Mayo Clinic Center for Tuberculosis

TB and the Eye

Wendy M. Smith, M.D.
Assistant Professor of Ophthalmology
Mayo Clinic, Rochester, MN USA
Disclosure

• No financial disclosures
TB and the Eye

Outline

• Introduction
• Ocular TB manifestations
• Case Examples
• Diagnosis
• Treatment

Objectives

• Identify the variety of manifestations of ocular tuberculosis
• Describe the challenges associated with diagnosing ocular tuberculosis
Pre-test Questions

• True or False: Mycobacterium tuberculosis is usually isolated from ocular specimens in cases of suspected TB uveitis.

• True or False: The presence of M. tuberculosis DNA is evidence of active infection.

• True or False: TB uveitis is only treated with anti-TB drugs.
Tuberculosis = *Mycobacterium tuberculosis*

- **Worldwide distribution**
  - ~1/3 latently infected
  - Incidence >9 million active TB cases/yr

- **Special populations**
  - People living in or immigrating from endemic regions
  - Immunocompromised people (HIV, elderly, diabetics, those on immunosuppressive medications)

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TB and the Eye

• Ocular disease is rare
• May affect any ocular tissue
• Direct invasion, hematogenous dissemination
• Hypersensitivity reaction to bacillus infection outside the eye

Mittal R et al. Ophthalmology. 2013 May; 120(5): 1103.e1-4
Ocular TB Epidemiology

• Varies worldwide
  • U.S. 1.4% of those with primarily pulm TB
  • Spain: 18% of randomly selected patients with culture-proven TB
  • Italy: 20% of newly diagnosed TB cases (only 5% with ocular symptoms)

• Subgroups of TB (reviewed in Cutrufello et al. 2010)
  • tubercular meningitis (16.2%), tubercular lymphadenopathy (23.2%), pediatric tubercular meningitis (~70%)
Ocular TB

- Tuberculosis of the conjunctiva and eyelids
- Tuberculous chancre and gumma of eyelids → atypical chalazion
- Mucopurulent conjunctivitis with regional lymphadenopathy
- Chronic blepharitis
- Interstitial keratitis
- Phlyctenular conjunctivitis
Ocular TB

• Scleritis (most often anterior necrotizing or non-necrotizing, less often posterior)

• Orbital or adnexal disease


Intraocular TB

- Tuberculoma
- Granulomatous uveitis
- Granulomatous choroiditis
- Retinal vasculitis
- Retinal or vitreous hemorrhages (Eales disease)
- Papilledema
- Optic neuritis, neuroretinitis
Most common presentations of ocular TB

- Demirci et al: review of 92 published case reports
  - Choroidal mass +/- inflammatory signs (34%)
  - Choroiditis/chorioretinitis (27%)
  - Vitritis (24%)
  - Iridocyclitis/anterior chamber reaction (13%)
  - Panuveitis (11%)
TB Uveitis

- Uveitis = inflammation of the uveal tract (iris, ciliary body, retina/choroid)

- Uveitis attributed to TB:
  - Once considered the most common cause of uveitis (up to 40% of granulomatous uveitis)
  - Now relatively rare:
    - US ~1%, China 4%, Italy 6%, Japan 7%, India up to 10%, Saudi Arabia 16%
IUSG Classification of Uveitis

- Anterior uveitis
  - iris and pars plicata (CB)

- Intermediate uveitis
  - pars plana and vitreous

- Posterior uveitis
  - retina + choroid

- Panuveitis
ANTERIOR UVEITIS
Granulomatous or Non-granulomatous

Keratic precipitates

Choroidal Tuberculoma

Choroidal tubercle with miliary TB


Serpiginous-like Choroiditis
Eales Disease

Idiopathic peripheral perivasculitis → proliferative vascular retinopathy, recurrent vitreous hemorrhages, and tractional retinal detachment

Young, otherwise healthy men, 20-40 yrs
India, PPD+

TB identified by PCR on aqueous, vitreous, ERM


Case: 28 yo M from Kenya, in US x 8 yrs

• 2 months earlier: clouding in peripheral vision
• Then, black spot in vision, not a floater
• A week ago: awoke with red, painful eye
• In college, PPD rxn left scar on his arm
• 2009: PPD 25mm
• 2013: nml CXR
VA cc: 20/50 OU, Ta 10, 9

K OU: inferior subepithelial opacification, neovascularization, pigmented KPs, endothelial debris
AC OU: 3+ cell, 1+ flare
Vit OU: 2+ cell, 1+ haze, veils
- CRP 14.5
- Quantiferon positive
- ANA low positive 1.1

- 28 yo M from Kenya

- Bilateral panuveitis
  - Keratitis
  - Anterior uveitis
  - Vitritis
  - Posterior uveitis/choroiditis

- wnl/neg: CBC (except low MCV), diff, Cr, UA, ESR, ACE, lysozyme, dsDNA, RF, CCP, toxoplasma IgG/M, Lyme abs, HepB/C, Syphilis IgG, HIV
Chest CT

- Calcified granuloma in the superior segment of the left lower lobe

- Scattered tiny indeterminant pulmonary nodules with an upper lung predominance

- These may all represent old granulomas, and are consistent with the diagnosis of prior TB lung infection, but can be seen with other granulomatous processes
Presumed TB Uveitis

- ID consult:
  - requested AC tap → neg acid fast smear and culture
- Quadruple drug tx (ethambutol, isoniazid, pyrazinamide, rifampin for 6 months)
- Oral prednisone taper
- One month after finishing prednisone and anti-TB meds, no active uveitis
Case: 45 yo F from Pakistan, U.S. x 11 yr
Sudden onset of “wavy lines” in vision

Aunt had tuberculosis, but no direct exposure
Yearly PPD for work (teacher)

Chest x-ray: normal
Quantiferon: indeterminate, but she was on systemic immunosuppression
Serpiginous vs Serpiginous-like Choroiditis

Differences from Classic Serpiginous:
- From TB endemic region
- More likely unilateral
- Multifocal lesions involve posterior pole, mid-periphery, periphery and spare juxtapapillary region (unlike classic serpig)
- Inflammation in anterior chamber & vitreous
- Inflammation stops in response to anti-TB meds
Diagnosis of Ocular TB

Clinical context + clinical findings

- immigration from or travel to TB endemic region
- exposure to active TB
- healthcare worker
- worker or resident of nursing home or prison
- Immunocompromised (HIV+, iatrogenic, chronic disease)
- Homeless, elderly
Diagnostic Testing

- Assessments for other uveitis etiologies including HIV
- Chest imaging (x-ray, CT, PET/CT)
- TST/PPD
  - False negative in 20-30% active TB
  - Low positive predictive value in non-endemic areas
- Interferon-gamma release assay
  - In vitro test using Mtb antigens to stimulate release of IFNg from peripheral blood cells
- Biopsy, Smear, Culture, PCR
Challenges in Ocular TB Diagnosis

• Limited specimen
  • aqueous – 150-200 uL
• Morbidity of obtaining specimen
  • Vitrectomy
  • Chorioretinal biopsy
• Low DNA yield, and presence of DNA not necessarily indicative of active disease
• Inflammation might be response to extraocular infection (no organism in the eye)

Ocular TB - Treatment

• Report to local health department

• Coordinate care with infectious diseases specialist

• Confirmed and Presumed Ocular TB
  • Both: quadruple drug tx x 6-12 mo
  • Longer if increased risk of relapse (cavitary pulm disease, sputum cx + after 2 months)

• Concurrent corticosteroids

• Therapy efficacy: 40-70%

• Enucleation rate up to 30%
Delayed diagnosis/treatment: Sight- and/or life-threatening consequences
Patel et al. JAMA Ophth 2013:

- Midwestern U.S. cohort of 14 patients
- Average delay from ocular disease onset to uveitis referral: 755.3 days
  - Non-Hispanic white race, posterior uveitis
- Vision loss associated with diagnosis after 500 days, age >50 yrs

Corneoscleral perforation
Choroiditis affecting macula, optic nerve
Choroidal neovascular membrane
Endophthalmitis

Post-test Questions

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References

Thank you!