

# Letters

## OBSERVATION

### Negative Treponemal Serologies in Syphilitic Panuveitis

Ocular syphilis has myriad manifestations and can be challenging to diagnose. Here, we report a case of an HIV-positive patient with bilateral syphilitic panuveitis, for whom diagnosis was initially delayed by negative treponemal testing.

**Report of a Case** | A young adult with HIV who was not receiving antiretroviral therapy presented with bilateral photophobia and decreased vision. CD4 count was 24 cells/mm<sup>3</sup> and HIV RNA level was 175 000 copies/mL. Multiple sexual partners with inconsistent protection were reported. Review of systems was positive for a pruritic back rash of crusting erythematous plaques.

Presenting uncorrected visual acuity was hand motions in both eyes. Intraocular pressures, measured by iCare, were 14 and 9 mm Hg in the right and left eye, respectively. Examination of the right eye showed corneal stromal haze, 3+ anterior chamber cell (26-50 cells/1 × 1 mm slitlamp field), posterior synechiae, vitreous cell and haze obscuring retinal vascular details, blurred disc margins, and superonasal peripheral retinal whitening. Examination of the left eye showed corneal haze, 1-mm hypopyon, posterior synechiae, vitreous cell and haze obscuring retinal vascular details,

blurred disc margins, and superotemporal peripheral retinal whitening (Figure 1A). Fluorescein angiography showed bilateral optic disc leakage and staining in the left eye of superotemporal retinitis (Figure 1B).

Given the presentation was concerning for acute retinal necrosis, intravitreal foscarnet was empirically administered, and frequent topical steroids were initiated. Aqueous fluid from both eyes returned negative for herpetic viral DNA by polymerase chain reaction. Results of *Treponema pallidum* serum antibody (DiaSorin LIAISON XL), T-spot, and *Toxoplasma gondii* serum antibody tests and urine cultures were negative, and echocardiogram and chest radiography were normal. Blood cultures grew polymicrobial bacteria of uncertain significance. Vitreous cultures were negative for bacteria and fungi. Cerebrospinal fluid was negative for VDRL and other microbiologic studies. Empirical treatment with intravitreal and systemic broad-spectrum antibiotic, antiviral, and antifungal yielded little improvement in posterior inflammation.

A direct scraping of skin lesions demonstrated spirochetes with histopathology (Figure 2). Rapid plasma reagin testing (initially not performed reflexively) was then performed, yielding a 1:64 titer. Cerebrospinal fluid *T pallidum* particle agglutination assay results were positive, confirming neurosyphilis. Repeat serum treponemal antibody testing remained negative. After 14 days of intravenous penicillin, visual acuity and vitritis improved, and peripheral retinitis

Figure 1. Multimodal Imaging From Left Eye

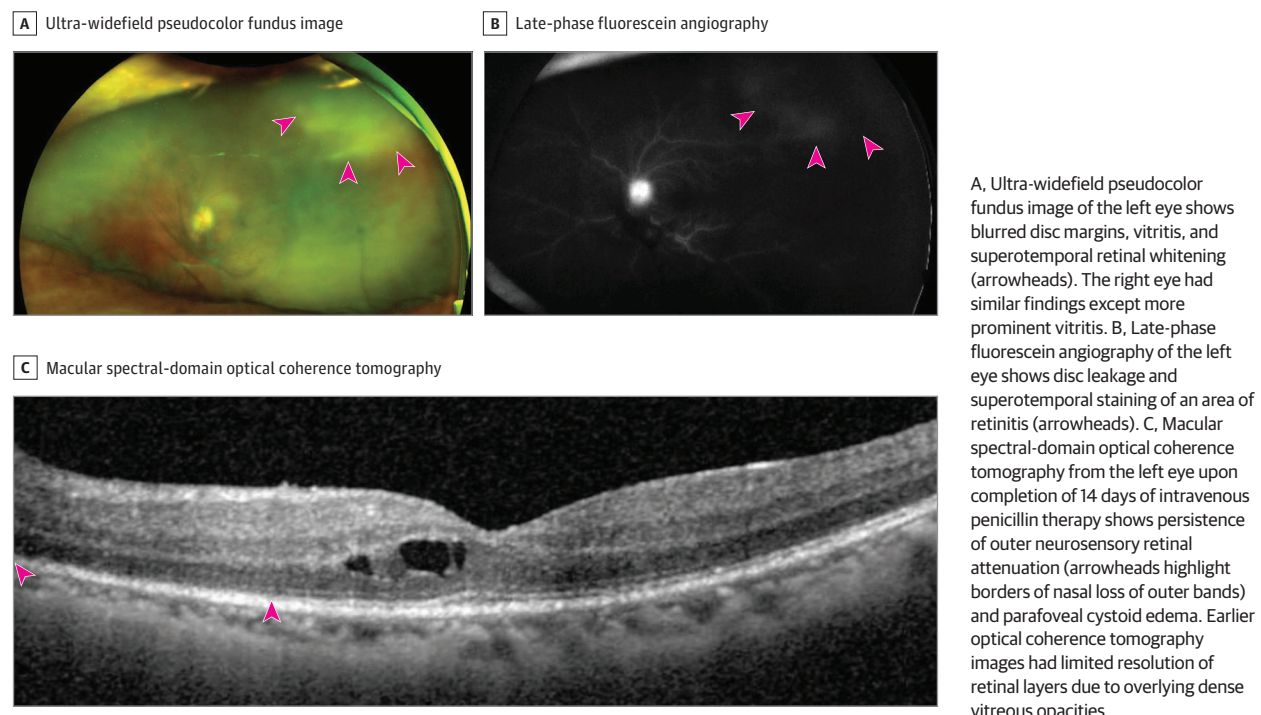
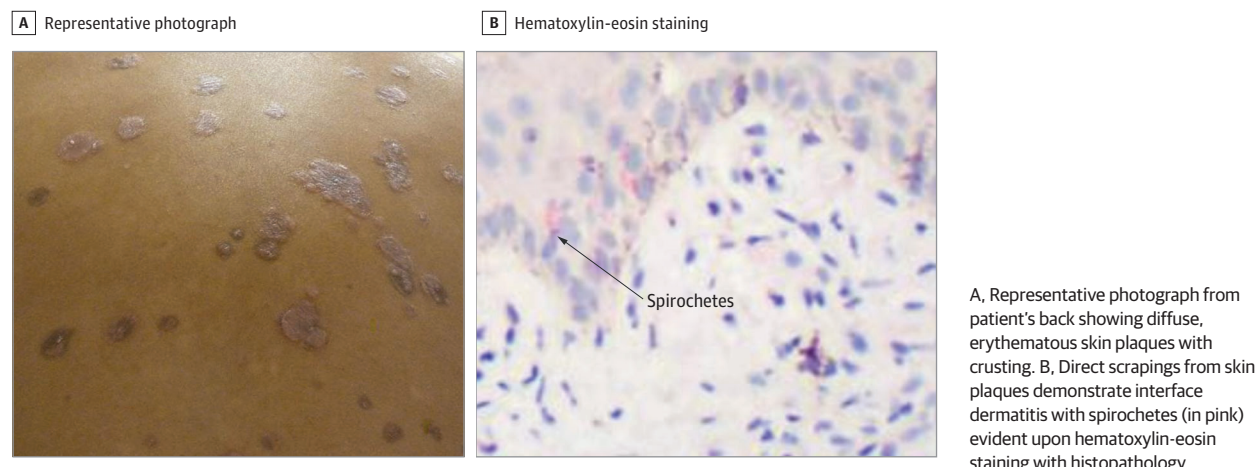


Figure 2. Photograph and Histopathology From Skin Lesions



resolved. Outer neurosensory retinal attenuation persisted on optical coherence tomography (Figure 1C). The patient was lost to follow-up.

**Discussion** | Diagnosis of syphilis can involve nontreponemal tests such as rapid plasmin reagin, which detect antibodies to nonspecific antigens triggered by syphilis infection, and treponemal tests, which detect antibodies specific to *T pallidum* proteins.<sup>1</sup> The traditional algorithm for diagnosing syphilis begins with a nontreponemal test (historically less expensive) and uses a treponemal test to confirm positive results. The reverse algorithm, which may have superior sensitivity for certain stages of syphilis, begins with a treponemal test for initial screening and uses a nontreponemal test to confirm positive results. The reverse algorithm has been adopted by a growing number of institutions, including the one where this patient received treatment. The 2024 Centers for Disease Control and Prevention guidelines state that either algorithm is acceptable and that HIV status should not affect interpretation of results. However, since an active immune system is required to generate treponemal-specific antibodies, our report highlights that reproducibly false-negative serum treponemal testing can occur in immunocompromised patients, even with modern assays. This patient did not report previous treatment for syphilis; previous treatment may reduce sensitivity of treponemal testing in HIV-infected patients.<sup>2</sup> Unlike in 2 previous reports of presumed ocular syphilis with negative treponemal serologies in HIV-positive patients that responded to empirical penicillin, additional tests in this patient confirmed the diagnosis of syphilis.<sup>3,4</sup> The

true sensitivity of treponemal testing in immunocompromised patients merits further study.

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