Dengue fever with Acute Liver Failure

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ABSTRACT

A virus belonging to the Flaviviridae group causes dengue haemorrhagic fever. Dengue presenting as acute liver failure is rare. Dengue is endemic in India. The last epidemic of dengue occurred in Delhi in 2003. During this epidemic, 2185 confirmed cases of dengue were reported. Dengue virus serotypes 2 and 3 were responsible for this epidemic. A 19-yr-old male presented to our hospital with the complaints of fever for 12 days, during this epidemic. He was diagnosed as having dengue shock syndrome, stage IV with acute liver failure. He had primary dengue infection. He made complete recovery with supportive management.

KEY WORDS: Dengue shock syndrome, acute liver failure

Dengue fever is caused by four different serotypes of dengue viruses. It is endemic in Southeast Asia. The last epidemic in the region was reported in Indonesia in 2004.[1] Dengue is endemic in India. The seroprevalence for IgG antibodies against dengue in Delhi was found to be at 77.6%, with the highest positivity of 100% in the age group of 31-40 years.[2] The last epidemic occurred in Delhi from June 2003 to November 2003. A total number of 2185 cases were reported.[3] Serotypes 2 and 3 were isolated during this epidemic. Dengue serotypes 1, 2 and 3 had caused the previous epidemics in Delhi.[4] Mild hepatic dysfunction in dengue haemorrhagic fever is usual. However, its presentation as acute liver failure (ALF) is unusual.[5-8]

Case History

A 19 year-old male, resident of Delhi, presented to the casualty with complaints of high-grade fever with chills, severe myalgia, nausea and non-bilious vomiting for 10 days, and progressive deterioration in sensorium with irrelevant speech, altered sleep-wake cycle, restlessness and violent behaviour for 2 days.

On examination, patient was restless. He was not oriented in time, person or place. He had icterus, epistaxis and gum bleeding. His pulse rate was 112/min, blood pressure was 84/60 mmHg, respiratory rate was 26/ min. Chest examination revealed decreased air entry in the right infrascapular and infra-axillary areas. Abdominal examination revealed a liver span of 10 cm. Neurological examination showed Glasgow coma score of E2M4V3. Fundus examination was normal. Bilateral plantar responses were withdrawal. There were no signs of meningeal irritation. Cardiovascular system examination was unremarkable. There was no past history of dengue fever.

Investigations

Chest radiograph showed right pleural effusion. His haemogram revealed: hemoglobin 11.5 g/dl, haematocrit 50%, total leucocyte count 10,000/mm³, differential leucocyte count: polymorphs 68%, lymphocytes 27% and platelet count of 120x10⁹ cells/mm³. Peripheral smear did not show malarial parasite. His blood glucose was 142 mg/dl. Liver function tests showed predominantly conjugated hyperbilirubinemia (4.4 mg/dl with total bilirubin of 6 mg/dl). Serum albumin was 2.8 g/dL and total protein was 6.8 g/dL. Serum alanine amino transferase was 4330 IU (normal upto 50 IU), aspartate aminotransferase was 2120 IU (normal upto 50 IU) and alkaline phosphatase was 267 IU (normal 80-280 IU). Prothrombin time was prolonged- more than 1 minute in comparison with 14 seconds in the control. Renal function studies were normal. LDH antigen tests for P. falciparum, malariae and ovale were negative. Ultrasound abdomen showed normal sized liver with
gall bladder wall thickening with minimal ascites and right-sided pleural effusion. Plain computerised tomography of the brain was unremarkable. Based on all these investigations, a provisional diagnosis of complicated malaria with acute liver failure was made.

Patient was fluid resuscitated. The first dose of artesunate, ceftriaxone 2 g and amikacin 375 mg were administered and he was shifted to intensive care unit. He had an episode of haematemesis and vomited about 200 ml of fresh blood. The Glasgow coma score deteriorated to 5. He was intubated and put on mechanical ventilation. Anti-cerebral edema measures were instituted and blood sugar was monitored. On second day, liver dullness was obliterated, platelet count decreased to 87x 10^9/ mm³, serum bilirubin, ALT and AST further increased to 7.2 mg/dl, 4860 IU and 2180 IU, respectively. Peripheral smear for malarial parasites, repeated five times, was negative. Blood samples were sent for dengue and leptospirosis serology. His sensorium improved on the third day. He was extubated on day four and shifted to the general ward on day five. By day 10 he had recovered fully and was discharged. Hepatitis A (Ig M type), hepatitis B surface antigen, Hepatitis C, Hepatitis E (Ig M type) serology were negative. Leptospirosis serology was negative. Ig M antibody against dengue was found in the serum using capture enzyme linked immunosorbent assay. As the patient had presented at the end of second week, virus isolation was not attempted.

Final diagnosis of dengue shock syndrome (DSS) stage IV with acute liver failure was made.

### Discussion

Acute liver failure in association with Dengue haemorrhagic fever (DHF)/DSS was initially reported during the epidemics in Indonesia in the 1970s. Later, it was reported during the 1987 epidemic in Thailand and the 1990 epidemic in Malaysia. Dengue virus serotypes 1, 2 and 3 have been isolated from the patients dying from liver failure with both primary and secondary dengue infections. Dengue antigens have been detected in hepatocytes, in Kupffer cells and occasionally in acute inflammatory cells in these patients. Whether this is due to the direct effect of dengue infection or to the host’s response to infection is not known. The DHF patients with secondary infections have a more severe clinical picture than the patients with primary infections. This does not seem to be the case with liver dysfunction. In the study by Nguyen et al., the difference in AST and ALT levels in primary and secondary infections was statistically not significant. Our case had primary infection.

The presentation of this case was like that of acute hepatic failure. The important differential diagnosis in a case presenting with fever with acute hepatic failure includes complicated malaria, leptospirosis, acute viral hepatitis and Reye’s syndrome. In complicated malaria ALT and AST levels will not be markedly elevated. Complicated malaria would present with features of multiorgan dysfunction like haemolysis and renal failure, which were not seen in this case. Peripheral smear for malarial parasites was negative and the malarial antigens were not demonstrable in the blood. Hence malaria was ruled out. Similarly, for leptospirosis, patient did not have features of renal involvement and the serological test was negative. Acute viral hepatitis presenting with high-grade fever preceding the onset of hepatic encephalopathy is rare. Moreover, all the viral markers of acute viral hepatitis were negative. Reye’s syndrome usually does not present with jaundice. The features of thrombocytopenia and plasma leakage seen in our case are not seen in Reye’s syndrome.

The presence of thrombocytopenia, signs of plasma leakage - pleural effusion, ascites and hypoalbuminemia, hypotension, positive IgM serology for dengue and its occurrence during the epidemic of dengue in Delhi strongly favour the diagnosis of DSS in this case. The treatment in such cases includes mainly supportive therapy in the form of adequate and cautious fluid replacement, timely ventilatory support, prophylactic antibiotic coverage to prevent secondary bacterial sepsis, anti-cerebral edema measures and continuous monitoring of neurological status. Most of the cases recover with good supportive therapy.[9-7]