ACUTE PANCREATITIS IN FATAL ANICTERIC LEPTOSPIROSIS

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Abstract We report a fatal case of anicteric leptospirosis with pancreatitis (acute hyperglycemia and insulin requirement, elevated lipase and amylase levels), pulmonary infiltrates, and refractory shock. In disease-endemic areas, leptospirosis with pancreatitis should be considered in patients with fever and abdominal pain, and serum pancreatic enzymes, blood glucose, and serum electrolytes should be closely monitored.

CASE REPORT

An 18-year-old mechanic was admitted to the Hospital Geral de Pedreira in São Paulo, Brazil, with a four-day history of fever, myalgia, diffuse abdominal pain, and progressive dyspnea. He had not traveled outside urban São Paulo during the previous month. He had no known animal exposures but had seen rats near his home. There had been no recent rainfall or flooding, and he had not walked barefoot through water or recently sustained cuts on his extremities. At the local hospital where he was initially evaluated, an abnormal urinalysis result prompted a diagnosis of urinary tract infection, and for this he had received three days of ciprofloxacin prior to admission. He took no other medications. His past medical history was notable for nephritis at age six that resolved without specific therapy. He denied tobacco, alcohol, or illicit drug use.

On admission, he was well-developed and alert but ill-appearing, with fever (41°C), a blood pressure of 100/60 mm Hg, a pulse rate of 112 beats/minute, and a respiratory rate of 48/minute with room air O2 saturation of 80%. He was dyspneic, and had diffuse abdominal pain but no abdominal wall ecchymosis. He had no conjunctivitis, epistaxis, petechiae, hemoptyis, hematemesis, hematochezia, or icterus. Urine output was normal. His chest radiograph showed diffuse bilateral lower lobe infiltrates. He was diagnosed with pneumonia, and ceftriaxone and ciprofloxacin were administered.

Within six hours of admission, his blood pressure decreased to 100/40 mm Hg and he was transferred to the intensive care unit where vasopressors were started, and he was intubated. Arterial blood gas measurement of pH showed a value of 7.01 with PO2 = 65 mm Hg (normal = 80–100 mm Hg), PCO2 = 47 mm Hg (normal = 35–45 mm Hg), bicarbonate = 18 mmol/L (normal = 22–28 mmol/L), and O2 saturation = 80%. Random plasma glucose levels were elevated by the third hospital day, with a range from 147 mg/dL to a maximum of 387 mg/dL (normal = 70–105 mg/dL) on hospital day 5 despite a mean insulin dose of 20 units per day (peak = 25 units per day). Additional peak laboratory values during hospitalization were lipase = 14,900 U/L (normal < 190 U/L), amylase = 2,860 U/L (normal = 30–100 U/L), serum creatinine 5.0 mg/dL (normal = 0.7–1.5 mg/dL), alkaline phosphatase = 347 U/L (normal = 40–150 U/L), creatinine phosphokinase = 210 U/L (0–190), white blood cell count = 54.8/ mm3 (5.0–10.0), and minimum platelet count = 65/mm3 (150–400). Amylase and lipase levels peaked on hospital day 1 and rapidly decreased thereafter.

Abdominal ultrasound showed mild hepatomegaly, and abdominal tomography showed no pancreatic abnormalities. Results of cranial tomography were normal. Serologic test results for hepatitis B virus, hepatitis C virus, human immunodeficiency virus, and blood and urine cultures were all negative. Antibody testing for leptospirosis (microwell serum enzyme-linked immunosorbert assay for IgM and IgG; Diagnostic Automation Inc., Calabasas, CA) was performed on two sets of sera. Results for IgM and IgG were initially negative (hospital day 2, IgM and IgG both < 0.3 optical density [OD] units) but both were positive (> 0.5 OD units) on repeat testing performed on hospital day 8 (IgM = 0.81 and IgG = 0.64). However, the patient died on hospital day 17 of shock, acute respiratory distress syndrome, and pancreatitis. An autopsy was not performed.

DISCUSSION

Pancreatitis is a rare complication of leptospirosis associated with poor prognosis. 2–5 Most patients with severe leptospirosis and pancreatic involvement have clinical evidence of jaundice, and fatal anicteric leptospirosis with hyperglycemia and insulin requirement is rare. This underscores the concept that overt renal, hepatic, and hemorrhagic manifestations (Weil’s disease) are not all invariably present in severe leptospirosis. The precise pathophysiology of pancreatic inflammation in leptospirosis has not been well described. In previously reported fatal cases, pancreatic histopathologic results showed mainly interstitial inflammation with lymphocytic infiltrates, fat necrosis, edema, hemorrhage, and rarely calcification. Histopathologic results did not always correlate well with serum pancreatic enzyme levels. 6

The clinical and laboratory diagnosis of acute pancreatitis is controversial in patients with leptospirosis. The interpretation of non-specific, unreliable abdominal symptoms, signs, and/or imaging studies is further confounded by the common co-presence of dehydration, shock, and acute renal failure. 1–3 Simultaneous determination of lipase (which is most specific for pancreatitis), amylase, and creatinine levels is recom-
mended for the evaluation of patients with abdominal pain in leptospirosis. Pancreatitis alone may induce a sepsis-like state, and renal failure alone may elevate amylase (and perhaps lipase) levels 2–3-fold. Scoring systems have been developed to help identify the patient at risk for adverse outcomes, and a variety of serum biomarkers are associated with the severity and prognosis of acute pancreatitis. Our patient’s extremely elevated lipase level (peak = 14,900 U/L) was unlikely to be solely caused by acute renal insufficiency lacking a need for dialysis. It was not possible to exclude a potential contributory or causal role of co-infection with viruses (e.g., cytomegalovirus, enterovirus, mumps virus) or bacteria (e.g., gram-negative enteric organisms most often seen with pancreatic necrosis), or a medication effect. Both ceftriaxone and ciprofloxacin may adversely affect pancreatic function in rare instances.

In disease-endemic areas, acute pancreatitis should be suspected even in anicteric leptospirosis patients with appropriate epidemiologic and clinical findings and abdominal pain; conversely, leptospirosis should be considered as a possible cause of pancreatitis. It is important to note that in our patient, acute serologic results obtained on day six of symptoms (hospital day 2) were negative, and the diagnosis was only obtained upon repeat testing six days later. Severe leptospirosis may be fatal before IgM antibody is reliably produced, and leptospiremia may be difficult to detect; negative serologic results and blood cultures (even placed into specific growth media) do not exclude the diagnosis. Repeat serology after the first week of illness and empirical treatment prior to serologic results may be essential for improving outcome in patients with severe leptospirosis.

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