A case of fulminant liver failure in dengue haemorrhagic fever

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Introduction

Currently, another epidemic of Dengue has emerged in Sri Lanka. Variations from the usual clinical pattern have been observed more frequently in this epidemic including very high transaminase levels in patients with Dengue. However only few cases were reported with acute hepatic failure and encephalopathy occurring in Dengue in adults[1,2,3,4,5].

Case report

A 28 year-old previously healthy, non-alcoholic male presented to us with a history of fever with chills for three days associated with vomiting and dizziness. He had no bleeding manifestations. On admission, he was plethoric with a temperature of 100F and blood pressure of 110/70 mmHg without a postural drop. His lungs were clear and the abdomen was soft. The initial full blood count showed a white cell count of 3,200/mm^3 (N-43%, L-55%, E-2%), Hb% of 16.9 g/dL with PCV of 48% and a platelet count of 20,000/mm^3. The blood picture was suggestive of dengue fever. On the following day, platelet count dropped to 10,000/mm^3 and the PCV rose to 50%. Twelve hours later he became drowsy. He was haemodynamically stable with no evidence of internal haemorrhage and also intracranial haemorrhage was excluded by a normal CT scan. Platelet count was 6,000/mm^3 then. By the next day patient's level of consciousness deteriorated further. His Glasgow Coma Scale was 9/15. There were petechial haemorrhages and mild gum bleeding. He was icteric with a tender hepatomegaly and a small amount of abdominal free fluid. His blood pressure was 140/90 mmHg with a normal pulse rate and volume. The platelet count was 20,000/mm^3 with a PCV of 40%. Blood picture showed no evidence of DIC. Blood urea and serum electrolytes were normal. The liver function tests were deranged: SGOT - 3,110 U/L and SGPT - 710 U/L, PT / INR - 1.5, total serum bilirubin - 120 µmol/L (direct fraction – 77 µmol/L).

We managed him as acute liver failure with hepatic encephalopathy and started him on standard liver failure regime including syrup lactulose 20 mL tds, oral metronidazole 400 mg tds, vitamin K 10 mg IV daily and bowel wash daily. At the same time we gave IV fluids to manage DHF and also transfused FFP and platelets. The patient was given ICU care with close monitoring in the critical stage. There were minor bleeding episodes attributed to coagulopathy although the platelet count was more than 20,000/mm^3. There was gradual improvement in patient's condition and hence we discharged him after 10 days of hospital stay. On discharge his platelet count was 90,000 /mm^3 with PCV - 34%, PT / INR - 1.0, SGOT - 93 U/L and SGPT - 56 U/L.

Both IgM and IgG antibodies for dengue were positive, but negative for hepatitis B virus surface antigen and hepatitis A IgM antibodies.

Discussion

Dengue infections are caused by a *flavivirus* which has four sero types (DEN1-4). It is the commonest arbovirus and a common cause of haemorrhagic fever in the world. The virus is transmitted by mosquitoes of *Aedes* genus, mainly *Aedes aegypti*. The severity of infection varies from mild undifferentiated febrile illness to dengue haemorrhagic fever to dengue shock syndrome.

Dengue virus can infect many cell types in the body to cause diverse clinical effects. Liver involvement appears to occur more commonly with serotypes DEN3 and DEN4[1]. Although liver is not the main target organ, direct infection of hepatocytes and Kupffer cells by dengue virus can be observed[6].

Hepatocellular necrosis in dengue mainly affects the mid-zonal area and sometimes centrilobular region[6]. In fact, dengue viral RNA and protein have been detected from mid-zonal hepatocytes[6]. Liver involvement is due to cytopathic effect by infection of liver cells by the virus *per se,* rather than a secondary immune reaction. Therefore, liver involvement can be seen both in primary infections[7] and re-infections.

An increase in liver transaminases is observed in the first week of dengue infection mainly in dengue haemorrhagic fever rather than in dengue fever. This can vary from 2-3 folds to more than 10 fold rise from normal level. SGOT rises more than SGPT which is different from other types of viral hepatitis[6]. This was the pattern observed in our patient as well. He was a non-alcoholic which excluded another common cause of SGOT > SGPT.

Acute liver failure is defined as rapid onset of acute encephalopathy and coagulopathy (INR ≥ 1.5) in the setting of liver failure of ≤ 6 weeks duration. Even though liver involvement is commonly observed with SGOT rising more than 10 folds of normal value, acute liver failure is not commonly seen in dengue infection as evidenced by extensive studies done locally and abroad[8,9]. In our patient PT / INR was 1.5 initially, which came down later. He was in encephalopathic coma which was evident by low GCS.

Acute hepatic failure due to dengue infection with subsequent complete recovery has been reported in two adult patients from India[4,5], one from Singapore[3] and one from USA[1]. A case with fatal outcome was reported in an immigrant to UK[2].

In dengue infection liver involvement is not chronic as in hepatitis B or C infection. Transaminase levels drop back to normal in about the third week of illness[6]. Same findings were seen in our patient as liver enzymes dramatically came down with clinical recovery.

Elevation of liver enzymes *per se* is not a bad prognostic sign in dengue[9]. With liver involvement the hospital stay will be prolonged with delayed recovery. However, with acute liver failure the mortality rate shoots up which adds to the toll of haemorrhagic phase and shock syndrome[6]. With acute liver failure a patient can develop haemorrhages even with a platelet count of >20,000/mm^3, as observed in our patient, due to coagulopathy[3].

Most patients with acute liver failure in dengue infection had hypotension which was not observed in this patient at any time[1,2]. The common causes of acute liver failure in tropics, hepatics A, hepatitis B, overdose of paracetamol and alcohol consumption were excluded in our patient.

References

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