Leptospirosis: An Uncommon Cause of Fever and Transaminitis in the Continental United States

Authors and Affiliates: Allen Byl, DO; Hope Oddo Moise, MD; Danielle Gilbert, DO, MPH; Michael Olejniczak, MD; Ashley Misky, DO; Tom Fox, MD; Alexa Lapointe, MD; Michael Modica, MD; Michelle Blyth, MD.

Case: A 24-year-old man presented with fevers, rigors, body aches, and headache for 6 days. He had recently returned from a 2-week trip to Colombia, during which time he went white water rafting, drank filtered stream water, had prolonged insect exposure with bites, and ate locally prepared food, including various meats. No one else from the trip experienced a similar illness. At time of hospital admission, he was febrile to 101.2 F. He had no rash, lymphadenopathy, or conjunctival injection. Physical exam was unremarkable. Initial workup significant for thrombocytopenia of 110x10^3 uL, elevated haptoglobin of 239 mg/dL, transaminitis (ALT 196 U/L, AST 131 U/L), total bilirubin 1.8 mg/dL, and EGFR 82 mL/min/1.73m^2 with unknown baseline kidney function. Testing for acute hepatitis was negative. Chest radiograph, CT head with contrast, and abdominal ultrasound were unrevealing. ID was consulted for fever of unknown origin in a returning traveler. The patient's presentation raised concern for leptospirosis, hantavirus, mononucleosis, and arthropod-transmitted diseases including malaria, dengue fever, chikungunya virus, and zika virus, for which send-out labs were ordered. By the afternoon after hospital admission, the patient reported feeling improved and requested to be discharged. His labs were not back to baseline but down trending. Per ID recommendation, he was discharged with seven days of empiric doxycycline 100 BID while awaiting results of workup. Several weeks later the patient's Leptospira IgM returned positive. He was seen in primary clinic post-hospitalization with resolution of all symptoms and LFTs and kidney function returned to baseline.

Discussion: Leptospirosis is a zoonotic and waterborne infection with global distribution caused by the spirochete bacterial genus *Leptospira* [1]. *Leptospira* has numerous reservoir host mammals, the most significant of which are small rodents, which can transmit infection (through urine or direct contact), importantly to cattle, swine, dogs, and humans [1]. Infected animals shed *Leptospira* from their renal tubules into urine, which can then spread to other animals and humans through affected soil or water via breaks in the skin or direct exposure to mucus membranes of the mouth, eyes, or nose [2]. Leptospirosis is more common in resource poor countries in tropical regions, and is associated with poor sanitation and housing, occupational exposure to environmental water (sewage workers, fishermen, farmers, etc.), as well as recreational water exposure (swimming, rafting, kayaking). While Leptospirosis is more common in endemic tropical regions, cases are increasingly being identified in temperate regions such as the United States [4].

Infection with *Leptospira* does not always result in clinically significant disease, manifestations are often subclinical but can be fatal. While most infections are subclinical, up to 10% of human infections result in a more severe form of the disease commonly characterized by rapid onset of fever, headache, and muscle aches. Gastrointestinal involvement is also common [1]. Conjunctival suffusion is common but not always present [4]. *Leptospira* infection can directly affect almost every organ system, especially microvascular structures, kidneys, liver, as well as

skeletal muscle (most commonly the muscles of the legs) [4]. Severe infection can result in multisystem organ failure. One of the most well-known manifestations of severe Leptospirosis, referred to as Weil's Disease, involves widespread hemorrhage accompanied by acute liver and kidney failure [3]. Diagnosis can be delayed due to low clinical suspicion in non-endemic regions and the non-specific nature of symptoms at onset, which can be confused for other diseases [1]. Early recognition and high clinical suspicion for leptospirosis are necessary to establish the diagnosis and initiate prompt treatment to prevent serious sequelae, morbidity, and mortality.

Citations

1. Guerra MA. Leptospirosis. J Am Vet Med Assoc. 2009 Feb 15;234(4):472-8, 430. doi: 10.2460/javma.234.4.472. PMID: 19222355.
2. Karpagam, K. B., & Ganesh, B. (2020). Leptospirosis: a neglected tropical zoonotic infection of public health importance—an updated review. *European Journal of Clinical Microbiology & Infectious Diseases*, *39*(5), 835-846.
3. Adler, B., & de la Peña Moctezuma, A. (2010). Leptospira and leptospirosis. *Veterinary microbiology*, *140*(3-4), 287-296.
4. Levett PN. Leptospirosis. Clin Microbiol Rev. 2001 Apr;14(2):296-326. doi: 10.1128/CMR.14.2.296-326.2001. PMID: 11292640; PMCID: PMC88975.