Case Report

Dengue presenting as Acute Liver Failure – A case report

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Abstract

Background: Dengue is the most common arboviral illness in humans. It is transmitted by mosquitoes of the genus *Aedes*, which are widely distributed in subtropical and tropical countries. The dengue virus has four related but antigenically distinct serotypes: DENV-1, DENV-2, DENV-3, and DENV-4. Many patients with dengue experience a prodrome of chills and facial flushing, which may last for 2-3 days. Other symptoms may include headache, retro-orbital pain, severe myalgias, nausea and vomiting, maculopapular or macular confluent rash over the thorax with islands of skin sparing, weakness, altered taste sensation, anorexia, sore throat, hemorrhagic manifestations (e.g. petechiae, bleeding gums, epistaxis and hematuria) and lymphadenopathy. The incubation period is 3-14 days. Criteria for the diagnosis of dengue hemorrhagic fever, according to the World Health Organization (WHO), are as follows: Fever, Hemorrhagic manifestations (e.g. hemoconcentration, thrombocytopenia, and positive tourniquet test), Circulatory failure, such as signs of vascular permeability (e.g. hypoproteinemia, effusions) and Hepatomegaly.

Aim: To know the atypical manifestations of Dengue such as acute liver failure, seizures and encephalopathy.

Material and methods: Study material obtained from Columbia Asia hospital Patiala along with all the records and detailed history of the patient. The study was carried out in Intensive Care Unit of the hospital where the patient was admitted.

Observation and conclusion: In our case, patient presented with Dengue Hemorrhagic Fever. He developed acute liver failure which was considered to be due to dengue infection as antigen for the same was positive and other viral markers were negative. Acute liver failure manifested in the form of raised liver enzymes, coagulopathy, and encephalopathy. Dengue can lead to mild to moderate elevation of liver enzymes but complication of acute liver failure is rare.

Key words

Acute liver failure, Dengue hemorrhagic fever, Dengue shock syndrome, Encephalopathy, Seizures.

Introduction

Dengue is the most common arboviral illness in humans. The vector mosquito thrives in endemic areas of the tropics which is an important risk factor for infection. Poorly planned urbanization combined with explosive global population growth brings the mosquito and the human host into close proximity [1, 2, 3, 4, 5]. Liver damage manifests as increases in levels of alanine aminotransferase and aspartate aminotransferase, low albumin levels, and deranged coagulation parameters [6, 7, 8]. Dengue can lead to mild to moderate elevation of liver enzymes but complication of acute liver failure and jaundice is rare. In this case report, atypical manifestations of dengue are discussed.

Neurologic manifestations such as seizures and encephalitis/encephalopathy have been reported in rare cases. Other neurologic complications include neuropathies, Guillain-Barré syndrome, and transverse myelitis. Complications and sequelae of dengue virus infections are rare and include cardiomyopathy, depression, pneumonia, iritis, orchitis and oophoritis.

Hyponatremia is the most common electrolyte abnormality in patients with dengue hemorrhagic fever or dengue shock syndrome. Metabolic acidosis is observed in those with shock. Elevated blood urea nitrogen (BUN) levels might be seen [9, 10, 11].

Case report

Male child weighing 60 kg (8 years, 5 months old) presented in emergency department of our hospital. As per history provided by his parents, he was febrile since 4 days, had vomiting and pain abdomen since a day. Before coming to our centre, he was admitted outside where his total leukocyte count was 21000 with platelets of 42000 and ultrasound abdomen showed mild ascites with pleural effusion. His vitals were recorded with heart rate of 155/min, respiratory rate was 28/min, with CFT 3 sec (approx), random blood sugar was 109, and blood pressure was 120/82 mmHg. Examination of systems revealed fine crepts in infra scapular area on both sides and the child appeared drowsy. He was electively intubated in emergency with paralysing agents and sedatives due to his present condition and a CT scan was done to rule out any intracranial pathology. Meanwhile his complete blood counts, renal and liver function tests along with coagulation parameters were sent. Cultures of bodily fluids were sent along with dengue serology/antigen and malaria antigen. After CT scan, he was shifted to ICU and put on mechanical ventilator support (volume controlled ventilation) Investigations revealed following results.

- Blood and urine cultures showed no growth.
- Tracheal secretions: Gram stain showed no bacterial morphology and culture showed no growth.
- Malaria (Vivax, Falciparum) was negative.
- Peripheral Blood Smear showed Normocytic normochromic erythrocytes, neutrophilic leukocytosis, reduced platelets, no abnormal cells or parasites.
- Blood group was B+ve.
- APTT was 120 seconds (Range – 30-40 sec).
- INR was 2.27.
- Dengue IgG was negative
- Dengue IgM was negative
- Dengue NS1 Ag was weakly positive.
- HbsAg was non reactive.
- Anti – HCV was non reactive.
- Anti HAV was non reactive.
- Anti HEV was non reactive.
- ANA was non reactive.
- Widal showed S. Typhi O, H - < 1:80 while S. Paratyphi AH, BH - < 1:80.

- Urine routine showed ++ proteins, no casts/crystals/epithelial cells, and leukocytes 3-4/hpf.
- ESR was 50 mm/1st hour.
- Reticulocyte count was 3%.

Hematocrit was elevated with raised total leukocyte counts, DLC showed 50% neutrophils. Platelets were 28000 cells/cumm. SGOT/SGPT was in thousands, low albumin with hyperbilirubinemia. Renal functions were within normal limits. ABG showed hypoxia with slightly raised anion gap. INR was deranged. PBF showed normocytic normochromic erythrocytes, neutrophilic leukocytosis, reduced platelets with no abnormal cells or parasites seen. Dengue NS1 Ag came out to be weakly positive. Possibility of Dengue Hemorrhagic fever with dengue shock syndrome was kept as there was evidence of hypotension and he was started on inotropic support. He was started on broad spectrum IV antibiotics for possible superadded bacterial sepsis along with PPI and Inj. Vitamin K. IV fluids were given for Dengue Shock Syndrome. He was started on L-ornithine L aspartate, Rifaximin and lactulose as there was evidence of encephalopathy, coagulopathy, hypoalbuminemia and SGOT/SGOT were raised suggesting the possibility of Acute Liver Failure. Blood sugars were regularly monitored during the hospital stay. SDP and FFP were transfused for thrombocytopenia and coagulopathy respectively and femoral venous line is inserted afterwards as there was poor peripheral access for medications. CT head revealed normal study. ECG showed sinus tachycardia. Chest X-ray was done which showed minimal right sided pleural effusion at day of admission and collapse left upper lobe, ground glass opacities in both lungs and bilateral pleural effusion after six days. Ultrasonography of abdomen revealed acalculous cholecystitis, mild ascites with bilateral pleural effusion.

Child developed hematoma formation after a day at the site of femoral venous cannulation. Hemoglobin was checked again which came out to be 5 g/dl after which two packed cells were transfused. Bleeding controlled with FFP and cryoprecipitate infusions. Reticulocyte counts were sent to rule out hemolysis which came out to be 3% (Range 0.5 – 2.5%). First and last investigations were as per **Table – 1 to 4**.

Table – 1: Complete blood counts.

Blood parameters	**First**	**Last**
Hemoglobin (g/dl)	15.7	8.3
Hematocrit (%)	48.9	25
MCV (fl)	84	87
MCH (pg)	27	28
MCHC (g/dl)	32	32
RDW (%)	13	16
TLC (cells/cumm)	18.2	24
DLC		
Neutrophils (%)	50	70
Lymphocytes (%)	35	25
Monocytes (%)	15	3
Eosinophils (%)	0	2
Platelets (cells/cumm)	28	95

Table – 2: Renal function tests.

Renal parameters	**First**	**Last**
Sodium (mmol/L)	137	137
Potassium (mmol/L)	4.68	5.3
Chloride (mmol/L)	94	86.5
Urea (mg/dl)	48.2	166
Creatinine (mg/dl)	0.64	5.3
Uric acid (mg/dl)	9.6	10.1

Table – 3: Liver function tests.

Liver parameters	**First**	**Last**
Total proteins (g/dl)	5.1	5.18
Albumin (g/dl)	2.5	1.9
Globulin (g/dl)	2.6	3.2
A/G Ratio	1.0	0.6
Bilirubin Total (mg/dl)	2.05	12.15
Bilirubin Direct (mg/dl)	1.25	8.65
Bilirubin Indirect (mg/dl)	0.8	3.5
SGOT (IU/L)	3244	1171
SGPT (IU/L)	3693	230
ALP (IU/L)	338	205
GGT (IU/L)	120	52

Table – 4: Arterial blood gas.

Parameters	First	Last
pH	7.36	7.26
pCO_2 (mmhg)	34	46
pO_2 (mmhg)	43	92
HCO_3 (mmol/L)	18.5	19.7
Anion Gap (mmol/L)	17.2	17.5

Inj. NAC infusion (150 mg/kg over 15 min, then 50 mg/kg over 4 hours followed by 100 mg/kg over 16 hours) was started for Acute liver Failure and attendants explained about transjugular liver biopsy along with possible need for liver transplant but they wanted a conservative approach. Hematoma size remained fairly constant during hospital stay. CT abdomen was done to rule out any evidence of retroperitoneal bleed which showed none evidence for the same.

He remained on mechanical ventilation and inotropic support along with bicarbonate infusions for metabolic acidosis. His urine output dipped on 3rd day of stay and creatinine rose on the 4th day with creatinine clearance of 39 ml/min/1.73m^2. Total bilirubin rose steadily from day of admission. SGOT rose until 3rd day of admission after which it started falling. SGPT fell constantly from day 1 after treatment was started. As total leukocyte counts were continuously rising over the 3rd day of admission, antibiotics were stepped up from Piperacillin/ Tazobactum to Carbapenems but the cultures of bodily fluids remained sterile. Patient developed upper GI bleed in the form of altered blood in nasograstric aspirate on 4th day after which the frequency of administration of PPI's is increased.

After that he had multi organ dysfunction in the form of respiratory failure (ARDS), acute liver failure and acute kidney injury. Patient started developing episodes of hypoglycaemia for which he was started on dextrose infusions. He was dialysed due to complete renal shutdown and metabolic acidosis via internal jugular catheter inserted under ultrasound guidance and under the cover of cryoprecipitate infusions. He had seizures (GTCS) which were controlled with benzodiazepines and levetiracetam. But due to multi organ involvement, eventually he had cardiac arrest and could not be revived.

Discussion

In our case, patient presented with Dengue Hemorrhagic Fever. Dengue NS1 Ag came out to be weakly positive. Patient was managed as mentioned. Patient developed acute liver failure which was considered to be due to dengue infection as antigen for the same was positive and other viral markers was negative. ANA was done to rule out autoimmune hepatitis but it came out to be negative. Patient developed super added sepsis during hospital stay as there was evidence of raised total leukocyte counts associated with neutrophilia. Acute liver failure manifested in the form of raised liver enzymes, coagulopathy, and encephalopathy. A 2005 review from Singapore found that useful predictors of death in dengue include atypical presentations, abnormal serum markers including albumin and coagulation studies and secondary infections [12].

A similar case report showed that mild hepatic dysfunction in dengue haemorrhagic fever is usual. However, its presentation as acute liver failure (ALF) is unusual [13]. Another case report suggested same finding that dengue presenting as acute liver failure is rare [14].

Conclusion

In this case report, atypical manifestations of dengue are mentioned which are acute liver failure, seizures and encephalopathy. These should be kept in mind, but other known causes and infections like leptospirosis, malaria, typhus and viral hepatitis which might contribute and lead to similar manifestations should be excluded.

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