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EDITORIAL

Syphilitic Uveitis

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The incidence of syphilis decreased dramatically in the United States and Europe in the latter half of the twentieth century, only to increase in the last two decades.[1–3] In 2005 the World Health Organization estimated the global prevalence of syphilis to be approximately 36 million, with 11 million new cases occurring in adults each year. Over 90% of those with syphilis live in developing countries, where the infection is typically both undiagnosed and latent.[4] In the developed world, syphilis is particularly common in men who have sex with men, where the rate of human immunodeficiency virus (HIV) co-infection is high.[5] Two articles in this issue of *Ocular Immunology & Inflammation* highlight the continued importance considering syphilis in patients with ocular inflammation and, when ocular syphilis is diagnosed, testing for HIV infection.[6,7]

Yap and associates described signs of syphilis in 18 eyes in 12 patients seen from 2004 to 2009 in their clinic in Singapore.[6] Over 90% were men and over 80% were heterosexual. Three were HIV positive and ocular inflammation was the presenting sign of syphilis in all but two patients. Ocular inflammation was bilateral in half of the patients, anterior or diffuse (panuveitis) in six eyes each, posterior in five eyes, and intermediate in one eye. Clinical images were not provided, but clinical features suggestive of syphilis that were described in the text included retinal vasculitis in five eyes (27.8%), optic disc edema in four eyes (22.2%), and retinitis in 3 eyes (16.7) – including two eyes with Acute Syphilitic Posterior Placoid Chorioretinopathy (ASPPC)[8] in an HIV negative patient. The vast majority of eyes returned to 20/40 vision or better following treatment. These findings support the generally held view that syphilitic uveitis may involve any part of the eye and is often fairly non-descript – occurring as simple anterior or panuveitis. Routine testing for syphilis is important, therefore, in all sexually active adults with uveitis. Specific treponemal and non-trepornemal (RPR and VDRL) tests should be viewed as complementary, since treponemal tests are quite sensitive and specific, but fail to reflect disease activity, whereas non-treponemal test titers rise during active infection and fall with treatment, but can have a false negative rate of 30% or higher.[9,10]

Lima and colleagues describe two patients with curvilinear outer retinal infiltrates involving the central macula, both of whom were initially thought to have Acute Zonal Occult Outer Retinopathy (AZOOR), but who on serologic testing were found to have evidence of syphilis.[7] Both patients were found to have abnormalities of the outer retina on SD-OCT, including disruption of the inner-segment/outer-segment photoreceptor junction (ellipsoid layer). In addition, one patient had irregularity of the RPE on SD-OCT, faint late staining of the involved area on FA, and a circular area of hypofluorescence on ICGA. One of the two patients was HIV positive and both responded to treatment with intravenous penicillin G with normalization of their clinical examination and restoration of vision. In retrospect, all of these features were fairly suggestive of ASPPC,[8] an uncommon, but clinically distinct manifestation of ocular syphilis first reported by de Souza and associates in 1988[11] and further defined by Gass and colleagues two years later - who introduced the name ASPPC.[12] Clinically, eyes with ASPPC present with a placoid, round or oval, yellow-white lesion involving or near the macula. Occasionally, a more active curvilinear 'leading edge' can be seen, as in the two cases described by Lima and colleagues. Fluorescein angiography of the lesion tends to show progressive hyperfluorescence, whereas ICGA may show either

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persistent hypofluorescence or late hyperfluorescent staining. Fluorescence in the area of the lesion may be variable with both techniques, producing a characteristic leopard-skin pattern. SD-OCT tends to be particularly suggestive with loss of the normally distinct hyper-reflective bands associated with the photoreceptor-RPE complex, typically with nodular irregularity of the RPE and often with a localized serous retinal detachment and punctate choroidal hyper-reflectivity.[13] Active lesions tend to show hyperautofluorescence, often in a punctate pattern. All of these changes tend to normalize and vision is typically restored following treatment for neurosyphilis, regardless of HIV status. This last point is important, since some authors, based on small numbers of patients from clinic-based cohorts, have suggested that HIV positivity may predict a more severe presentation and portend a worse clinical outcome. In fact, however, at least two comprehensive retrospective reviews would seem not to support this contention.[14,15] First, the comprehensive review of ASPPC by Eandi and colleagues cited above compared the clinical findings at presentation and the visual acuity at last visit in 35 affected eyes in 23 HIV-positive patients to 58 affected eyes in 37 HIV-negative patients, and found no meaningful differences in either severity of clinical presentation or vision outcome.[8] Second, Amaratunge and associate reviewed 41 original reports on syphilitic uveitis in the English language literature published from 1984 to June, 2008, including 93 HIV-positive and 50 HIV-negative patients.[16] They found that only 1 of the 50 HIV-negative patients (2%) had isolated anterior or intermediate uveitis, compared to 27 of the 93 HIV-positive patients (29%; $p = 0.000023$, Fisher's exact test).[15] Given that isolated anterior or intermediate uveitis tend to be less likely to cause permanent vision loss than posterior or panuveitis, this large retrospective review would seem to suggest that HIV co-infection alone does not put patients at increased risk for a more severe, vision-threatening uveitis at presentation. Of note in this regard, Tucker and colleagues comprehensively reviewed published series and case reports among HIV-infected individual with ocular syphilis (n=101), and found that 97% of patients improved following treatment with intravenous antibiotics supporting the notion that HIV infection per se does not portend a poor outcome.[17] Clearly, however, HIV co-infection is common and so should be both tested for and, when found, treated appropriately.

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DECLARATION OF INTEREST

The author reports no conflicts of interest. The author alone is responsible for the content and writing of the paper.

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