

## Leptospirosis Presenting as Acute Acalculous Cholecystitis and Pancreatitis

Dear Editor,

Acute cholecystitis in the absence of any detectable stones is known as acute acalculous cholecystitis (AAC) and has been often associated with severe illness or major surgeries in patients with significant co-morbid conditions. Acute pancreatitis is commonly due to gallstone diseases. Infectious disease presenting as AAC or pancreatitis is rare. We report a case of leptospirosis presenting with AAC and acute pancreatitis as the initial manifestations.

A 41-year-old gentleman presented with a 3-day history of fever, intermittent right upper quadrant pain and vomiting. He did not have any significant past medical history except for previous excess alcohol ingestion and smoking (10 to 20 cigarettes/day). He worked as a cleaner. He had been well and denied any infectious diseases contacts or recent travel abroad. On examination, he was icteric, lethargic, had non-specific right upper quadrant tenderness and was in some respiratory distress, but did not require any respiratory support. Otherwise, he was haemodynamically stable. Admission electrocardiogram showed tachycardia with non-specific T waves changes. Chest radiography was unremarkable. Blood investigations showed leukocytosis ( $17 \times 10^9/L$ ), mild thrombocytopenia ( $105 \times 10^9/L$ ), hyperbilirubin ( $171 \mu\text{mol/L}$ ), coagulopathy (INR 2.03), hyperamylasaemia ( $328 \text{ U/L}$ ) and mild dehydration (serum urea  $9.1 \text{ mmol/L}$  and serum creatinine  $130 \mu\text{mol/L}$ ). The rest of parameters were unremarkable or showed only mild abnormalities. A clinical diagnosis of acute cholecystitis with cholangitis was made.

An urgent ultrasound scan (USS) showed a thickened gallbladder wall (7 mm) and pericholecystic collection. There was no evidence of biliary dilatation, gallbladder stones or sludge. A computer tomography scan confirmed the USS findings and showed mild pancreatitis. In view of the clinical and radiological findings, he was treated as per AAC and acute pancreatitis. He was kept nil per orally and initiated on intravenous antibiotics (ceftriaxone 2 gm daily and metronidazole 500 mg t.i.d) and continuous somatostatin infusion. However, his condition deteriorated rapidly over the next 24 hours, leading to septic shock and respiratory failure requiring ventilation and inotropic support. Post-intubation radiography showed features of acute respiratory distress syndrome. Repeat serum amylase was elevated at  $3049 \text{ U/L}$  the following day. His renal function also rapidly deteriorated and required renal replacement therapy. Serum

bilirubin peaked at more than  $800 \mu\text{mol/L}$  and he had features of disseminated intravascular coagulopathy. His condition was later complicated by bradyarrhythmia, leading to complete heart block requiring temporary cardiac pacing. A septic screen that included several blood cultures, sputum and urinary cultures were unrevealing. Viral hepatitis markers for hepatitis A, B and C were negative. Serology for *leptospira* (ELISA IgM) came back strongly positive, indicating leptospirosis. He made a slow recovery, eventually being weaned off the ventilator and renal support. It was only later that a history of recent exposure to a contaminated environment was obtained. He had been involved in clearing and cleaning of an environment infested with rats the week before becoming ill. He was discharged after 40 days of hospitalization and he was making slow progress on his rehabilitation at the last follow up.

There are an increasing number of reports of AAC in association with infectious diseases including leptospirosis (Table 1). Leptospirosis is a widespread zoonosis caused by a ubiquitous spirochete and commonly occurs after exposure to water or soil contaminated by infected animal urine, typically that of rats. It is common in developing countries and in areas where there is frequent contacts with contaminated water. Similarly, leptospirosis is uncommon in Singapore. Data from the Communicable Disease Surveillance Singapore showed that 34, 29, 9 and 32 cases of leptospirosis were notified in the years 2002, 2003, 2004 and 2005 respectively.<sup>1</sup>

Manifestations can be self-limiting (80% to 90%), presenting with fever, myalgia and malaise. Weil's disease, the fulminant form (5% to 10%) usually presents with kidney and liver involvement and is associated with significant morbidity and mortality (5% to 10%). Diffuse vasculitis is thought to be the underlying cause. Generally, presentations of leptospirosis are non-specific and any organs can be affected. Cardiac involvements such as

Table 1. Microbes that have been Associated with Acute Acalculous Cholecystitis

Virus	Hepatitis A, Cytomegalovirus, Dengue virus
Bacteria	<i>Salmonella typhi</i> , <i>Vibrio cholerae</i> , <i>Escherichia coli</i> , <i>Klebsiella</i> species, <i>Staphylococcus</i> species, <i>Serratia marcescens</i> , <i>Leptospira</i> species
Parasites*	<i>Isospora belli</i> , Microsporidia, Malaria
Fungus	<i>Candida</i> species

\* Microbes associated with HIV infection

myocarditis and vasculitis have also been reported and it is possible that the subsequent cardiac arrhythmia in our patient was directly related to the infection. However the patient also had risk factors for ischaemic heart disease. Unfortunately, no confirmatory test was performed.

Leptospirosis presenting as AAC and pancreatitis is rare and has only been reported 3 times, twice in adults and once in a child.<sup>2-4</sup> All reported cases had complicated diseases requiring intensive supports. Early diagnosis requires suspicion as presentations may be non-specific. The diagnosis in our patients was not initially suspected due to a lack of suspicion and rapid progression. Leptospirosis has been associated with hyperamylasaemia and it has been suggested that leptospirosis should be included in the differential diagnosis of acute pancreatitis of unknown aetiologies. Edwards and Evarard<sup>5</sup> reported that 23% of patients with leptospirosis had elevated serum amylase 3 times above the normal level without any other causes for the elevations.

In our case, the diagnosis was based on the strongly positive ELISA, clinical features and laboratory investigations that were supportive of the diagnosis. ELISA IgM for leptospira has been reported to have low sensitivity due to cross reactions with other organisms such as *Chlamydia pneumoniae*, viral hepatitis, Epstein-Barr virus (EBV) and cytomegalovirus (CMV) infections, giving false positive results.<sup>6</sup> However, we are certain in our case that the aetiology is due to leptospirosis as extensive investigations failed to reveal any other possible causes. The diagnosis is further supported by the history of exposure that was only evident after the patient's recovery.

In conclusion, our case highlights important manifestations of leptospirosis and clinicians should consider leptospirosis in patients presenting with AAC and acute pancreatitis, particularly if there are risk factors.

#### REFERENCES

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