

Acute acalculous cholecystitis secondary to dengue fever

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ABSTRACT

Patients with dengue fever usually present with typical symptoms such as fever, frontal headache, retro-ocular pain, myalgia, arthralgia, nausea, vomiting, rash, leucopaenia and thrombocytopaenia. However, they can also manifest with atypical symptoms. Acute acalculous cholecystitis is an atypical manifestation of dengue fever. In dengue endemic areas such as Brunei Darussalam, it is imperative that typical and atypical presentations of dengue fever are recognised so that early diagnosis can be made. We report a case of an 18-year-old Malay lady who presented with fever, cough, abdominal pain, and generalised myalgia. She was found to have acute acalculous cholecystitis secondary to dengue fever.

Keywords: Cholecystitis, complications, dengue haemorrhagic fever

INTRODUCTION

Dengue fever is a mosquito-borne viral disease transmitted by the infected female *Aedes aegypti* mosquitoes and is endemic in the tropical and subtropical countries, including Brunei Darussalam. ¹ Patients typically present with fever, frontal headache, retro-ocular pain, myalgia, arthralgia, nausea, vomiting, rash, leucopaenia and thrombocytopaenia. ^{2,3} Atypical presentations are infrequent, and if unrecognised, may potentially result in delayed diagnosis leading to potentially catastrophic consequences. ² We report a case of an 18-year-old Malay lady who presented

with abdominal pain, and generalised myalgia. She was found to have acute acalculous cholecystitis (AAC) secondary to dengue fever.

CASE REPORT

An 18-year-old Malay lady with no known past medical history presented to RIPAS Hospital with a three-day history of fever, cough, abdominal pain, and generalised myalgia. She also complained of loss of appetite. Her sister and brother had been recently diagnosed with dengue fever. There was no history of rash and recent travel. On examination, she was alert and appeared well. She had a temperature of 40.1°C, with a blood pressure of 95/60 mmHg, pulse rate 112 per min and respiratory rate of 22 per min. There was no pallor,

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or lymphadenopathy. Examination of the abdomen revealed mild epigastric and right upper quadrant tenderness. There was no rebound tenderness, guarding, masses, organomegaly or ascites. Bowel sounds were present. Her respiratory, cardiovascular, neurological and ear, nose and throat examinations were unremarkable.

Laboratory and haematological investigations on admission were as follows: total white cell counts $3.2 \times 10^9/L$ (4.0 to 11.0) with 76.5% neutrophils (40 to 75) and 13.1% lymphocytes (15 to 41), haemoglobin 12.0 g/dL (12.0 to 16.0), platelets $81 \times 10^9/L$ (150 to 450), haematocrit 36.8% (36 to 46), prothrombin time 14.3 seconds (9.9 to 12.9), APTT 38.4 seconds (25.6 to 41.5), INR 1.29 (0.8 to 1.2), C-reactive protein (CRP) 0.95 mg/dL (0 to 0.50). Liver function test and electrolyte panel were normal. Blood culture, peripheral blood film for malarial parasite, serology for viral hepatitis A, B and C were all negative. Chest radiography was normal. Serology for dengue was positive with dengue IgM antibodies.

The patient was given intravenous fluids and was started on regular intravenous antibiotics consisting of amoxicillin-clavulanic acid (augmentin, 1.2gm t.i.d) and metronidazole (500mg t.i.d). Daily full blood count showed a decreasing trend of platelets from 81 to the nadir point of $26 \times 10^9/L$ and she was given four units of platelets.

On the third day of admission, an ultrasound scan of her abdomen was done to evaluate the right upper quadrant pain, suspected to be cholecystitis. The scan showed a thickened and oedematous gall bladder (8mm, normal <3mm). No stones or sludge were seen and the common bile duct and hepatic ducts were normal. There was also ascites and left pleural effusion. The scan was consistent with a diagnosis of AAC and this was attributed to the dengue infection.

The patient was continued on conservative treatment with intravenous fluids and was later given an additional four units of platelets. Her fever settled within 24 hours of admission with resolution of her abdominal

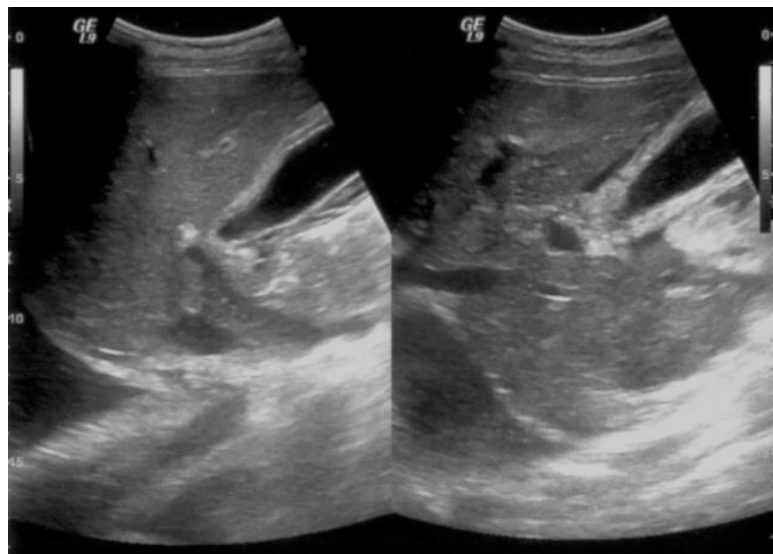


Fig. 1: Ultrasound scan shows marked thickening of the gallbladder and pericholecystic fluid in the absence of any stones or sludge.

pain on the third day. The platelet level came up to $321 \times 10^9/L$ on the ninth day of admission. She was discharged well on the ninth day with oral metronidazole (400mg t.i.d) for 10 days. She defaulted her clinic follow up appointment but had remained well when she was contacted via telephone.

DISCUSSION

Dengue fever is endemic in tropical and subtropical countries in Southeast Asia, the Pacific, East and West Africa, the Caribbean and the Americas. ¹ In Brunei Darussalam, there has been an outbreak of dengue fever with the main focus located at the water village (Kampong Ayer) in Bandar Seri Begawan. Our patient was also from the water village. Therefore in our setting, any patients admitted from Kampong Ayer with fever and thrombocytopenia needs to have dengue infection excluded.

Most presented with typical symptoms as did our patient. However, it is important to realise that not every patient will manifest

the whole range of symptoms. It is also interesting to note that our patient had manifested with an atypical manifestation despite the mild degree of her dengue fever. Hence, it is imperative that clinicians are familiar with both the typical and atypical manifestations. ⁴ Atypical presentations (Table 1) are infrequent, and if unrecognised, may potentially lead to catastrophic illness. ²

AAC has been reported to account for approximately 10% of all cases of acute cholecystitis. ⁶ Patients with AAC present with fever, right upper quadrant abdominal pain, positive Murphy's sign, and abnormal liver function tests. Ultrasonographic findings for diagnosis of AAC include thickening of the gallbladder wall over 3mm, gallbladder distention, localised tenderness, pericholecystic fluid and sludge. ⁴

AAC is traditionally known to occur in the critically ill patients with mortality as high as 90%. ⁶ A variety of clinical conditions is associated with AAC which includes burns,

Table 1: Atypical manifestations of dengue infection

| System | Manifestations |
|-------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Gastrointestinal | Acalculous cholecystitis, acute pancreatitis, acute parotitis febrile diarrhoea, hepatitis / fulminant hepatic failure |
| Cardiovascular | Conduction abnormalities Atrioventricular blocks (first degree AV block, Mobitz type I second degree AV block, complete heart block, atrial fibrillation, sinus node dysfunction (sinus bradycardia, sinoatrial exit block), ectopic ventricular ectopic Myocarditis, pericarditis |
| Respiratory | Acute respiratory distress syndrome, pulmonary haemorrhage |
| Neurological | Encephalopathy, encephalitis, septic meningitis, intracranial haemorrhages, thrombosis, mononeuropathies, polyneuropathies, Guillian-Barre syndrome, myelitis |
| Renal | Haemolytic anaemia, renal failure |
| Lympho-reticular | Spontaneous splenic rupture, lymph node infarction, haemophagocytosis |
| Musculoskeletal | Myositis, rhabdomyolysis |

Adapted from Gulati S and Maheshwari A. ¹

Table 2: Infections associated with acute acalculous cholecystitis.

| Genus | Organism |
|------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Virus | Hepatitis A, Cytomegalovirus, Ebstein Barr virus, Dengue |
| Bacteria | Salmonella species, Vibrio cholera, Escherichia coli, Klebsiella species, Staphylococcus species, Serratia marcescens, Leptospira species, Mycobacterium avium-intracellulare |
| Parasites | Isospora bellis, Microsporidia, Cryptosporidium, Malaria |
| Fungus | Candida species |

Adapted from Chong VH and Goh SK.¹⁴

childbirth, cholesterol emboli, coronary heart disease, diabetes mellitus, immunosuppression, major trauma, mechanical ventilation, medications (e.g. opiates), multiple transfusions, nonbiliary surgery, sepsis/hypotension, total parenteral nutrition, and vasculitis.⁷⁻¹³ AAC can also occur in outpatients with no evidence of acute illness or trauma. It is also interesting to note certain infections have been reported to be associated with AAC.^{4,14} Dengue infection has been reported to be associated with AAC in up to 7.6% in a study from Taiwan. In our local setting, to our knowledge, this is the only case of AAC associated with dengue fever.

The exact pathogenesis of AAC is unknown, but cholestasis and increased bile viscosity from prolonged fasting, spasms of the ampulla of Vater, infection, endotoxaemia, microangiopathy and ischaemia-reperfusion injury have been suggested. Dengue virus has been shown to be present in the brains of patients with neurological manifestations. Whether, the virus itself has any direct effect on the pathogenesis of AAC is unknown. In dengue fever, the main pathophysiological changes of AAC could be due to increased

vascular permeability, causing plasma leakage and serous effusion with high protein content, which then causes thickening of the gallbladder wall.¹ A thickened wall can lead to motility problem. The associated hypoalbuminemia may be an important contributory factor.

AAC needs to be diagnosed early and requires prompt management, especially in critically ill patients. Management includes starting broad spectrum antibiotics after blood cultures have been obtained. The definitive therapy for AAC is cholecystectomy with drainage of any associated abscess via percutaneous cholecystostomy.⁶ AAC in dengue fever is usually self-limiting, and the gall bladder wall thickness usually returns to normal. Thus, management is conservative with antibiotic therapy. Cholecystectomy is usually not indicated in dengue patients unlike other subsets of patients. It is however indicated if there are complications like gangrene and perforation.¹

In conclusion, AAC can manifest in dengue fever. In dengue endemic areas, it is important that typical and atypical presentations of dengue fever are recognised.

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