A 23-year-old Man with Leptospirosis and Acute Abdominal Pain

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Abstract

Leptospirosis is a zoonosis caused by the spirochete Leptospira interrogans. *Most cases of leptospirosis are mild to moderate, and self-limited. The course of disease, however, may be complicated by multiorgan dysfunction such as in Weil's disease. We present a case of Weil's disease with pancreatitis in a young Caucasian man residing in Hawai'i. Although leptospirosis is common in Hawai'i, few patients present with pancreatitis. This report of leptospirosis-induced pancreatitis should help raise awareness of clinicians to assess for pancreatitis when evaluating a patient with leptospirosis and acute abdominal pain.*

Keywords

Leptospirosis, Weil's disease, pancreatitis, multiorgan dysfunction, hyperbilirubinemia, acute abdominal pain

Introduction

Leptospirosis is a zoonosis caused by the spirochete *Leptospira interrogans*. Compared to temperate regions, the incidence of this disease is significantly higher in tropical and subtropical regions.[1] In the United States, an estimated 100-200 leptospirosis cases are identified annually, of which 50% occur in Hawai'i.[2] The infection is primarily transmitted to humans through direct contact with water, mud, or soil contaminated with the urine of chronically infected mammals and rodents.[3] An incubation period of 5-14 days is typical. During this time, the spirochetes proliferate in the bloodstream and then disseminate hematogenously. The clinical manifestations of leptospirosis in humans vary from a subclinical infection to severe illness with multiorgan dysfunction. Usual disease presentation includes a flu-like illness with mild hepatic and renal impairment, whereas severe disease forms are characterized by hepatorenal failure, encephalopathy, and pulmonary hemorrhage.[4-6] The illness itself has a biphasic nature: an initial septicemia phase and consequent immune phase. During septicemia, patients will present with fever, headache, myalgia, conjunctival suffusion, and various non-specific findings such as mild cough, rash, lymphadenopathy, nausea, and vomiting.[7] Subsequently, patients may have a brief afebrile period of variable duration whereafter they develop organ derangements, most commonly of the liver and kidneys. In rare cases, it is reported to directly affect other organs such as the eye, bone marrow, and pancreas. Weil's disease, the most severe form of illness, is characterized by jaundice, renal failure, and hemorrhage with a variable clinical course.[4] Infected patients with acute renal failure may demonstrate elevated serum amylase levels, however, clinical symptoms of pancreatitis are uncommon.[4] We present a case of Weil's disease accompanied by pancreatitis.

Case Report

A 23-year-old Caucasian man from the continental United States residing in Hawai'i presented to the emergency department (ED) three days prior to admission with a two-day history of fever (104F/40C), chills, headache, neck stiffness, productive cough, nausea, and diffuse myalgias. At that time, he denied photophobia, rash, abdominal pain, and diarrhea. On exam, he was found to be tachycardic (119 beats per minute [bpm]) and febrile (101.4F/38.5C). He received 2 L normal saline. He was reassessed and found to be hemodynamically stable. He was discharged by the ED physician with prescriptions for acetaminophen and ondansetron. The patient reported that his fever was controlled with acetaminophen, however, his nausea was unremitting.

Two days after his first ED visit, the patient developed symptoms of photophobia, non-bloody, watery stools, non-bloody, non-bilious emesis up to seven times per day, bloody sputum, and dark tea-colored urine. On the night prior to his second ED visit, the patient also noticed yellowing of his eyes and face and onset of abdominal pain prompting him to return to the ED. The patient reported swimming in freshwater 2 weeks prior to admission, but denied skin abrasions and water ingestion. He further denied history of recent travel, sick contacts, eating uncooked foods, animal bites, and positive purified protein derivative (PPD) status. Upon questioning, the patient admitted to recreational alcohol consumption, his last episode being consumption of 4 beers (48 fluid ounces) twelve days prior to onset of illness.

Abbreviations

ALT: alanine aminotransferase
AST: aspartate aminotransferase
bpm: beats per minute
CDC: Center for Disease Control
CT: Computerized tomography
ED: Emergency Department
ICU: Intensive Care Unit
IgM: Immunoglobulin M
INR: International Normalized Ratio
PPD: Purified Protein Derivative
PT: Prothrombin Time
PTT: Partial Thromboplastin Time

Upon admission, the patient's vital signs were significant for hypertension (149/81 mmHg), tachycardia (120 bpm), pyrexia (101.1F/38.4C), and tachypnea (24 breaths per minute); he also demonstrated pulse oximetry of 94% on room air, and BMI 22 kg/m^2. In addition, he was icteric, with conjunctival injection but no suffusion. He had decreased breath sounds bilaterally, abdominal rigidity, and arthralgias of his hips, knees, and ankles, but no effusions. Kernig's and Brudzinski's signs were absent. On abdominal exam, bowel sounds were hyperactive. Abdominal organomegaly could not be assessed because the patient had severe rigidity and tenderness to palpation and percussion. There was no rebound tenderness.

Laboratory studies demonstrated leukocytosis (approximately 18,000/mm^3) with neutrophil predominance (83%), thrombocytopenia (42,000/mm^3), hyponatremia (132 mEq/L), hypokalemia (3.0 mEq/L), respiratory acidosis, metabolic alkalosis, and wide anion gap acidosis, as well as acute kidney injury (creatinine levels 4.4 mg/dL). Total creatine kinase was elevated (1162 IU/ml), alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were elevated (184 mEq/L and 144 mEq/L, respectively), and there was significant hyperbilirubinemia (total 13.0 mEq/L, direct 9.9 mEq/L, indirect 3.1 mEq/L). Coagulation studies demonstrated prothrombin time (PT) 13.2 seconds, partial thromboplastin time (PTT) 28.9 seconds, and international normalized ratio (INR) of 1.0. Urinalysis revealed large amounts of blood and bilirubin. Troponin I was not elevated. Computed tomography (CT) scan of the chest (Figure 1) revealed diffuse, bilateral peribronchial thickening and consolidation with extensive bud nodular opacities. Abdominal ultrasound was performed and did not demonstrate gallbladder inflammation, common bile duct dilatation, or evidence of gallstones. CT scan of the abdomen was performed without oral or intravenous contrast, due to the patient's acute kidney injury, and demonstrated hepatosplenomegaly without biliary dilatation and an unremarkable pancreas.

The patient was admitted for systemic inflammatory response syndrome with suspicion for infection or inflammation in the hepatobiliary system. Differential diagnoses included chol-

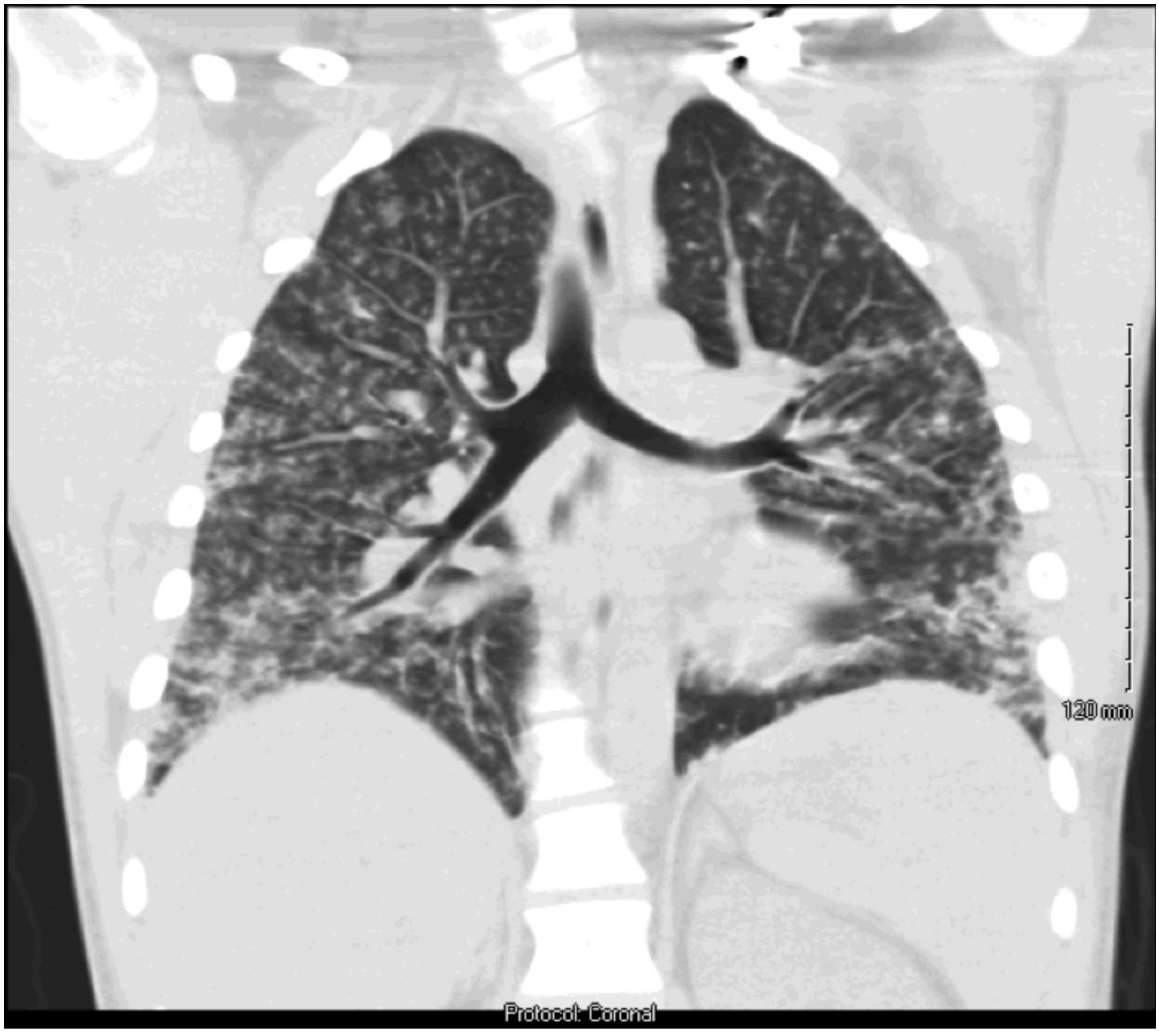

Figure 1. Computed tomography (CT) scan of the chest demonstrating diffuse, bilateral peribronchial thickening and consolidation with extensive bud nodular opacities.

angitis, pancreatitis, hepatitis (viral, autoimmune, drug- or toxin-associated), leptospirosis, dengue, murine typhus, and typhoid fever. As such, he was started on empiric intravenous antibiotics (doxycycline, ceftriaxone, and metronidazole) while awaiting blood/sputum/urine/stool cultures, gram stains, and serological test results.

Shortly after admission to the medical floor, the patient developed respiratory distress. He was found to have oxygen saturation of 80% on room air. He was tachycardic, tachypneic, and expectorated a large volume of blood. The patient quickly became less responsive to verbal stimuli. Given his acute respiratory failure, the patient was transferred to the intensive care unit (ICU) where he was supported with supplemental high flow oxygen via Venturi mask and close monitoring. At this time, the patient's serum lipase was found to be 1750 Units/Liter (normal range 13-60 U/L). The patient became increasingly lethargic and he was unable to tolerate oral intake. The patient's condition slowly improved with intravenous fluids and empiric triple antibiotic therapy. He was weaned to supplemental oxygen via nasal cannula and had no further respiratory distress or evidence of recurrent pulmonary hemorrhage.

Back on the hospitalist ward team, the patient demonstrated jaundice, decreased abdominal rigidity, and tenderness to palpation predominantly in the right upper quadrant and epigastric region. Laboratory values demonstrated down-trending hepatic transaminases, serum creatinine, and creatine kinase. However, serum bilirubin levels were increased (total 18.7 mEq/L, direct 16.5 mEq/L, indirect 2.2 mEq/L). Abdominal ultrasound was repeated and showed an unremarkable pancreas and gallbladder, but demonstrated hepatomegaly without evidence of biliary dilatation or ascites. The patient was started on a clear liquid diet and continued to demonstrate nausea and epigastric pain without emesis. Serological tests returned significant only for leptospira immunoglobulin M (IgM). The Center for Disease Control (CDC) would define a positive leptospira IgM as a probable case. The patient's antibiotics were narrowed to intravenous doxycycline. The patient was discharged after demonstrating clinical improvement on completion of seven-days of intravenous doxycycline. At the time of discharge, the patient was able to tolerate a regular diet without nausea. The patient was educated that his illness was likely related to freshwater exposure to the infectious agent and counseled on methods for decreasing risk.

Discussion

Leptospirosis is a disease with a variable grade of severity and organ involvement. Neurologic injury is seen in up to 25% of all cases and is most commonly associated with aseptic meningitis; however, intracranial hemorrhages, cerebellitis, and myelitis have been reported as well.[4,8] Hepatic injury is associated with disruption of cellular cohesion, plugging of bile canaliculi, and occasional acute inflammatory infiltrates.[4] This pathophysiology is consistent with the laboratory findings of hypertransaminemia, and direct hyperbilirubinemia. Pulmonary injury often presents with hemorrhage, as in our patient, and has been related to toll-like receptor (TLR) activation from *Leptospira* lipoproteins.[4,5] Cardiac involvement may present with non-specific electrocardiogram abnormalities or findings consisting with pericarditis or myocarditis (PR interval prolongation, T-wave inversion, first degree atrioventricular block).[4] Acute renal failure, also associated with TLR activation, is reported in 16%-40% of cases where oliguria is a significant predictor of death.[4,9]

Although acute pancreatitis has been recognized as a rare involvement of the multiorgan dysfunction of leptospirosis, most reported cases are of patients who developed hemorrhagic or necrotizing pancreatitis several days after the onset of disease. Furthermore, most reports deal with leptospirosis cases occurring in under-developed countries and involving mainly elderly patients.[10-13] The case presented herein adds to the body of knowledge in that leptospirosis-induced pancreatitis occurred in a young patient and at the early onset of disease. This patient developed acute abdominal pain and rigidity coupled with high lipase level and inadequate pancreatic imaging. He became critically ill from a combination of acute kidney injury, acute respiratory failure, pancreatitis, acute cholestatic hepatitis, and immune dysfunction. In the context of this report, it is important to consider alcohol consumption as a possible cause of pancreatitis. However, the patient reported last ingestion 12 days prior to disease onset, decreasing the likelihood of alcohol-induced pancreatitis. Also, patients often minimize the amount consumed. Animal studies suggest alcohol consumption is usually not associated with pancreatitis unless 5 drinks or more per day (60 g of ethanol) are consumed.[14] Nonetheless, such results suggest that ethanol could sensitize the pancreas to injury while additional factors may trigger the development of overt pancreatitis. In the setting of leptospirosis, this may be *Leptospira* antigen-associated vascular endothelial damage, which has been associated with the various other organ dysfunctions of leptospirosis.[4] Vascular injury most likely causes ischemic effects on the pancreas such as through decreased removal of reactive oxygen species, intracellular enzymes and toxins, and increased stasis of injurious elements that, together, may manifest as acute pancreatitis. *Leptospira interrogans*-induced acute pancreatitis seems rare. However, because of the high mortality rate associated with pancreatitis, clinicians should keep in mind the possibility of *Leptospira*-induced pancreatitis when confronted with leptospirosis.[15]

Conclusions

Leptospirosis is a frequently encountered infectious disease in Hawai'i and certain other parts of the world. Weil's disease represents the most severe form of leptospirosis. While multiorgan dysfunction is common, pancreatitis is rare. Furthermore, significant alcohol consumption may predispose leptospirosis patients to pancreatitis. Acute pancreatitis is associated with significant morbidity and mortality, resulting in the death of 20% of patients.[16] Thus, it is essential to assess risk factors for pancreatitis, such as alcohol consumption and gallstones, in patients presenting with leptospirosis.

Conflict of Interest

None of the authors identify any conflict of interest.

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