CLINICAL VIGNETTE

Ocular Syphilis Manifesting as Acute Zonal Occult Outer Retinopathy

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Introduction

Over the past few years, the Centers for Disease Control and Prevention has reported an increase in the number of cases of ocular syphilis, especially along the western coast of the United States. Between December 2014 and March 2015, there were 12 reported cases in San Francisco and Seattle, and more than 200 cases from over 20 states over the past 2 years.[1] The majority of cases have occurred in men who have sex with men (MSM) who are co-infected with HIV, but ocular syphilis can affect both heterosexual men and women without HIV. Most commonly, ocular syphilis manifests during the secondary stage of syphilis and presents as anterior uveitis, optic neuropathy, or retinal vasculitis.[2] However, it has been reported to involve almost any eye structure and can lead to irreversible vision loss if left untreated. Its rarity, variability in presentation, and delayed onset make it a diagnostic challenge that can be easily misdiagnosed.

We present a 71-year-old male with new onset blurry vision. He was initially diagnosed with an outer retinopathy until laboratory studies revealed an elevated rapid plasma reagin (RPR) titer, indicating ocular syphilis as the primary etiology.

Case Presentation

A 71-year-old male with a history of hypertension presented with four months of worsening vision. The patient described gradually increasing blurry vision of both eyes, right worse than left, and decreased color vision. Around the time his vision began to worsen, he recalled a one-day episode of gastroenteritis symptoms and the development of a "canker sore" on his tongue that persisted for "a few weeks." He reported no prior history of aphthous ulcers. He denied any additional symptoms including confusion, fatigue, hearing loss, tinnitus, headache, neck stiffness, paresthesias, tremors, or muscle weakness. He denied any additional ocular symptoms including photophobia, photopsia, or floaters. He reported no known history of sexually transmitted infections. He also denied family history of eye disease.

He initially presented to an outside ophthalmologist who diagnosed him with retinal cone dystrophy and referred him to our institution for further retinal assessment. Upon initial evaluation by ophthalmology at our institution, the patient's visual acuity was 20/125 in the right eye and 20/50 in the left eye. The patient subsequently underwent electroretinography, which revealed reduced cone amplitudes relative to age-matched controls but normal timing, making a pan-retinal cone dystrophy less likely. Further evaluation with optical coherence tomography (OCT) and fundus autofluorescence (FAF) revealed bilateral macular ellipsoid zone disruption, greater in the right eye (Figures 1, 2A, and 2B). Humphrey visual field testing demonstrated central threshold elevations and scattered areas of reduced sensitivity in both eyes, right worse than left (Figure 3A). The patient's asymmetric symptoms (right worse than left), relative acute onset of symptoms, and history of gastroenteritis and possible aphthous ulcer around the time of onset of ocular symptoms favored a diagnosis of acute zonal occult outer retinopathy (AZOOR) as it is thought to be a post-viral inflammatory retinopathy.[3]

About two weeks later, the patient's ophthalmologist obtained laboratory studies to evaluate for syphilis. The patient's RPR resulted positive with a titer of >1:1024. The *Treponema pallidum* particle agglutination assay (TP-PA) was confirmatory. The diagnosis now favored ocular syphilis. HIV testing was negative.

The patient was admitted to the hospital for further evaluation and treatment. He underwent a lumbar puncture and cerebral spinal fluid (CSF) analysis demonstrated a positive Venereal Disease Research Laboratory Test (VDRL) titer of 1:4 in addition to a pleocytosis (38 cells/cmm) and an elevated protein level (76 mg/dL). Fundoscopic and slit lamp examinations at the time of admission did not demonstrate any structural evidence of ocular syphilis.

The infectious disease service was consulted and started intravenous penicillin G, 4 million units every four hours, with a planned 14-day course. The patient tolerated antibiotic treatment well without evidence of Jarisch-Herxheimer reaction. At his two-week post-hospital discharge appointment, he reported incremental improvement in his vision. At a four-month follow-up ophthalmology appointment, the patient reported his vision had improved to near baseline. Visual acuities improved to 20/30 in the right eye and 20/25 in the left eye (previously 20/125 and 20/50, respectively). Repeat FAF and Humphrey visual field testing demonstrated marked improvement as well (Figures 2C, 2D, and 3B). Repeat lumbar puncture six months after initial presentation demonstrated resolution of the pleocytosis and a non-reactive CSF VDRL. Repeat RPR titer at this time decreased to 1:64.

Following confirmation of the diagnosis of ocular syphilis and the wide possible time frame for initial infection, the patient acknowledged he was bisexual with a female partner for the past 12 years and male partner for the past 20 years. He also reported high-risk sexual activity with a prostitute 10-15 years prior to presentation and a history of anonymous oral sex, most recently 4-6 months prior to presentation. He denied any history of genital ulcerations or other lesions.

Discussion

Of eight cases of ocular syphilis reported in San Francisco between December 2014 and March 2015, six were in MSM and seven were HIV-infected (6 MSM and one female commercial sex worker).[1] They presented with a variety of visual complaints and eventual ophthalmological diagnoses, including anterior uveitis, various forms of retinitis, and optic neuritis. While these are some of the most common presentations of ocular syphilis, the disease can affect any ocular tissue.[4] Ocular syphilis manifesting as AZOOR has only been sparingly reported in the English literature.[5,6]

An initial diagnosis of AZOOR was favored by OCT and FAF findings, relative acute onset of symptoms, and temporal association of visual symptoms with a preceding gastrointestinal infection (suggesting a viral etiology). Furthermore, the rare association of AZOOR with ocular syphilis, combined with the lack of known high-risk sexual behavior at the time of initial evaluation by ophthalmology, likely explains why laboratory testing for syphilis was delayed.

The patient's case was further clouded by his rapid and early progression of disease, which is atypical for ocular syphilis and makes his case unique. Ocular syphilis typically presents in the late latent stage of the disease, usually 5-10 years after exposure, however it can occur at any stage.[7] Samoff et al[8] demonstrated in a review of over 10,000 cases of syphilis that while RPR titers are imperfect, they at times can aid in distinguishing the stage of the disease. They demonstrated that titers may remain low in the first six weeks of infection, rise, and then begin to decrease in the late latent stage.[8] By extrapolating the information in their study to our patient whose titer was >1:1024, he was most likely in the secondary stage of syphilis on presentation. His history of the mucocutaneous lesion on his tongue four months prior, possibly his primary chancre, further corroborates this staging.

This case highlights the importance of maintaining a high clinical suspicion for potentially reversible alternative causes of retinal and other ocular disease. As demonstrated in this case, the patient experienced marked deterioration of his vision over a four-month period. Initially diagnosed with AZOOR, he would have likely suffered further vision loss without additional treatment. The vigilance of his ophthalmologist to evaluate for syphilis – the "great mimicker" – ensured this patient's eventual correct diagnosis and the initiation of needed treatment. Following a 14-day course of IV penicillin G for treatment of his underlying ocular syphilis, he noted significant improvement in his vision and near complete resolution of his symptoms four months after completing antibiotic therapy. Had the diagnosis been delayed further, he could have suffered irreversible vision loss as has been previously reported.[7]

Figures

Figure 1. Heidelberg optical coherence tomography (OCT). At initial presentation, OCT demonstrated significant ellipsoid zone disruption of the right eye (area between arrowheads) and posterior vitreous detachment.

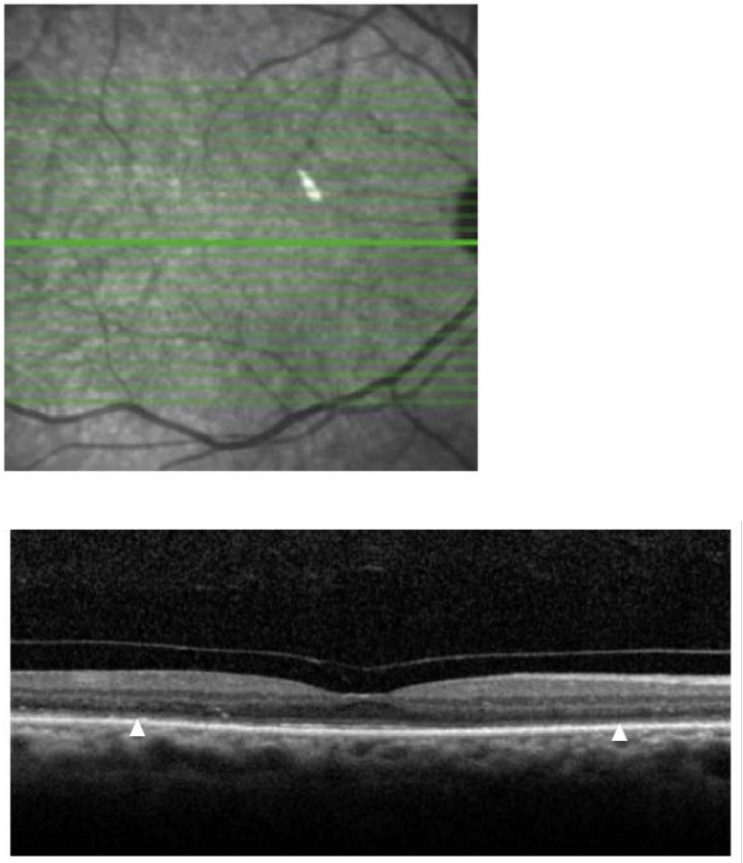
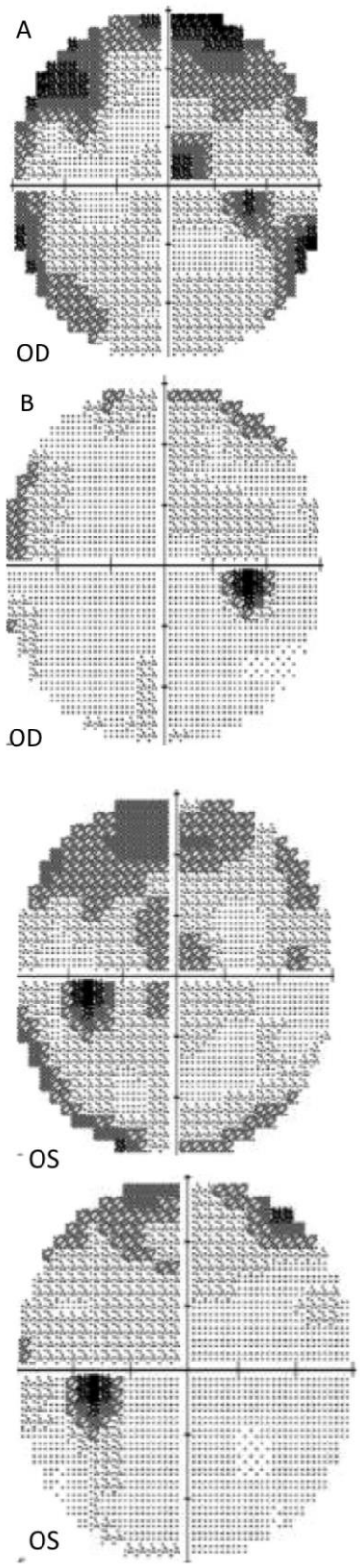


Figure 2. Fundus autofluorescence (FAF). At time of presentation (A and B), FAF demonstrated an almost complete macular area of hypo-autofluorescence in the right eye. Following antibiotic therapy (C and D), normal autofluorescence of the right eye suggests resolution of pathology.

Figure 3. Humphrey visual field testing. (A) Approximately three weeks after initial presentation, testing demonstrated central threshold elevations and scattered areas of reduced sensitivity in both eyes, right worse than left. (B) Following two weeks of intravenous antibiotics, testing demonstrated marked resolution of visual field defects.



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Submitted January 14, 2017