Leptospirosis

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Overview

- Definition
  - One of the most common zoonotic infections in the world, caused by gram-negative helical spirochete *Leptospira interrogans*
  - Infection occurs via direct contact with animal blood or urine (farmers and abattoir workers, veterinarians, laboratory workers), or more commonly via indirect contact with contaminated water (farmers, sewer workers, freshwater swimmers/boaters); there is a higher incidence after heavy rainfall and flooding in temperate and tropical climates
  - Panuveitis is by far the most common ocular presentation
- Symptoms
  - Conjunctival redness
  - Photophobia
  - Blurry vision
  - Floaters
- Laterality
  - More commonly bilateral
- Course
  - Systemic disease presents acutely, typically 2 days to 4 weeks after exposure
  - Uveitis tends to occur in the late immune phase (see below), which can be months after acute systemic illness
- Age of onset
  - Young to middle-age adults
- Gender/race
  - Males are more often affected due to occupational exposures
  - Central and South America, the Caribbean, Southeast Asia, and the Pacific Islands

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- Systemic association
  - Extremely wide spectrum of presentations, as the spirochete can invade any organ. Disease severity depends on serovar of the infecting organism and host's immune response
  - In general, leptospirosis is biphasic
    Spirochetemic phase: abrupt headache, fever, vomiting, myalgia following the incubation period of 2–26 days; spirochete is found in blood, cerebrospinal fluid (CSF), and kidneys
    Spirocheturic (immune) phase: recurrence of fever, development of complications, including meningitis, leptospiruria, nerve palsies, jaundice, renal failure, pulmonary hemorrhage, ocular symptoms, etc.; 90% of patients have mild, anicteric disease that gets resolved without treatment; the other 10% can have severe icteric disease with jaundice and azotemia, with up to 30% mortality rate
    Weil's syndrome: a particularly serious presentation of leptospirosis in which jaundice and renal failure occur; the biphasic nature is often obscured by rapid deterioration to multi-organ failure and death

Exam: Ocular

Anterior Segment

- Conjunctival hyperemia and subconjunctival hemorrhage
- Non-granulomatous anterior uveitis with diffuse Keratic Precipitates
- Posterior synechiae
- Hypopyon
- Rapid cataract formation (but may resorb in some cases)

Posterior Segment

- Frequently severe vitritis with large clumps and membranes
  - Vitreous membranes are highly suggestive of diagnosis in the right clinical setting, after toxoplasmosis and infectious endophthalmitis are ruled out
- Non-occlusive periphlebitis
- Papillitis with optic nerve head hyperemia and edema
- Cystoid Macular Edema (CME) is very rare

Exam: Systemic

- Fever
- Jaundice
- Aseptic meningitis
- Respiratory symptoms
- Neuropathy

Imaging

- FA
  - Vascular staining
  - Late optic disc hyperfluorescence

Laboratory and Radiographic Testing

- Testing is imperfect; if there is high clinical suspicion, empiric treatment may be appropriate
- Culture of body fluids (blood and CSF during the first week of infection, and urine after the first week of infection, can remain positive for up to 30 days after symptoms resolve) with Ellinghausen-McCullough-Johnson-Harris (EMJH) medium: growth can take several weeks but can be negative if antibiotics are given prior to collection of samples
- Leptospiral antibody detection (serology) by Enzyme-Linked Immunosorbent Assay (ELISA) antibodies can be found after 5–7 days of illness in naïve patients
  - Background seropositivity in endemic areas makes this strategy challenging for diagnosis of acute infection
  - Paired serum (acute/convalescent samples) are preferred
- Polymerase Chain Reaction (PCR) for leptospiral DNA: test blood during bacteremic phase, CSF, and urine a few days after onset of symptoms, aqueous and vitreous fluids
- Microscopic agglutination test (MAT) is the reference standard for testing and may be requested through the Center for Disease Control and Prevention if ELISA or PCR is positive

Differential Diagnosis

- HLA-B27 uveitis
- Pars planitis
- Behcet's disease
- Eales disease
- Lyme disease
- Tuberculosis

Treatment

- Observation may be appropriate for mild cases
- Doxycycline, azithromycin, or amoxicillin for mild disease
- Intravenous (IV) penicillin, doxycycline, or third-generation cephalosporin (ceftriaxone, cefotaxime) for severe cases; systemic corticosteroid is controversial
- Treatment should be promptly started within the first 4 days of illness

- Doxycycline is preferred when differential diagnosis includes rickettsial infection, which can be clinically similar to leptospirosis
- Because ocular compartments can harbor live leptospira long after acute systemic disease, we recommend systemic antibiotic treatment, along with judicious use of topical and periocular steroids, for uveitis
- Jarisch–Herxheimer reaction can occur following therapy

Prevention

- Vaccination of domestic/farm animals
- Avoiding exposure to stagnant water, rodents, contaminated food
- Prophylactic antibiotics for patients at high risk of exposure (e.g., during outbreaks or flooding in endemic areas): doxycycline—200 mg weekly

Referral/Comanagement

- Infectious disease