Special Feature
CASE REPORT/FOCUSED REVIEW

Leptospirosis in New Orleans

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Abstract: Leptospirosis is an unusual but reemerging zoonotic infectious disease in the United States where the diagnosis may not be suspected when patients initially present. The case report of a patient from New Orleans who presented with jaundice, hypotension and acute kidney injury is presented. In this patient, a broad differential diagnosis was considered on presentation and serologic testing for leptospirosis eventually confirmed the diagnosis. A review of the clinical manifestations, diagnostic studies and treatment are discussed so that leptospirosis will be considered more carefully in the initial evaluation and management of similar patients.

Key Indexing Terms: Leptospirosis; Weil's disease. **[Am J Med Sci 2014;347(2):159–163.]**

The diagnosis of leptospirosis can present a daunting task as it mimics several other infectious and noninfectious illnesses. It is also an unusual disease in the United States and may not be considered in the evaluation of patients who present with signs and symptoms that might be more easily recognized in countries where this disease is more common and endemic. It is therefore important for clinicians to consider leptospirosis in the evaluation of patients who present with acute multisystem disorders, especially when jaundice and acute kidney injury are primary problems. A case of leptospirosis in New Orleans is therefore reported where other diagnoses seemed initially more likely, but leptospirosis emerged as the final diagnosis. The clinical features and diagnostic tests are described to facilitate the diagnosis and treatment of this disorder in other patients in the United States.

CASE REPORT

A 46-year-old man presented to the emergency department with a 4-day history of fever and chills. Around the same time, the patient developed a dry cough, nausea, vomiting, diarrhea and generalized abdominal pain. He had no blood in his vomitus or in his stool and noted that he had limited oral intake. He also noticed his urine output had decreased during the previous 4 days. Two days before his presentation to the hospital, the patient began suffering from severe myalgias and weakness in his legs that progressed to the inability to walk. He also noticed significant yellow discoloration of his skin, which prompted him to seek medical attention. The patient had no significant medical history and was taking no medications. He first emigrated to the United States 7 years earlier from Honduras and had no recent travel history. He is a construction worker whose symptoms began, whereas he was working on the rooftop of a gutted flood-damaged house. He denied any recent sick contacts or new medications. On further questioning, he reported the presence of rats on the upper levels of the house in which he was working.

The patient initially had a temperature of 102.7°F, blood pressure of 82/37 mm Hg, heart rate of 130 and respirations of 26. In the emergency department, his blood pressure did not improve with intravenous normal saline, and thus, dopamine was started. The patient was visibly jaundiced and diaphoretic without any lymphadenopathy. There was scleral icterus present. He had crackles at both lung bases bilaterally. The heart examination revealed tachycardia but no other abnormalities. There was moderate diffuse tenderness to palpation on abdominal examination without any distinct masses. The liver edge was slightly palpable. He displayed no lower extremity edema. The patient's neurological examination was significant for decreased patellar and Achilles tendon reflexes, decreased lower extremity strength and normal sensation. He had generalized muscle tenderness in his legs.

Initial investigations revealed markedly abnormal liver function tests, including an aspartate aminotransferase level of 710 IU/L, an alanine aminotransferase level of 220 IU/L, an alkaline phosphatase level of 74 IU/L, a total bilirubin level of 13.0 mg/dL and an albumin level of 1.6 g/dL. The patient's international normalized ratio was within normal limits. Other significant laboratory examinations on admission were total white blood cell count of 12,000/mm^3, hemoglobin 7.1 mg/dL,

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platelets 59,000/mm^3 and creatine kinase >8,000 mg/dL. Serum chemistries were significant for potassium 5.1 mEq/L, blood urea nitrogen 108 mg/dL, creatinine 7.5 mg/dL and lactate 4.4 mg/dL. Urinalysis was significant for 50 protein, large amount of blood, 6 white blood cells, 2 to 5 red blood cells/high-powered field and rare amorphous phosphate crystals, and the urine sodium was 67 mEq/l. The fractional excretion of sodium was calculated to be > 1.4%. Hepatitis panel, urine cultures, blood cultures, stool cultures, HIV serology and urine drug screen were all negative. Computed tomography of the patient's abdomen and pelvis revealed only sludge in the gallbladder and a noncalcified left lower lobe nodule. A chest radiograph revealed normal lungs. Abdominal ultrasound revealed an enlarged echogenic liver and unremarkable bilateral kidneys. In lieu of the patient's clinical presentation and his history of working in an abandoned building in the presence of rodents, enzyme-linked immunosorbent assay (ELISA) for leptospirosis was obtained.

The patient was admitted to the intensive care unit and intravenous broad-spectrum antibiotics including vancomycin and piperacillin/tazobactam were initiated because of the concern for presumed septic shock and renal replacement therapy (RRT) with slow low efficiency dialysis was begun. His blood pressure improved, his abnormal chemistries began to improve and, by day 4, the patient was nonoliguric with improving renal function. By day 5, he was afebrile and antibiotics were discontinued on day 7. The patient's jaundice slowly disappeared, his muscle weakness resolved, he was able to ambulate by day 5 and he was discharged on day 7. Postdischarge, a diagnosis of leptospirosis was confirmed with a positive Leptospira IgM-ELISA.

DISCUSSION

It is vital to include leptospirosis in the differential diagnosis of any illness that presents with acute kidney and liver injury, neurological manifestations, hemorrhagic sequelae or a combination thereof as illustrated by this patient. In our patient, sepsis was considered as the most likely diagnosis and broad-spectrum antibiotics were begun on admission. Leptospirosis was considered but given thought less likely, primarily because of its rare occurrence. This is not surprising, given that the incidence of Weil's disease is extremely low in the United States, with only 100 to 200 cases reported per year.[1] However, one of the purposes of this report is to bring attention to an important and potentially fatal disorder that is increasing in incidence.

Leptospira interrogans is the only pathogenic species of the genus. It is mobile, aerobic and unable to be Gram stained. In endemic areas, the microscopic agglutination test (MAT) is the standard of diagnosis and offers quick and reliable confirmation. Most American hospital laboratories, secondary to low incidence, are not likely to offer this test, so the IgM-ELISA is most likely to be the preferred method of diagnosis. This may delay confirmation as this study is usually performed at a reference laboratory. Leptospirosis is considered a "reemerging" infectious illness by both the World Health Organization and the Centers for Disease Control and is recognized as the most common zoonotic disease in the world.[2] It is caused by the spirochete of the genus *Leptospira* and contains 17 different species that are grouped based on DNA relatedness and antigenic differences in the lipopolysaccharide envelopes that surround the cell wall. This classification coexists with the older serological classification where antisera are used to establish antigenic relatedness between isolates.[3] Therefore, based on antigenic differences, there are 2 recognizable species: *L interrogans*, which is known to cause most pathological disease in humans and other mammals, and the saprophytic *Leptospira biflexa*.

Epidemiology

It is estimated that 100 to 200 cases of leptospirosis occur annually in the United States, with approximately 50% of those cases occurring in Hawaii.[1] The disease has a worldwide distribution but is exceedingly more common in tropical environments where freshwater and climate make transmission more favorable. This includes areas such as Hawaii where from the years 1974 through 1994, Hawaii had the highest reported annual incidence rate of leptospirosis in the United States.[4] Reports are more likely from underdeveloped areas, including Ecuador, Peru, Thailand, Costa Rica, Columbia and Malaysia, but the disease does occur in industrialized nations as well. The true incidence is unknown because of a lack of awareness of the disease and the inability to accurately and quickly make the diagnosis. Environmental conditions such as seasonal flooding, walking barefoot through deforested areas, freshwater swimming holes and wells serving as a source for portable water for domestic use all support vector transmission.[5]

Human infection generally occurs through contact with infected urine from a carrier mammal, most commonly dogs and rats in industrialized regions, whereas in more tropical regions, reservoirs can include marsupials and wild mammals as well.[5] Colonized renal tubular epithelial cells allow for passage of urine containing the organism, which, in turn, comes in contact with skin while walking barefoot on soil or water or through exposure to freshwater sources containing the infected urine.[6] Although it is known that animals can remain asymptomatic and be a chronic carrier of *Leptospira*, human beings have never been shown to be significant vectors of transmission, although some individuals can shed the organism in the urine for weeks or rarely months.[7]

Pathogenesis and Clinical Presentation

After initial infection with the organism, the incubation period typically lasts 2 to 21 days. The disease is characterized by a biphasic timeline, usually with an acute, or bacteremic phase, followed by an immune stage where antibody production begins and spirochetes can be found in the urine of infected hosts.[8] A substantial number of people who are initially infected only experience subclinical disease and thus do not seek medical attention. The spectrum of manifestations of milder nonicteric disease is broad and documented in a case series involving 771 patients.[7] Fever and headache are near-universal symptoms and were present in 97% and 98% of cases, respectively. A significant majority (78%) of patients experience myalgias. Nausea and vomiting were reported in 41% of cases, whereas other nonspecific findings of cough, diarrhea and arthralgia accounted for <30% of cases. Conjunctival suffusion is highly associated with leptospirosis.[9] Resolution of these milder symptoms seems to occur in conjunction with the beginning of antibody production and the initiation of shedding of the organism in the urine.

When fever returns after a period of 3 to 4 days, it produces a biphasic illness that is clinically indistinguishable from other febrile syndromes. However, when acute kidney injury, jaundice, pulmonary hemorrhage or a constellation of these symptoms develop, the illness is termed "Weil's disease[5]." Weil's disease is the most severe manifestation of leptospirosis and occurs in 5% to 10% of cases.[10] In the event of disease progression to include the above symptoms, this usually occurs after the acute phase.