Clinical Brief

Fulminant Hepatic Failure in an Infant with Severe Dengue Infection

R. Soundravally, P. Narayanan, B. Vishnu Bhat[1], Jayanthi Soundraragavan[2] and Sajita Setia

Departments of Biochemistry, [1]Pediatrics, and [2]Pathology, Jawaharlal Institute of Postgraduate and Medical Research, Pondicherry, South India

ABSTRACT

Fulminant hepatic failure due to dengue infection is rare, although mild liver dysfunction is common. Here we report a fatal case of fulminant hepatitis in an infant infected with dengue 3 serotype. Attention must be given to the use of hepatotoxic drugs in some cases of dengue especially in infants. **[Indian J Pediatr 2010; 77 (4) : 435-437]** *E-mail: soundy27@yahoo.co.in*

Key words *: Dengue hemorrhagic fever; Fulminant hepatitis; Histopathological features; Infant*

Dengue hemorrhagic fever (DHF) and Dengue shock syndrome (DSS) are important causes of morbidity in South-east Asia and occur almost exclusively in young children in some parts of the world.[1] Though liver involvement with significant increase in transaminases is common in DHF/DSS, fulminant hepatic failure is rarely seen.[2-5] Here, we describe an unusual course of an infant with DSS and fulminant hepatic failure.

REPORT OF CASE

A seven-month-old infant was admitted with complaints of high fever, cough, vomiting, loose stools and respiratory distress of 5 days duration. He was irritable at presentation with tachycardia (140/min), tachypnea (48/min) and normal blood pressure. Clinical examination revealed pallor, petechial rashes over the trunk and extremities and hepatomegaly. His respiratory system examination showed decreased air entry in the right hemithorax and bilateral rhonchi. Hematological and biochemical investigations at admission and on subsequent days are shown in table 1. Chest radiograph revealed right sided pleural effusion. The CSF examination was normal. The infant was treated with a presumptive diagnosis of septicemia with parenteral cefotaxime and amikacin. He developed features of shock by day 2 of admission and was started on fluid regimen.

Correspondence and Reprint requests : Dr R Soundravally, Assistant Professor, Department of Biochemistry, Jawaharlal Institute of Postgraduate and Medical Research, Pondicherry, South India.

[DOI-10.1007/s12098-010-0027-z]

[Received May 31, 2009; Accepted September 3, 2009]

By day 3 of admission, he developed massive ascites and bilateral pleural effusion necessitating ventilator support. Jaundice was also noted from day 3 of admission. As we

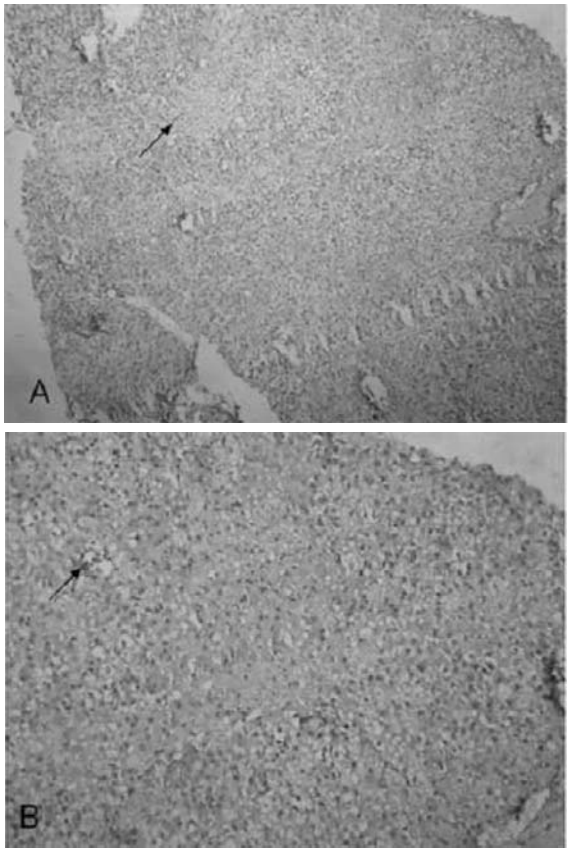

Fig. 1. Hepatic tissues showing necrotic foci and apoptotic cells: (A) Necrotic foci (arrow) are seen (4×), (B) Apoptotic hepatocytes (arrow) are mostly seen at the periphery of the foci of necrosis (10×).

Table 1. Clinical and Laboratory Profile of the Case During the Course of Infection

Hematological and Biochemical parameters	Day of hospitalization					
	1	2	3	4	5	6
Bleeding manifestations	*Extensive petechiae *ecchymosis	*Upper GI bleeding	* G.I.bleed *shock	*Multiple bleeding manifestations	* Multiple bleeding manifestations	* Multiple bleeding manifestations
Hb	11.7	11.1	14.8	8.6	3.7	6.7
PCV	-	50	56	32	20	26
Total WBC count (cells/cu.mm)	2,900	2,900	4,200	3,800	2,500	2,700
Differential count (%)	-	-	$N_{74}L_{20}E_1M_1$	$N_{64}L_{27}E_1$ M_1	$N_{73}L_{20}E_1$ M1	$N_{73}L_{16}E_2M_1$ MoM^2_4
Platelets (cells/mm^3)	1,75000	1,30000	86000	28,000	22,000	9500
Peripheral smear	-	-	Neutrophilic shift	Neutrophilic shift	Moderate Anisocytosis, eranated frig cells	Crenated RBC, neutroplilic shift.
ESR (mm/hr)	30.4	31.6	32.5	32.9	32.9	33.2
BT(min)	9	>10	>10	>10	>10	>10
CT(min)	>20	>20	>20	>20	>20	>20
PT(INR)	2.6	2.8	2.8	3.0	3.8	3.8
Fibrinogen (mg%)	-	-	38	-	-	-
FDP[1]	-VE	-VE	+VE	+VE	+VE	+VE
Total Bilirubin (mg%)	2.1	2.3	4.0	3.9	4.1	4.8
Direct Bilirubin (mg%)	0.8	0.8	1.8	2.0	1.9	1.8
Total protein (gm%)	4	4.1	3	3	3	4
Albumin (gm%)	2.8	2.6	1.5	1.5	1.4	1.3
AST[3] (IU/L)	814	567	1500	1506	1410	1320
ALT[4] (IU/L)	212	765	1649	1049	506	223
ALP[5] (IU/L)	122	120	122	138	90	57

[1]FDP: Fibrinogen degradation products, [2]MoM: Myelomonocytes, [3]AST: Aspartate amino transferase, [4]ALT: Alanine amino transferase, [5]ALP: Alkaline phosphatase.

had experienced a recent dengue epidemic, the infant was investigated for dengue specific IgM and IgG antibodies and for virus isolation by RT-PCR. Dengue specific IgM/IgG ratio of > 1.8 is considered as primary infection and < 1.8 as secondary infection.[6] The infant had primary dengue infection (IgM/IgG= 2.4) and RT-PCR was found positive for type 3 serotype. Investigations for HIV, hepatitis B and C infections were negative. His mother was also found positive for IgG antidengue antibodies. His hemodynamic status and coagulation profile kept on worsening inspite of all supportive measures and the infant expired by day 6 of admission. Postmortem liver biopsy was consistent with fulminant hepatitis (Fig. 1).

DISCUSSION

The incidence of dengue virus infections in infancy amounted to 5-20% of dengue infections in children. Management of infants with DHF and DSS is challenging because early diagnosis is rather difficult as many of them present with unusual manifestations and complications such as hepatic dysfunction and fluid overload and also the case fatality rate is higher.[4]

Over the last few yrs, several atypical manifestations of dengue have been described, including involvement of the central nervous system, cardiac alterations, and elevations in aminotransferase levels, with reactive hepatitis.[1] In dengue infection, mild elevation of transaminases (<5x) is a common finding. Elevation more than 10 times is rarely reported.[5] These unusual clinical forms of hepatic disease are frequently associated with more serious states, and they often result from multifactorial conditions, such as the use of hepatotoxic drugs, in addition to the direct aggression by the dengue virus. Liver damage has been found to be greater in patients with complicated dengue infection *e.g.,* DHF.[7]

In the present study the transaminases elevation was 15-40 times the upper limit of normal. The peaks of both the enzymes were on day 7 which is consistent with other reports.[5] Unlike other viral infections, in dengue the rise in AST is usually more than ALT and is believed to be due to release from injured myocytes. In our patient also AST level was the first to rise as reported earlier.[7] However, peak of ALT was found to be on par with AST. This finding reflects the severity of hepatic tissue necrosis.

Fulminant hepatitis is unusual in dengue infection and comparatively more common in pediatric age group than adults. In the present patient, the post mortem liver histopathology revealed fatty necrosis, hemorrhagic necrosis and apoptotic changes suggestive of fulminant hepatitis. Similar changes have been reported in severe liver involvement with dengue infection.[7] Dengue antigens have been detected in hepatocytes, and kupffer

cells. However, it is not known whether the extensive necrosis seen is due to the direct effect of dengue infection or because of host's response to infection.[8]

Pediatricians should be aware of this complication of dengue infection. Usage of hepatotoxic drugs like anti-pyretics and anti-emetics during the early phase may initiate or potentiate the liver damage. Thus the prudent use of these drugs and serial measurement of AST, which was found as an early marker of liver dysfunction in DHF, may help in early detection and initiating appropriate supportive measures.

Acknowledgements

The authors acknowledge Dr.S.Soundraragavan for guidance in manuscript preparation. The authors thank pediatricians and nurses in pediatric intensive care unit of JIPMER for their guidance.

Contributions : RS acquired the data and drafted the manuscript. PN carried out the treatment, read and approved the final manuscript. BV revised critically and guided to draft the manuscript. JS reported on the histopathology and read the manuscript. SS helped to draft the manuscript. All authors read and approved the final manuscript.

Conflict of Interest: None.

Role of Funding Source: None.

REFERENCES

1. Chongsrisawat V, Hutagalung Y, Poovorawan Y. Liver function test results and outcomes in children with acute liver failure due to dengue infection. *Southeast Asian J Trop Med Public Health* 2009; 40: 47-53.
2. Gulati S, Maheshwari A. Atypical manifestations of dengue. *Trop Med Int Health* 2007; 12: 1087-1095.
3. Osorio J, Carvajal C, Sussman O, Buitrago R, Franco-Paredes C. Acute liver failure due to dengue virus infection. *Int J Infect Dis* 2008; 12: 444-445.
4. de Souza LJ, Goncalves Carneiro H, Souto Filho JT, Ferreira de Souza T, Azevedo Cortes V, Neto CG *et al*. Hepatitis in dengue shock syndrome. *Braz J Infect Dis* 2002; 6: 322-327.
5. Kuo CH, Tai DI, Chang-Chien CS, Lan CK, Chiou SS, Liaw YF. Liver biochemical tests and dengue fever. *Am J Trop Med Hyg* 1992; 47: 265-270.
6. Innis BL, Nisalak A, Nimmannitya S, Kusalerdchariya S, Chongswasdi V, Suntayakorn S *et al*. An enzyme-linked immunosorbent assay to characterize dengue infections where dengue and Japanese encephalitis co-circulate. *Am J Trop Med Hyg* 1989; 40: 418–427.
7. Ling LM, Wilder-Smith A, Leo YS. Fulminant hepatitis in dengue haemorrhagic fever. *J Clin Virol* 2007; 38: 265–268.
8. Seneviratne SL, Malavige GN, de Silva HJ. Pathogenesis of liver involvement during dengue viral infections. *Trans R Soc Trop Med Hyg* 2006; 100: 608-614.