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Dengue fever presenting as acute liver failure- a case report

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ABSTRACT

Dengue fever (DF) and dengue haemorrhagic fever (DHF) are important mosquito-borne viral diseases of humans and recognized as important emerging infectious diseases in the tropics and subtropics. Compared to nine reporting countries in the 1950s, today the geographic distribution includes more than 100 countries worldwide. Dengue viral infections are known to present a diverse clinical spectrum, ranging from asymptomatic illness to fatal dengue shock syndrome. Mild hepatic dysfunction in dengue haemorrhagic fever is usual. However, its presentation as acute liver failure (ALF) is unusual. We report a patient with dengue shock syndrome who presented with acute liver failure and hepatic encephalopathy in a recent outbreak of dengue fever in Delhi, India.

1. Introduction

Dengue viral infection can present a diverse clinical spectrum, ranging from asymptomatic illness to dengue shock syndrome, as well as unusual manifestations, such as hepatitis, encephalitis, myocarditis, Reye's syndrome, hemolytic uremic syndrome and thrombocytopenic purpura[1]. Mild hepatic dysfunction in dengue haemorrhagic fever is usual. However, its presentation as acute liver failure (ALF) is unusual[2,3]. We report a patient with dengue shock syndrome who presented with acute liver failure and hepatic encephalopathy in a recent outbreak of dengue fever in Delhi, India.

2. Case report

A 19 year-old male, resident of Delhi, came to the casualty with complaints of high-grade fever with chills, myalgia, nausea and non-bilious vomiting for 7 days, and progressive deterioration in sensorium with irrelevant speech, altered sleep-wake cycle, restlessness and violent behaviour for 2 days.

On examination, the patient was restless and 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, and 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. Microsection of liver biopsy with PAS showing confluent areas of hepatocyte necrosis with moderate stenosis and inflammation (Figure 1). 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.

His haemogram revealed: hemoglobin 12.5 g/dL, haematocrit 50%, total leucocyte count 10 000/mm^3, differential leucocyte count: polymorphs 68%, lymphocytes 27% and platelet count of 124 × 10^3 cells/mm^3. Peripheral smear did not show malarial parasite. 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 4 330 IU (normal upto 50 IU), aspartate aminotransferase was 2 120 IU (normal upto 50 IU) and alkaline phosphatase was 267 IU (normal 80-280 IU). Prothrombin time was prolonged to more than 1 minute in comparison with 14 seconds in the control. Renal function studies were normal. LDH antigen test for malarial parasite was negative. Chest radiograph showed right pleural effusion. Ultrasound abdomen showed normal sized liver with gall bladder wall thickening with minimal ascites and right-sided pleural

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effusion. Plain computerized tomography of the brain was unremarkable. Based on all these investigations, a provisional diagnosis of acute liver failure secondary to complicated malaria was made.

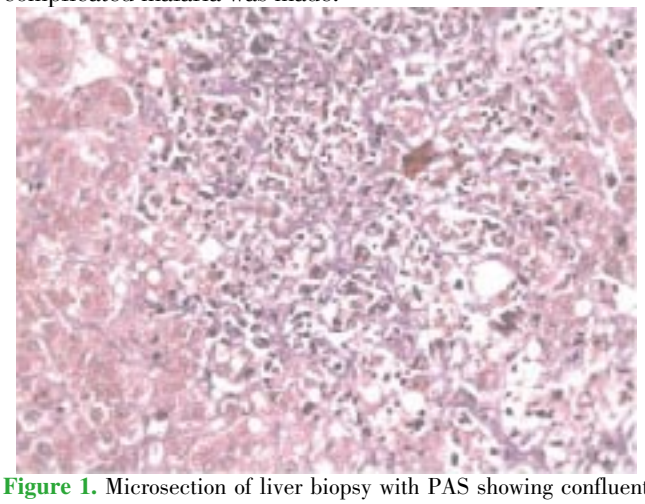

Figure 1. Microsection of liver biopsy with PAS showing confluent areas of hepatocyte necrosis with moderate stenosis and inflammation.

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 $87\times10^3/mm^3$ and serum bilirubin, ALT and AST further increased to 7.2 mg/dL, 4 860 IU and 2 180 IU, respectively. Peripheral smear for malarial parasites, repeated five times, was negative. Blood samples were sent for dengue and leptospira serology. His sensorium improved on the third day. He was extubated on day four and shifted to the 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. Leptospira 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.

3. Discussion

Dengue virus infection can present with a diverse clinical spectrum. Acute liver failure in association with 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[4]. Dengue virus serotypes 1, 2 and 3 have been isolated from the patients dying from liver failure with both primary and secondary dengue infections. The pathogenic mechanisms of acute liver failure have not yet fully elucidated. Some believe that it is related to combined interactions of the virus, the host and the duration of disease[5,6].

The virus may have a replication phase in hepatocytes, causing hepatic injury, stimulating apoptosis, microvesicular steatosis and the development of Councilman-Rocha Lima bodies, similar to yellow fever infection and other viral hemorrhagic diseases[7-9], The histopathological observation of liver specimens is restricted to fatal cases because of the risk of bleeding diathesis in acutely ill patients.

In India due to superimposed geographical areas for malaria, viral hepatitis, Reye's syndrome and leptospirosis represent a challenge for identifying etiology of acute febrile syndrome complicated by hepatitis. 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. 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, hypotension, positive IgM serology for dengue and its occurrence during the outbreak of dengue in Delhi strongly favors 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, anti-cerebral edema measures and continuous monitoring of neurological status[4]. Most of the cases recover with good supportive therapy as was with our case[2,9,10].

Conflict of interest statement

We declare that we have no conflict of interest.

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