Case Report

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Acute liver failure in a young patient with dengue shock syndrome: a case report

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Abstract

Dengue fever is caused by dengue virus, which has four different serotypes and is transmitted by the *Aedes* mosquitos. This disease is endemic to Southeast Asian countries, including Nepal. Liver involvement in dengue is a crucial feature, and the effect ranges from an asymptomatic rise in liver enzymes to the development of acute liver failure. Acute liver failure often results in multiorgan dysfunction including hemodynamic instability, renal failure, cerebral edema, and even death because of shock. Prompt diagnosis and management are necessary to prevent complications. However, there is no proven proper treatment for this condition, and the only treatment modality is to prevent the symptoms. We presented the case of a young female with dengue fever who developed a life-threatening acute liver failure because of dengue shock syndrome.

Keywords: acute liver failure, dengue fever, dengue shock syndrome

Introduction and importance

Dengue fever, cause by dengue virus is an arboviral infection of a significant burden in tropical countries. *Aedes aegypti* and *Aedes albopictus* transmit this disease[1]. The dengue virus has four distinct serotypes, namely DEN 1 to DEN 4[2]. Dengue fever is endemic in Southeast Asian countries, including Nepal. The previous infection protects against reinfection with the same serotype, but reinfection with different serotypes results in a worse clinical prognosis[3]. Clinically, dengue fever is diagnosed by the presence of fever with at least two additional symptoms like ocular pain, headache, muscle/joint pain, rash, or leukopenia[4]. The incubation period of this illness is 3–7 days, and it is divided into three phases; a febrile phase (2–7 days) this phase is marked by an unexpectedly high temperature (38.5°C), headache, vomiting, myalgia, arthralgia, and, in rare cases, a brief macular rash[5–7]. a critical phase (days 3–7 of illness, with vascular leakage), followed by a convalescent phase[2]. Liver is one of the major organ that is damage due to dengue virus through multiple mechanisms. The virus directly affects the Kupffer cells and hepatocytes. There is immunological hyperactivity that leads to T-cell–mediated cytokine storm and circulatory failure, leading to decreased hepatic perfusion[8]. Effects of the disease on the liver range from asymptomatic transaminitis to ALF. We present a case of a young female with dengue fever complication leading to ALF and about her management. This case report follows all the SCARE criteria[9].

HIGHLIGHTS

- Dengue fever is caused by dengue virus, which has four different serotypes.
- The clinical presentation can range from asymptomatic to life-threatening acute liver failure (ALF).
- Liver involvement in dengue is a crucial feature, and the effect ranges from an asymptomatic rise in liver enzymes to the development of ALF.
- People infected more than one time with different serotypes increase the risk of severe complications and mortality.
- Prompt diagnosis and management are necessary to prevent complications.

Case presentation

A 26-year-old nonalcoholic female presented to the emergency department with a history of 4 days fever which was intermittent; the maximum temperature recorded was 102°F, associated with headache, retroorbital pain, and myalgia but without chills and rigor. There was no history of mucocutaneous bleeding or bruises. There was a history of multiple episodes of nausea and vomiting along with diffuse abdominal pain and distension, loss of appetite, and the generalized weakness associated with acute shortness of breath. There was no history of chest pain, palpitation, orthopnea, dizziness, loss of consciousness, abnormal body movements, or altered sensorium. There was no similar history in the past.

On examination, her blood pressure was 100/60 without a significant postural drop, pulse was 106 beats/min, oxygen saturation at room temperature was 98%, respiratory rate was 20/min, and the temperature was 101.4°F. She was well-oriented to time, place, and person. On abdominal examination, it was

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Table 1

Investigations done on the day of admission

Investigations	Results	Reference range
Total leukocyte count (cells/mm^3)	11 950	4000–11 000
Differential count (%)	Neutrophils: 60.90, lymphocytes: 34.30	Neutrophils: 40–70, lymphocytes: 20–45
Hemoglobin (g%)	12.4	11.9–14.6
Packed cell volume (%)	35.20	40–50
Platelets (cells/mm^3)	78 000	150 000–450 000
Alanine transaminase (U/l)	2202	9.0–52
Aspartate transaminase (U/l)	74 160	14–36
Total bilirubin (mg/dl)	4.70	0.2–1.3
Conjugated bilirubin (mg/dl)	1.40	0–0.3
Unconjugated bilirubin (mg/dl)	1.20	0.01
Alkaline phosphatase (U/l)	311	30–126
Prothrombin time (s)	19.50	11.0–16
Control (s)	14	
Random blood glucose (mg/dl)	60	80–140
C–reactive protein (mg/l)	87	0–10
Creatinine (mg/dl)	0.60	0.52–1.04
Urea (mg/dl)	19	15–45
Total protein, serum (g/dl)	5.30	6.3–8.2
Albumin, serum (g/dl)	2.20	3.5–5.0
Serum lactate (mmol/l)	5.1	0.7–2.0

grossly distended with dull percussion with decreased bowel sound. There was the presence of crackles over the lower surface of both lung fields. Her heart sound was normal. A necessary initial investigation showed (Table 1) were sent.

The blood investigations for malaria, hepatitis viruses, scrub typhus, and leptospira were negative. But the dengue viral antigen nonstructural protein 1 was detected in her blood. The ultrasound of the abdomen and pelvic done on the day of admission showed moderate ascites with bilateral pleural effusion. The following day after the admission, she had four to five episodes of nausea and vomiting, for which she was kept nil per oral. She was started on intravenous fluids and antiemetic due to worsening lactate levels and persistent tachycardia; later that day, she complained of severe abdominal pain and respiratory difficulty, for which she was shifted to the ICU. During the third day, her abdominal distension progressively increased, and she became tachypneic, confused, drowsy, and restless. She was subsequently diagnosed with Dengue shock syndrome with ALF and grade III Hepatic Encephalopathy evidenced by altered liver biochemistry with coagulopathy, severe lactic acidosis, and altered level of the sensorium. She was started on antibiotics, enema, diuretics, proton pump inhibitors, methylprednisolone, lactulose, 20% albumin infusion, N-acetylcysteine, and was kept on total parenteral nutrition. Hepatotoxic medications were avoided. She was intubated due to altered level of consciousness to protect her airway. The computed tomography scan of whole abdomen was done on the third day of hospital admission (Fig. 1). Therapeutic tapping of ascitic fluid was done to provide relief to the patient.

Over time, her deranged transaminases (Fig. 2) level was improved. Her coagulopathy which was deranged (Fig. 3), was appropriately managed with fresh frozen plasma and vitamin K. Slowly her clinical status as well as biochemical profiles was improved. She was completely weaned off the ventilator on the fifth day of intubation. After 20 days, she was discharged from the hospital. Later during a follow-up visit, her transaminase levels were within normal range.

Clinical discussion

The spectrum of dengue fever caused by different serotypes of dengue virus dengue fever clinical spectrum extends from asymptomatic to dengue fever, dengue hemorrhagic fever, and the most lethal dengue shock syndrome with ultimate ALF[1,4]. The most common definition of ALF involves any degree of mental deterioration (encephalopathy) in a patient without underlying cirrhosis and an illness lasting less than 26 weeks[10]. Evidence of coagulation irregularity, often an international normalized ratio of 1.5, is also included. Dengue hemorrhagic fever is diagnosed by the presence of fever with signs of hemorrhages, thrombocytopenia, and plasma leakage[4]. Dengue shock syndrome is the most severe form of dengue, which can affect several organs, including the liver, brain, and kidney, and result in fatal outcomes[1,4].

Liver involvement in dengue is a crucial feature, and the effect ranges from an asymptomatic rise in liver enzymes to the development of ALF[4]. Dengue patients who presented with abdominal

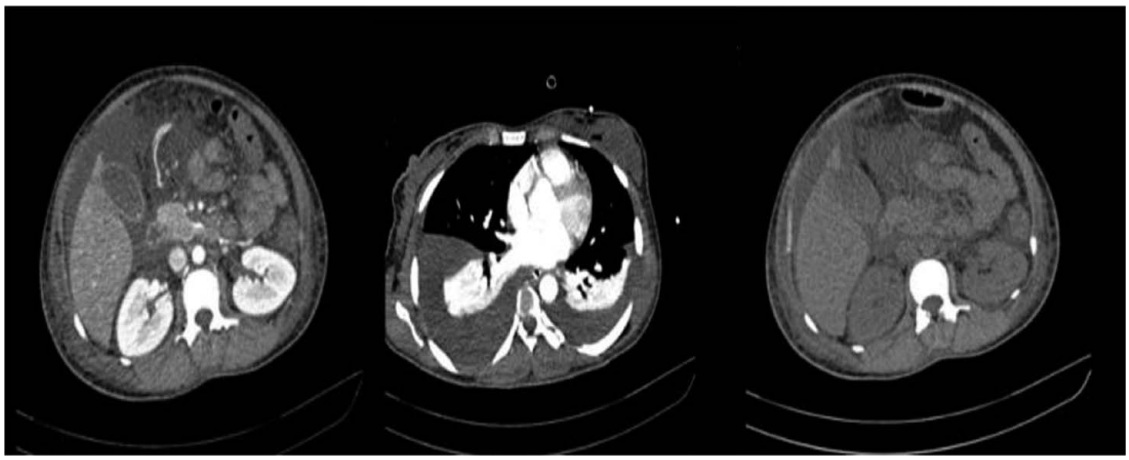

Figure 1. Computed tomography scan of whole abdomen: Gross ascites with large amount of bilateral pleural effusion with bilateral lower lobe atelectasis.

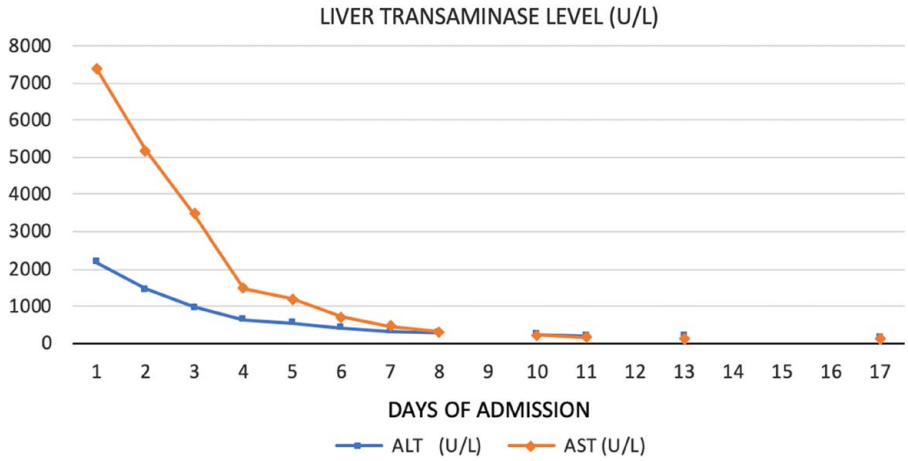

Figure 2. Liver transaminases level. ALT, alanine transaminase; AST, aspartate transaminase.

pain, nausea, vomiting, and anorexia should be evaluated for liver involvement[11]. The exact pathophysiology behind liver failure in dengue is not clear. The possible hypothesis includes T-cell–mediated host immunity and the underlying cytokine storm, which is also known as cytokine "Tsunami"[4,12,13]. Interleukin-22 and interleukin-17 are particularly responsible for liver injury[14].

ALF often results in multiorgan dysfunction including hemodynamic instability, renal failure, cerebral edema, and even death because of shock[4,12]. Souza *et al.*[14] found that 74.2% of patients with serologically confirmed dengue had significantly elevated transaminase. Many studies have point that the elevation of AST is more than alanine aminotransferase (ALT). The change in the ratio of aspartate aminotransferase (AST)/ALT is rarely observed in hepatitis A, B, or C viruses–induced acute hepatitis but only in Dengue fever[4]. Later Kuo *et al.*[15] and Nguyen *et al.*[16] found that the level of AST was higher than that of ALT. Damaged striated muscle, cardiac muscle, and erythrocytes release the AST, which could be the reason for the high level of AST as compared with ALT[17,18]. The prothrombin time and activated partial thromboplastin time are prognostic variables used to evaluate the degree of liver damage and serve as indicators of bleeding in individuals with ALF[19]. Severe coagulopathy-like disseminated intravascular coagulation, severe sepsis, renal impairment, increased intracranial pressure resulting in cerebral edema, and cardiopulmonary collapse resulting in multiple organ failure are all complications of ALF[20,21].

During ALF, complications like metabolic abnormalities, either due to infections or electrolyte abnormalities, should be corrected. Hepatic encephalopathy is usually corrected by restricting protein intake along with the administration of lactulose and antibiotics like rifamixin and neomycin (nephrotoxic). However, lactulose is frequently prescribed to patients who have hepatic encephalopathy as a result of chronic liver illness. However, its utility in cases of sudden liver failure is debatable. According to one study, receiving lactulose helped patients with ALF live a small increase in

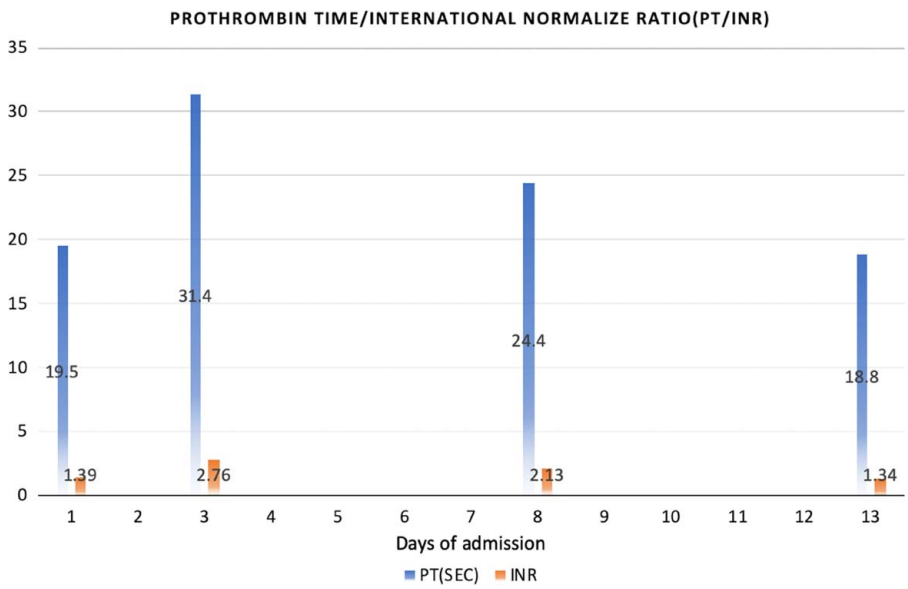

Figure 3. Change in prothrombin time (PT)/international normalized ratio (INR) levels.

survival time[22]. Coagulations disorders should be addressed as well. Other treatment principles include the administration of N-acetyl cysteine, which has a crucial role in preventing free radicals-mediated hepatocyte damage and prevention of hypoperfusion, dengue shock syndrome, or dengue hemorrhagic fever. Although this plays a specific role in mitigating the process, none is proven beneficial in all cases. Only a few therapeutic options are available in the current era for severe liver disease. The last resort is a liver transplant in the case of ALF; however, it is not that feasible due to a limited number of donors. Therefore, new methods should be developed to prevent as the dengue virus spread and new drugs should be discovered to prevent hepatotoxic injury[23,24].

Conclusion

Dengue fever has been a significant burden in countries with poor resources. Since most dengue cases are better with conservative treatment, few develop serious complications. Although liver involvement is mild in many cases, there are ALF cases associated with high morbidity and mortality due to complications such as encephalopathy, severe bleeding, renal failure, and metabolic acidosis. People infected more than one time with different serotypes increase the risk of severe complications and mortality. To accurately diagnose dengue and prevent misdiagnosis as viral hepatitis in dengue-endemic areas, clinicians must be aware of the need for early patient monitoring and measurement of suitable laboratory data. The afflicted patient's health, bleeding, and laboratory-determined markers such as complete blood count, serum transaminase levels, prothrombin time, and international normalized ratio should thus be constantly monitored while assuring adequate supportive care and treatment. Resource-limited countries like many countries in South Asia are facing an increasing case of dengue fever with increasing serious complications.

Provenance and peer review

Not commissioned, externally peer reviewed.

Ethical approval

Exempted by our institution.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Authors' contribution

E.A.: design of the study, data collection, evidence collection, manuscript writing, and revision.

L.A.: design of the study, data collection, design of the study, involved in patient management, manuscript writing, and revision, corresponding author.

S.S.: data collection, design of the study, manuscript writing, and revision.

A.B.S.: design of the study, evidence collection, manuscript writing, and revision.

Conflicts of interest disclosure

The authors declare that they have no financial conflict of interest with regard to the content of this report.

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Not applicable.

Guarantor

Eliz Achhami, Sukraraj Tropical & Infectious Disease Hospital.

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