Mayo Clinic Center for Tuberculosis

TB and the Eye

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Disclosure

• No financial disclosures
TB and the Eye

Outline

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

Objectives

• To identify the variety of manifestations of ocular tuberculosis
• To understand the challenges associated with diagnosing ocular tuberculosis
Mycobacterium tuberculosis is usually isolated from ocular specimens in cases of suspected TB uveitis.

A. True
B. False
The presence of M. tuberculosis DNA is evidence of active infection.

A. True
B. False
TB uveitis is only treated with anti-TB drugs.

A. True
B. False
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

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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 $\rightarrow$ 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
Serpinous 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 M tb 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

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References

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