

CASE REPORT

Dengue shock syndrome

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Abstract

Dengue fever is a mosquito-borne arthropod-borne viral (arboviral) tropical disease in humans affecting 50–528 million people worldwide. The acute abdominal complications of dengue fever are acute appendicitis, acute pancreatitis, acute acalculous cholecystitis and non-specific peritonitis. Acute pancreatitis with new onset diabetes in dengue shock syndrome (DSS) is very rarely reported. We describe a case of 30-year-old man admitted in intensive care unit and was diagnosed with DSS with RT-PCR, NS1 antigen and dengue IgM antibody being positive. Abdominal ultrasound and computerized tomography confirmed acute pancreatitis. Patient required insulin after recovery. Diabetes mellitus caused by DSS is under-reported and lack of awareness may increase mortality and morbidity.

INTRODUCTION

Dengue fever (UK /ˈdɛŋɡeɪ/ or US /ˈdɛŋɡiː/), also known as break-bone fever, is a mosquito-borne tropical disease and the most common arboviral illness in humans. Worldwide around 2.5–3 billion people live in 112 countries that experience dengue transmission. Estimates suggest that number of people infected range from 50 to 528 million per year, resulting in ~0.5 million hospitalizations [1, 2]. Dengue infection occurs commonly in >110 countries. For the decade of the 2000s, 12 countries in Southeast Asia were estimated to have around 3 million infections and 6000 deaths annually. Dengue hemorrhagic fever (DHF) is an endemic disease in India [3]. Four serotypes of dengue virus were documented till now which are DEN-1, DEN-2, DEN-3 and DEN-4 [3].

Each year DHF worldwide causes 22 000 deaths (mainly in children) [4]. In the last 50 years, dengue incidence increased 30-fold according to WHO [5]. Various common complications include encephalitis, myocarditis, acute motor weakness, Guillain–Barre like syndrome, acute liver failure, lupus erythematosus, hamophagocytic syndrome, acute kidney injury, etc. [6–8].

CASE REPORT

A 30-year-old man was brought to emergency room in a state of gasping for breath. As Glasgow Coma Scale was 5/15, patient was intubated and managed in intensive care unit. History from relatives revealed fever with chills since 6 days and shortness of breath from 2 days for which he was admitted in local

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clinic and was treated with intravenous fluids and prophylactic antibiotics. Patient was diagnosed with dengue fever as the NS1 antigen and dengue IgM antibody was positive.

Relatives informed the presence of infected people with dengue fever in his village. His physical examination showed fever (40°C), hypotension (BP: systolic 70 mm of Hg), cyanosis and other signs of systemic inflammatory response syndrome, including increased respiratory (38/min) and heart (136/min) rates. Systemic examination revealed bilateral basal crepitations.

Chest radiography showed bilateral pleural effusion with alveolo-interstitial infiltrate in right hemithorax (Fig. 1). Patient was started on antibiotics levofloxacin 750 mg 24 hourly in view of increased WBC count (25 900/mm³) and chest radiography features. Three samples of blood culture, reverse transcriptase-polymerase chain reaction (RT-PCR) for dengue and endotracheal tube aspirate for influenza were sent.

Investigations revealed hemoglobin of 10.3 mg/dl, platelet count of 9000/microliter, red blood cell (RBC) of 42 300/ml, and hematocrit of 48.5. The arterial blood gases had pH of 7.32, a PO₂ of 61 mmHg, PCO₂ of 35.5 mmHg and 17.2 mmol/l of bicarbonate. Renal function test was abnormal with creatinine of 2.6 mg/dl and blood urea of 70 mg/dl. Mild elevation of serum glutamic-oxaloacetic transaminase and serum glutamic-pyruvic transaminase in liver function tests noted. Electrocardiogram showed tachycardia and ST-T changes in lead 3. Echocardiography was normal with ejection fraction of 60% (Fig. 2). Ultrasound abdomen revealed bulky and hypoechoic pancreas indicative of pancreatitis, fatty liver and ascites (Fig. 3). RT-PCR, NS1 antigen and dengue IgM antibody were positive.

Computerized tomography (CT) of abdomen revealed diffusely enlarged pancreas with scattered non enhancing areas suggestive of necrosis, extensive peripancreatic fat stranding, moderate ascites and bilateral pleural effusion (Fig. 4). Investigations revealed hyperlipasemia and hypocalcaemia with serum amylase of 2350.0 U/L (normal range 30–110 U/L); serum lipase of 975.0 UI/L (normal range 23.0–300.0 UI/L) and calcium 6.16 mg/dL (normal range 8.4–10.2 mg/dL).

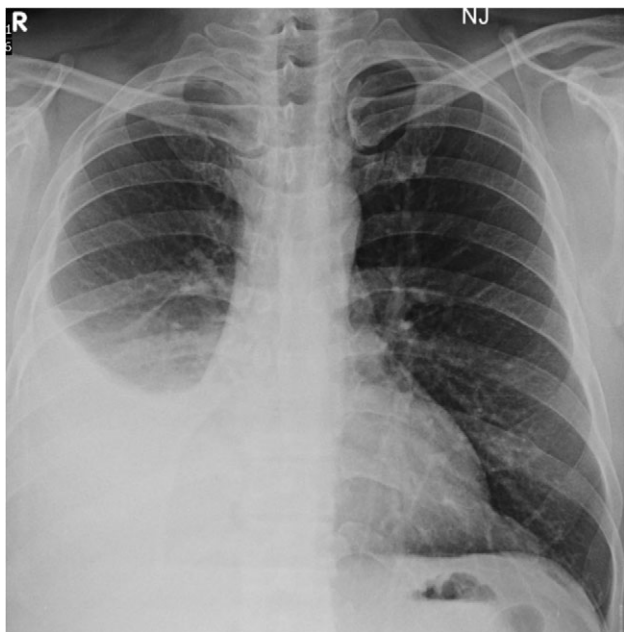


Figure 1: Chest radiograph showing bilateral pleural effusion and alveolar infiltrates

Investigations done 4 days ago in a local clinic including fasting and post prandial blood sugars, lipid profile were normal.

On admission random blood sugar was 200 mg/dl. Patient relatives reported no family history or treatment for diabetes mellitus. Fourth hourly general random blood sugar was persistently high above 200 mg/dl. Glycosylated hemoglobin was 5.1. Patient was diagnosed as severe DHF with acute pancreatitis, new onset diabetes mellitus, acute kidney injury and decompensated shock. Dengue shock syndrome (DSS) was diagnosed based on 1997 WHO classification, which classifies DHF in to four grades and Grades 3 and 4 being classified as DSS. Diagnosis of acute kidney injury was based on RIFLE (Risk, Injury, and Failure; and Loss; and End-stage kidney disease) classification system, which designates Injury with 2-fold increase in the serum creatinine, or glomerular filtration rate decrease by 50%, or urine output <0.5 ml/kg per hour for 12 h.

Mechanical ventilation was continued with positive end-expiratory pressure of 8 cm of H₂O. Intravenous fluids 0.9% NS at 20 ml/kg/h initially and then infusion of 10 ml/kg/h was given. Condition of patient deteriorated on second day with oliguria, shock and multiple organ dysfunction syndrome. Patient required blood transfusion, inotropic support (Dopamine at 15 µg/min) and crystalloids. Patient was given two packed RBC transfusion, two single donor platelets and fresh frozen plasma.

Condition of patient improved progressively on Day 3 with increase in blood pressure, no bleeding manifestations and radiography revealing reduction in pulmonary infiltrates. Patient was extubated on Day 6 with continuation of antibiotics. All other blood cultures as well as serological tests including HIV were negative. On Day 8, investigations were normal. But, patient continued to have high blood sugars and was advised insulin to be continued. On Day 10, patient was discharged after repeat ultrasound abdomen showing reduction of pancreatitis and ascites.

DISCUSSION

Infection with one dengue serotype results in lifelong homotypic immunity and a very brief period of partial heterotypic immunity, but an individual can be infected by all four serotypes separately. Dengue is transmitted by the bite of an infected *Aedes* (subgenus *stegomyia*) mosquito [9]. Female *Aedes* mosquitoes feed during daytime inflicting an innocuous bite, on the back of the neck and the ankles usually. Transmission occurs after 8–12 days of viral replication in the salivary glands of mosquito (extrinsic incubation period). Life span of *Aedes aegypti* ranges from 15 to 65 days.

Incubation period of dengue infection is 3–14 days (average 4–7 days) and viral replication occurs in target dendritic cells. Infection of target cells in reticuloendothelial system, such as dendritic cells, hepatocytes and endothelial cells occur [10]. The four cardinal features of DHF are increased vascular permeability, fever, hemorrhage and marked thrombocytopenia (100 000 cells/mm³ or lower). DSS is usually characterized by a rapid, weak pulse with narrowing of the pulse pressure (<20 mmHg (2.7 kPa), regardless of pressure levels, e.g. 100/90 mmHg (13.3/12.0 kPa)) or hypotension with cold, clammy skin and restlessness.

Acute pancreatitis diagnosis was based on clinical features, history of epigastric pain, fever, abdominal tenderness, enlargement of the pancreas on ultrasound examination and CT abdomen with normal hepatobiliary function, increased serum amylase and lipase three times above normal. One series regarding DHF outbreak in Taiwan (2002) reported pancreatitis (defined by a lipase level 3-fold greater) in three patients with

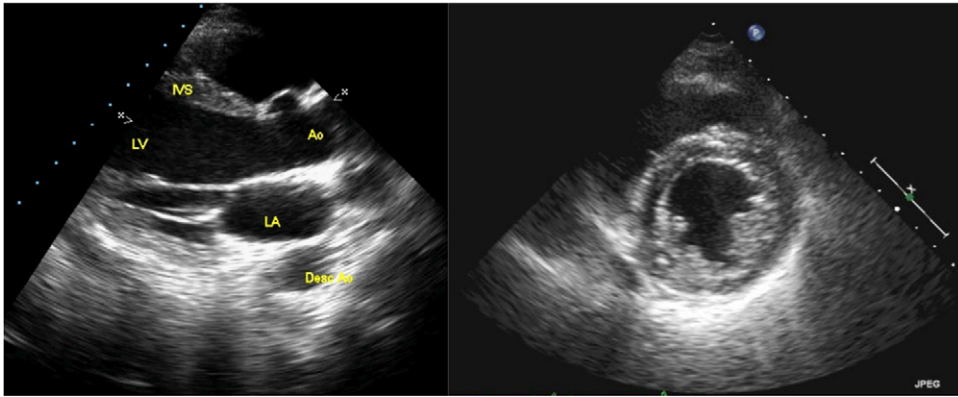


Figure 2: Normal 2D echocardiography of patient

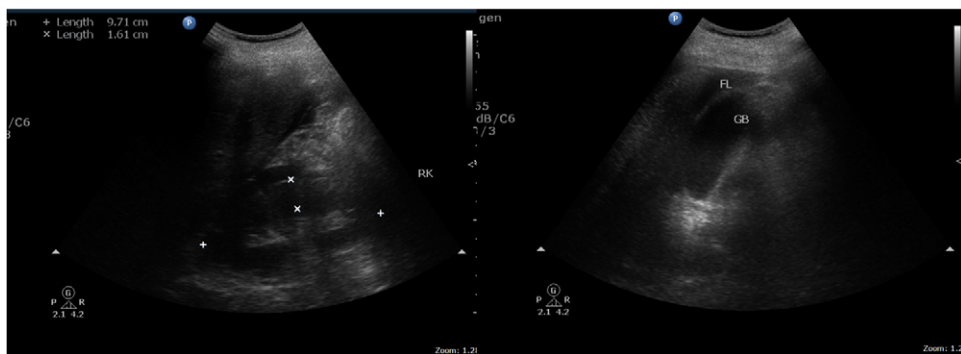


Figure 3: Ultrasound abdomen showing bulky and hypoechoic pancreas indicative of pancreatitis, fatty liver and ascites

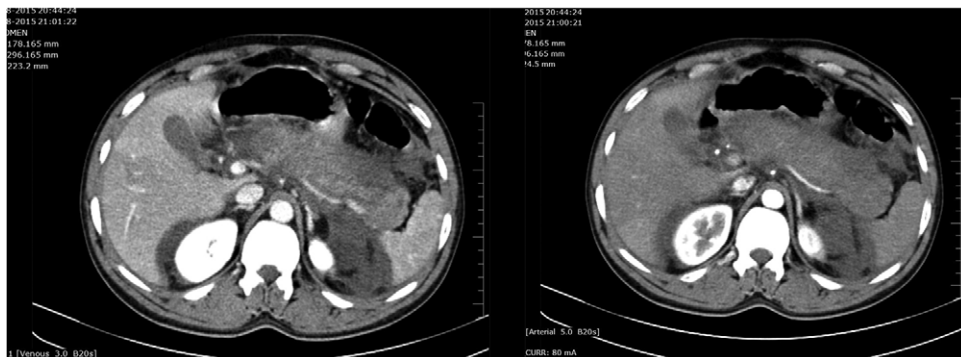


Figure 4: CT abdomen showing diffusely enlarged pancreas with scattered non enhancing areas suggestive of necrosis, extensive peripancreatic fat stranding, moderate ascites and bilateral pleural effusion

acute DHF and few other reports from other Asian countries [11]. Acute pancreatitis causing diabetes mellitus is a very rare manifestation of dengue [12]. The main clinical features of described 17 cases of pancreatitis in dengue infection are illustrated in Table 1.

The exact mechanism of pancreatitis is not clear and was thought to be multifactorial. Several hypotheses were proposed include direct inflammation, destruction of pancreatic acinar cells; autoimmune response to pancreatic islet cells with viral infection as a trigger, similarity between viral and islet cells antigens inducing autoimmune response, edema of the ampulla of Vater causing obstruction to the outflow of pancreatic fluid. The mechanism of injury may be similar to liver and kidney injury

caused by dengue virus infection. Dengue virus is hepatotropic, causing liver cell injury and aminotransferase elevation. Aspartate aminotransferase (AST) levels are usually higher than alanine aminotransferase levels, possibly due to coexisting myositis and release of AST from injured muscle cells. Serotypes 3 and 4 are associated with greater aminotransferase elevation.

Liver biopsies in patients with DHF showed microvesicular steatosis, centrilobular focal necrosis, acidophilic bodies, Kupffer cell hyperplasia and mononuclear portal tract inflammation. Kidney injury might be due to glomerular injury caused by direct invasion of virus and deposition of immune complex in glomeruli. Dengue virus causing deposition of antigen-antibody complex in Langerhan's cells has been found.

Table 1: Common clinical features of pancreatitis in dengue virus infection (including DHF and DSS)

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- Epigastric pain
 - Nausea
 - Vomiting
 - Loss of appetite
 - Fever
 - Hemodynamic instability, including hypotension and shock
 - Tachycardia
 - Respiratory distress
 - Hiccups
-

Very few cases were reported dengue infection causing pancreatitis [12–14] and further leading to insulin requiring diabetes mellitus. This complication is under-reported and lack of awareness may prove fatal to a patient in DSS. Even though pancreatitis treatment does not differ from other causes, more chances of bleeding and increased capillary permeability causing third space loss should be addressed more aggressively.

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CONFLICT OF INTEREST STATEMENT

None declared.

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ETHICAL APPROVAL

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CONSENT

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GUARANTOR

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