Ocular Neurosyphilis as First Manifestation of Infection in a non-immunosuppressed patient

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Introduction

Syphilis is a sexually transmitted infection caused by spirochete *Treponema pallidum*. In 2018, combined cases of syphilis, gonorrhea, and chlamydia hit an all-time high. 35,000 cases of primary and secondary syphilis were reported in the U.S. in 2018, representing a 14% increase from 2017.

Case

History of Present Illness:

59-year-old male presents to his primary care provider with 5 days of visual disturbances in the left eye. He describes episodes of cloudiness, appearance of blue strings of lights (photopsia), and tunnel vision only in the left eye. These episodes last only seconds and occur intermittently throughout the day. He denies headache, pain with extraocular movements, vision loss, dizziness, or history of similar episodes. Earlier in the year, his blood pressure was poorly controlled, but is currently well-controlled on lisinopril. His PCP placed an urgent ophthalmology referral due to concern for retinal detachment.

Funduscopic exam reveals a pale, swollen optic disc in the L eye with peripapillary venous congestion and a preserved physiologic cup (Figure 1A). Retinal imaging called Optical Coherence Tomography (OCT) shows retinal nerve fiber layer (NFL) edema OU, but worse in left eye. Due to concern for ischemic optic neuropathy due to Temporal Arteritis, his ophthalmologist orders a CRP/ESR. CRP 1.7 mg/dL and ESR 40 mm/hr, both mildly elevated. He immediately starts 80mg prednisone daily and is sent for temporal artery biopsy 3 days later. Tunnel vision improves, but he still sees 'wavy blue lines' and has an intermittent 'blurred spot' in his vision. Temporal artery biopsy is negative.

2-week follow-up with ophthalmology. Although symptoms improved, his visual field testing is worse in the left eye and OCT shows worsening NFL edema in both eyes (Figure 1B). Given worsening inflammation despite high-dose steroids, ophthalmologist recommends emergent brain MRI and Neurology consult.

PMH: HTN, HLD, migraines, anxiety, benign prostatic hypertrophy
SH: Never smoker. Does not drink alcohol or use recreational drugs. He is widowed and lives alone. Currently does not have health insurance.
FH: Father had HTN. Mother had COPD and T2DM. Sister has T2DM.
Medications: Lisinopril-HCTZ, Loratadine, Tamsulosin, Excedrin migraine, Tadalafil, Alprazolam PRN
Allergies: None

Physical Exam:

Vitals: Temp 37˚C, BP 102/70, **Heart rate 116** at first outpatient visit
GEN: Awake, alert, oriented, well appearing. In NAD.
HEENT: Sclerae anicteric. Conjunctivae noninjected. No discharge.
Neck: No lymphadenopathy, masses, or thyromegaly. No JVD. No neck stiffness.
CV: +S1/S2. Tachycardic. Regular rhythm. No murmurs, rubs, or gallops.
Neurologic: Visual acuity grossly intact. PERRLA, EOMI, no afferent pupillary defect. Strength, sensation, reflexes intact. Normal gait. CN II-XII intact.

Ophthalmologic Imaging

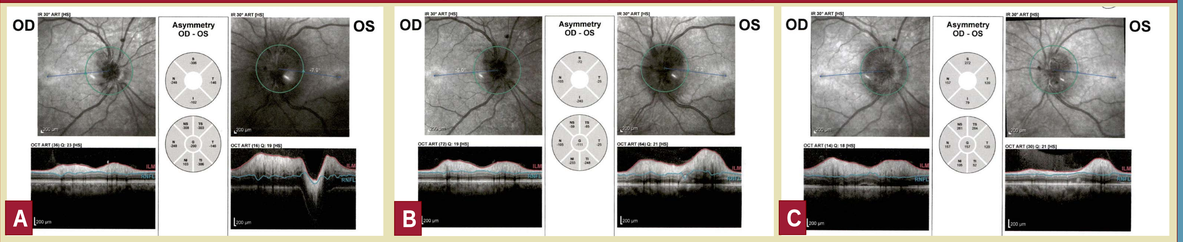

Figure 1. Optical coherence tomography (OCT) using Spectralis Tracking Laser Tomography. The top images represent the retina and the bottom images represent a cross section of the retina with the optic nerve in the middle. A) 11/26/2019 first visit to ophthalmologist. B) 12/10/2019 follow-up after 8 days of high-dose prednisone. C) 1/28/2020 follow-up 3 weeks after completing IV Penicillin treatment.

Hospital Course and Treatment

- 15 days after initial visit, presents to ER for workup & Neurology consult
- MRI brain w/o gadolinium: No significant abnormality
- MRI/MRA/MRV head w/ gadolinium: No significant abnormality.
- Lumbar puncture: Traumatic tap. Difficult to interpret initially; the traumatic tap may account for elevated WBC and protein.
- 7 days later, develops **ringing in both ears** and new headache.
- RPR, Treponemal EIA, and CSF VDRL are positive, suggesting neurosyphilis
- 4 weeks after initial visit, he is admitted for 2 days of IV Penicillin G 5 million units Q4 hours, then discharged with midline to receive 20 million units by continuous infusion for total 14-day course.
- 3-week follow-up: Auditory disturbance resolved promptly. Vision gradually improving since treatment. Retinal imaging shows marked improvement (Fig 1). He will continue follow-up with serial RPRs.

Laboratory Findings

87% PMNs

16.4		
25.8	414	
49		

133	101	44
4.8	23	1.06

137

LFTs normal
CRP: **1.7** (< 1)
ESR: **40** (0-20)

CSF Studies (traumatic tap):

- Glucose: 66 mg/dL (nl 50-80)
- Protein: 82 mg/dL (15-45)
- RBC: 11,000/mm^3 tube 4 (14,000 tube1)
- WBC: 24/mm^3, 53% PMNs, 47% Monos (corrected for RBCs: 23.95)
- Gram stain: 1+ PMNs, no growth
- EBV PCR (-); HSV DNA: Not detected
- ACE CSF <0.4 (normal)
- 0 CSF Oligoclonal bands seen
- **CSF VDRL titer 1:2 (Low positive)**

Other Blood tests:

- Lyme Ab Scrn (+); Confirmatory Western blot (-)
- Quantiferon Gold (-), HIV1/2 (-), ACE: <5 (normal)
- Neuromyelitis Optica/AQP4 FACS negative
- **RPR Screen: Reactive**
- **RPR Titer: 1:128**
- **Syphilis IgG (Treponemal EIA): Positive**

Testing Algorithms for Syphilis

Testing for Syphilis Infection

- Darkfield microscopy and PCR are definitive tests, but infrequently used as they are difficult to perform
- Presumptive diagnosis requires: **Nontreponemal test (**Venereal Disease Research Laboratory (VDRL) or Rapid Plasma Reagin (RPR)) **+ Treponemal Test** (i.e. Fluorescent treponemal antibody absorbed (FTA-ABS), *T. pallidum* passive particle agglutination (TP-PA) assay, enzyme immunoassays (EIAs))
  - Nontreponemal tests have high false-positive rates and are associated with many other medical conditions
- Traditional Screening Algorithm: Screen with Nontreponemal test -> if positive, confirm with Treponemal test
- Reverse Screening Algorithm: Screen with Treponemal test to determine if patient has ever been exposed to *T. pallidum* -> if positive, follow with Nontreponemal test to determine if patient has active infection

Further testing for Neurosyphilis

- CSF VDRL preferred test, highly specific but not sensitive
  - False-positives can be due to contamination with peripheral blood
  - False-negative may occur in >25% of patients
- CSF WBC often elevated with lymphocytic predominance
- Fluorescent treponemal antibody absorption (FTA-ABS) is sensitive, but less specific test
- Serum RPR titer ≥ 1:32 is associated with increased likelihood of neurosyphilis in patients with syphilis infection

Discussion

Clinical Presentation

- Syphilis can present in 3 stages, often with periods of latency (no symptoms, but positive serologies) in between:
  - Primary: painless chancre at site of transmission
  - Secondary: development of systemic symptoms including fever, lymphadenopathy, skin rash, mucocutaneous lesions
  - Tertiary: gummatous disease, tabes dorsalis, cardiovascular disease
- Neurosyphilis and Ocular Neurosyphilis can present during any stage
  - Syphilis can affect any part of the eye itself and can cause range of symptoms, including eye pain, vision loss, photopsia, Argyll Robertson pupil, eye pressure, photophobia. Uveitis is most common ocular manifestation.
  - Ischemic optic neuropathy can occur as part of ocular neurosyphilis
- Persons with CNS involvement can present with symptoms of meningitis, encephalitis, dementia, stroke, altered mental status, cranial nerve findings, auditory or ocular defects, tabes dorsalis, and paresis.
- HIV infection is a major risk factor for syphilis infection.
  - **Rate of HIV co-infection with syphilis ranges between 20-70%.**
  - Patients with HIV and syphilis co-infection are at higher risk of developing neurosyphilis.

Therapy

- Parenteral Penicillin G is preferred for all patients with syphilis
- Refer to CDC Guidelines for which Penicillin G formulation (i.e., benzathine, aqueous procaine, aqueous crystalline) is appropriate for each stage of syphilis infection

Neurosyphilis:

- Aqueous crystalline Penicillin G 18-24 million units per day (3-4 million units IV every 4 hours or continuous infusion for 10-14 days)
- OR Procaine penicillin G 2.4 million units IM once daily + Probenecid 500mg PO 4 times daily for 10-14 days
- Adjunctive steroid treatment is thought to improve optic nerve function and prevent Jarisch-Herxheimer reaction but needs more data to support its routine use.

References

- Centers for Disease Control Sexually Transmitted Diseases Online Resource: 2015 Sexually Transmitted Diseases Treatment Guidelines. Accessed March 2020.
- DynaMed [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - . Record No. *T115794*, *Neurosyphilis*; [updated *2018 Nov 30*, cited 2020 Mar 23]. Available from https://www-dynamed-com.ezproxy.library.tufts.edu/topics/dmp~AN~T115794.
- Parthopratim Dutta Majumder, Elizabeth J. Chen, Janika Shah, Dawn Ching, Wen Ho, Jyotirmay Biswas, Leo See Yin, Vishali Gupta, Carlos Pavesio & Rupesh Agrawal. Ocular Syphilis: An Update. Ocular Immunology and Inflammation 2019; 27:1, 117-125, DOI:10.1080/09273948.2017.1371765
- Kelly Meehan and Julie Rodman. Ocular Perineuritis Secondary to Neurosyphilis. Optometry and Vision Science 2010; 87:10, E790-E796, DOI:10.1097/OPX.0b013e3181f361b0
- Ameeta E. Singh. Ocular and neurosyphilis: epidemiology and approach to management. Current Opinion in Infectious Diseases 2020; 33:1, 66-72, DOI:10.1097/QCO.0000000000000617
- UptoDate. Neurosyphilis. Accessed March 2020.
- Christina M. Marra. Neurosyphilis. Continuum (Minneap Minn) 2015; 21(6):1714-1728. DOI:10.1212/CON.0000000000000250.