Clinical Features and Incidence Rates of Ocular Complications in Patients With Ocular Syphilis

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• PURPOSE: To describe the clinical outcomes of ocular syphilis.
• DESIGN: Retrospective chart review.
• METHODS: The charts of patients with ocular syphilis (regardless of human immunodeficiency virus [HIV] status) seen in a uveitis referral center between 1984 and 2014 were reviewed.
• RESULTS: The study included 35 patients (61 eyes). Panuveitis was the most common type of ocular inflammation (28 eyes), independent of HIV status. Thirty-three of 35 patients received systemic antibiotics with 24 patients treated with intravenous (IV) penicillin only. When compared to the HIV-positive patients, HIV-negative patients with ocular syphilis were older ($P < .001$), were more likely to be female ($P = .004$), and had poorer visual acuity at presentation ($P = .01$). During follow-up, the incidence rates of visual impairment were 0.29 per eye-year (EY; 95% confidence interval [CI]: 0.06/EY-0.86/EY) and 0.12/EY (95% CI: 0.01/EY-0.42/EY) among the HIV-negative and the HIV-positive patients, respectively. The incidence of blindness was 0.07/EY (95% CI: 0.009/EY-0.27/EY) and 0.06/EY (95% CI: 0.002/EY-0.35/EY) among the HIV-negative and the HIV-positive patients, respectively. Longer duration of uveitis prior to diagnosis and chorioretinitis in the macula at presentation were associated with ≥2 Snellen lines of visual loss ($P < .01$) and visual acuity loss to 20/50 or worse ($P = .03$) in HIV-negative patients, respectively.
• CONCLUSIONS: Syphilis is an uncommon cause of ocular inflammation in both HIV-negative and HIV-positive patients. Visual loss and ocular complications were common among HIV-negative patients even with systemic antibiotic treatment. Delay of diagnosis and chorioretinitis in the macula were associated with visual loss in these patients. (Am J Ophthalmol 2015;159:334–343. © 2015 by Elsevier Inc. All rights reserved.)

ACQUIRED SYPHILIS IS A CHRONIC SEXUALLY TRANSMITTED disease caused by the spirochete *Treponema pallidum*. Any portion of the body may be affected, including the eyes.[1] Based on the progression of the infection, acquired syphilis is classified into early (primary, secondary, and early latent) syphilis, late syphilis, and neurosyphilis.[2,3] Diagnosis of syphilis is based on medical history, clinical findings, and serologic tests.[4,5]

The eye is a relatively uncommon site of syphilitic infection. However, almost any portion of the eye may be involved in syphilis, and it may mimic different ocular inflammatory disorders.[3,6] Therefore, a high index of clinical suspicion is crucial to the accurate clinical diagnosis.[2,3,5-8] Syphilis rarely affects the eyes in the primary stage of infection but may affect the eyes in the secondary stage and, more frequently, in late, latent, and tertiary stages.[3,6,9,10]

Typically the most common ophthalmic finding in ocular syphilis is panuveitis.[6,11] However, additional ocular manifestations have been reported, including anterior uveitis, intermediate uveitis, interstitial keratitis, chorioretinitis, retinal vasculitis, retinitis, perineuritis, papillitis, retrobulbar neuritis, optic atrophy, optic nerve gumma, and various stroke syndromes.[2,6,10] Even though co-infection with human immunodeficiency virus (HIV) is a common finding in the setting of ocular syphilis, ocular syphilis may occur in immune competent hosts as well.[2,6,7]

A PubMed online database search using the following terms: (syphilis OR treponema pallidum) AND (eye OR ocular, iridocyclitis, chorioretinitis, uveitis, retinitis, optic neuritis, OR conjunctivitis) revealed a paucity of published studies on the rate of ocular complications and visual outcomes in eyes with syphilitic uveitis, especially in the HIV-negative population. This retrospective study provides the demographics and ophthalmic manifestations of ocular syphilis, incidence rates of ocular complications, and management of both HIV-positive and HIV-negative patients with ocular syphilis seen at a single tertiary care center.

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METHODS

• **STUDY POPULATION:** A retrospective chart review was performed on all patients with ocular syphilis (International Classification of Disease [ICD] codes 090-099) who presented to the Division of Ocular Immunology at the Wilmer Eye Institute of The Johns Hopkins Hospital between 1984 and July 1, 2014. The diagnosis of ocular syphilis was made by a uveitis specialist based on clinical history, ophthalmic findings, imaging, and positive serologic testing. To confirm the diagnosis and exclude other causes of uveitis, all patients had a laboratory examination and imaging studies, which included a chest x-ray, rapid plasma regain (RPR) test, fluorescent treponemal antibody absorption test (FTA-ABS) or microagglutination assay for *Treponema pallidum* (MHA-TP), lumbar puncture for cerebrospinal fluid (CSF) analysis for venereal disease research laboratory (VDRL), and Lyme antibody test. Additional diagnostic testing, including serologies for toxoplasmosis and viral causes when clinically suspected and polymerase chain reaction (PCR) of anterior chamber or vitreous samples, was performed as clinically indicated. The preservation of data confidentiality was addressed properly during this study, since it was conducted with the approval of The Johns Hopkins University School of Medicine Institutional Review Board (IRB) and in accordance with the principles of the Declaration of Helsinki. Data collection was compliant with the Health Insurance Portability and Accountability Act (HIPAA).

• **DATA COLLECTION:** Data of all patients evaluated and treated for ocular syphilis, dating to the establishment of the service in 1984, were collected retrospectively from clinical charts and entered into a database for subsequent statistical analysis. These charts use flow sheets that require the treating ophthalmologist to enter specific clinical information on each patient at each visit, as well as clinic notes.[12]

Other data collected by chart review included demographic features (including age, sex, race, ethnicity, tobacco use, men who have history of sex with men, and intravenous drug use); past medical history (such as diabetes and hypertension); past history of syphilis infection and the duration of infection; and past history of ocular syphilis and the duration of ocular inflammation at presentation. Ophthalmic findings at every visit included visual acuity, intraocular pressure, slit-lamp examination findings, the grade of inflammation in the anterior chamber and in the vitreous, and fundus examination and findings. SUN (standardization of uveitis nomenclature) guidelines were used to classify the ocular inflammation.[13]

Data on ocular surgeries and procedures were obtained. Syphilis-associated serologic test results (FTA-ABS or MHA-TP ± RPR ± CSF VDRL) were documented. Treatment data collected included the route and dose of systemic antibiotics, ophthalmic antibiotic drops, and the use of topical or periocular corticosteroids.

• **MAIN OUTCOME MEASURES:** Main outcome measures were incidence of visual acuity loss and ocular complications. Visual impairment (defined as decrease in best-corrected visual acuity to 20/50 or worse) and blindness (defined as decrease to 20/200 or worse) were the 2 main functional visual outcomes in this study. Change in visual acuity was designated based on the gain or loss of 1 or 2 Snellen lines and categorized into groups of stable vision, visual gain, or visual worsening. The incidence rates of structural ocular complications were assessed based on the presence of findings on dilated ophthalmic examination and confirmed by appropriate imaging modalities if clinically indicated. Ocular hypertension was defined as an intraocular pressure (IOP) of greater than 21 mm Hg in an eye with no documented history of IOP ≥22 mm Hg. The development of new-onset cataract was defined as the presence of 1+ nuclear sclerosis, 1+ cortical change, or trace posterior subcapsular change seen on clinical examination in an eye in which no cataract had been reported on prior visits.

• **STATISTICAL ANALYSIS:** The statistical analyses were performed using Stata statistical software (version 10.0, 2007; Stata Corp, College Station, Texas, USA). Demographics and clinical characteristics at presentation were tabulated for study patients and the affected eyes in Tables 1 and 2, respectively. Numerical and categorical variables were compared among HIV-negative and HIV-positive patients/eyes and *P* values were calculated using *t* test and χ^2 (Fisher exact test), respectively. All *P* values were nominal. Incidence rates for ocular complications were calculated as the number of events divided by the sum of the eye-years (EY) of the at-risk eyes. Poisson 95% confidence intervals (CI) were calculated for the estimated incidence rate of ocular complications during the follow-up period. Regression analyses on possible confounding factors were not performed owing to the small sample size.

RESULTS

• **CLINICAL CHARACTERISTICS OF THE ENTIRE COHORT AT PRESENTATION:** Thirty-five patients (61 eyes) met study criteria and were included in the study (Table 1). These 35 patients comprised 2.25% of 2707 new patients with active ocular inflammation seen during the study period and tested for syphilis. The median age at presentation was 45 years (range 24-80 years). Nine patients were female (25.7%). African-Americans comprised 60% of patients (n = 21); the remainder were white. Smoking data were available for 28 patients and of these, 15 (54%) were current or former smokers. Two of our patients reported a history of intravenous drug use and 9 of the men

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