Ocular Syphilis, the Great Masquerader

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Introduction

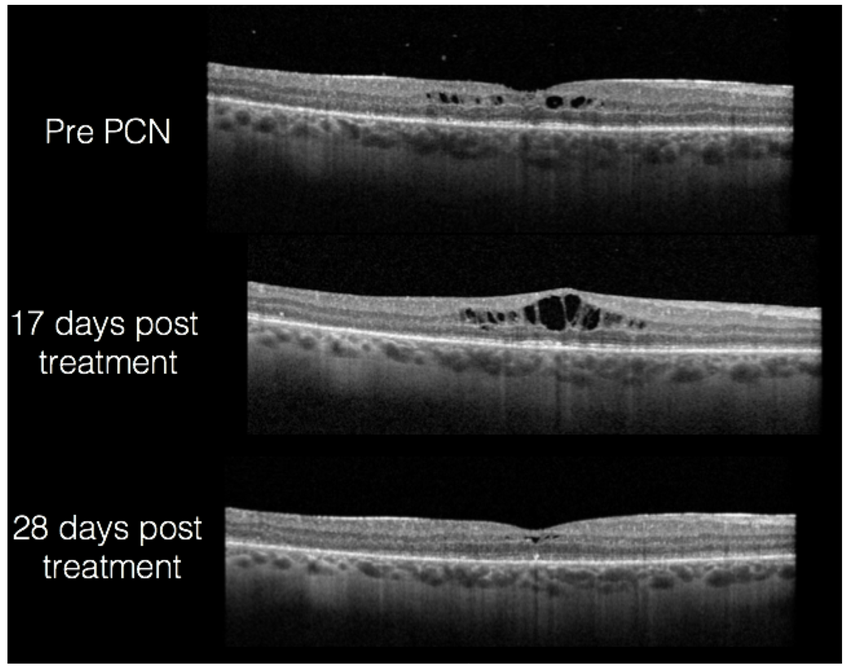
- Syphilis typically advances through four different stages
  - Primary
  - Secondary
  - Latent
  - Tertiary
- Ocular syphilis can develop during **any** of these stages!
  - It is a rare condition that can involve any structure of the eye and mimic a variety of eye diseases:
    - Uveitis
    - Diminished visual acuity
    - Optic neuropathy
    - Retinal vasculitis

Case Description

- A 47-year-old man with no PMH presented with six months of decreasing vision in his right eye
  - Initial ophthalmology exam revealed cystoid macular edema
  - He was treated with local steroids with minimal relief, and then developed retinal detachment
  - After retina surgery, his vision did not improve and he had worsening inflammation
- A broad serological workup later revealed **RPR of 1:128 and +FTA**, prompting hospital admission
- He denied STIs, but had penile lesions in the past and had a history of high-risk sexual behavior
- Physical exam showed **diffuse, pruritic, maculopapular rashes** scattered throughout his body (see below)
  - The patient later endorsed that the rashes had been present for roughly three months prior to admission

- Visual acuity was 20/400 right eye, 20/30 left eye with bilateral uveitis
- Neurological exam was benign
- Lumbar puncture showed 101 WBC (86% lymphocytes), with **CSF VDRL titer 1:8**
- The patient was started on IV penicillin G and continued on anti-inflammatory eye drops
- He completed a **14-day infusion of IV Penicillin G**, with progressive improvement in his visual and dermatologic symptoms
  - Follow up labs showed decreased RPR titer

Macular Edema Throughout Treatment Course



- The patient displayed evidence of a **Jarisch-Herxheimer reaction** via Optical Coherence Tomography (OCT) imaging
  - **Pre-penicillin**: OCT displays mild cystoid macular edema
  - **17 days post-treatment**: OCT displays paradoxical worsening of inflammation and macular edema
    - This is secondary to lysis of organisms, release of endotoxin-like lipoproteins, and increase in TNF-a, IL-6, and IL-8
    - Note: although OCT shows worsening of macular edema during this stage, clinical symptoms improved with the IV penicillin (PCN)
  - **28 days post-treatment**: improved macular edema, completely resolved

Review: Stages and Treatment of Syphilis

	Clinical manifestations	Treatment	Post-treatment monitoring
Early syphilis	• **Primary**: single painless chancre +/- regional lymphadenopathy • **Secondary**: systemic illness + rash (often palms and soles) • **Early latent**: infected by blood testing, but no symptoms (< 1yr)	• **Penicillin G benzathine IM x1** • Alternatives: Doxycycline, ceftriaxone, tetracycline, amoxicillin + probenecid	• Clinical exam and blood testing with RPR at 6 and 12 months
Late syphilis	• **Tertiary**: late syphilis with cardiovascular manifestations and gummatous disease • **Late latent**: infected by blood testing, but no symptoms (> 1 yr)	• **Penicillin G benzathine IM once a week for 3 weeks** • Alternatives: doxycycline or ceftriaxone	• Clinical exam and blood testing with RPR at 6, 12, and 24 months
Neurosyphilis (can occur **at any time** of infection course)	• **Early Neurosyphilis:** can have meningitis, meningovascular disease (meningitis + stroke), vision or hearing loss • **Late neurosyphilis:** involves the brain and spinal cord (dementia and tabes dorsalis)	• **Aqueous penicillin G IV for 10-14 days** • Patients allergic to penicillin should be desensitized • Alternatives: ceftriaxone	• Clinical exam and blood testing with RPR (frequency depends on stage) • May need to do CSF testing

Discussion

- Ocular syphilis can present with any visual symptom, thus internists should be on the lookout for signs that will guide us towards the diagnosis
  - Early treatment drastically improves outcomes
  - One retrospective chart review determined that visual acuity improved significantly in 89% of patients treated
  - The main factor associated with poor prognosis was over 28 days of ocular symptoms before diagnosis (1)
  - Early recognition and treatment is key!
- Detecting ocular syphilis early is difficult because of its varied symptomatology
  - One case series reported that macular edema was present in 52% of ocular syphilis patients (2)
  - Another case series reported that uveitis was the most common symptom, and that case series featured six patients with retinal detachment (3)
  - As internists, if we see mention of such symptoms on chart review in a patient with unspecified ocular symptoms and high-risk sexual behavior, then a syphilis work-up should be pursued!
- While ocular syphilis is typically associated with neurosyphilis, this is not always the case
  - A case series determined that only 22% of patients with ocular syphilis had neurological symptoms (3)
  - Thus, a benign neurologic exam does not rule out ocular syphilis, as was the case with this patient!

Teaching Points

- Early diagnosis and treatment (within 28 days of symptom onset) is key to good patient outcomes
- Patients respond well to IV penicillin G
- If a patient presents with macular edema, uveitis and/or retinal detachment, think of ocular syphilis, especially if they have high-risk sexual behavior
- The majority of patients with ocular syphilis have benign neurological exams, thus not a rule out test!

References

1) Tsuboi M, et al. Prognosis of ocular syphilis in patients infected with HIV in the antiretroviral therapy era. *Sexually Transmitted Infections*. 2016;92(8):605-610.
2) Shen J, Feng L, Li Y. Ocular syphilis: an alarming infectious eye disease. *International Journal of Clinical and Experimental Medicine*. 2015;8(5):7770-7777.
3) Oliver SE, Aubin M, Atwell L, et al. Ocular Syphilis – Eight Jurisdictions, United States, 2014 – 2015. MMWR Morb Mortal Wkly Rep 2016;65:1185-1188.