

Dengue Hemorrhagic Fever and Acute Hepatitis: A Case Report

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Introduction

Bangladesh has achieved a remarkable progress in controlling communicable diseases, but still facing pressure in public health problems especially controlling the emerging or re-emerging diseases. Increase in dengue cases introduce threats to public health. Most of the cases of dengue virus infection remain asymptomatic; but it can cause a wide spectrum of clinical manifestations from mild illness to spontaneous recovery and also haemorrhagic dengue fever (DF) and/or dengue shock syndrome (DSS).¹ There are four serotypes of dengue virus (DEN1-4) with 25-40% heterogeneity.² Infection with one serotype confers lifelong immunity against that particular serotype but subsequent infection by another serotype often creates fatal outcomes if remains untreated.¹

Since 1970, liver injury due to dengue infection has been described and it's not uncommon. Dengue hemorrhagic fever (DHF) is associated with hepatomegaly in 30% of patients, and its magnitude has no relationship with the severity of the disease. On the other hand, 90% of people with dengue infection presented with an increase in aminotransferases, with levels of aspartate aminotransferase (AST) higher than those of alanine aminotransferase (ALT). Acute liver failure is a severe complicating factor in dengue infection, predisposing to life-threatening hemorrhage, disseminated intravascular coagulation and encephalopathy.³

The case

A 28-year-old woman was admitted in Dhaka Medical College Hospital in April 2019. She was from--- Written informed consent was obtained from patient. She had a history of dengue fever three years earlier.

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developed fever, headache, chills, myalgia and arthralgia. She tested Dengue NS1 with the advice of family physician and it was positive. She took acetaminophen at standard dosages according to the instruction of that physician. On the fourth day of her symptoms, after a decrease in fever and headache, she had cold clammy skin, abdominal pain, repeated vomiting, per vaginal (PV) bleeding and diarrhoea. So, she was admitted in hospital on 5th day of her illness. On evaluation in the emergency department, she was well-nourished but icteric. Vital signs revealed pulse 100/min and BP 90/60 mm of Hg. A few petechial lesions were observed on the upper extremities and mildly painful liver enlargement was evident. The tourniquet test was not performed due to bleeding manifestations. The patient was hospitalised and submitted to a management protocol for DHF cases. She was given oral fluids and also intravenous saline solution. The results of laboratory tests were done. Tests of IgM HAV, HBsAg, anti HCV, and IgM HEV were also negative (table I). Ultrasound exam of her abdomen showed hepatomegaly with gall bladder wall thickening, minimal ascites and retained products of conception.

During the first 24 hours of hospitalisation the patient had moderate PV bleeding, right upper abdominal pain, vomiting and unstable BP. She was managed conservatively with continuous IV fluids and daily vital monitoring. On the 7th day, her platelet count became 65000/ μ L, on 8th day it increased to 60000/ μ L, and on the 9th day it reached 1.3 lakhs/ μ L. Both IgM and IgG antibodies against dengue were strongly positive at day 6. One unit of packed cell was transfused on day 7. Her PV bleeding decreased from day 8. So, repeat ultrasound was done to see the condition of retained products. As there were no products, no D&C was performed. Jaundice slowly

disappeared from day 9 and she was discharged on the 13th day. Her LFT and ultrasound of whole abdomen were normal at the time of discharge.

Table I: Laboratory results of a dengue hemorrhagic fever patient, according to the day of illness. The patient first sought medical care on day 5

Investigations	Day 5	Day 7	Day 8	Day 9	Day 13
Leukocytes (4000-11,000/cmm)	9400		20800		11000
Neutrophils (%)	66		55		45
Lymphocytes (adult 20-50%)	25		41		38
RBC (x 10 ⁶ /μL)	4.3				
Hemoglobin (g/dL)	10		9		10
Hematocrit (%)	42	46	40	32	31
Platelet (x 10 ³ /μL)		65000	60000	130000	160000
PT		13 sec	15 sec		12 sec
Albumin (g/dL)			2.7	2.5	3.4
AST U/L (<34)	7380		4765	2500	310
ALT U/L (<40)	2185		1280	500	220
ALP U/L (100-360)	499		360	280	80
LDH U/L (140-280)	5000		2020	800	300
Total bilirubin (0.1 -1.2 mg/dL)	4		2.5	1.5	0.7
S Ceatinine (mg/dL)			1.4		1.1

Discussion

Dengue virus infection can be presented with a diverse clinical spectrum. In Indonesia in 1970s, acute liver failure was initially reported in association with DHF/DSS. After that, 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 infection.⁵

Another study reported that DENV-3 and DENV-4 are related with a greater degree of hepatic involvement. Furthermore, there is a suggested correlation between acetaminophen administration for fever, and the degree of liver damage.⁶

The mechanism of liver failure is not fully cleared yet. It may be combined interactions of the virus, the host and the duration of disease. Replication phase in hepatocytes which causes hepatic injury, stimulating apoptosis, micro vesicular steatosis and the development of Councilman-Rocha Lima bodies, may contribute to disease aggravation.⁷ The histopathological observation of liver specimens is restricted to fatal cases because of the risk of bleeding diathesis in acutely ill patients.⁵

The liver involvement due to dengue infection in Thailand and Malaysia was reported as mild from 1973 to 1982, and it manifested exclusively as elevated liver enzymes. But, several cases of fulminant hepatitis with high mortality rate have been reported after this period, mainly in children and young adults.⁸ The increase in aminotransferases, mainly AST, has been associated with disease severity and may serve as an early indicator of dengue infection. Certainly, liver injury is a good positive predictive factor for the development of DHF.⁹ This increase usually happens within the first nine days of symptoms and normalizes in about two weeks. Increased levels of alkaline phosphatase and serum bilirubin are noted in some cases.⁶

In this case, patient had fever and was diagnosed as dengue (NS1 positive) with 6 weeks pregnancy and was on home management. But on the 5th day, when she developed abdominal pain, repeated vomiting, PV bleeding and diarrhea, she was admitted in hospital. She was hemodynamically unstable at that time. The appearance of jaundice with thrombocytopenia along with PV bleeding, all features made the condition of the patient unstable. The elevation in the AST level is usually greater than that of ALT in dengue infection, which is uncommon in patients with viral hepatitis A, B, or C.¹⁰ This patient also had greater elevation of AST compared to ALT elevation. Dengue fever should be considered when liver functions are deranged, because they are potential candidates for

acute fulminant hepatic failure apart from routine hepatotropic viruses.⁹

The hypoalbuminaemia found in this case was probably a result of both capillary leakages induced by dengue infection and liver failure. Leukocytosis may be the cause of extensive acute hepatocyte necrosis.¹¹

Conclusion

A high suspicion of dengue should be present when clinical and laboratory criteria are present in addition to that of jaundice. Countries that are endemic to dengue that have possible epidemic outbreaks should be kept in mind the different presentations which may mask dengue fever.

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