Grand Rounds

A 36-year-old man with a red eye

Drew Chronister, MD, and Evan Waxman, MD

Author affiliations: University of Pittsburgh Eye and Ear Institute

History

A 36-year-old Caucasian man with a six-day history of right eye redness and right brow pain presented with new onset blurry vision. The pain was a mild, dull ache and was fairly constant. The redness began laterally and then spread over his entire right eye. He was seen at an outside emergency room 4 days prior to presentation where he was started on oral cephalexin for presumed preseptal cellulitis. He denied photophobia, periorbital redness or swelling, pain with eye movement, or recent trauma. His past ocular history was significant for a left eye “prosthesis” that he had had for 19 years after suffering a gunshot wound to the left eye.

His past medical history was significant for juvenile rheumatoid arthritis and rheumatic fever as a child. He had no drug allergies and his only medications were vicodin and keflex. He denied tobacco or alcohol use and was employed as a prison guard. On review of systems, he had a flu-like illness 10 days prior with fever, myalgias, nausea, vomiting and diarrhea. All of these symptoms had since resolved. He had stable chronic knee pain which was controlled with vicodin. He denied headache, cough, sore throat, shortness of breath, hemoptysis, chest pain, rash, new joint pain, cold sores, genital lesions, dysuria, or mood changes.

Examination

On examination, the visual acuity was 20/20–2 in the right eye. The right pupil was reactive (6 mm to 3 mm) and the intraocular pressure was 14 mm Hg by applanation. His right eye extraocular movements were intact, and his visual field was full to confrontation. He had a prosthesis over his left eye.

Slit lamp examination (see Figures 1–3) revealed a scleral shell prosthesis on the left. His eyelids were flat

Figure 1. Photograph of the right eye (post-dilation) displaying ciliary flush.

Figure 2. Photograph of the right eye demonstrating anterior chamber cell and flare.

without erythema or swelling bilaterally. His conjunctiva had 3+ injection with ciliary flush on the right and was quiet on the left. There were fine keratic precipitates on

Published April 13, 2008.

Copyright ©2008. All rights reserved. Reproduction in whole or in part in any form or medium without expressed written permission of the Digital Journal of Ophthalmology is prohibited.

doi:10.5693/djo.03.2008.007

Correspondence: Drew Chronister, MD (email: chronisterdr@upmc.edu).

Figure 4. Fundus photo of the right eye demonstrating multiple creamy, placoid, deep retinal lesions in the macula and temporal periphery. The optic nerve and vessels were normal.

the right cornea. The left cornea was opaque due to panus. There was no view of any deeper structures in the left eye. The right eye had 4+ cell and flare in the anterior chamber, a round and regular iris with no synechiae, and a clear lens. There was vitreous haze in the right eye.

Funduscopy exam of the right eye (see Figure 4) showed a normal optic nerve with a cup to disc ratio of 0.3. The vessels were within normal limits, but there were multiple creamy, placoid, deep retinal lesions extending from the right macula to the temporal periphery. There was no view of the left fundus.

Ancillary Testing

A fluorescein angiogram was performed (see Figures 5–8). Laboratory studies and chest x-ray results are listed in Table 1.

Treatment

Table 1 shows several labs that were ordered prior to treatment initiation. The patient was placed on oral and topical steroids (prednisone 80 mg and prednisolone acetate 1% 8×/day), oral cyclosporine 125 mg 2×/day, and topical homatropine. In addition, he was placed on oral famotidine 20 mg for gastrointestinal prophylaxis and doxycycline 100 mg 2×/day to cover any possible infection until the labs returned. The patient was initially followed daily in the outpatient setting.

Differential Diagnosis

We considered multiple inflammatory, infectious, and neoplastic causes in our patient with panuveitis. Of all

Figure 5. A red free photo showing placoid lesions of the right fundus.

Figure 6. The arterial phase of the right eye fluorescein angiogram shows early blockage of the lesions.

Figure 7. Venous phase of the right eye fluorescein angiogram.

Figure 8. The late phase of the right eye fluorescein angiogram demonstrates late hyperfluorescence of the lesions.

Table 1.

Labs and studies that were obtained are listed above with abnormal values in bold.

Hemoglobin	15.7
Hematocrit	45.8
Platelets	378 (normal 156-369)
White blood cells	10.9 (upper limit of normal 10.6) with a normal differential
Rapid plasma reagin	Non-reactive
Erythrocyte sedimentation rate	30 (normal 0-15)
Anti-nuclear antibody	<40
ACE-level	9 (normal 9-67)
Lyme titer	Negative
Toxocara antibody	Negative
Toxoplasma IgM	Negative
Toxoplasma IgG	Negative
HLA Typing	Converted A1, A31, B60, B57
PPD	Negative
Chest X-ray	Normal

the inflammatory causes of panuveitis, sarcoidosis may be the most common, but it affects African-American patients much more commonly than Caucasian patients. The keratic precipitates are classically mutton-fat and not fine as in this case. Vogt-Koyanagi-Harada (VKH) disease causes a diffuse granulomatous uveitis with a flu-like prodrome. Typically, however, it affects dark-skinned patients, particularly Asians or American Indians.¹ Also, it is often associated with central nervous system or dermatologic signs including hearing loss, seizures, meningismus, focal neurologic deficits, alopecia, or vitiligo, all of which our patient did not have. When considering the diagnosis of sympathetic ophthalmia, the patient indeed had the necessary history of a penetrating eye trauma. While the majority of sympathetic ophthalmia cases present within the first year, there have been cases presenting as long as 66 years after the trauma.² A rare cause of panuveitis, Behcet disease requires recurrent oral and/or genital ulcers in addition to uveitis (often with a hypopyon) for diagnosis.¹ Our patient did not present with any of these findings other than the uveitis. A white dot syndrome was considered and of all the disease entities that cause white

dots, the fundus lesions were most similar to those found in acute posterior multifocal placoid pigment epitheliopathy (APMPPE). This disease does occur in young healthy adults with a viral prodrome; however, our patient had more anterior chamber cells than would be expected in APMPPE.

Other than working as a prison guard, our patient gave no other risk factors or history of exposure to any possible infectious cause. He also did not show any systemic signs of illness at the time he was evaluated. Nevertheless, we considered syphilis, tuberculosis, toxoplasmosis, endogenous endophthalmitis, Lyme disease, and toxocariasis as possible infectious causes that needed to be ruled out.

Lastly, we considered neoplastic masquerade syndromes as they constitute 2–3% of all uveitis cases seen at a tertiary uveitis center.¹ Primary CNS lymphoma is the most common cause; however, this neoplasm presents in a much older population than our patient. Leukemia was also unlikely and more commonly presents as a retinopathy. Metastases represents the most common intraocular malignancy in adults and most often presents as choroidal metastases with vitritis,¹ but our patient had no history of a primary tumor.

Diagnosis

Our patient was treated with immunosuppression for sympathetic ophthalmia and was closely monitored in the outpatient setting. His labs returned and excluded the other diseases in the differential. He developed nausea, anorexia, fatigue, and a mild rise in his blood pressure over the first week. He then developed periorbital pain around the left eye with a severe headache. He was admitted for a 3-day course of IV methylprednisolone. Rheumatology was consulted and the patient was switched from cyclosporine to mycophenolate mofetil. His symptoms and intraocular inflammation greatly improved. The choroidal lesions also improved (Figure 9). Oral prednisone and prednisolone drops were very slowly tapered and mycophenolate mofetil was gradually increased. Approximately 2 months later, the anterior chamber cells had finally cleared. At six months after initial presentation, the patient is currently on prednisone 12.5 mg and mycophenolate mofetil 1000 mg 2×/day. His right eye has remained quiet with subretinal scarring and 20/20 vision.

Sympathetic ophthalmia is a non-necrotizing, granulomatous panuveitis that generally spares the choriocapillaris.² The incidence is reported to be 0.2% after accidental trauma and less than 0.1% after surgical trauma.³ It is

Figure 9. A right eye fundus photo shows fading of the choroidal lesions after 2 weeks of treatment.

theorized that sequestered intraocular antigens gain access to the lymphatic system after a penetrating ocular injury and the predominant cellular infiltrate has been found to be T lymphocytes.⁴ Although sympathetic ophthalmia has been found to occur up to 66 years after injury, 65% of cases present between 2–8 weeks after injury and 90% of cases occur within 1 year.²

Patients often complain of vision loss, photophobia, and/or pain. Signs can include panuveitis, multifocal infiltrates at the level of the RPE or choroid, thickening of the uveal tract, optic nerve swelling, and/or exudative retinal detachment.

The diagnosis is one of exclusion but is suggested by bilateral uveitis after trauma or injury. Treatment initially consists of corticosteroids (topical, systemic, and/or periocular) and topical cycloplegics or mydriatics. When treated with steroids, the majority of patients

retain 20/60 vision or better.⁵ Given the long-term need for immunosuppression, a steroid-sparing agent becomes necessary to avoid the dangerous adverse effects of long-term steroid use. There is strong evidence that low-dose cyclosporine (a T-lymphocyte inhibitor) should be considered a first-line immunomodulator with or without concomitant low-dose corticosteroids in cases of chronic non-infectious uveitis (including sympathetic ophthalmia).⁶ Mycophenolate mofetil is a newer immunomodulator with a better side effect profile. There is moderate evidence of efficacy showing that mycophenolate mofetil should be used for chronic non-infectious uveitis when other immunosuppressive drugs have failed or have not been tolerated.⁷ Alkylating agents (i.e. chlorambucil or cyclophosphamide) and antimetabolites (i.e. azathioprine) or a combination of two immunosuppressive agents may also be considered in patients with resistant vision-threatening inflammation.⁷

References

1. Opremcak, EM. Uveitis New York: Springer-Verlag; 1995.
2. Boyd SR, Young S, Lightman S. Immunopathology of the Noninfectious Posterior and Intermediate Uveitides. *Survey of Ophthalmology* 2001;46(3):209-233.
3. Kilmartin DJ, Dick AD, Forrester JV. Prospective Surveillance of Sympathetic Ophthalmia in the UK and Republic of Ireland. *British Journal of Ophthalmology* 2000;84:259-263.
4. D'Amico FM, Kiss S, Young LH. Sympathetic Ophthalmia. *Seminars in Ophthalmology* 2005;20(3):191-197.
5. Chu D, Foster CS. Sympathetic Ophthalmia. *International Ophthalmology Clinics* 2002;42(3):179-185.
6. Jabs DA, Rosenbaum JT, Foster CS, et al. Guidelines for the Use of Immunosuppressive Drugs in Patients with Ocular Inflammatory Disorders. *American Journal of Ophthalmology* 2000;130(4):492-513.
7. Okada AA. Immunomodulatory Therapy for Ocular Inflammatory Disease. *Ocular Immunology and Inflammation* 2005;13:335-351.