



Case report

Necrotizing retinitis due to syphilis in a patient with AIDS

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ABSTRACT

The ocular manifestations of syphilis are varied. Ocular syphilis can occur during any stage of infection and involve virtually any part of the eye. In immunocompetent individuals, the most common etiologies include syphilitic uveitis. Although the clinical presentation of ocular syphilis in HIV-infected patients is also widespread, posterior segment involvement has been more commonly described particularly in patients with AIDS. The diagnosis of syphilitic retinitis is challenging since its clinical presentation mimics retinitis caused by other viral etiologies. In addition, HIV-infected individuals with syphilis are more likely to develop aberrant serologic responses. Recognition of syphilitic retinitis and prompt initiation of penicillin therapy is of critical importance since syphilitic retinitis generally responds well to treatment and loss of vision is reversible. In this report, we describe a 39-year-old female with advanced stages of AIDS who developed necrotizing retinitis due to syphilis. Prompt initiation of intravenous penicillin led to excellent visual outcome for this patient despite significantly decreased visual acuity on presentation.

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Introduction

HIV-infected individuals are at increased risk of developing a wide variety of ophthalmologic opportunistic infections with advanced degrees of immunosuppression. Retinitis or acute retinal necrosis (ARN) is commonly caused by various viruses, such as CMV, HSV and VZV, in patients with AIDS [1–4]. Other non-viral etiologies of retinitis or ARN also include toxoplasmosis, lymphoma and syphilis [5–7]. Although syphilis can involve any anatomical structures of the eye, anterior uveitis is the most common presentation in immunocompetent hosts [8]. Importantly, however, posterior segment involvement has been more commonly described in patients with AIDS [8]. Necrotizing retinitis due to syphilis poses a diagnostic challenge for a number of reasons. Its clinical presentation closely mimics retinitis caused by viral etiologies. Additionally, HIV-infected individuals with syphilis may demonstrate aberrant serological responses. For example, seronegative secondary syphilis has been reported in HIV-infected patients [9–12]. Hicks et al. reported a case of secondary syphilis in an HIV-infected man with Kaposi sarcoma. Serology testing of syphilis was repeatedly nonreactive which necessitated biopsy of a skin lesion for diagnosis [9]. Non-

treponemal tests may also be negative in HIV-infected patients with ocular syphilis [13]. Syphilitic retinitis generally responds well to intravenous penicillin leading to favorable visual outcome, thus a high clinical suspicion and recognition of syphilitic retinitis in HIV-infected individuals followed by prompt initiation of treatment are crucial for clinicians even in the absence of objective evidence of syphilis. Herein we report a case of necrotizing syphilitic retinitis in a patient with AIDS.

Case presentation

A 39-year-old African American female with a history of AIDS was in her usual state of health until 5 days prior to presentation when she developed sudden onset of loss of vision. She was diagnosed with HIV infection 2 months prior to presentation and she was not yet on highly active antiretroviral therapy (HAART). Her markedly decreased vision started in the left eye. Two days later, she also developed decreased vision with blurriness in the right eye. She denied eye pain, conjunctival redness, and flashes of light or floaters in her visual fields. Her past medical history was also significant for gonorrhea and syphilis diagnosed 13 years before. The patient recalled uncertainly that she was treated with penicillin for syphilis. She had not been evaluated for neurosyphilis. On physical examination, the patient appeared cachectic, but not in acute distress. The temperature was 98.2 °F, blood pressure 111/65 mm Hg, pulse 95 beats per minute, respirations

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16 breaths per minute and oxygen saturation 95% on room air. Her heart sounds were regular without murmurs and her lungs were clear to auscultation. No rash or edema was observed. A 0.5 cm ulcerative lesion with irregular edges was noted in the genital area posterior to the anus. The ophthalmologic examination revealed visual acuity of hand motion in right eye and light perception in the left. The pupils were round without defects and reactive to light. The pupil size was 2.5 mm in the right eye and 4.5 mm in the left. Extraocular movement was full and intraocular pressure was normal in both eyes. Fundoscopy showed vitritis and extensive white-yellow retinal lesions, compatible with necrotizing retinitis. Laboratory studies revealed a white blood cell count of 4800 cells/mm³, hemoglobin of 12.3 g/dL, and platelets of 157,000 cells/mm³. Comprehensive metabolic panel was unremarkable. The CD4 count was 29 cells/ μ l and the HIV viral load was 3,100,000 copies/ml. Based on the fundoscopic examination demonstrating necrotizing retinitis, a presumptive diagnosis of CMV retinitis was made and the patient was started on intravenous ganciclovir. On the third day after admission, the patient underwent left anterior chamber aspiration. PCR analysis of aqueous humor for CMV, HSV and VZV were negative. PCR analysis for the peri-rectal ulcerative lesion returned positive for HSV. The patient demonstrated minimal visual improvement with ganciclovir therapy. Based on the patient's past medical history of syphilis and positive Treponema antibody (TP-PA) on admission, the patient was started on intravenous penicillin for suspected syphilitic retinitis, though serum RPR was negative. Subsequently, the patient underwent lumbar puncture; CSF was colorless with WBC 8 cells/mm³, protein 69 mg/dl and glucose 34 mg/dl. The patient demonstrated dramatic improvement of her vision and fundoscopic examination of both eyes. At the time of completion of 10 days of penicillin therapy, her visual acuity was 20/30 in the right eye and 20/50 in the left. HAART was initiated 21 days later without signs of immune reconstitution syndrome.

Discussion

In this report, we described a case of necrotizing retinitis due to syphilis in a patient with AIDS. Retinal involvement due to syphilis has been described in individuals with advanced HIV infection [13–16]. Our case posed a diagnostic challenge since the fundoscopic findings were suspicious for viral retinitis, particularly CMV. Although the patient has a remote history of presumably treated syphilis, RPR was non-reactive at the time of admission. In fact, the patient was initially treated with ganciclovir for a presumptive diagnosis of CMV retinitis. After various viral PCR assays obtained from the anterior chamber aspiration returned negative, the decision was made to initiate penicillin which resulted in dramatic clinical improvement. In HIV-infected individuals with syphilis, atypical clinical manifestations are not uncommon. More severe clinical manifestations, lack of response to penicillin therapy and inappropriate antibody responses, have been described in the literature [17]. Seronegative secondary syphilis has been reported in HIV-infected patients [9–12]. Non-treponemal tests may be negative in HIV-infected patients with ocular syphilis [13]. Our patient demonstrated inadequate serology responses to RPR due to her immunosuppressed status with advanced stages of HIV-infection. Conversely, polyclonal gammopathy and possible coexistent anticardiolipin antibodies in the presence of HIV may make non-treponemal tests be falsely positive. [18,19]. In addition, a failure to decrease serologic titers of syphilis in the absence of immune reconstitution with antiretroviral therapy has been reported [20]. Considering the uncertainty regarding syphilis serology testing in HIV-infected individuals, clinical judgment with a low threshold for penicillin therapy would be a reasonable approach.

The ocular manifestations of syphilis are diverse since it can involve any anatomical structures of the eye. In a study of 22 cases of ocular syphilis in HIV-negative individuals, non-granulomatous anterior uveitis was the most common presentation (18/22) [8]. Although anterior uveitis is common in immunocompetent individuals, posterior segment involvement has been described more commonly in HIV-infected individuals with advanced stages of immunosuppression. In a retrospective study of ocular syphilis in HIV-infected patients, panuveitis accounted for 38% whereas isolated anterior uveitis accounted for 31% [21]. Tran et al. investigated ocular manifestations due to syphilis for 20 eyes in 12 HIV-infected individuals; necrotizing retinitis was noted in 7 eyes (35%), posterior chorioretinitis in 6 eyes (30%) and optic nerve involvement in 5 eyes (25%) [22]. In addition, syphilitic retinitis is more commonly seen in HIV-infected individuals with more advanced stages of immunosuppression. In a study of 101 HIV-infected patients, posterior uveitis was significantly more common in those with CD4 count <200 cells/mm³ ($p=0.002$) [13].

Ocular syphilis may be complicated by central nervous system involvement, thus investigation for neurosyphilis should be considered especially for patients with AIDS. In a study of neurosyphilis during the AIDS epidemic in San Francisco, 11 patients had concomitant uveitis among 38 patients with early neurosyphilis [23]. Another study reported a high proportion of neurosyphilis in HIV-infected patients with syphilitic uveitis; 7 of 9 patients (77.8%) demonstrated CSF abnormalities [22]. Even with no evidence of neurosyphilis, syphilitic retinitis should be treated with the same regimen for neurosyphilis; a 10–14 day course of intravenous penicillin is recommended. Syphilitic retinitis generally responds well to penicillin therapy with good visual outcome [24,25].

Conclusions

Although ophthalmologic manifestations of syphilis are diverse, posterior segment involvement is common in HIV-infected individuals with more advanced stages of immunosuppression. Necrotizing retinitis due to syphilis is particularly diagnostic challenging in the presence of AIDS. Its clinical presentation mimics retinitis cause by viral opportunistic infections. Serological responses may be atypical in HIV-infected individuals with syphilis. Lack of appropriate clinical responses to ganciclovir for presumed viral retinitis, negative PCR analysis for viral retinitis, remote history of syphilis led us to initiate penicillin therapy empirically with excellent visual outcome. Recognition of syphilitic retinitis in patients with AIDS is paramount for clinicians and a threshold to initiate penicillin should be lower even in the absence of objective evidence of syphilis.

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