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Acute Syphilitic Posterior Placoid Chorioretinitis; a Case Report and Review

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Acute Syphilitic Posterior Placoid Chorioretinitis; a Case Report and Review

Abstract

Background: Acute syphilitic posterior placoid chorioretinopathy (ASPPC) is a rare but defining characteristic of ocular syphilis. Clinical findings are subtle, geographic, yellowish, macular lesions, affecting the outer-retina and inner choroid, and often associated with subretinal fluid in the early phase. This case report will review the clinical signs of ASPPC to aid the practitioner in identification and recognition of its clinical importance as it relates to early diagnosis, treatment and prognosis.

Case Report: A 79-year-old African American male presented to clinic with a chief complaint of blur in the right eye for the past two days. Spectral Domain Optical Coherence Tomography (SD-OCT) of the macula revealed a shallow retinal pigment epithelial detachment with subretinal fluid centrally with some loss of the retinal pigment epithelium (RPE) and photoreceptors nasally, in the right eye. There was rapid progression over a week to full loss of RPE and photoreceptors with reduction of vision to hand motion in the right eye suggesting an infectious eitiology. Serologic testing was ordered and an RPR and FTA-ABS were both reactive. A diagnosis of acute syphilitic posterior placoid chorioretinopathy was made. Infectious disease treated the patient with IV penicillin G. There was complete resolution of ocular findings.

Conclusion: Syphilis should be considered for any ocular inflammatory condition. ASPPC is highly suggestive of syphilis. All patients with ocular syphilis should be evaluated for neurosyphilis. Treatment is IV penicillin G for 10-14 day and considered successful when there is a four-fold reduction in titers. Full visual recovery typically occurs within 12 weeks of treatment if a diagnosis and treatment are initiated early in the course of ocular disease.

Keywords

ocular syphilis, chorioretinitis, central serous chorioretinopathy, acute syphilitic chorioretinopathy

BACKGROUND

Syphilis has been increasing in prevalence once again in the United States and is one of the leading causes of uveitis.[1] However, it can present with a wide range of ocular manifestations and can affect the eye at any stage of infection, making its diagnosis challenging. Therefore, it is critical that eye care providers keep syphilis high on their list of differentials for many ocular conditions. Acute syphilitic posterior placoid chorioretinopathy (ASPPC) is a rare but defining characteristic of ocular syphilis. Clinical findings reveal one or multiple, subtle, geographic, yellowish, macular lesions, affecting the outer-retina and inner choroid, sometimes associated with subretinal fluid in the early phase. This case report will review the clinical signs of ASPPC to aid the practitioner in identification and recognition of its clinical importance as it relates to early diagnosis, treatment, and prognosis. A review of syphilis and its ocular manifestations will also be discussed.

Case Report

A 79-year-old African American male presented to the clinic with a chief complaint of blur in the right eye for the prior two days. The blur was constant, worse centrally, and gradually worsening in severity and size over the course of two days. His medical history was remarkable for obstructive sleep apnea, asthma, hypertension, atrial fibrillation, hyperlipidemia, and gout. His medications were allopurinol, albuterol, diltiazem, hydrochlorothiazide/triamterene, loratadine, simvastatin, and warfarin, and he had a known drug allergy to penicillin. His social history was positive for occasional alcohol use, negative for recreational drug use, and smoking cessation 30 years ago. He was alert and oriented to person, place, and time.

His last eye exam was five months prior for which he was routinely monitored as a glaucoma suspect due to the asymmetry of optic nerve head cupping and history of borderline elevated intraocular pressures. His retinal nerve fiber layer scans and Humphrey visual fields were historically normal. Entering corrected distance visual acuities were 20/50 in the right eye with no improvement with pinhole, and 20/20 in the left eye. Confrontation visual fields were full to finger count in each eye, and extraocular motilities were full and extensive for the right and left eye without pain or diplopia. Pupils were equal, round, reactive to light, and there was no afferent pupillary defect noted. His refraction was +1.00+0.50 x177 OD and +0.50+1.00 x168 OS with a +2.50 add at near. His best corrected visual acuities after refraction were 20/40 OD and 20/20 OS.

Slit lamp examination was relatively unremarkable; lids and lashes were clear, conjunctiva had trace injection bilaterally, no follicles or papilla were noted, and corneas were clear bilaterally. Anterior chambers were deep and quiet, and no cell or flare was noted in either eye. Irides were flat and uniform bilaterally, and lenses had early nuclear sclerotic and cortical changes outside the visual axis bilaterally. Intraocular pressures were 15 mm Hg OD and 14 mm Hg OS as measured with Goldmann applanation tonometry. Dilated evaluation revealed a cup to disc ratio of 0.6 round in the right eye and 0.4 round in the left eye, nerves were distinct, pink, and flat OU. The artery and veins appeared to be normal. There was a small intraretinal hemorrhage in the right macula with a blunted yellowish reflex centrally which suggested thickening/elevation. The left macula was flat with a distinct foveal reflex. There was a large posterior vitreal detachment with syneresis in the right eye; the left vitreous was noted to be clear. The peripheral retinas were flat and intact bilaterally. A spectral domain-optical coherence tomography (SD-OCT) of the macula was obtained and revealed a small amount of subretinal fluid (SRF) centrally with some loss of the inner-segment/outer-segment (IS/OS) photoreceptor junction and retinal pigmented epithelium (RPE) nasally OD. There were a few hyper-reflective foci in the vitreal cavity. The left macula was unremarkable on SD-OCT (see Figure 1).

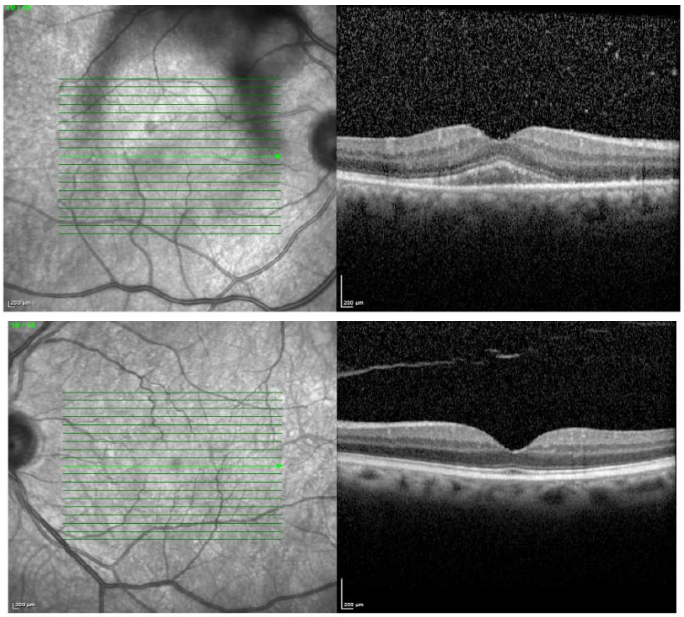


Figure 1. Spectralis SD-OCT (Heidelberg) images of subfoveal heterogenous subretinal fluid and nasal loss of the RPE and EZ, a large vitreal floater along with vitreal cells and a few small intraretinal hyperreflective vitreal foci in the right eye, upper image. A normal retinal scan in the left eye, lower image.

Differential Diagnosis

Differential diagnosis for this patient includes variants of pachychoroid including, acute central serous chorioretinopathy (CSCR), diffuse retinal pigment epitheliopathy, acute posterior multifocal placoid pigment epitheliopathy (APMPPE), exudative age-related macular degeneration, and acute syphilitic posterior placoid chorioretinitis (ASPPC). Variants of choroidal neovascular membranes such as polypoidal choroidal vasculopathy and myopic degeneration should also be included in the list of differentials. All of these differentials can present with detachments of the RPE as noted on the OCT and posterior placoid yellowish lesions in the macular region.

There were no signs of drusen or pigment abnormality in either eye to suggest age related macular degeneration. APMPPE was also unlikely as this typically affects younger patients and is most often multifocal with many creamy yellowish placoid lesions throughout the posterior pole.[2] With no apparent history of syphilis, patient demographic, and the rarity of this clinical finding, ASPPC was lower on our list of differentials. At this time the patient was diagnosed with a subfoveal retinal pigment epithelial detachment possibly due to CSCR. Although CSCR is common, this presentation was slightly atypical due to the age of the patient, the slight heterogenous nature of the subretinal fluid, and the extensive loss of RPE and IS/OS photoreceptor junction, which is typically preserved in acute CSCR but may be affected in chronic CSCR; this was not consistent with the patient's reported 1 day history of vision loss.[3] Therefore, the patient was asked to return to clinic in 1 week for a follow up to ensure the stability of findings or explore further testing if worsening was noted.

At the one week follow up, the patient's vision had dropped significantly to hand motion in the right eye but remained 20/20 in the left eye. Confrontation visual fields were reduced centrally in the right eye. There was a right afferent pupillary defect, extraocular motilities were full in both eyes and intraocular pressures were noted to be 14 mm Hg OD and 16mm Hg OS. Anterior segment evaluation was unchanged. Dilated fundus examination revealed rare blot intraretinal hemorrhages temporal to the macula and nasal to the nerve in the right eye. There was a yellowish placoid subfoveal lesion in the right eye as well as vitreous cells. The left eye was unremarkable (see Figure 2). SD-OCT revealed diffuse loss of outer retinal structures and a nodular deposit at the level of the RPE/photoreceptor junction, subfoveally in the right eye. The left eye remained unremarkable (see figure 3).

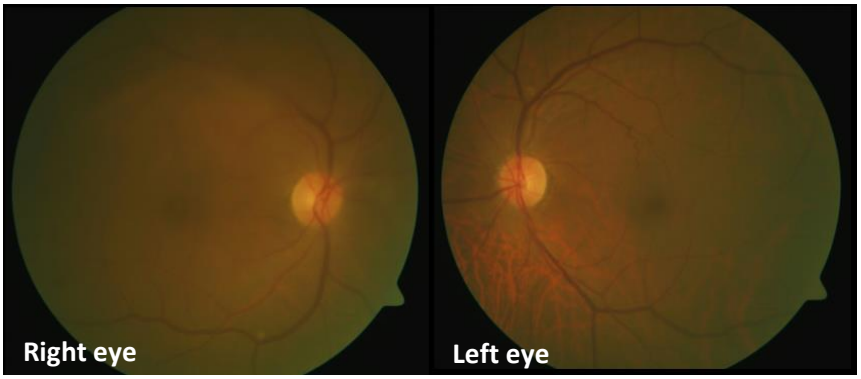


Figure 2. Fundus photography reveals a large yellowish subfoveal placoid lesion in the right eye with overlying vitreal haze. The fundus of the left eye appears unremarkable.

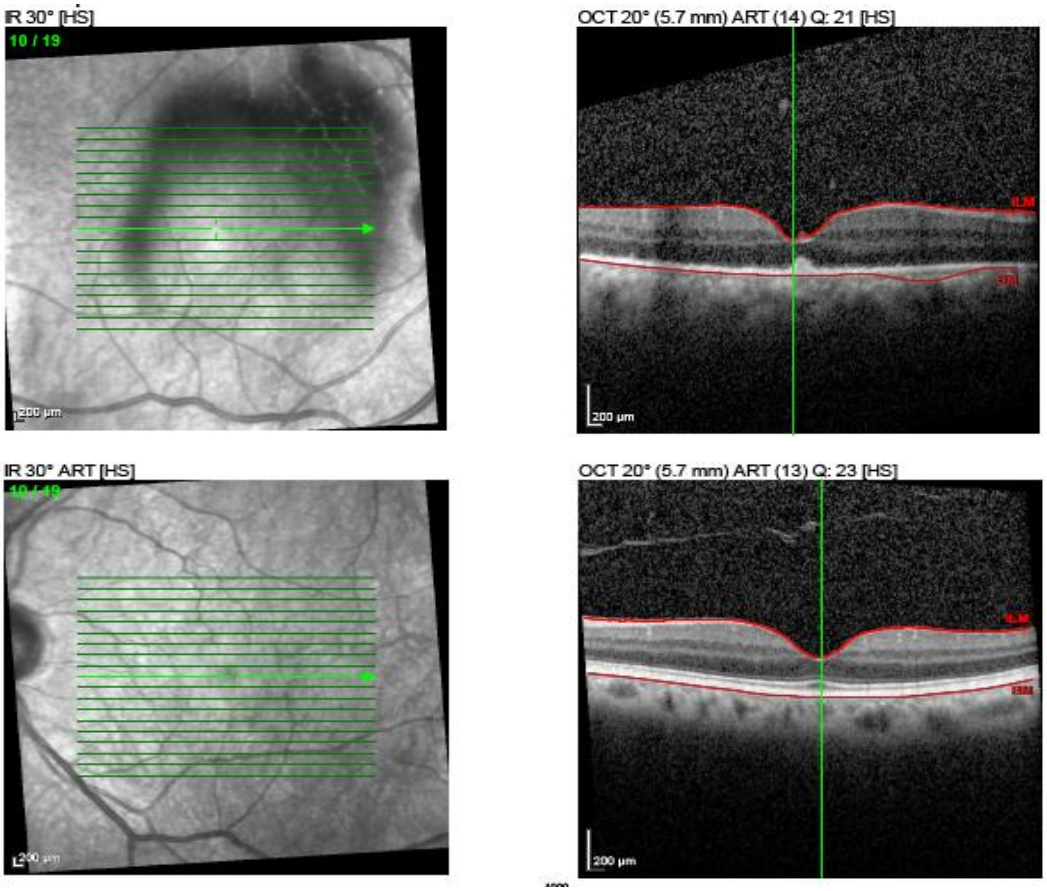


Figure 3. Spectralis SD-OCT (Heidelberg) images of diffuse loss of the outer retinal structures with subfoveal deposit OD, upper image. A normal retinal scan OS, lower image.

Fluorescein angiography revealed a few pinpoint hyperfluorescent deep spots parafoveally, and the macula revealed a mild stippled hyper- fluorescence in the late phase consistent with an RPE dysfunction in the right eye. The left eye showed a few pinpoint hyperfluorescent deep spots parafoveally (see figure 4).

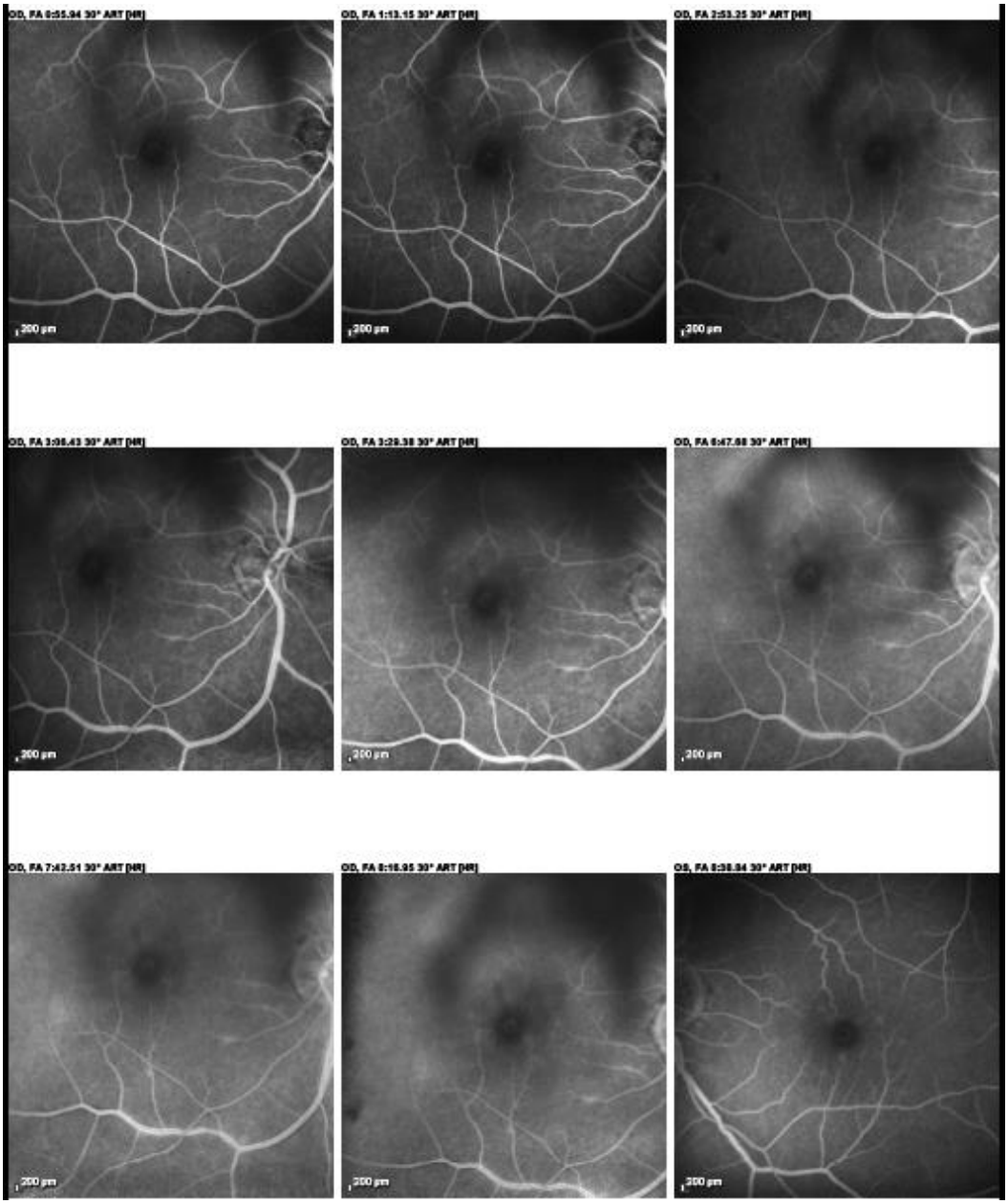


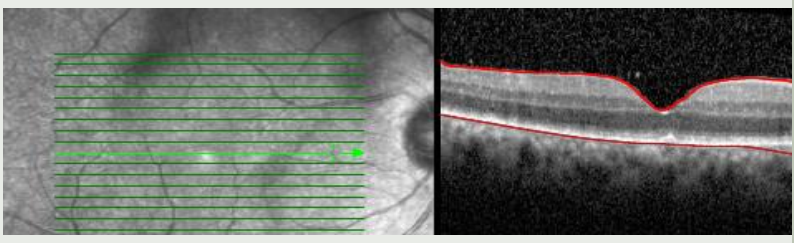
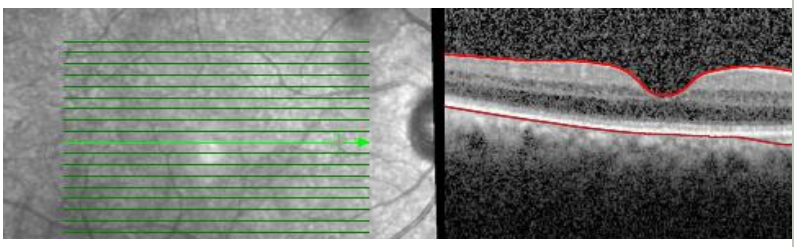
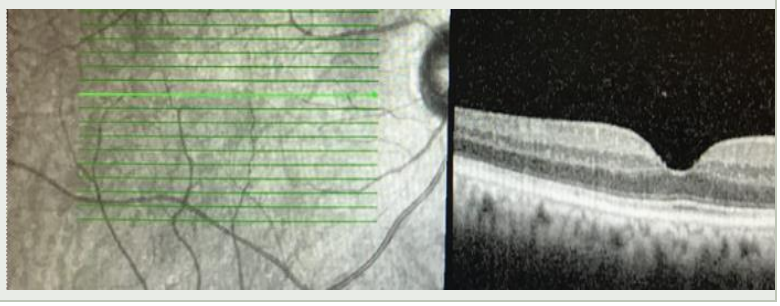
Figure 4. Fluorescein angiography reveals small hyperfluorescent parafoveal spots in the late phase OU.

Based on the significant change after a duration of 1 week and the new clinical findings of an extensive loss of the outer retinal structures, the clinical suspicion for an infectious etiology, notably syphilis, was explained to the patient. A chest X-ray was ordered which showed no signs of tuberculosis or sarcoidosis. HIV testing came back negative, an RPR and FTA-ABS were ordered, and both came back reactive with an RPR titer of 1:8192. The diagnosis of ASPPC with posterior vitritis was made, and our patient was admitted to the infectious disease service for treatment of ocular syphilis and evaluation for neurosyphilis.

An infectious disease physician saw the patient the same day. During this exam, the patient recalled being treated for a venereal disease in his late 20's. He stated he was treated, and it resolved; he denied any history of male-to-male sexual encounters. A lumbar puncture with cerebral spinal fluid (CSF) analysis was ordered to evaluate for neurosyphilis; it revealed 2 white blood cells per microliter with a 79% lymphocyte predominance and elevated protein at 48 mg/dL. The CSF VDRL came back negative, however, the ocular manifestations along with RPR titers and elevated CSF protein was enough to suggest the diagnosis of neurosyphilis. Treatment with IV penicillin for 10-14 days was recommended. Since he had a reported allergy to penicillin, he was first admitted to the ICU for penicillin desensitization followed by treatment with a loading dose of 4 million units of penicillin G IV, followed by 3 million units every four hours for 14 days.

The patient continued to be examined closely with visual acuity checks, tonometry, dilated fundus examinations, serial OCT imaging and fluorescein angiography. Vision slowly improved as the RPE and ellipsoid zone (EZ) repaired itself after treatment was completed, with complete resolution by week 12 (see Table 1). The infectious disease doctor continued to monitor the patient's RPR titers until a four-fold decrease was noted to suggest successful treatment. One-month post treatment, RPR titers were 1:512, and 6 months post treatment, RPR titers were 1:128, suggesting successful treatment. The patient continues to be monitored every 6 months and continues to be stable with no recurrence of ocular signs.

Table 1. OCT imaging reveals gradual resolution of RPE nodule with increasing clarity of IS/OS and photoreceptor structures, with complete resolution by week 12 in the right eye.

Follow Up	Visual Acuity	SD-OCT
Week 2	**20/125**	
Week 4	**20/60**	
Week 12	**20/25**	

DISCUSSION

Syphilis is caused by the bacterium Treponema pallidum. It is most commonly transmitted by direct lesion contact during unprotected sex and less commonly via blood transfer or needle sharing.[4] Often regarded as "The Great Mimicker," syphilis can progress through multiple stages each with a variety of often subtle and variable clinical and ocular findings, making its diagnosis challenging. The prevalence of syphilis was at its highest rates in the United States in the 1990's largely in heterosexual individuals during the crack cocaine epidemic.[4] This was followed by a significant rate reduction in 2000. More recently, since about 2010, there has been a significant resurgence in prevalence, most commonly in middle aged men who have sex with men (MSM).[1,4-6] This resurgence is hypothesized to be related

to the emergence of successful HIV treatment and resultant increased risky behavior and unprotected sex.[5,6]

Primary syphilis is the first stage of the disease. Its characteristic lesion is a chancre which is noted at the site of inoculation. T. pallidum shows slow growth and can take up to 3 weeks for the primary lesions to occur after initial exposure.[1] Chancres are most often found in the genital region, are densely infiltrated with lymphocytes, which are also the target of human immunodeficiency virus (HIV), and therefore provide a portal of entry for HIV coninfecion.[4] Lesions are often solitary, ulcerated, painless, and resolve without treatment in 3-6 weeks, or a few days if identified and treated.[4]

Secondary syphilis occurs when the bacterium disseminates within the bloodstream. During this stage a macular type rash occurs, often spreading throughout the body onto the palms of the hands and soles of the feet. Patients might develop a fever, sore throat, and swollen lymph nodes. Symptoms typically resolve within a few weeks to a few months.[1] If secondary syphilis remains untreated, it can develop into a latent or dormant phase that can last for many years, or indefinitely, without any signs or symptoms. Of these, about 15% to 30% of untreated cases will progress into late or tertiary syphilis. Tertiary syphilis can manifest in a variety of ways including cardiovascular syphilis, late neurosyphilis, and gummatous syphilis.[4,7] Syphilis is transmissible to others during the primary, secondary, or early latent phases. Diagnosis is most commonly made through performing serological testing. However, in the early stage, titers may be falsely nonreactive, therefore clinical signs/suspicion are critical for making an accurate diagnosis early in the disease course. Two different tests are typically used. Non-treponemal tests which include rapid plasma reagin (RPR) and venereal disease research laboratory (VDRL) tests. A reactive test indicates an active infection and titers from these tests will assist in monitoring the response to treatment.[4] A fourfold drop in titers or return to nonreactive state indicates successful treatment.[4,8] Treponemal tests include, fluorescent treponemal antibody adsorbed (FTA-ABS) tests and Treponema pallidum particle agglutination (TPPA). These tests detect antibodies to T.pallidum, where a reactive test indicates a current or past infection, and will remain positive for life despite successful treatment.[4]

Ocular syphilis can occur at any stage of infection but is most commonly reported during the second or third stage of syphilis.[1,9] Treponema pallidum can affect all layers of the eye and therefore has a wide range of ocular manifestations including, interstitial keratitis, scleritis, iridocyclitis, posterior uveitis, retinitis, choroiditis, serous detachment, and optic neuropathy.[1,10] There are a few distinctive clinical

findings that can aid in a rapid diagnosis. These include small, creamy-white, superficial retinal precipitates overlying a region of inflamed retina, and acute syphilitic posterior placoid chorioretinopathy.[6] ASPPC is increasingly recognized but has an overall low prevalence rate. First described by Gass et. al in 1990, ASPPC is clinically characterized by one or more, subtle, deep, yellow, circular lesions in the macular region.[1,6,11-13] While not fully understood, these lesions are thought to consist of an accumulation of lipofuscin or photoreceptor outer segment remnants.[12] The lesions are more apparent with false color imaging technology with red/green laser systems or auto-fluorescent imaging than on clinical exam which typically reveals increased autofluorescence.[9] Fluorescein angiography reveals early phase hypo-fluorescence with later phase hyper-fluorescence, occasionally with round areas of hypo-fluorescence, mimicking leopard spots, within the fundus lesions.[1,9,11] Typical lesions will show characteristic thickening and nodularity of the RPE on SD-OCT with areas of loss of the IS/OS photoreceptor junction.[9,12] If patients present within a few days of vision loss, SD-OCT imaging on day one or two of presentation may reveal subretinal fluid which may mimic CSCR, but will typically resolve in seven to nine days, when loss of IS/OS and OS/RPE bands and nodular elevations at the level of the RPE and photoreceptors become apparent.[9,12,14] It is hypothesized that these lesions are due to an inflammatory process at the level of the choriocapillaris and RPE.[1,11-12] With early diagnosis and treatment, full reversal of OCT abnormalities and complete visual recovery can be expected. However, with late treatment, permanent scarring and loss of vision may occur.[10] Other studies have found spontaneous resolution of ASPPC lesions prior to initiation of treatment.[1] ASPPC has been found more commonly in middle aged MSM, and also more commonly in patients with an HIV coinfection.[1] All cases of ocular syphilis warrant testing for neurosyphilis and all cases of ocular syphilis should be treated with the standard treatment for neurosyphilis with a 10-14 day course of intravenous penicillin G at a dose of 18 million to 24 million units per day.[4-9]

Neurosyphilis can occur at any stage of infection; a reactive CSF VDRL is the gold standard diagnostic test but has a low sensitivity.[1,4-5,8] Approximately 30-70% of neurosyphilis cases will have a nonreactive CSF VDRL.[1] Therefore, clinical judgement, elevated CSF white blood cells (>5/microliters with lymphocyte predominance) and elevated protein (>45mg/dL) can also support the diagnosis of neurosyphilis in a patient with untreated syphilis.[4-5,8]

Penicillin G is the gold standard for treatment of syphilis. IV aqueous penicillin G 18 million to 24 million units per day for 10-14 is the recommended treatment

for neurosyphilis and ocular syphilis.[4-8] Treatment is considered successful when there is a four-fold reduction in titers. Full visual recovery typically occurs within 12 weeks of treatment if a diagnosis and treatment are initiated early in the course of ocular disease.

CONCLUSION

Syphilis is increasing in prevalence in the United States, more commonly in MSM, and can have a wide range of systemic and ocular manifestations mimicking many other conditions. It is critical for eye care providers to keep syphilis on their list of differentials for any inflammatory ocular condition. ASPPC is a clinical finding that, if present, is highly suggestive of syphilis and can assist the provider in making an early diagnosis and providing early treatment and thus reduce visual morbidity.

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