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Acute acalculous cholecystitis in a patient with leptospirosis

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Introduction

Leptospirosis is a potentially serious but treatable tropical zoonotic disease (1). It is caused by pathogenic spirochete that belonged to genus leptospira. This spirochete's life cycle is maintained in rodents, livestock, canines and wild animals. From these animals leptospira is transmitted to human via direct and indirect methods; direct inoculation of infected animal tissues, body fluids or indirectly by contact of contaminated urine via damaged skin or mucous membranes (2).

Variety of occupational groups are vulnerable to leptospirosis such as farmers, labourers, people who work in marshy lands, white water rafting and abattoir workers (2).

In Sri Lanka, leptospirosis is reported throughout the year and annually two outbreaks can be seen related to monsoons (during March - May and October - December) (2). According to the latest available data in Sri Lanka, during the 2nd Quarter of 2023, 3276 cases and 69 deaths (CFR 1.8) due to Leptospirosis were notified (3).

There are myriads of manifestations of infection on the host ranging from self-limiting febrile illness to fatal organ dysfunctions such as hepatitis, myocarditis, acute renal failure, rhabdomyolysis, aseptic meningitis and pulmonary hemorrhage (4,5). Acalculous cholecystitis is an uncommon complication of leptospirosis which is emphasized in this case report (6).

Case presentation

A 37-year-old previously healthy woman presented with a 3-day history of fever with chills, diffuse frontal headache, arthralgia, myalgia, back pain and right sided abdominal pain. She denied of coughing, difficulty in breathing or haemoptysis. Patient did not have dysuria, hematuria, lower abdominal pain, dyspeptic symptoms or change in bowel habits. She is a paddy cultivator and had been in contact with mud frequently prior to the illness. There was no contact history of febrile illness or any contact with patients suspected of dengue fever. She denied intravenous drug administration and there was no high-risk sexual behaviour. Menstrual cycles were regular and her regular menstrual period was 10 days prior to the illness.

On examination, the patient was febrile, not pale or icteric. There were no conjunctival injections, skin rashes or lymphadenopathy. She was haemodynamically unstable with blood pressure of 90/50 mmHg, pulse rate was 56 beats per minute and jugular venous pressure was not elevated. Heart was in dual rhythm. Abdominal examination showed positive Murphy's sign with tender right hypochondrium, without organomegally or free fluid. Respiratory and neurological systems were unremarkable on examination.

Initial haematological investigations revealed leukocytosis (WBC - 11,740 /µl) with neutrophil predominance (96.5%). The platelet count was 84,000 /µl per microliter and hemoglobin was 11.5

g/dL. Urine analysis revealed 5-10 pus cells and moderately field full red cells and culture was sterile. C-reactive protein level was elevated (169 mg/L) and ESR was 62 mm /1st hour. Dengue NS1 antigen and dengue IgM antibody were negative. Though her serum creatinine and blood urea were normal she had initial hypokalaemia (K - 3.2 mmol/L) and elevated creatine kinase (440 U/L). Liver transaminases were elevated (SGOT - 83I/L, SGPT - 95U/L) while bilirubin level, alkaline phosphatase level were normal. Serum amylase (83 U/L) coagulation profile and blood culture all were negative.

Ultrasound examination of the abdomen revealed a thickened gallbladder (GB) wall (5 mm) without calculi or sludge, co-existing free fluid in the Morrison's pouch and GB fossa (Figure 1). Ultrasonographically Murphy's sign was positive. However, there was no free fluid in the pelvis or thoracic cavities.

Her electrocardiogram (ECG) showed sinus bradycardia and cardiac troponins was 0.54 ng/ml (normal value 0 - 0.04 ng/ml). 2D Echocardiogram showed reduced ejection fraction (EF - 45 %) without evidence of regional wall motion abnormalities.

Given her presentation, exposure history and laboratory workup, she was empirically treated for leptospirosis with IV ceftriaxone 1 gram 12 hourly and oral doxycycline 200 mg twice daily with best supportive medical care. Later, leptospirosis was confirmed with the positive leptospira IgM antibody by ELISA. Because of the limited resource availability and emergence of COVID 19 pandemic we could not arrange leptospira microagglutination (MAT) in our patient.

Surgical consultation was arranged and cholecystitis was managed with IV fluid and IV proton pump inhibitors 40 milligrams twice daily and IV Metronidazole 500 milligram 8 hourly was added to the management. Her magnetic resonance cholangiopancretography (MRCP) was negative for GB calculous disease. Surgical team frequently reviewed the patient. Hence, there was no deterioration of the condition, acute acalculous cholecystitis (AAC) was clinically suspected and managed conservatively.

Leptospirosis associated myocarditis was suspected with a constellation of sepsis due to the unstable hemodynamic parameters (low blood pressure, bradycardia), ECG, cardiac troponins and 2D Echo findings.

Gradually, the patient's clinical condition improved after around eight days of IV antibiotics and laboratory parameters were also improving. After nine days of inward care the patient's clinical and laboratory parameters were improved. Follow up ultrasound scan of the abdomen revealed resolution of cholecystitis.

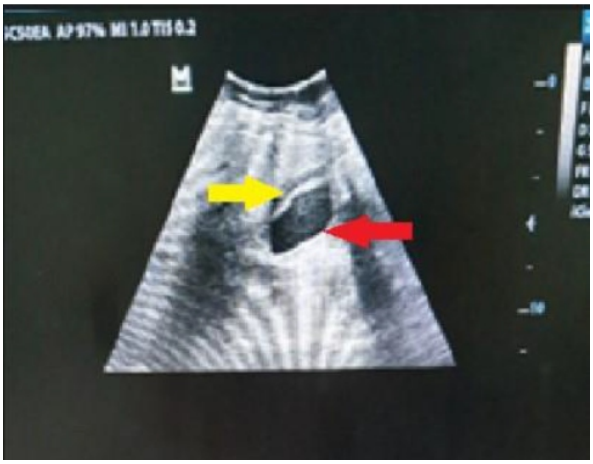

Figure: 1: Thickened GB wall (red arrow) with pericholecystic fluid collection (yellow arrow) without evidence of cholelithiasis

Discussion

The average incubation period of leptospirosis is 5 - 14 days but it can range from 2 - 30 days. Leptospirosis is a biphasic disease with bacteraemic and immunologic phases. Bacteraemic phase involves classical high fever with chills and rigors, arthralgia, myalgia and headache. Conjunctival injections can be seen in the third day of illness. In the immune phase of illness there will be multiple organ involvement. Severe disease will manifest as acute renal failure, acute pulmonary haemorrhages, myocarditis, aseptic meningitis, ARDS and multi-organ dysfunction (1).

Laboratory confirmation of leptospirosis is by a positive culture or a positive PCR test for leptospira or MAT titre of ≥ 1 : 320, a four-fold rise or seroconversion from acute and convalescent

sera (7). MAT is the gold standard serological test for diagnosis (2). With the above available evidence, leptospirosis was entertained as our diagnosis. Elevation of creatine kinase, hypokalaemia and sterile pyuria are other laboratory markers that suggest leptospirosis (2).

Fulminant disease spectrum which is known as Weil's disease presents with progressive renal failure and jaundice (9). These variety of complications are due to an underlying vascular and endothelial injury causing a vasculitis by the spirochetes (10). AAC is a complication due to leptospirosis related vasculitis (2).

AAC is an uncommon cause of acute cholecystitis. It accounts for 2-15% of all acute cholecystitis cases (11, 12). Risk factors for AAC are post-abdominal surgeries, diabetes, trauma, burns and malignant tumours (liver, biliary tract, pancreas, melanoma, breast cancer and gastric cancer) (9, 13). Patients who underwent biliary surgeries such as closure of intrahepatic bile ducts and percutaneous transhepatic biliary drainage also have an increased risk (12, 14). Infections such as bacteria (leptospirosis, systemic candida infection, tuberculosis, salmonella infection of the bile duct), viruses (EBV, CMV, HIV), parasites (cryptosporidium) and spread of distant infections from other sites would also endangers the patients to develop AAC (13). AAC has been reported secondary to GB infection following systemic leptospirosis (13).

Diagnosis of AAC basically depends on the ultrasonic evidence of thickened GB wall more than 3 mm, pericholecystic fluid and subserous edema (9). In addition, there are positive sonographic evidence such as sonographic Murphy's sign, emphysematous GB wall, striated GB and absence of calculi or sludge (9). But the specificity of ultrasound on diagnosing AAC is lower than that of acute cholecystitis (4). The accuracy of contrast CT scan to diagnose AAC is similar to that of USS (4). Technetium-labeled hepatobiliary iminodiacetic acid (HIDA) scan would be more sensitive in the diagnosis of AAC (15). Cholescintigraphy will be positive if the GB fails to opacify after one hour of HIDA injection (15). However these tests are not freely available in our setting.

Management of AAC depends on the underlying systemic condition. As in the case of underlying systemic infection, primary treatment would be the treatment for primary infection. But some cases can be complicated with gangrenous GB, abscess formation and perforation, which warrants emergency cholecystectomy where usual conservative management is not curable (16). In our scenario patient was managed with expectant care with supportive management and IV antibiotics for the AAC associated with leptospirosis. Prognosis of AAC is worse than classic acute cholecystitis due to the high incidence of morbidity such as gangrenous changes, perforations and abscess and lead to high incidence of mortality (14).

This case scenario depicted an uncommon association of leptospirosis which is related to variable organ dysfunction in leptospirosis. Improved recognition of this uncommon but lethal condition would improve the patient care.

Informed written consent obtained from the patient and the relatives for publication of this case report. Author would like to acknowledge Dr. Arosha Abeywickrama, Consultant Physician, Teaching Hospital Karapitiya.

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