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Case report

Ocular syphilis in an immunocompetent host

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ABSTRACT

Syphilis is an old disease that experienced a resurgence with the emergence of HIV/AIDS. Syphilis is a reportable infection that is monitored by the Centers for disease Control (CDC) in the U.S. and rates have been rising since 2000. Although ocular syphilis is a well known consequence of syphilis infection it continues to be less frequently diagnosed, partially because ocular manifestations are not reportable to CDC. While the majority of recent cases in the U.S. have been reported in men who have sex with men (MSM) population, 50 % of these cases are HIV negative. We present a case of acute iridocyclitis and ocular hypertension due to syphilis infection. This case reiterates the need to increase healthcare workers' awareness of the importance of timely recognition of potential ocular syphilis to prevent visual sequelae from the infection. Ocular syphilis should be kept in the differential diagnosis in immunocompetent/HIV negative patients, and the importance of obtaining a detailed sexual history should not be forgotten.

Background

Syphilis is a disease that is introduced to medical students early in their undergraduate curriculum, but nonetheless is often missed by seasoned healthcare providers in clinical practice. In this case, secondary syphilis with maculopapular rash was misdiagnosed as a viral exanthem, and our patient progressed to ocular syphilis. This case reiterates the importance of detailed history taking skill in this hectic age of technology driven healthcare. Fortunately, our patient responded well to treatment for ocular syphilis and on follow up his visual acuity had returned to 20/20 in both eyes.

Case presentation

A 52-year-old male with history of smoking and hyperlipidaemia initially presented to an outpatient general medicine clinic with complain of acute onset left eye redness, pain, clear discharge and blurred vision. He denied any recent trauma,sick contacts and recent viral illnesses. He was started on gentamicin eye drops and appropriate referral to ophthalmologist was made due to acute vision loss. He was misdiagnosed with acute bacterial conjunctivitis. On follow-up with an ophthalmologist, he was diagnosed with iridocyclitis, adhesions of the iris due to inflammation with some swelling of cornea was noted on detailed examination. A detailed sexual history by the ophthalmologist revealed high risk sexual behaviour, with reported unprotected sex with two male partners over the last year. Patient was subsequently started on neomycin -polymyxin -dexamethasone ointment, atropine eyedrops and testing to evaluate cause of iridocyclitis was sent. Syphilis IgG resulted positive, with RPR quantitative titre of 1:128 and he was admitted to the hospital for initiation of intravenous antibiotic treatment. On admission to the hospital, external eye examination revealed left pupil with irregular border, slight conjunctiva erythema and no purulent discharge was noted (Fig. 1).

On further questioning, our patient reported a diffuse rash over his trunk and back that he first appreciated 3 months prior to the onset of his eye pain. He reported being diagnosed with viral exanthem at that time, was treated symptomatically. He denied noticing any genital lesions in the past 12 months. Patient had pigmented macular truncal rash (Fig. 2).

Investigations

Due to acute onset of symptoms and progressive worsening, multiple testing as shown below in Table 1 were performed.

After the blood test returned positive for syphilis, patient was admitted to the hospital for treatment with IV antibiotic. Patient underwent lumbar puncture to rule out neurosyphilis. Lumbar puncture result were as mentioned below in Table 2.

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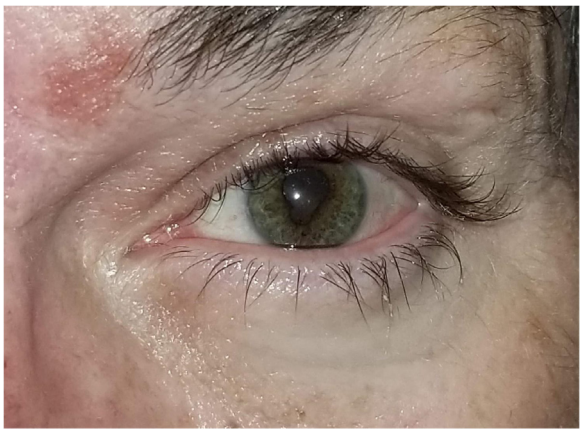

Fig. 1. External examination of left eye showing irregular pupil.

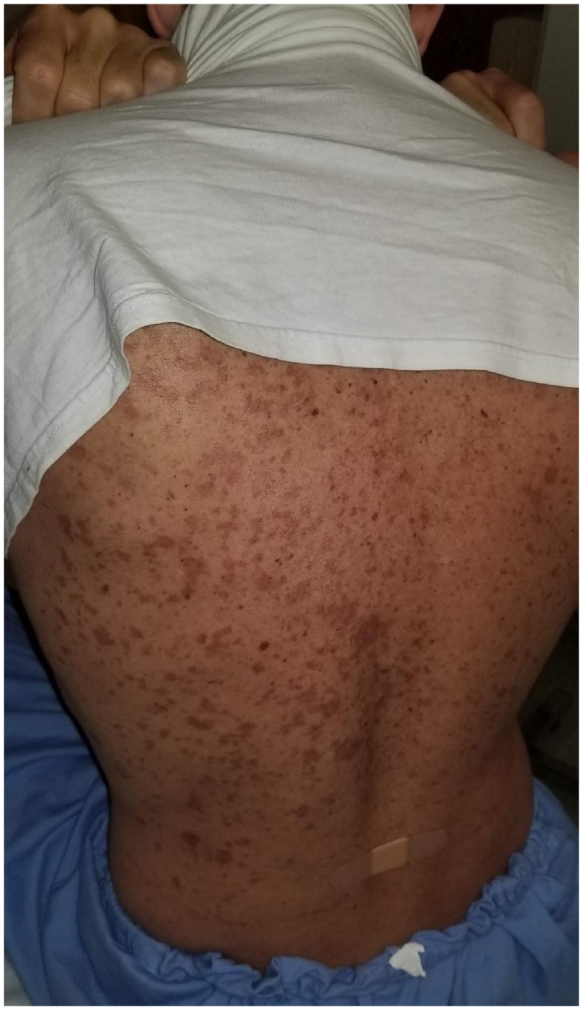

Fig. 2. Pigmented macular rash over back.

Other tests performed included complete blood count on presentation that showed absence of leukocytosis with total white blood cell count of 9350/ml but patient had a leftward shift with slight increase in neutrophil percentage to 72.7. C reactive protein level was normal at 0.28 mg/dl.

Differential diagnosis

Anterior uveitis can broadly be classified by cause as infectious, non-infectious, human leukocyte antigen associated (HLA-B27) or idiopathic. Most cases are idiopathic [1]. About 50 % of cases have been associated with HLA-B27 [2]. In our patient HLA-B27 testing was negative. Corneal trauma can present with similar complaint of acute onset eye pain and can be ruled out based on history. For patients presenting with recurrent, chronic or bilateral symptoms, sarcoidosis and tuberculosis should be kept in possible differentials. Angiotensin converting enzyme and Quantiferon tests were negative in our patient. Reiter syndrome with triad of urethral, conjunctival and synovial symptoms should be considered in patients with symptoms following a genitourinary or gastrointestinal infection. Our patient did not report history consistent with it. Infectious conjunctivitis due to bacterial or viral etiology is the most common diagnosis made in primary care setting when a patient presents with acute onset eye pain and redness. Our patient did not report mucopurulent discharge consistent with bacterial conjunctivitis.

Treatment

Patient was admitted in the hospital and started on aqueous crystalline penicillin G potassium 24 Million Units in sodium chloride continuous infusion. A peripherally inserted central catheter(PICC) was placed in right upper extremity, and home infusion through continuous ambulatory deliver device(CADD) pump was arranged to complete total 14 days of treatment.

Outcome and follow-up

Follow-up complete blood count: WBC count 8200/dl, with normal neutrophil percentage of 59.1. On one-month follow-up after completion of antibiotic the patient reported resolution of pain and improvement of visual acuity to 20/20 in bilateral eyes. Due to his risk factor he was started on HIV pre-exposure prophylaxis. Repeat RPR titer at 6 months was 1:2.

Discussion

Treponema pallidum is an ubiquitous pathogen. Overall incidence of syphilis is rising world wide with approximately 75,000 cases reported in United States in 2015, greater than 22,000 cases reported from European countries in 2013, and greater than 400,000 cases in China reported in 2016 [5]. Actual incidence or prevalence of ocular syphilis is unclear due to lack of good surveillance. Retrospective case investigation of data from reported cases of syphilis in the United States in 2014–2015 recorded that 0.6 % of these cases also had symptoms of ocular syphilis [6]. After the initial inoculation, the organism is thought to disseminate via the blood and lymphatic system and accumulate in perivascular spaces of organs. The organism invades structures of the eye to cause local inflammation and edema.

Most cases of ocular syphilis occur in HIV-infected MSM. Few cases have been reported among HIV-uninfected persons including heterosexual men and women, but clinicians should be aware and vigilant to make early diagnosis of the infection as ocular syphilis can include any eye structure and lead to permanent blindness [3]. This case highlights the need to obtain good social history to identify patients at risk of the infection and also to make clinicians aware of an increase in the incidence of ocular syphilis in immunocompetent hosts. Recently a single centre identified HIV co-infection in only two of a series of 12 patients with ocular syphilis in France [4]. Clinicians should be aware of dramatic rise of syphilis and other sexually transmitted diseases in individuals uninfected with HIV. Early consideration of diagnosis and prompt treatment is essential to halt the epidemic of sexually transmitted diseases.

Table 1
Blood testing to determine the cause of acute iridocyclitis.

Test	Result
HLA- B27	*Negative*
Rheumatoid factor	*Negative*
Angiotensin converting enzyme	*41 u/l – (reference range: 16–85 u/L)*
QuantiFERON-TB Gold Plus	*Non Reactive*
ANA screen	*Negative*
HIV 1&2 antigen antibody screen	*Non reactive*
Syphilis IgG	*Reactive*
RPR screen	*Reactive*
RPR quantitative titer	*1:128—(reference range: <1:1)*
Urine gonorrhea and chlamydia nucleic acid amplification test (NAAT)	*Negative*

Table 2
Result of cerebral spinal fluid analysis.

Test	Result
Color	*colorless*
CSF GLUCOSE	*62 ml/dl(reference range: 40–70 ml/dl)*
PROTEIN CSF: 35.1	*35 mg/dl(reference range:12–60 mg/dl)*
FLUID, TOTAL NUCLEATED CELLS:	*2 /mm3(reference range: 0-cells/mm3)*
CSF NEUTROPHILS	*3*
CSF LYMPHOCYTES	*95*
CSF MONOCYTES	*2*
CSF MACROPHAGES	*0*
CSF EOSINOPHILS	*0*
FLUID RBC COUNT	*23/mm3*
CSF VDRL	*Negative*

Treponema pallidum infection causing ocular syphilis can involve any part of the eye. Ocular syphilis is usually seen in early syphilis but can present in any stage of syphilis. Uveitis is usually the most common presentation of ocular syphilis as reported in prior studies [7–9]. Other ocular presentations may include iritis, retinitis and optic neuritis. Most common symptoms include blurry vision, seeing flashing lights and blindness. Neurological symptoms such as headache, altered mental status or acute hearing loss can be found in about 20 % cases of ocular syphilis. Because ocular involvement can occur in any stage of infection, clinicians should enquire and perform thorough examination for presence of syphilitic ulcer or rash. Our patient was noted to have a pigmented macular rash over his back at time of presentation to the hospital. In retrospect, this was a feature of secondary syphilis which unfortunately was misdiagnosed as viral exanthem.

Direct diagnostic methods include microscopy, PCR or histology. Testing for syphilis include non-treponemal tests used for screening, rapid plasma reagin (RPR) test and Venereal Disease Research Laboratory (VDRL) slide test. Positive non-treponemal test is confirmed by treponemal tests which include fluorescent treponemal antibody absorption (FTA-ABS), treponemal pallidum particle agglutination (TPPA) and treponemal antibody-linked enzyme immunoassays (EIA) or chemiluminescent immunoassays (CIA). In the traditional test screening algorithm, non-treponemal testing is performed first, then confirmed by a direct treponemal testing. A reverse sequence algorithm has increased sensitivity in cases of latent infection, previously treated cases and rarely in very early syphilis infection [5,10]. Based on expert opinion, some ophthalmologists recommend using the reverse sequence by direct antibody tests as initial screening test for ocular syphilis followed by indirect tests. Patients diagnosed with ocular syphilis should be tested for HIV and also for other sexually transmitted diseases.

Ocular syphilis may be a manifestation of neurologic infection or may occur independent of CNS involvement. It may occur at any stage of infection, from primary to tertiary syphilis. Asymptomatic neurosyphilis always precedes symptomatic neurosyphilis, hence CSF analysis is important in ocular syphilis. CSF examination should be performed in all cases of ocular syphilis and treated for neurosyphilis irrespective of CSF finding. Though checking the CSF does not change management, it is recommended that patients with CSF pleocytosis should have repeat CSF testing done after completion of treatment to assess for response and every 6 months until cell count normalize. As per Marra et al., CSF pleocytosis is the most sensitive measure to check for response to treatment. CSF protein and CSF-VDRL can stay elevated for longer duration. If cell count in CSF remains elevated 6 months after completion of treatment or CSF-protein and VDRL are abnormal upto 2 years after completion of treatment, repeat treatment should be considered [11,12]. In our patient, CSF study was normal.

Recommended treatment for ocular syphilis includes aqueous crystalline penicillin G 18–24 million units per day, administered as 3–4 million units IV every 4 h or continuous infusion, for 10–14 days. Alternate therapy includes Procaine penicillin G 2.4 million units IM once daily in addition to Probenecid 500 mg orally four times a day, both for 10–14 days. Our patient was treated with continuous infusion of penicillin G.

Learning points

1 Ocular syphilis cases are on a rise over the last decade and clinicians should be aware of presentation.
2 Late identification of ocular syphilis can lead to blindness.
3 In cases of uveitis or iritis seen by primary care providers, detailed sexual history should be obtained and patients with high risk behaviours should be tested for syphilis irrespective of HIV status.
4 CSF study should be obtained on all ocular syphilis cases to rule out neurosyphilis.

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