THE RETINA PARTNERS

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Case of the Month – October 2020

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A 66-year-old male was referred for evaluation of iritis in both eyes with complaints of blurry vision in the right eye greater than the left eye. His past medical history was significant for hypertension, difficulty with gait since a cerebrovascular accident 12 years ago, and an old rash on his body, including his hands and feet, which resolved without treatment. As he walked, he had a high steppage gait, and his feet slapped the ground.

Visual acuity was 20/60 in the right eye (OD) and 20/40 in the left eye (OS). Intraocular pressures were 14 OD and 13 OS. There was light-near dissociation of the pupils, with minimal response to light noted and constriction to a near stimulus. Slit lamp exam OD revealed a deep anterior chamber with 2+ cell and 2+ flare, as well as corectopia, with nasal displacement of the pupil, and a well-centered 1-piece intraocular lens (IOL) in the capsular bag. Slit lamp examination OS revealed a deep anterior chamber with 1+ cell and 1+ flare and corectopia, with inferonasal displacement of the pupil, and a well-centered 1-piece IOL in the bag. Dilated fundus exam showed 1+ vitritis with mild vitreous floaters in both eyes. There was slight erythema of the optic nerve in each eye. The macula and periphery were normal in clinical appearance without retinal whitening, chorioretinal scarring, or RPE changes. Optical coherence tomography (OCT) showed mild vitreous floaters and a normal retinal contour without intraretinal or subretinal fluid in either eye. Fluorescein angiography (FA) showed late leakage from both disks, suggestive of a mild papillitis.

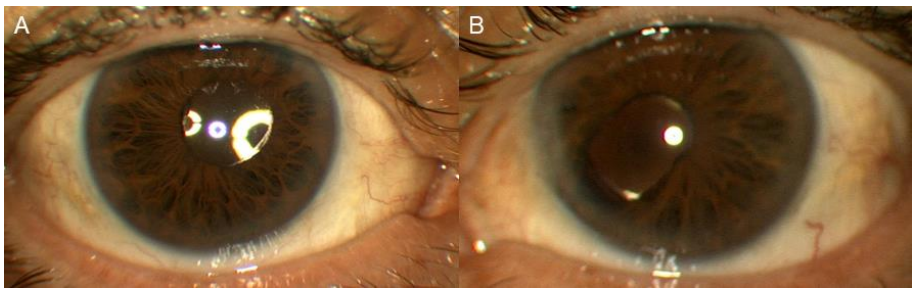

Figure 1: (A) Slit lamp photograph shows mild nasal corectopia OD and (B) inferonasal corectopia OS.

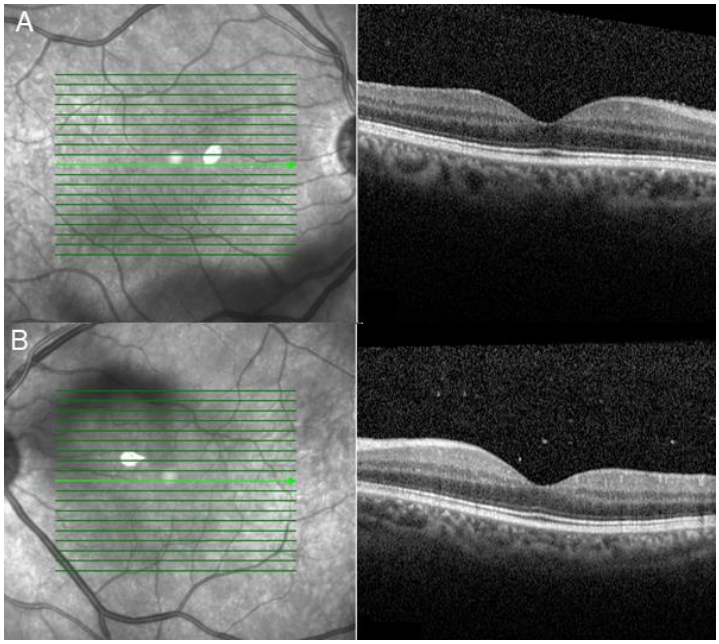

Figure 2: (A) Optical coherence tomography (OCT) OD shows mild vitreous floaters with a normal foveal contour, no macular edema, nor subretinal fluid. (B) OCT OS shows mild vitreous floaters, with an otherwise normal appearance of the retina.

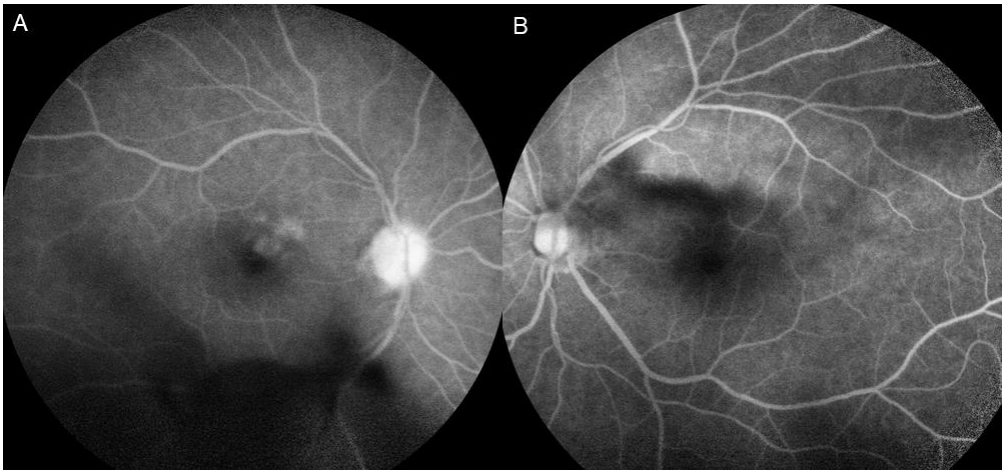

Figure 3: (A) Fluorescein angiography (FA) OD shows late leakage of the disc, suggestive of a mild papillitis, mild perifoveal hyperfluorescence, and hypofluorescent blockage from the vitreous floaters. There is no vasculitis noted. (B) FA OS shows late leakage of the disc and blockage from the floaters.

Clinical Course:

The clinical findings and ancillary testing supported a diagnosis of panuveitis. Laboratory workup for panuveitis revealed a positive fluorescent treponemal antibody absorption (FTA-ABS) test and rapid plasma reagin (RPR) test, confirming a diagnosis of ocular syphilis. A spinal tap conveyed a reactive CSF-VDRL, consistent with Neurosyphilis. HIV, chlamydia, and gonorrhea were all negative. The rest of the laboratory workup for infectious and noninfectious panuveitis was negative.

In concert with his Primary Care Physician and an Infectious Disease specialist, arrangements were made for placement of a peripherally inserted central catheter (PICC) line and the patient underwent 2 weeks of treatment with Penicillin G 2.4 million units intravenously, daily. After treatment of the infection, the inflammatory component was then treated with oral Prednisone and topical prednisolone on a slow taper. The anterior chamber inflammation resolved, and there was a significant reduction in the vitreous floaters. Visual acuity improved to 20/30 OD and 20/20 OS. The patient's partner was also tested and treated.

Discussion:

Infection with the spirochete *Treponema Pallidum* results in the systemic and ocular findings seen in syphilis. The most common route of infection is by sexual transmission, through direct contact with an active lesion or direct transmission of the spirochete. Dissemination then occurs via the blood and lymphatic system. There are an estimated 12 million new cases globally each year, with about 90% of these cases occurring in developing nations. The only known reservoir for syphilis is the human. At the microscopic level, diffuse or focal lymphocytic infiltration is seen surrounding blood vessels of affected organs. Chronic granulomatous inflammation, including epithelioid histiocytes and multinucleated giant cells can be seen, as well as mononuclear cells, sensitized T lymphocytes, macrophages, and plasma cells.

Ocular syphilis is typically associated with tertiary disease or neurosyphilis, and it can manifest with a wide array of ophthalmic findings, earning its reputation as "the great masquerader." Uveitis is the most common ocular finding of syphilis, occurring in 2.5-5% of patients with tertiary disease. Iritis and iridocyclitis may manifest as either granulomatous or nongranulomatous inflammation. In one series, patients with ocular syphilis presented with iridocyclitis in 33% of eyes, vitritis in 11%, retinitis or neuroretinitis in 56%, and papillitis in 22% of eyes. Two-thirds of the patients had concomitant HIV-AIDS infection and 78% had a dramatic improvement in ocular signs after treatment with high-dose intravenous penicillin. Exudative retinal detachment, uveal effusion, central retinal vein occlusion, subretinal membrane formation, retinal necrosis, and neuroretinitis have all been described in the setting of ocular syphilis. Multiple reports suggest that ocular syphilis can be a presenting sign of HIV-AIDS, and thus testing for both is critical. In patients with HIV-AIDS, posterior uveitis is more common.

Interstitial keratitis, conjunctival chancre, nonspecific conjunctival papillary reaction, episcleral and scleral inflammation can also be seen. In cases of congenital syphilis, cataract can present. Glaucoma may occur secondary to uveitis. The classic pupillary finding in syphilis is the Argyll Robertson pupil, which is seen in neurosyphilis. This pupillary finding manifests with anisocoria and light-near dissociation, whereby the pupils respond to near stimulus (accommodation) more robustly than to light stimulus. Corectopia has also been noted.

Yellow or gray placoid lesions may also be seen in the macula or juxtapapillary location in some cases, and are thus termed acute syphilitic posterior placoid chorioretinitis. The lesions may have atrophic centers and be flat, without fluid or hemorrhage. In these cases, fluorescein angiography reveals early hypofluorescence and late staining of the lesion, giving a distinctive "leopard spot" hypofluorescent appearance. In addition to considering the patient's history and examination, the diagnosis is made with serological testing. A positive RPR typically indicates an acute infection, while the FTA-ABS remains positive throughout the patient's lifetime. In

cases with an elusive diagnosis, a PCR of the aqueous or vitreous may be helpful in establishing the diagnosis, but this is rarely required.

Findings in neurosyphilis may vary and depend on the stage of the disease. They can include stroke-like symptoms due to vasculitis with vascular compromise, which can affect cranial nerve nuclei and centers of saccadic and smooth pursuit. Focal intracranial gummas may result in visual field defects and superior orbital fissure syndrome. Horner syndrome and internuclear ophthalmoplegia may be observed. Finally, late neurosyphilis can result in general paresis and tabes dorsalis. Tabes dorsalis is characterized by slow demyelination of neural tracts in the dorsal root ganglia of the spinal cord. This may result in a broad variety of neurological problems, including weakness, diminished reflexes, paresthesias (shooting and burning pains), gait difficulties (classically with a tabetic gait where there is high stepping and foot slapping), loss of coordination, personality changes, dementia, and urinary incontinence,

Primary and secondary syphilis can be treated with a single intramuscular injection of 2.4 million units benzathine Penicillin in patients with and without HIV infection. Serological testing after treatment is the primary method for assessing response to treatment, with a reduction of nontreponemal antibody to unreactive levels. In the case of tertiary syphilis, treatment with intravenous Penicillin 2.4 million units, for at least 2 weeks, should be initiated. In patients with a Penicillin allergy, Ceftriaxone may be used. In patients with HIV-AIDS, this component of their disease also requires treatment. After adequate control of the infectious component of the disease, the inflammatory sequelae can then be treated, whether by local or systemic steroids. In cases of anterior uveitis, topical prednisolone alone can be used with or without a cycloplegic. In cases of panuveitis, systemic steroids may also be required. The patient requires close monitoring and coordination of care with their Infectious Disease specialist and Primary Care Physician during their treatment course.

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Take Home Points: Ocular Syphilis

- Ocular syphilis is typically associated with tertiary or Neurosyphilis and requires treatment with intravenous Penicillin.
- Ocular manifestations of syphilis span varied breadth and severity, leading to the moniker “the great masquerader.”
- Patients with syphilis should be tested for HIV and other sexually transmitted infections, as rates of coinfection are high.

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