Ocular syphilis in an HIV-infected patient: active disease or immune reconstitution syndrome?

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ABSTRACT

In patients coinfected with HIV the natural history of syphilis may be altered and the immune defect may account for differences in the host immune response to Treponema pallidum. Anyway many questions remain about interactions between HIV and syphilis during the HAART-related restoration of protective pathogen-specific immune responses. We describe the case of a HIV-positive patient with ocular syphilis who presented an unexpected immune response to coinfection.

Introduction

Recent findings indicate that syphilis is somehow modified with concurrent HIV infection. HIV-positive patients may present syphilis with non-typical features: infection may be more aggressive, more difficult to treat and it is possible to observe an increased rate of early neurological involvement; in addition is always more frequent neuro-ophthalmic manifestations. The inability of HIV patient to establish an adequate immune response to Treponema pallidum may account for a more rapid progression of syphilis. In fact in patient with co-infection the natural course of syphilis may be modified with contemporaneous presence of multiple manifestations. On the other hand syphilis does not seem to involve virological and immunological course of concurrent HIV disease. The immune defect may account for some differences in the host immune response to syphilis in patients infected with HIV. Anyway many questions remain about changes of the host immune response during HIV-syphilis co-infection and interactions between HIV and Treponema pallidum.

Case report

We present the case of a 28 years-old bisexual asymptomatic HIV-infected male, who was hospitalized because of a two days history of ocular pain, reduction of left eye’s visual acuity and headache. The HIV seropositivity has been diagnosed two months before when the CD4 count was 142 cells/mmc and HIV-RNA>100000 copies/ml. He has been treated with lamivudine/ zidovudine and lopinavir/ritonavir for 28 days. On admission, a neuro-ophthalmological examination revealed reduction of visual acuity and an acute retinal inflammation of left eye with necrosis areas; right eye was normal. There was no abnormality in the physical and neurological examination. The CD4 count was 227 cell/mmc and HIV-RNA was undetectable. On a suspicious diagnosis of acute herpetic necrosis of left eye’s retina, based on the ophthalmic findings, acyclovir, corticosteroids plus local anti-inflammatory therapy were administrated. After seven days, the left eye did not show reduction of retinal inflammation and a progressive reduction of visual acuity was seen. Serologies for Syphilis, Lyme, Brucella, Chlamydia, Toxoplasmosis, EBV, CMV were negative. Magnetic resonance of the brain was normal. Analysis of cerebrospinal spinal fluid (CSF) was negative, including CSF serologies for Syphilis. After ten days ophthalmological examination revealed a bilateral uveo-papillitis associated to left eye retinal detachment. On the 3rd week from admission tests for syphilis showed VDRL ++++, TPHA 1:2560, Beia (Syphilis Ig Mab Capture, ELISA assay, Bouty, Milan, Italy) IgM positive, Beia IgG positive. CD4 count was 389 cell/mmc. Therapy with intravenous penicillin G (24.000.000 IU) and prednisone 25 mg/die for 14 days was given. On the 4th week the patient was discharged: left eye vision was lost and right visual acuity was 7/10. Intramuscular benzathine penicillin (2.400.000 every week for 3 weeks) was given and after 2 months serology tests for
syphilis showed VDRL ++++, TPHA 1:640, Beia IgM negative, Beia IgG positive. CD4 count was 452 cell/mmc. A neuro-ophtalmological examination confirmed the reduction of inflammatory activity in both eyes; however the patient lost visual acuity of left eye (Fig 1).

**Discussion**

Our case underlines the importance to consider always syphilis infection as first clinical manifestation of HIV infection. In fact syphilitic eye disease may be asymptomatic, insidious and is not recognized. A suspicion is required for patients with latent or indeterminate syphilis, but it has been observed ocular compromission as first manifestation of infection too. In patients coinfected with HIV the natural history of syphilis may be altered. Moreover our patient showed ocular involvement in the absence of positive serology. It is largely discussed about the accuracy of serologic tests for *Treponema pallidum* during HIV infection.² Often lumbar puncture is useful for CSF evaluation in patients with ocular syphilis; anyway it can be also negative. This data permit us to speculate that the absence of positive serologies for syphilis was somehow related to severe immunocompromise. The immune defect may also account for the inability of HIV-infected patient to establish an adequate cell-mediated immune response to *Treponema pallidum* and may implicate a more rapid progression of ocular involvement. Many questions remain about the ability of *Treponema pallidum* to persist in the presence of a brisk host response. Antigenic variation has been hypothesized to be one mechanism of escaping immune surveillance. If a Th1 response is elicited in primary syphilis, progression of disease is accompanied by a shift to a Th2 response, allowing for incomplete clearance of the pathogen. Moreover during HIV co-infection, an imbalance in the Th1-type and Th2-type responses contributes to the immune dysregulation associated with HIV infection. Suppression of HIV replication by highly active antiretroviral therapy (HAART) often restores protective pathogen-specific immune responses. Anyway some patients present an immunopathological restoration of immune response that may trigger an inflammatory reaction. The immunopathogenesis of immune restoration disease is not clear but data suggests that immunopathogenic mechanisms are determined by the pathogen. During dynamic changes of the host immune response, the exposition to spirochetal, not more sequestered beyond the damaged blood-ocular barrier, and the use of antiretroviral therapies may favour intraocular inflammatory reactions. If before the use of protease inhibitors ocular syphilis was described in 0.6% of HIV-positive patients, after the introduction of HAART researchers reported a prevalence between 4.3 and 9% in patients coinfected with HIV. Phadungchai et al hypothesize that syphilitic uveitis may be related to a complex interaction between *Treponema pallidum* and immunologic recovery HAART-related.³ On the other hand Tran et al. report that ocular syphilis is not correlated with HIV-infection staging and does not seem to be correlated with CD4 counts.⁴ Moreover the immune reconstitution inflammatory syndrome has not been previously

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**Fig 1.** Viro-immunologic evolution of HIV infection and follow-up of syphilis markers in serum and cerebrospinal fluid
described with syphilis. In all cases of ocular inflammatory manifestations it is important to consider syphilis. In fact atypical syphilitic ocular manifestations may not be understood and concurrent HIV infection may lead to an accelerated course of syphilis with a risk of severe ophthalmic involvement.

References