

Dengue causing fulminant hepatitis in a hepatitis B virus carrier

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Summary

Dengue is an acute febrile illness resulting from infection by a flavivirus transmitted by the *Aedes* mosquito. It is characterized by bleeding manifestations and a plasma leak syndrome. Hepatic involvement in the form of elevation in transaminases is common. However, acute hepatic failure is uncommon. It is not known how the presence of an underlying chronic hepatitis or liver disease affects the likelihood of severity of hepatitis from dengue. The present report is of a 33-year-old man, a carrier of hepatitis B virus, who presented with fever, altered sensorium, thrombocytopenia, and coagulopathy. He was diagnosed to have developed acute hepatic failure due to dengue. The patient improved with supportive measures.

Keywords: Dengue, acute liver failure

1. Introduction

Dengue is an arbo-viral disease transmitted by the bite of the *Aedes* mosquito. It is endemic in many areas of the world including India. Apart from causing fever and severe myalgias and arthralgias, dengue results in a phenomenon of plasma leak manifesting as hemoconcentration, serositis, and occasionally shock. Thrombocytopenia is common and can result in bleeding manifestations (1). Hepatic involvement in the form of raised transaminases is common but usually of no clinical importance. Sometimes dengue can cause acute hepatic failure (2). However, the effects of dengue infection on chronic liver disease or a chronic carrier state are not known.

2. Case report

A 33-year-old male, resident of Delhi (India) presented with a history of 5 days of fever. The fever was documented to be as high as 40°C. The fever was associated with chills and rigors. Two days prior to presentation there had been a gradual deterioration in his sensorium. He had started behaving abnormally and was irritable and abusive to his relatives. Around

eight hours prior to his presentation to us the patient had one episode of generalized tonic movements of the body associated with clenching of teeth. The patient had no associated rash, neck stiffness, cough, urinary, or bowel complaints. There was no past history of any seizures, jaundice, or long standing fever. There was no history of any herbal drug intake. Patient had taken paracetamol (500 mg three times per day) for two days prior to presentation.

On examination, the patient was unconscious. His blood pressure was 116/78 mmHg, pulse was 104/min, and regular oral temperature was 38.5°C. His oxygen saturation on room air was 98%. He had mild icterus. Chest auscultation revealed diminution of breath sounds on the right side with stony dullness on percussion. The cardiovascular examination was normal. On palpation of abdomen liver was palpable two fingers below costal margin, spleen was not palpable. He was unconscious and moved his limbs only to deep painful stimulus. There was no neck rigidity, pupils were normal size and reacted normally to light and the plantars were flexor.

His investigations revealed a hemoglobin of 18.4 g/dL (PCV-55%), total leukocytes of 2,600/mm³, and a platelet count of 18,000/mm³. His serum total bilirubin was 3.5 mg/dL, with a direct of 1.5 mg/dL (Table 1). Alanine transaminases (ALT), aspartate transaminase (AST), and serum alkaline phosphatase (SAP) were 768, 882, and 132 IU/L, respectively. Serum albumin was 3.5 g/dL (Table 1). His prothrombin time was 32 sec (control, 12 sec) (Table 1). His serologies for

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Table 1. Trend of liver function tests during admission

Parameters	Days				
	D1	D3	D8	D10	D14
Bilirubin (total) (mg/dL)	3.5	2.6	1.8	1.6	1.5
Bilirubin (direct) (mg/dL)	1.5	1.2	0.6	0.3	0.3
ALT (IU/L)	768	308	112	80	35
AST (IU/L)	882	450	205	115	52
SAP (IU/L)	132	112	98	111	108
Albumin (g/dL)	3.5	3.2	3.2	3.5	3.4
prothrombin time (sec)*	32 (12)	–	–	–	15 (13)

* Control time is shown in parenthesis.

viral hepatitis including IgM anti-hepatitis A virus, IgM anti-hepatitis E virus, and anti-hepatitis C virus were negative. He was, however, positive for hepatitis B surface antigen (HBsAg). He was negative for hepatitis Be antigen (HBeAg) but positive for anti-hepatitis Be antibody. His IgM anti-hepatitis Bc (HBc) antibody was negative. A peripheral smear for malaria and a card test for parasite lactate dehydrogenase (pLDH) for *Plasmodium vivax* and *P. falciparum* were negative. His blood cultures were returned sterile. His chest roentgenogram was remarkable for presence of right sided pleural effusion. His ultrasound confirmed the presence of hepatomegaly. Presence of mild ascites and gall bladder wall edema was also noted. Magnetic resonance imaging of his brain was normal. IgM enzyme-linked immunosorbent assay (ELISA) for dengue was positive. The patient improved with conservative management (including fluid resuscitation, platelet transfusion, and anti-cerebral edema measures, *i.e.*, head end elevation, *i.v.* mannitol). Anti-virals (nucleoside analogues) were not administered. The patient was discharged after 2 weeks when his liver functions had returned to normal. The patient remained positive for HBsAg, with normal transaminases and hepatitis B virus (HBV) DNA of 1,880 IU/mL at six months.

3. Discussion

This patient presented with fever and altered sensorium. The differentials for this are broad and include among others meningitis, encephalitis, cerebral malaria, CNS tuberculosis, *etc.* The investigations in this patient were suggestive of leucopenia, thrombocytopenia, deranged liver functions especially transaminase elevation, and mild pleural effusion. These pointed to the possibility of dengue. Dengue was suspected as the patient presented with symptoms during an epidemic of dengue. The absence of IgM anti-HBc and low viral DNA levels argue against acute hepatitis B or an acute flare up of chronic hepatitis B. Also, the presence of severe thrombocytopenia and serositis argue against HBV as

the responsible etiological agent. The diagnosis was confirmed with a positive IgM ELISA for dengue.

Dengue is an arboviral disease caused by a member of flaviviridae. Dengue virus is a single strand RNA virus having four serotypes. Hepatitis is very common in dengue and can result in acute hepatic failure (3). Some reports have indicated that dengue is one of the most common etiologies responsible for acute hepatic failure in endemic areas (4).

However, not much is known about the effect of dengue coinfection in a HBV carrier state. There are some reports which have documented acute hepatitis resulting from dengue in a patient with chronic liver disease (5). However, it is not clear if dengue coinfection will result in more severe hepatitis or a higher likelihood of liver failure. A study in China examined the effect of co-infection of dengue on patients with HBV and found a difference of cytokine profiles in these patients. It noted that in cases of coinfection less interleukin (IL)-6 and tumor necrosis factor- α were formed whereas levels of IL-4, IL-10 and interferon- γ were similar (6). The clinical consequences of this difference are not clear and the study offered no evidence regarding any difference in liver function tests of dengue patients coinfecting with HBV. To the best of our knowledge the present report is the first one implicating dengue in causation of acute hepatic failure in a HBV carrier. The present case highlights the need to consider dengue as a possible cause of acute liver failure in endemic regions.

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