SYPHILITIC UVEITIS AS THE INITIAL MANIFESTATION OF HIV INFECTION

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Abstract: Syphilis is an uncommon cause of uveitis in HIV-infected patients. We report a case of bilateral panuveitis and describe its characteristics as the initial manifestation of HIV infection. A 74-year-old heterosexual male complained of blurred vision and floaters in both eyes for 40 days. Slit lamp examination showed diffuse keratic precipitates and cells in the anterior chamber of both eyes. Fundus examination revealed multiple small white dots and scattered retinal hemorrhage over the mid-equatorial retina with marked vitritis. Physical examination disclosed multiple erythematous papules over bilateral palms compatible with secondary syphilis. Serologic tests — the venereal disease research laboratory (VDRL) test, fluorescent treponemal antibody absorption (FTA-ABS) test, and Treponema pallidum hemagglutination (TPHA) test — were all positive. Aqueous fluid also showed positive FTA-ABS reaction. Under the impression of acquired secondary syphilis, enzyme-linked immunosorbent assay and Western blot test were performed and revealed concurrent HIV infection. After intravenous administration of penicillin-G, 18 million units daily for 2 weeks, the vitritis and retinochoroiditis improved. All patients with panuveitis of unknown cause should undergo VDRL and FTA-ABS screening. Subsequent testing for HIV antibody in leutoic uveitis is also mandatory.

CASE REPORT

In May 2001, a 74-year-old man presented with progressively blurred vision and floaters in both eyes of 40 days’ duration. Best-corrected visual acuity was 3/60 in the right eye and 6/60 in the left. Slit lamp examination showed diffuse keratic precipitates and 1+ cells in the anterior chamber of bilateral eyes. There were multiple small, yellow-white, oval lesions in the deep retina and

Syphilis is a sexually transmitted disease caused by the spirochete Treponema pallidum. It can cause a wide variety of ocular inflammatory conditions that mimic other diseases and thus cause confusion for ophthalmologists [1]. Uveitis, scleritis, chorioretinitis, interstitial keratitis, retinal vasculitis, papillitis, and optic atrophy are all well-known ocular manifestations of syphilis. With the introduction of penicillin in the 1940s, the incidence of syphilis decreased markedly [2]. However, a resurgence of this disease was noted over the past two decades and has been linked to drug abuse, prostitution, and increased coinfection as part of the HIV epidemic [3]. We report a case of syphilitic infection with panuveitis in a patient who was found to be HIV seropositive. This case shows the importance of considering syphilis infection in patients with panuveitis of unknown cause. Furthermore, as the number of HIV-infected people is increasing in Taiwan [4, 5], the prevalence of HIV coinfection with ocular syphilis may also be increasing. As in this case, leutoic uveitis can be the initial presentation of HIV infection.

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retinal pigment epithelium (RPE) distributed over the extramacular area to the mid-equatorial retina, accompanied by marked vitritis (Fig. 1). Scattered retinal hemorrhage and localized vessel cuffing were also noted. Fluorescein angiography disclosed early hypofluorescence of the yellow-white spots that became hyperfluorescent through the mid phase to the late phase. Color vision was not impaired.

Physical examination showed general weakness and poor nutrition. His body weight had decreased by 11 kg in the last year. The patient denied any history of drug abuse, homosexuality, or exposure to sex with prostitutes. Physical examination revealed multiple painless, circular, erythematous papules over the bilateral palms consistent with secondary syphilis, as confirmed by dermatologists (Fig. 2). Chest roentgenography and abdominal sonography both showed no pathologic lesions. Complete blood counts revealed 4,800 white blood cells/mm$^3$ with 61% neutrophils, 26% lymphocytes, 10% monocytes and 1% eosinophils. The C3 and C4 complement levels were 76 mg/dL and 16 mg/dL (normal C3, 55–120 mg/dL; normal C4, 14–51 mg/dL). Serum IgG was 2,580 mg/dL (normal, 751–1,560 mg/dL), IgA was 366 mg/dL (normal, 82–453 mg/dL), and IgM was 191 mg/dL (normal, 46–304 mg/dL). Neurologic examinations were all within normal limits.

Subsequent serologic tests confirmed the diagnosis of syphilitic infection. Venereal disease research laboratory (VDRL) test, fluorescent treponemal antibody absorption (FTA-ABS) test, and $T. pallidum$ hemagglutination (TPHA) test were all positive: VDRL 1:16, and FTA-ABS test 2+ in serum and 1+ in aqueous humor. Lumbar puncture for cerebrospinal fluid (CSF) study was suggested, but the patient refused. In addition, enzyme-linked immunosorbent assay (ELISA) and Western blot for HIV were both positive. The CD4$^+$ T-lymphocyte count was 454 cells/$\mu$L and HIV viral load was 102,621 copies/mL.

Because examinations of serum and aqueous humor all demonstrated syphilitic uveitis, antibiotic treatment with 18 million units of intravenous penicillin-G daily was started. After 1 week of therapy, his visual acuity remained 3/60 in the right eye and improved to 6/30 in the left. The patient also reported decreased floaters. The yellow-white retinal lesions decreased in number, showed progressive hyperpigmentation, and became more superficial. Slightly increased peripapillary hemorrhage was noted. The vitritis also improved. After 14 days of full-course therapy, the patient was discharged and was given intramuscular penicillin-G 2.4 million units/week for 3 weeks at the outpatient clinic.

**Discussion**

This patient presented with syphilitic uveitis as the initial manifestation of HIV infection with multiple yellow-white chorioretinal lesions and vitritis. Studies have indicated that syphilis accounts for 1 to 3% of all cases of uveitis [6–8]. Shalaby et al reported a syphilis incidence of 0.6% in 2,085 HIV-infected patients in their clinic from 1983 to 1995 [9]. They also found that panuveitis was the most common ocular manifestation of syphilis in patients coinfected with HIV. The most
common posterior segment manifestations of acquired syphilis are chorioretinitis and retinal vasculitis [2]. Two forms of syphilitic chorioretinitis are generally recognized. The first form, seen in this case, is a diffuse bilateral chorioretinitis that exhibits multiple white-yellow, inflammatory, chorioretinal lesions with associated vitritis, retinal vasculitis and retinal edema. This diffuse form typically occurs during secondary syphilis. Belin et al described a patient with syphilitic uveitis who had yellow-white chorioretinal lesions with progressive pigmentation and anterior migration similar to those of our patient [10]. The second form is a localized, large, solitary, placoid, pale yellow, subretinal lesion that typically affects the region of the optic disc and macula [11]. This localized form is thought to occur in late-stage systemic syphilis and may be associated with asymptomatic infection.

Although patients concurrently infected with HIV and syphilis usually have more florid and aggressive ocular disease, no unique patterns of syphilitic posterior uveitis have been reported [12]. HIV-positive patients are reported to have more bilateral involvement, more posterior segment disease, and more neurologic disease than HIV-negative patients [13]. In addition, positive CSF serology and pleocytosis are commonly found in HIV-positive patients [9]. Our patient had bilateral involvement and mainly posterior segment lesions. However, he refused lumbar puncture for CSF examination as no neurologic deficit was noted.

HIV-infected patients do not face markedly increased risk of opportunistic infection until all T4 cell counts fall below 250. The CD4 cell count in our patient was 454 cells/µL, which is below the normal range (normal, 600–1,500 cells/µL). Cytomegalovirus retinitis, acute retinal necrosis, and progressive outer retinal necrosis tend to occur in patients with more advanced HIV disease, having CD4 cell counts less than 50 cells/µL, which may be useful in the differential diagnosis [13].

Our patient had positive results on FTA-ABS, TPHA, and VDRL tests, which demonstrated syphilitic uveitis. FTA-ABS test of the aqueous humor was also positive. The diagnosis of ocular syphilis is primarily dependent on serologic tests [1]. Treponemal tests (FTA-ABS and TPHA) are the most sensitive and will remain positive over time and after treatment. Nontreponemal tests (VDRL and rapid plasma reagin) are less sensitive than treponemal tests, but more useful for therapeutic monitoring. Obtaining only a serum VDRL test without a serum FTA-ABS test will miss 30 to 40% of cases of ocular syphilis [8].

Penicillin remains the antibiotic of choice for the treatment of syphilis. We treated this patient with intravenous aqueous penicillin-G 18 million units/day for 14 days followed by intramuscular benzathine penicillin-G 2.4 million units/week for 3 weeks. Ocular syphilis should be treated as neurosyphilis, because the retinal and optic neuroepithelial structures are embryologically derived from the brain. Many studies have suggested that intravenous aqueous penicillin-G 12 to 24 million units/day for 10 to 14 days followed by intramuscular penicillin-G 2.4 million units/week for 3 weeks is the most appropriate regimen [1, 9, 14, 15]. Benzathine penicillin-G alone should not be used in the treatment of ocular syphilis because only low drug levels accumulate in the CSF and eye. Relapse of ocular syphilis after treatment with benzathine penicillin has been reported in both immunocompetent and HIV-infected hosts [16, 17]. Hence, HIV-infected patients with ocular syphilis should be treated with high-dose intravenous penicillin-G for a full 14 days, and always supplemented with intramuscular benzathine penicillin-G 2.4 million units/week for 3 weeks to prevent relapse [1].

The ability of syphilis to mimic different ocular diseases can lead to misdiagnosis and delay in appropriate therapy. The findings in this case suggest the need for routine FTA-ABS and VDRL screening in patients with uveitis and unexplained ocular inflammation. High suspicion of ocular syphilis is mandatory, because prompt and proper antibiotic treatment is almost always effective and omission of treatment is disastrous. Subsequent testing for HIV antibody in leutics is important, as HIV coinfection with ocular syphilis is common in the era of AIDS.

References