubii meningitis

Summary of Case
Examination of the CSF on the final LP revealed yeast forms on the gram stain consistent with Cryptococcal neoformans. Cryptococcal antigen titre was 1: 512. Amphotericin B and Flucytosine were started IV with high dose IV steroids. With treatment, acuity, color vision and fields all returned to normal. Cryptococcal antigen of the CSF from the initial LP was negative. However, a mucicarmine stain of the pituitary biopsy was positive, consistent with the presence of mucopolysaccharides on the capsule of cryptococcal yeast at the time of the biopsy. It remained unclear as to whether the primary diagnosis was cryptococcal meningitis in an immunocompetent host, or if instead, a fungal meningitis complicated a case of neurosarcoidosis in the context of immunosuppression secondary to IV steroids. The speciation of the yeast was Cryptococcus neoformans var grubii, commonly found in eucalyptus plant, wood and pigeon feces and found around the world. Inoculation may have occurred via trans-sphenoidal biopsy, as Cryptococcus is usually acquired via inhalation of spores. Biopsy could have introduced fungal elements into the CNS. HIV was negative (tested twice), but CD4 counts were decreased. In culture growth occurs in 3-7 days with identification in 3-4 days; however occasionally growth is slower and incubation should be continued for 4-6 weeks. Cryptococcus neoformans is a saprophytic fungus that may cause disease in normal hosts as well as the immunocompromised. In the immunocompetent individuals Cryptococcus neoformans var. gattii is implicated more often compared to the immunocompromised with Cryptococcus neoformans var neoformans. In those who are immunocompromised with defective cell mediated immunity, such as those being treated with corticosteroids, HIV, lymphoma and leukemic patients, infections can be more serious with rapid progression and dissemination. Infections are more often pulmonary than meningoencephalitis. In the immunocompetent infections are usually of the basal leptomeninges.

Struggle/Dilemma of the Clinical Presentation Description
This case illustrates the difficulties in treating a patient with rapid visual decline with an exquisitely steroid responsive optic neuropathy and chiasmitis in whom the diagnosis is uncertain. Repeated negative fungal cultures reflected cryptococcal’s fastidious nature. Once cryptococcosis was identified, it remained unclear whether or not megadose steroids should be continued in the face of a fungal infection since vision appeared to be dependent on their presence.

Keywords: Cryptococcal Meningitis, Leptomeningeal disease, Chiasmopathy

References
**History & Exam**

A healthy 6-month old boy was sent to a pediatric neurologist because his parents had noted “irregular eye movements” for 1 month. The neurologist found horizontal nystagmus with a rare vertical component and ordered a brain MRI that demonstrated a suprasellar mass, prompting hospital admission. We found him to be alert and behaving normally. Vital signs and general physical examination were normal. He could fix and follow objects. Pupils reacted normally to bright light without afferent pupillary defect. He had a multivector nystagmus with rare intermittent convergence movements. Fundus and neurologic examinations were normal. Review of the outside brain MRI showed a mass perhaps arising from the diencephalon with high T2 signal and low T1 signal and intense enhancement. It compressed the third ventricle superiorly, extended anteriorly along the planum sphenoidale, and postero-inferiorly into the pre-pontine cistern. The imaging features, apparent site of origin, and the patient’s young age strongly suggested a diagnosis of pilocytic astrocytoma. In view of the considerable risks in operating on such a young patient with such a large tumor, chemotherapy (carboplatin and vincristine) began without a tissue diagnosis. Four days later, the patient was readmitted for poor feeding and lassitude. Features of a dorsal midbrain syndrome were present. Brain CT demonstrated interval increase in the size of the lateral and third ventricles. A procedure was performed.

**Financial Disclosures:** The authors had no disclosures.
A Case of Mistaken Identity

Answer

Final Diagnosis
Final Diagnosis: High-grade glioma

Summary of Case
The procedure was a ventriculoperitoneal shunt and biopsy of the mass. The biopsy showed microvascular proliferation, infiltrative growth, mitotic figures, areas of necrosis, and a MIB-1 proliferation index of 22%, characteristics of a high-grade glioma. The patient’s chemotherapy was changed to a drug regimen appropriate for this tumor (CCG protocol 9921 induction regimen A). The 3rdmost common malignant brain tumors in children under 2 years (1), high-grade gliomas, usually occur in the cerebral hemispheres with only 11-24% arising from the diencephalic region, the presumed source in our patient (2, 3). Because malignant brain tumors rarely arise in this region in young children, and because pilocytic astrocytomas commonly originate in this region, are known to enhance avidly, and typically grow without invading brain, we believed that pilocytic astrocytoma was a strong enough presumptive diagnosis to preclude the need for biopsy. We were wrong. Although high-grade gliomas of youths and adults are pathologically indistinguishable, there are differences in tumor behavior. High-grade gliomas in very young patients are remarkably chemosensitive, with a 5-year overall survival rate of over 50% with appropriate multi-drug chemotherapy (4). Still unresolved issues are whether age at diagnosis, histologic features of malignancy, or the degree of surgical resection influence prognosis (4).

Struggle/Dilemma of the Clinical Presentation Description
Pilocytic astrocytomas contain networks of leaky blood vessels that cause them to enhance avidly, mimicking malignant brain tumors (5). In youth, they often arise in the diencephalon. These facts misled us into thinking that our patient had a pilocytic astrocytoma, justifying empiric chemotherapy without a biopsy. When tissue was later obtained after tumor expansion caused hydrocephalus, we discovered that the tumor was a high-grade astrocytoma demanding an entirely different chemotherapy regimen.

Keywords: High-grade glioma, Pilocytic astrocytoma, Magnetic resonance imaging

References

History & Exam
A 46 year old Hispanic male presented to the ER with progressive visual loss over 1 week in both eyes to the point where he could only see light. He denied pain on eye movements, but reported a history of headaches for the past 8 months that became more severe in the last few weeks. They were pressure like, came and went, started occipital and radiated to the front. He was able to get initial relief with ibuprofen, but for the past week it didn’t help. CT head in the ER was within normal limits (no bleed/mass/midline shift). His past medical history was significant for DM, HTN and hyperlipidemia. He reported being treated for several months for rheumatoid arthritis 8 years ago. Review of systems was negative. He was on oral diabetic and hypertensive medications as well as simvastatin. Social history was significant for 30 pack years of smoking – he quit approximately 4 months prior to presentation. On exam he was hand motion OD and NLP OS. His pupils were sluggish (os more than od) but round and reactive with a trace APD OS. IOP was normal as was extraocular motility. Slit lamp exam showed nuclear sclerotic cataracts OU and DFE showed non proliferative diabetic retinopathy. He was admitted for work up. The following labs were negative/normal: SS-A, SS-B, thyroid function, homocysteine, fasting lipid panel, liver panel, coags, toxicology screen, HIV, RPR, rheumatoid factor, anti-DS DNA; Positive/Elevated labs included: ESR 115, CRP 66.8, ANA (positive nuclear pattern 1:80). MRI brain/orbits showed diffuse enhancement of the dura with apparent thickening greater on the left side. In addition bilateral enhancement of the posterior aspect of the intracranial optic nerve sheath was seen.

Financial Disclosures: The authors had no disclosures.
Final Diagnosis
IgG4 pachymeningitis.

Summary of Case
A repeat ophthalmic exam two days after presentation showed vision to be hand motion OU. CSF analysis showed 1 RBC, 21 WBC, lymph 80%, glucose 90 (serum 164), protein 44 and negative cytology as well as no organisms or host cells on gram stain. The decision was made to start IV solumedrol to salvage vision. Other CSF studies that were negative included: CMV PCR, CMV IgG/IgM, crypto Ag, HSV, RPR and FTA-ABS. Chest-Xray was normal, PPD was negative. The patient also reported scrotal pain and a rash on his legs. Biopsy of the rash and a scrotal ultrasound were non-revealing. MRI T- and C-Spine were normal as well. Four days after initiation of IV methylprednisolone the patient’s vision improved to 20/20 OU. On exam he still had a trace APD OS and his color plates were 1/8 OU. More CSF studies returned showing an elevated IgG synthesis rate (31.1mg/24hr), a high IgG index (1.09) and normal albumin (20.9). A dural biopsy showed pachymeningitis with increased IgG4 plasma cells. The patient was discharged on PO prednisone 60 mg with follow up. IgG4 pachymeningitis appears to be one of the manifestations in the newly recognized IgG4-related disease spectrum. This disease was first recognized in 2001 in sclerosing pancreatitis and in 2003 as a systemic condition. At this point in time there are only a few papers describing reports on the rare presentation of involvement of the CNS, with little information being available about clinical presentation, diagnostic criteria and optimal treatment. The treatment modalities available are based on Class IV evidence. Most of the information is currently being extrapolated from the more common presentation of autoimmune pancreatitis and include initial treatment with IV steroids, followed by glucocorticoid sparing agents and/or rituximab in the case of refractory disease.

Struggle/Dilemma of the Clinical Presentation Description
This was a very challenging case given the rarity of this disease. The initial differential diagnosis included meningitis, lymphoma, a granulomatous process, and less likely metastatic disease. Blood work and skin biopsy were non revealing. Reviewing the case, the only potential early clue was the elevated IgG in the CSF analysis. However, there was no firm diagnosis until pathology confirmation established this to be a case of IgG4 pachymeningitis.

Keywords: Vision loss, Headaches, Lumbar puncture

References