

The Construction Worker With Deteriorating Vision

For most of his working life, Jim West* was a construction worker. A few weeks before we saw him, he began to notice floaters and flickering in his right eye. His vision had also become intermittently blurry at near and distance. Mr. West's optometrist diagnosed cataract in both eyes, and he was referred to our clinic for evaluation.

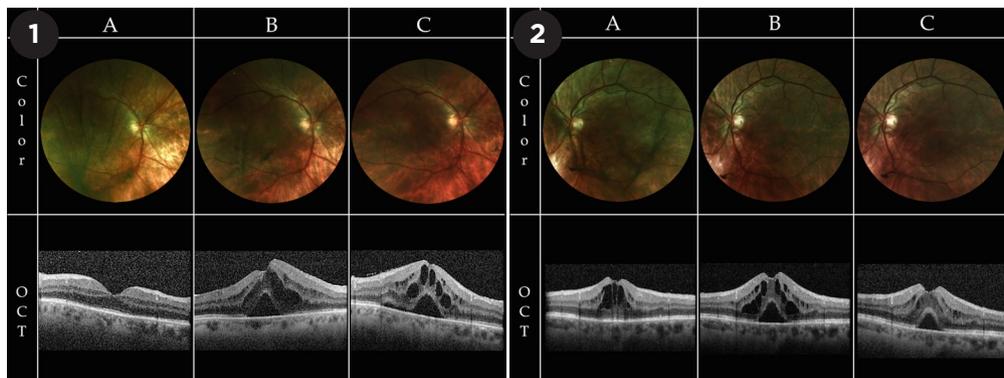
We Get a Look

Mr. West had been diagnosed with HIV in 2011. Since then, he has been on highly active antiretroviral therapy (HAART). His most recent CD4 count was 707 cells/mm³ (500-1,200 cells/mm³ is usual in healthy adults¹). His past medical history was relevant for hypertension and hyperlipidemia.

On examination, his BCVA was 20/60 in the right eye and 20/70 in the left eye. His intraocular pressure (IOP) was 13 mm Hg in the right eye and 11 mm Hg in the left. There was no afferent pupillary defect, and his ocular motility was intact.

The slit-lamp exam showed 1+ flare and 1+ cells in the anterior chamber of the right eye and trace flare and ± cells in the left eye. Nuclear sclerosis (2+) was apparent in the lens of each eye. There were 1-2+ cells in the anterior vitreous of each eye.

The dilated examination revealed vitreous veils in each eye and a faint whitening of the retina at 12 o'clock in



FUNDUS COLOR AND OCT IMAGES. Over the course of 3 months, the right eye initially (1A) reveals a normal foveal contour on OCT, with multiple vitreous veils in the clinical image; the next month (1B) it shows fewer vitreous veils and development of macular edema on OCT; and the third month (1C) it demonstrates resolution of vitreous veils but worsening of macular edema. Over the same 3 months, the left eye (2A) shows loss of the foveal contour with multiple intraretinal cysts on OCT, and vitreous veils are observed inferiorly in posterior pole in the clinical image; (2B) demonstrates improvement of the intraocular inflammation with fewer vitreous veils, while concomitant worsening of macular edema was seen on OCT; and (2C) reflects improvement of vitreous veils but persistence of macular edema.

the right eye. Although optical coherence tomography (OCT) of the right eye was hampered due to a poor signal caused by the vitreous veils, it showed a normal foveal depression with a central macular thickness of 261 µm. OCT of the left eye showed multiple cystic spaces in the fovea with a central macular thickness of 537 µm.

We ordered a laboratory workup that included CBC (complete blood count), CD4 count, ACE (angiotensin-converting enzyme), RPR (rapid

plasma reagin), Lyme titer, Quantiferon gold, toxoplasmosis, HSV (herpes simplex virus), and CMV (cytomegalovirus) serology. An anterior aqueous humor sample was obtained and sent for CMV, HSV, VZV (varicella-zoster virus), and toxoplasmosis PCR (polymerase chain reaction).

Differential Diagnosis

Clinically, Mr. West presented with bilateral nongranulomatous uveitis, unilateral retinitis, and cystoid macular edema.

Given the patient's history of HIV, our differential diagnosis was broad, including viral retinitis, toxoplasmosis, syphilis, tuberculosis, sarcoidosis, and

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primary intraocular lymphoma.

Lab results. His serology was positive for CMV IgG and HSV-1. The ACE level was elevated at 65 μ /L, and the RPR titer was reactive (1:1,024). The rest of the tests were within normal limits. The positive RPR prompted us to check TP-PA (*Treponema pallidum* particle agglutination), which was also reactive, confirming a diagnosis of syphilis. Of note, during the previous 10 months, Mr. West's RPR was non-reactive.

The patient did not complain of any neurological symptoms, but based on this additional information, a lumbar puncture was performed, and the VDRL (Venereal Disease Research Laboratory) test of cerebrospinal fluid (CSF) was reactive at 1:32.

Treatment

Mr. West was admitted to the hospital and completed a 14-day course of intravenous aqueous crystalline penicillin G. His ocular inflammation was treated with topical prednisolone acetate 1% and cyclopentolate 1%. Incidentally, while he was hospitalized, a diagnosis of rectal gonorrhea was made.

At the conclusion of his intravenous therapy, we reevaluated Mr. West. The vitritis had improved and the retinitis had resolved, but his visual acuity remained unchanged. We discovered that he had not adhered to his topical treatment regimen. There was now cystoid macular edema (CME) in both eyes. OCT demonstrated a central macular thickness (CMT) of 659 μ m in the right eye and 649 μ m in the left eye. There was no improvement of the CME over the following month, despite restarting topical prednisolone acetate 1% and adding topical ketorolac 0.5%.

At this point, Mr. West was managed with a sub-Tenon injection of triamcinolone (40 mg in 1 mL) in the right eye. Given a lack of response to the sub-Tenon injection, the decision was made to continue with topical treatment only.

Mr. West's most recent follow-up was 8 weeks after he had restarted topical therapy, and both his visual acuity and macular edema were improving bilaterally.

Discussion

The origins of syphilis are still debated. The first written record of a large outbreak described the epidemic as starting in Naples, Italy, during the 15th century. However, it is also believed that syphilis was described by Hippocrates in Classical Greece.²

Ocular syphilis is on the rise. A multistate outbreak during 2014-2015 resulted in a clinical advisory issued by the Centers for Disease Control and Prevention (CDC).³

"The great imitator." Ocular involvement can accompany any stage of the disease. It can involve any structure of the eye, but its most common presentation is uveitis.

Many recent cases of ocular syphilis have affected HIV-infected men who have sex with men, but the disease also occurs in heterosexual relationships.⁴ Therefore, it is important to screen any patient who complains of nonspecific symptoms associated with signs of unexplained ocular inflammation.

There is evidence to support the concept that syphilis may induce an autoimmune response.⁵ The majority of patients show chorioretinitis, but anterior uveitis, necrotizing retinitis, vasculitis, neuroretinitis, vitritis, and panuveitis may occur. Anterior uveitis with vitritis, as in this case, is more common than isolated anterior uveitis.⁶ Macular edema can be expected in the setting of uveitis and may be asymmetric at times, as was first noted in our patient.

Delayed diagnosis can be deadly. Unfortunately, syphilis is often overlooked as a cause of uveitis. Similar to other infections, delay in diagnosis may have potentially serious ocular repercussions (e.g., cataract, glaucoma, retinal and choroidal atrophy and scar, and blindness) and may result in systemic morbidity (e.g., paralysis, dementia, and hearing loss) and possibly death.⁶ It is of paramount importance to begin treatment with penicillin prior to starting steroids.

There are very specific serologic tests that can easily establish the diagnosis. Per CDC guidelines, all patients with ocular syphilis should undergo CSF analysis and HIV testing.³ Regardless

of the results, we believe that patients should be treated as neurosyphilis cases, although there is some debate about this—see "Ocular Syphilis or Neurosyphilis?" (Letters, January).

Treatment regimens differ between patients with and without HIV. HIV-positive patients are less likely to manifest serologic improvement, and the decrease in RPR titers seems to be slower.⁷ Therefore, screening of high-risk patients, as well as follow-up, is recommended every 3 to 6 months.

Syphilis resurgence is a public health threat. Every new case should be reported to the CDC, and sexual partners of the patients must be tested. After all, syphilis is one of the few uveitides in which the majority of cases can be cured.

1 www.aids.gov. Accessed Jan. 25, 2016.

2 Frith J. *Journal of Military and Veterans Health*. 2012;20(4):49-58.

3 www.cdc.gov/std/syphilis/clinicaladvisoryos2015.htm. Accessed Jan. 13, 2016.

4 www.cdc.gov/mmwr/preview/mmwrhtml/mm6440a6.htm. Accessed Jan. 13, 2016.

5 Wozniczko-Orlowska G, Milgrom F. *J Immunol*. 1981;127(3):1048-1051.

6 Tamesis TT, Foster CS. *Ophthalmology*. 1990; 97(10):1281-1287.

7 Marra CM et al. *Clin Infect Dis*. 2004;38(7): 1001-1006.

*Patient name is fictitious.

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Further Reading

See "Be on the Lookout for Ocular Syphilis" (Clinical Update, November), including a Web Extra, "Ocular Features of Acquired and Congenital Syphilis," and read the subsequent correspondence, which includes a letter from the CDC (Letters, January)—go to www.eyenet.org and click "Archive."