Case Report

A CASE OF DOUBLE TROUBLE: OCULAR SYPHILIS IN A PATIENT WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION

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ABSTRACT

Syphilis has always been known as "the great mimicker" as it can have a plethora of clinical presentations. Ocular manifestations occur in the secondary and tertiary stages of syphilis, however it may occur at any stage of the disease. The resurgence of syphilis has resulted in an increased number of cases. Syphilis is an important facilitator of human immunodeficiency virus (HIV) with reported coinfection rates of 50-70 %. The ocular syphilis in patients with HIV co-infection has both diagnostic and management challenges as HIV alters the clinical presentations. We report a case of HIV infection who "defaulted" highly active antiretroviral therapy *(HAART) for 1 year due to COVID-19 pandemic. He presented with bilateral blurring of vision secondary to syphilis pan-uveitis.*

INTRODUCTION

The incidence of syphilis has increased markedly over the last decade, particularly among men who have sex with men (MSM). Ocular involvement is a potentially devastating clinical manifestation of syphilis. Human immunodeficiency virus (HIV) infection appears to increase the risk of ocular syphilis [1]. Because of the lack of pathognomonic features for ocular syphilis and its ability to occur in both immunocompetent and immunosuppressed individuals, high index of suspicion is required for prompt diagnosis and treatment. Thus MSMs and HIV -infected patients presenting with blurring of vision, ocular syphilis should be highly suspected [2]. We share a case of ocular syphilis in a HIV positive young adult male.

CASE REPORT

A 31-year-old male presented with bilateral acute progressive visual loss worse in the left eye over the past 2 weeks. There was no associated pain or redness. He had intermittent floaters with no flashes a few months prior. He reported to only being able to make out shadows in the left eye and blurry figures in the right eye. He had on and off fever with no chills or rigors for the past 2 to 3 months and had been taking over the counter medications for the symptoms.

He had no headache, photophobia, neck stiffness, diplopia, nausea, vomiting, or limbs weakness. He had no cough or chest pain. He denied history of penile ulcer or discharge or rashes, however he had mouth ulcer a week prior which had healed. There was no history of loss of weight or appetite. He had used intravenous methamphetamines for the past 10 years and was undergoing rehab at a rehab center at the time of presentation, and was free of the drug for 8 months. He denied using other illicit drugs or alcohol. He was however an active smoker. He also admitted to having unprotected sex with several men (MSM) in the past 10 years, although he had been in a monogamous relationship for the last 1 years.

He is HIV positive, diagnosed in December 2019, just prior the COVID-19 pandemic. Previously he was being followed- up at a clinic in Selangor and was receiving highly active antiretroviral therapy (HAART) for one year. However his follow and treatment was interrupted by the pandemic and he was out of HAART for the last one year.

On physical examination, his vital signs were normal. Right best corrected visual acuity (BCVA) was 6/24,

and only able to perceive light in the left eye. The right anterior segment was unremarkable. The left anterior segment revealed keratic precipitates, cells of 2+, and mild flare (Figure 1). In both eyes, there was no evidence of posterior synechiae and the pupils were round and reactive. There was left relative afferent pupillary defect. The fundus view was hazy due to severe vitritis, visualisation of retina or any retina/chorioretinal detail was poor. There were vague views of both discs which appeared hyperaemic (Figure 2A, 2B).

Laboratory investigation revealed mild increase in total WBC, 12.02 x 10^3/uL HIV Ag/AB (CIMIA) was reactive with Particle Agglutination (PA) was positive for HIV-1 The CD4+ cell count was 428 cells/mm3, HIV viral load 40111 copies/mm3 , CD4/CD8 ratio was 0.27. A rapid plasma regin (RPR) for syphilis screening was reactive with a titer of 1: 512. Veneral disease research laboratory (VDRL) was reactive with titre 1:512, Treponema Pallidum Agglutination Test TPPA/TPHA was also Positive. Serology test done for Toxoplasma and Hepatitis B and C were negative. Tracheal aspirate was negative for AFB. Mantoux test showed no induration.

Cerebrospinal fluid (CSF) analysis demonstrated 0 red blood cells/µL, 3.6 white blood cells/µL, 3.4 mg/dL glucose, and 301 mg/dL protein. No microorganisms were seen by Gram stain. The CSF VDRL and bacterial culture were negative. Serum and CSF cryptococcal antigen tests were also negative. Chest X-ray showed no evidence of pulmonary tuberculosis. Brain CT did not show any evidence suggestive of neurosyphilis. A diagnosis of right posterior uveitis and left panuveitis secondary to syphilis infection with HIV co-infection was made.

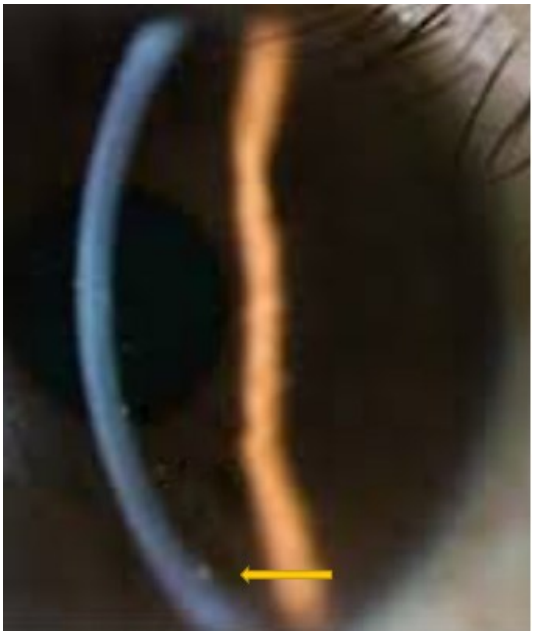

Figure 1: Left anterior uveitis with keratic precipitates (KPs)

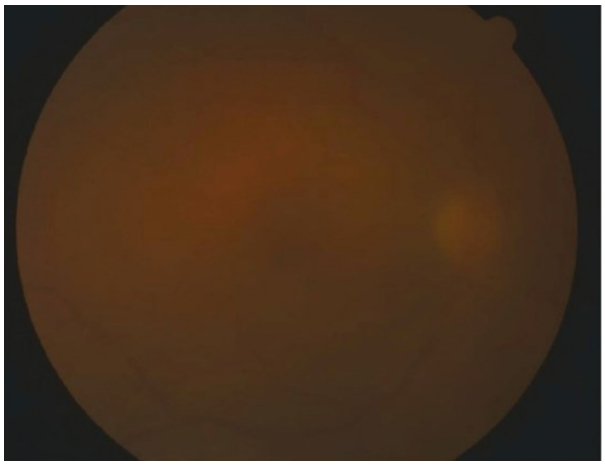

Figure 2A: Right fundus: Hazy view

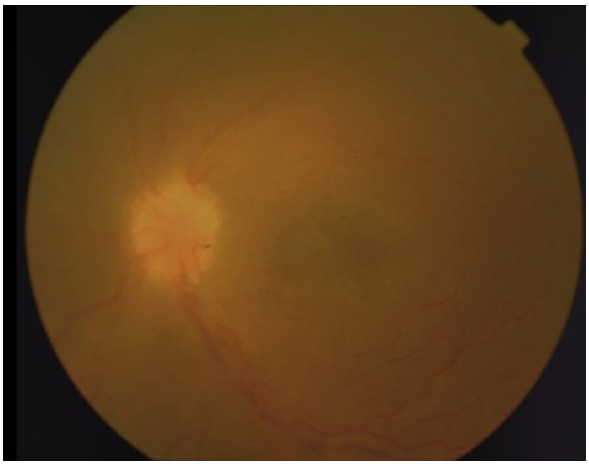

Figure 2B : Left Fundus: Hazy view due to severe vitritis with vague appearance of swollen and hyperaemic disc.

The patient was informed of the diagnosis of syphilis infection with ocular involvement. He was immediately started on Procaine penicillin 2.4 million units IM once daily plus Probenecid 500mg 4 times per day, both for 14 days. He also received gutt Dexamethasone 0.1% 2-hourly and gutt Atropin% TDS to both eyes. It was recommended that his partner undergoes evaluation for HIV and syphilis. Patient voluntarily agree to continue his HAART treatment and follow up. At an ophthalmology clinic visit two weeks later, the patient's right BCVA improved to 6/12, however his left vision remained perception to light most probably related to optic nerve dysfunction.

DISCUSSION

Syphilis is a sexually transmitted infection caused by a spirochete bacterium, Treponema pallidum. *Treponema pallidum* has the ability to infect multiple organs leading to multiple clinical manifestations with devastating consequences if left untreated [1].

The incidence of primary and secondary syphilis has increased markedly over the last decade, from 2.1 per 100,000 people in 2000 to 4.5 per 100,000 in 2011 [3,4]. The epidemic has disproportionately affected the MSM population, while rates in women and men who have sex with women have steadily decreased. The Centers for Disease Control and Prevention (CDC) estimated that, in 2011, 72% of all primary and secondary syphilis cases occurred in MSM, which increased from just 7% in 2000 [5,6]. The epidemic in this population, including in Malaysia, is exacerbated by high rates of coexisting HIV infection and risky sexual and drug behaviours [6,7].

In a study of MSM presenting to sexually transmitted disease clinics, a significantly higher proportion of HIV-infected individuals had coexisting primary or secondary syphilis compared with those who were HIV-negative (10.1% versus 2.6%) [6]. Some studies suggest that syphilis facilitates HIV transmission by increasing expression of its CCR5 receptors or inducing expression of the HIV-1 gene in human monocytes [8]. The natural history of syphilis leading to unusual and more aggressive clinical manifestations as well as earlier neurologic involvement is altered by HIV infection [9].

Panveitis is the most common ocular syphilis manifestation. It can occur at any stage of infection and may be the only clinical manifestation of infection as seen in our case [10]. Clinically, patients may present with eye pain and reduced vision, central scotomas, and unilateral or bilateral [11]. As syphilis comprises less than 1-2% of all cases of uveitis, delays in diagnosis are common. The diagnosis is often not considered until a patient has failed to respond to corticosteroid therapy [9].

Ocular syphilis in the setting of untreated HIV is more frequently bilateral as illustrated by our case, as his HAART therapy was interrupted by the pandemic for almost a year [12]. Ocular syphilis however does not require immunosuppression to occur; it is therefore important to consider the diagnosis in HIV-infected patients with visual complaints regardless of CD4+ cell count.

When ocular syphilis is suspected, lumbar puncture should be performed with CSF analysis in addition to serum serologic tests. Lumbar puncture also serves to confirm the diagnosis of neurosyphilis [12]. A positive CSF VDRL is highly specific for neurosyphilis, although lacks sensitivity [6]. CSF examination may also reveal a lymphocytic pleocytosis or elevated protein; however, such findings may also be seen in HIV-infected patients without syphilis. Given the potential reduced sensitivity of serologic tests for syphilis in HIV-infected patients, any clinical suspicion for syphilis not supported by serologic findings warrants an attempt to visualize spirochetes microscopically [8].

Therapy for ocular syphilis is the same as for other forms of neurosyphilis. Current Guideline, first-line therapy is intravenous aqueous crystalline penicillin G 18-24 MU per day administered as 3 to 4 MU every 4 hours or continuous infusion for 10- 14 days. Alternatively, Procaine Penicillin 2.4 MU administered intramuscularly once daily plus Probenecid 500mg orally 4 times per day, both for 10-14 days [10,13]. Treatment failure in cases of ocular syphilis may occur. Therefore, patient was counselled regarding the importance of compliance to treatment and follow up as timely diagnosis and treatment are essential for good outcomes.

CONCLUSION

Re-emergence of syphilis has resulted in the rise of ocular syphilis. A high index of suspicion is needed to diagnose and treat these cases. Panuveitis is the most common ocular manifestation. Ocular syphilis is treated as neurosyphilis even when there are no CSF and CT Brain evidence of the infection. It is recognised that MSMs are at a higher risk for syphilis and thus more prone to have ocular syphilis.

CONFLICT OF INTEREST

The authors of this paper declare that they have no financial or nonfinancial conflict of interests.

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