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Introduction

Here, we report a case of syphilis in a patient who presented with blurred vision, in the setting of an unknown Human Immunodeficiency Virus (HIV) infection to highlight that syphilis should always be considered in the differential when caring for an individual who presents with monocular symptoms such as monocular papillary disc edema. We also want to bring into discussion the interplay of HIV and syphilis in terms of clinical manifestations. We want to focus on the underappreciated manifestation of ocular syphilis, which has been increasingly reported in the last several years and may be more common among persons with HIV.

Background

Syphilis is a sexually and vertically transmitted bacterial infection caused by spirochaete bacterium *Treponema pallidum*. In 2022, the Centers for Disease Control and Prevention (CDC) reported a total of 207 255 cases of syphilis in the United States, marking an 80% increase since 2018 and reflecting a consistent upward trend over several decades (1).

Syphilis manifests in three stages. Primary syphilis appears within 10-70 days of acquiring the infection and is characterized by the development of a primary chancre at the site of inoculation. Secondary syphilis presents with symptoms such as a desquamating rash at the palms and soles, oral ulceration, or mucous patches, and generalized lymphadenoma within weeks to a few months. The symptoms of secondary syphilis resolve within a few weeks in the absence of treatment, as the disease enters a latent stage. Without treatment, about a third of patients develop tertiary syphilis (2).

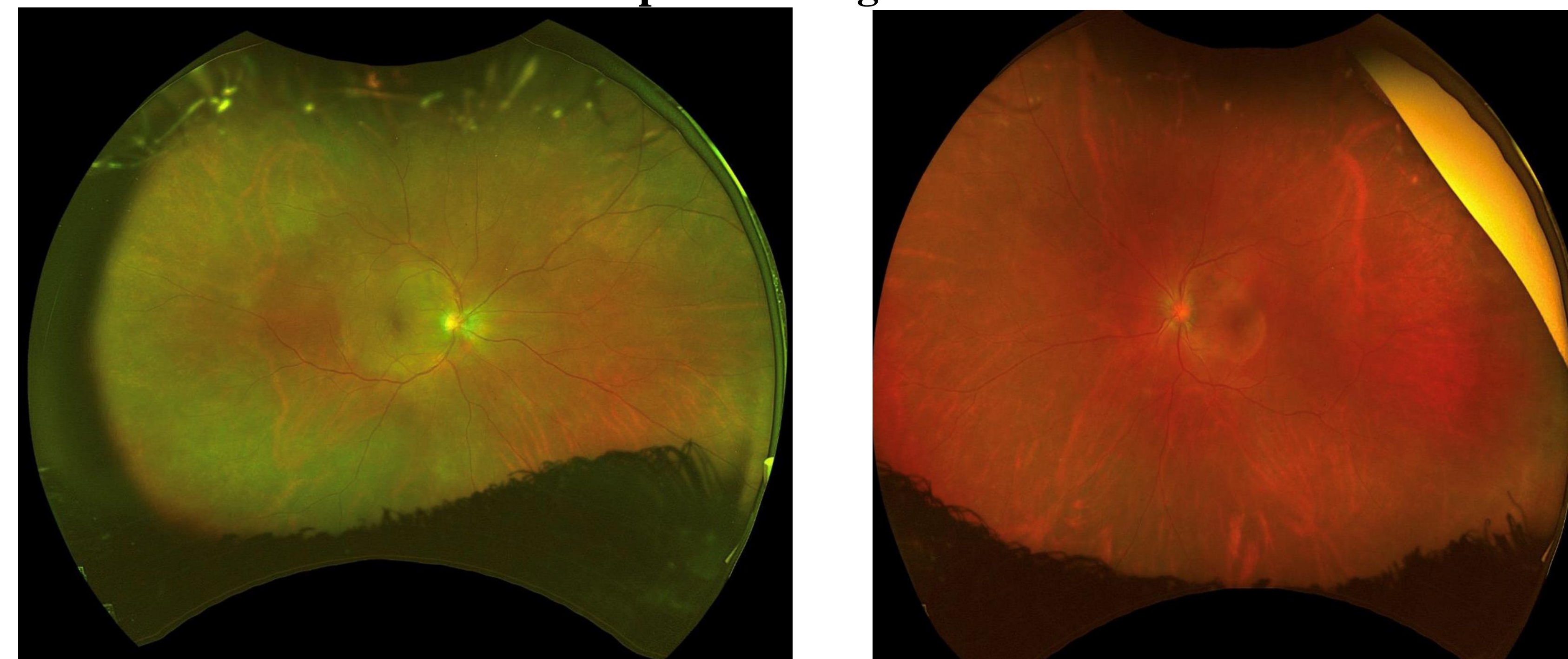
Neurosyphilis, a form of tertiary syphilis, occurs when *T. pallidum* invades the nervous system, affecting the brain, spinal cord, and peripheral nerves, and can occur at any time after the initial infection (3). Approximately 25-40% of patients develop neurosyphilis, with many clearing the infection from the cerebrospinal fluid without requiring treatment and sometimes remaining asymptomatic of the infection (3). Patients with a compromised immune system who cannot clear the infection, are more likely to develop CNS involvement, which can be asymptomatic, and ocular manifestations (1,4).

Presentation

A 38-year-old African American woman with a medical history notable for Turner Syndrome (45XO) presented to the Emergency Department with a chief complaint of blurred vision, more pronounced in the left eye, accompanied by intermittent floaters and retro-orbital pain. Patient reported that she had bilateral conjunctival injection, approximately eight months prior, after which she continued to have floaters in her vision. She also reported feeling unsteady due to visual changes as well as fatigue. Initial vital signs were recorded were: Bp 191/105 mmHg, HR 72 bpm, RR 16, Temp 36.8°C PO. A comprehensive stroke workup encompassing chest x-ray, non-contrast head CT scan, head and neck CT angiography, and non-contrast MRI, yielded unremarkable findings. Ophthalmological evaluation revealed acute optic disc edema of Frisen grade 1 in her left eye. Given monocular clinical findings, a syphilis EIA and RPR screening tests were ordered. The patient was discharged and instructed to follow-up at an outpatient ophthalmology center the following day. At her outpatient follow-up, the patient was informed of her positive EIA and reactive RPR test results and advised to return to the ED for further testing and treatment. Further questioning, the patient reported experiencing alopecia, and a rash on her palms about a year ago, however had not sought medical attention as these symptoms had self-resolved. During the current patient inpatient admission, the patient's partner, who was present at the bedside, disclosed he had been treated for syphilis 8 years ago. During admission, patient was also found to be HIV positive.

Key Diagnostic Results

Ophthalmologic Exam



Right image: right eye has some white specks which represent posterior placoid syphilis.
Left image: left eye has some whitening in the macular, but not as prominent as the right eye.

Labs

Syphilis workup		Lumbar puncture	
EIA	18.08	RBC	11
RPR	1:512	Nucleated cells	10
VDRL – CSF	Reactive 1:4	Protein	
HIV workup			
HIV AB Geenius	Positive	HIV Ag/Ab Combo	Reactive
CD4 Absolute	294	Ultra-Sensitive HIV viral load	3,200

Treatment

The patient completed a 14-day course of intravenous penicillin G, 4,000,000 units IVPB every 4 hours. The patient did not receive an oral steroid treatment as adjunct of treatment in case of possibility for a Jarisch Herxheimer reaction and tolerated the penicillin infusion well. Bictegravir/emtricitabine/tenofovir (Biktarvy) treatment was also initiated.

Discussion

HIV infection often co-occurs with Syphilis, yet the reciprocal effects of each infection remain poorly elucidated. The convergence of HIV and syphilis introduces nuances in diagnostic challenges, notably in asymptomatic neurosyphilis. This becomes particularly intricate in HIV-positive individuals where manifestations of syphilis can range from overt neurological symptoms to complete absence of clinical signs. Acknowledging the propensity for asymptomatic neurosyphilis is those with HIV underscore the importance of including syphilis in the diagnostic algorithm, especially when ocular symptoms emerge as the sole presentation.

Remarkably, recent reports highlight a compelling correlation wherein ocular syphilis prompts the discovery of previously undiagnosed HIV infections in a notable proportion of cases. This underscores the necessity for HIV screening in patients presenting with ocular syphilis. Such screening efforts are particularly advantageous given that many newly diagnosed HIV patients exhibit relatively preserved CD4(+) cell counts, affording the opportunity for timely monitoring and intervention before progression to AIDS (5,6).

Moreover, it is of importance that clinicians test for HIV for those presenting with ocular symptoms from syphilis as it has been pointed in literature that an HIV infection may affect mainstay neurosyphilis treatment outcomes (7). Recognizing the interplay of HIV and syphilis allows clinicals to perform additional monitoring in the form of frequent cerebrospinal exams and modifications to treatment regimen to prevent treatment failure of neurosyphilis.

References

- Assistant Secretary for Public Affairs. (2024). *HHS announces department actions to slow surging syphilis epidemic*. HHS.gov. [https://www.hhs.gov/about/news/2024/01/30/hhs-announces-department-actions-slow-surgin-syphilis-epidemic.html#:~:text=According%20to%20Centers%20for%20Diseases%20and%20Prevention%20\(CDC\),%20syphilis%20cases%20increased%20by%2080%20percent%20since%202018](https://www.hhs.gov/about/news/2024/01/30/hhs-announces-department-actions-slow-surgin-syphilis-epidemic.html#:~:text=According%20to%20Centers%20for%20Diseases%20and%20Prevention%20(CDC),%20syphilis%20cases%20increased%20by%2080%20percent%20since%202018)
- Peeling, R. W., Mabey, D., Xiang-Sheng, C., & Garcia, P. J. (2023). Syphilis. *The Lancet*, 402(10398), 336-346. doi:https://doi.org/10.1016/S0140-6736(22)02348-0
- Marra CM, Gary DW, Kuyper J, et al. (1996). Diagnosis of neurosyphilis in patients infected with human immunodeficiency virus type 1. *J Infect Dis*; 174: 219-21. doi:10.1093/infdis/174.1.219
- Marra CM. (2009). Update on neurosyphilis. *Curr Infect Dis Rep*. 11: 127-34. doi:10.1007/s11908-009-0019-1
- Ceccarelli, G., Borrazzo, C., Lazzaro, A., Innocenti, G. P., Celani, L., Eugenio, N. C., ... Gabriella d'Ettore. (2019). Diagnostic issues of asymptomatic neurosyphilis in HIV-positive patients: A retrospective study. *Brain Sciences*, 9(10), 278. doi:https://doi.org/10.3390/brainsci9100278
- Kunkel J, Schürmann D, Pleyer U, Rütger K, Kneifel C, Krause L, Reichert M, Ignatius R, & Schneider T. (2009). Ocular syphilis—indicator of previously unknown HIV-infection. *J Infect Dis*; 200: 1100-1104. Epub 2008 Dec 10. PMID: 19081634.
- Gordon, Steven M., et al. "The Response of Symptomatic Neurosyphilis to High-Dose Intravenous Penicillin G in Patients with Human Immunodeficiency Virus Infection." *The New England Journal of Medicine*, vol. 331, no. 22, 1994, pp. 1469-1473. ProQuest. <https://ezproxy.msu.edu/login?url=https://www.proquest.com/scholarly-journals/response-symptomatic-neurosyphilis-high-dose/docview/1983903307/se-2>. doi:https://doi.org/10.1056/NEJM199412013312201.