Abstract

Atypical manifestations of dengue fever (DF) and dengue haemorrhagic fever (DHF) involving different organs are being increasingly recognised, especially in the dengue endemic areas. We report an atypical presentation of DF in a 22 year old lady presenting with fever and acute pain in the right hypochondrium, diagnosed to be acute acalculus cholecystitis (AAC).

Introduction

Dengue fever is an arboviral illness quite endemic in tropical countries like India. The disease is transmitted by female Anopheles mosquito and caused by four antigenically distinct dengue virus serotypes (DEN 1, DEN 2, DEN 3 and DEN 4). Dengue infections may be asymptomatic or may lead to characteristic DF with headache, arthralgia, retro-orbital pain, rash with associated leucopenia or may have occasionally fatal manifestations of DHF and dengue shock syndrome. Atypical Clinical manifestations are increasingly being reported.

Case Report

A 22 year old unmarried lady, with no known past medical history of note, was admitted with high grade fever associated with generalised myalgia and arthralgia of 3 days’ duration. There were no associated symptoms of sore throat, cough, dysuria, haemorrhagic manifestations or rash. Her menstrual history was normal. Since the second day of her admission, she complained of intense right upper quadrant pain without radiation to any direction, accompanied by nausea and loss of appetite. Examination revealed a conscious, ill-looking lady who had mild pallor. She neither had icterus, cyanosis, clubbing, oedema, nor was there any lymphadenopathy. Her vitals were stable and the temperature was 38.2°C. Gastrointestinal system examination revealed mild muscle guarding with tenderness over the right upper quadrant and right lumbar region. At the bedside, Murphy’s sign was not clinically appreciable. There was no clinically demonstrable fluid in the abdomen, no organomegaly and the bowel sounds were within normal limits.

Preliminary investigations showed haemoglobin level of 10.8 g/dl, haematocrit of 36, leucopenia with total leucocyte count of 3200/ mm³ and a differential count of 68% neutrophils, 29% lymphocytes and 3% monocytes. Her platelet count was 1.8 lacs/ mm³ An ESR of 24 mm in 1st hour (Westergren) was noted. Blood sugar, urea, creatinine, electrolytes were essentially normal. Liver function tests revealed alkaline phosphatase 90 U/L (ALP normal value 32-103), aspartate transaminase 435 U/L (AST normal value 15-33), alanine transaminase 342 U/L (ALT normal value 7-36) and total bilirubin 1.4 mg/dl (conjugated fraction 0.6 mg/dl and unconjugated fraction 0.8 mg/dl). Serum amylase and lipase were only mildly elevated. Peripheral blood slides for malaria parasites and blood test for malaria parasite dual antigen were negative. A provisional diagnosis of hepatitis owing to a viral fever, resulting in leucopenia...
with elevated transaminase level, was entertained. Acute cholecystitis in the background of viral fever was also a possibility although Murphy's sign was negative clinically. Viral markers for Hepatitis A, B, C and E were negative. Our patient was put on two litres of dextrose-saline daily along with parenteral piperacillin-tazobactum with metronidazole infusion as broad spectrum coverage for gastrointestinal sepsis. Her fever, abdominal pain and nausea persisted. Blood culture sent on the day of admission came out to be negative. The dengue serology report sent on the third post-admission day showed positive dengue IgM with negative dengue IgG antibody against nonstructural protein 1 (NS1) antigen of dengue virus by NS1 capture enzyme-linked immunosorbent assays (ELISAs).

Her platelet count and coagulation profiles, done thrice, were within normal limits all the time. Abdominal ultrasound suggested acute cholecystitis with a thickened gall bladder wall with no evidence of stone or sludge. An abdominal computed tomography (CT) scan showed a thickened distended gall bladder with peri-cholecystic collection (Figure 1), suggestive of 'acute acalculus cholecystitis'; the other organs including the pancreas were absolutely normal on CT scan. The opinion of the surgeon was to continue conservative management with close sonographic follow-up so far as acute cholecystitis was concerned. Fever subsided by the tenth day with marked diminution in abdominal pain. Abdominal ultrasound repeated twice over the next week showed resolution of the peri-cholecystic collection and a decrease in the gall bladder wall thickness. The patient was discharged and followed up in the outpatients' department. She had no clinical symptoms with normal liver function tests and abdominal ultrasound one month after the onset of fever.

**Discussion**

Classical DF is rare in the endemic areas. Some unusual clinical manifestations like fulminant hepatitis, parotitis, encephalopathy, myocarditis, cardiomyopathy, acute pancreatitis and AAC are more common in the endemic areas. AAC as an atypical presentation of DF has been reported earlier from India. Acalculus cholecystitis has been described in association with burns, trauma, vasculitis, post-surgical conditions, and certain infections such as salmonellosis or cytomegalovirus in immunocompromised patients.

Our patient suffered from DF as diagnosed from the positive dengue IgM antibody against NS1 antigen of dengue virus which is a quite sensitive and specific laboratory test for acute DF. Dengue Fever according to WHO guidelines, is an acute febrile illness of 2-7 days duration (sometimes with two peaks) with two or more of the following manifestations like headache, retro-orbital pain, myalgia/arthralgia, rash, haemorrhagic manifestation (petechiae and positive tourniquet test) and leucopenia. Thrombocytopenia may be present with no evidence of plasma loss. The platelet count on admission was 1.8 lacs/mm$^3$ and thereafter decreased slightly but was always within normal limits. There was no evidence of DHF or Dengue shock syndrome. Therefore, a thickened distended gall bladder with peri-cholecystic collection in the absence of gallstone, in the backdrop of DF was considered as AAC. The patient recovered completely after resolution of fever and her ultrasound also normalised.

The exact pathophysiology in the development of AAC from infection with dengue virus is unknown. Some experts in this field suggested cholestasis and increased bile viscosity from prolonged fasting, spasms of the ampulla of Vater, infection, endotoxaemia, microangiopathy, and ischaemia-reperfusion injury. Various studies done worldwide have detected dengue virus or their antigens in the Kupfer cells and sinusoidal lining cells in the liver. Sonographic evidence of fluid collection was seen in subjects infected with dengue virus who did not show any evidence of dengue haemorrhagic fever. These findings shed light on possible mechanisms of plasma leakage and its role in the pathogenesis of DF and DHF. There is a significant association between thickening of the gallbladder wall and severity, as well as progression of DF. Thickened gall bladder wall of > 3.5 mm, positive sonographic Murphy’s sign which is the maximum tenderness of sonographically localised gall bladder are considered consistent with AAC. However, in DF patients with AAC, the course of DF is usually self-limiting and thickening of the gallbladder wall returns to normal after several days. Contrary to this, some authors have described a typical reticular pattern of gall bladder wall thickness that can be used to diagnose and follow up on patients with severe DF but should not be considered as an acalculus cholecystitis. Surgery is not indicated initially for DF patients with AAC as the tendency for bleeding can be a complicating factor.

**Conclusion**

Gastrointestinal manifestations of DF are varied and some appear innocuous. However, a rapid downhill course of these atypical manifestations are known to occur. AAC may progress to gangrene and perforation. A high degree of clinical suspicion with appropriate management is necessary to reduce morbidity and mortality in this clinical setting.
References


