

# Case report: Acute Liver failure; An Unusual Complication of Dengue Fever

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## Abstract

Dengue is one of the most prevalent viral equatorial diseases which has recently become a major health concern globally. This case report exemplifies a case of Expanded Dengue Syndrome in 29 years old male who was received by a Tertiary Care Hospital in Karachi and expired due to liver failure.

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## **CONSENT:**

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## **Abstract**

Dengue fever is one of the most prevalent viral equatorial diseases which has recently become a major health concern globally. The disease stems from a single-stranded positive RNA virus, which belongs to the family Flaviviridae, genus flavivirus. The disease is characterized by fever along with two of the following associated symptoms; (1) headaches, (2) myalgias, (3) leukopenia, and (4) rash. Plasma leakage is also a usual finding and its progress manifests as either compensated, or uncompensated shock. The shock syndrome may confer lethality by causing multi-organ failure or death. The term Expanded Dengue Syndrome (EDS) was coined by WHO in 2012 when the clinical presentation became vague and showed generalized impacts on normal physiology which could not be confined to a specific clinical spectrum. It amalgamates the findings exacerbating from the usual clinical picture and manifesting as an unusual presentation. Liver involvement is among the mainstay features of DF. Liver injury in DF is usually manifested by nausea, vomiting, abdominal discomfort, and anorexia concurrent with the findings of hepatomegaly and elevated serum transaminase levels. Laboratory parameters including a mean Platelet count  $< 20,000/\text{mm}$ , Aspartate Transaminase Levels  $> 45 \text{ IU}$ , and lymphocytes  $< 1500$  were significantly associated with severe disease. This case report exemplifies a case of Expanded Dengue Syndrome in 29 years old male who was received by a Tertiary Care Hospital in Karachi and expired after a week secondary to liver failure.

## **Introduction**

Dengue fever is one of the most prevalent viral equatorial diseases which has recently become a major health concern globally. The disease stems from a single-stranded positive RNA virus, which belongs to the family

Flaviviridae, genus flavivirus. The Dengue Virus has four identified serovars labeled as DENV-1, DENV-2, DENV-3, and DENV-4 and is transmitted by the vector, female Aedes Mosquito, particularly Aedes aegypti and Aedes albopictus [1]. It is now endemic in more a than hundred countries including The Americas, South-East Asia, and Western Pacific regions [2].

Dengue virus has an incubation period of 3-7 days, followed by symptoms that can appear in three distinct phases; febrile phase (2-7 days and persists throughout the illness), critical phase (3-7 days when the disease may disseminate and involve further organ systems), and finally the convalescent, or recovery phase [3].

The disease is characterized by fever along with two of the following associated symptoms; (1) headaches, (2) myalgias, (3) leukopenia, and (4) rash [3]. Dengue hemorrhagic fever (DHF) is among the clinically complicated pictures which may present with a severe fever, hemorrhage with or without hepatosplenomegaly, and occasionally circulatory failure [1]. Dengue Shock Syndrome (DSS) is another variant characterized by hypotension and accompanying chills and agitation [4]. The term Expanded Dengue Syndrome (EDS) was coined by WHO in 2012 when the clinical presentation became vague and showed generalized impacts on normal physiology which could not be confined to a specific clinical spectrum [5].

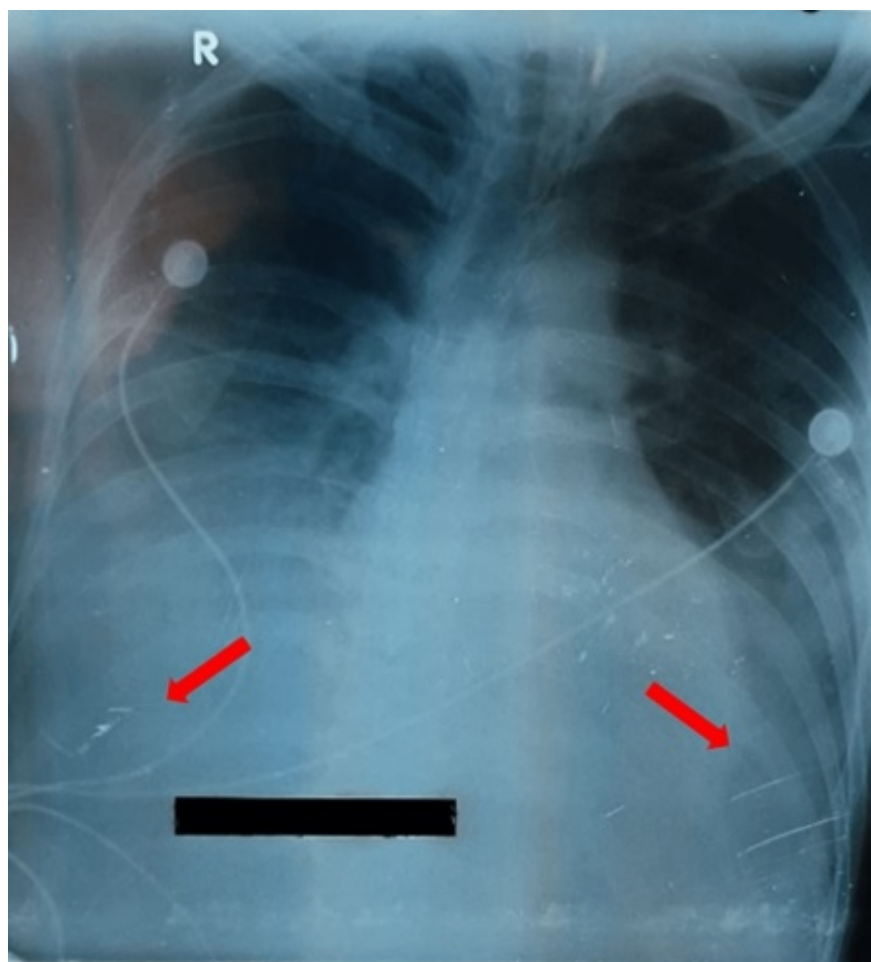
Liver involvement is among the mainstay features of DF [3]. Dengue virus blunts the physiologic hepatic functioning by diverse mechanisms involving direct disruption of hepatocytes and Kupffer cell function, and indirectly by impairment of the immune system via a cytokine surge mediated by t-cells and circulatory failure causing ischemic liver injury [6]. Liver injury in DF is usually manifested by nausea, vomiting, abdominal discomfort, and anorexia concurrent with the findings of hepatomegaly and elevated serum transaminase levels [7].

A recent outbreak of DF occurred in Pakistan starting from 1st January to 27th September 2022, with around 25,932 people being afflicted and 62 deaths reported by the National Institute of Health in Islamabad [8].

### Case Presentation

A 29-year-old Pakistani male was presented to the Emergency Department of a Tertiary Care Hospital in Karachi on 19th October 2022 with altered level of consciousness for 1 day and a history of fever, vomiting, and abdominal pain for the past 5 days.

On history, the fever was reported to be high-grade (maximum spike of 104°F), with rigors and chills, intermittent with a peak after every twelve hours. Vomiting was described as projectile, occurring three to four times a day, watery, and not blood-stained. Abdominal pain was localized to the right hypochondriac regions, with no shifting or radiations. It was described as an aching, intense pain that aggravated after vomiting and was not relieved despite the administration of analgesics. He then gradually developed an altered loss of consciousness which initiated with irrelevant conversation and progressively worsened. The patient was under hospital care for 4 days before being referred to the current set-up after behavioral alterations were evident. His viral markers for Hepatitis A ,B and hepatitis E infection were negative, Dengue Antigen and Malaria parasite were also negative on 17th October 2022. A chest X-Ray was also performed (Figure 1).



**Figure 1: Chest X-ray dated 17th October showing bilateral pleural effusion**

Upon receiving the patient in the Emergency Department, pulse and blood pressure were recorded as 63 beats/minute and 94/50 mmHg, and he was physically assaulting family and staff members alike along with displaying resistance to therapeutic care by removing cannulas and nasogastric tubes; he also showed impedance to taking medicine. On evaluation by the Psychiatry Department, he was under the impression of delirium. The Laboratory investigations conducted are reported in Table 1, which evidently reports deranged Liver Function Test values. The patient was injected with one liter of Ringer's Lactate to stabilize his vitals and was then advised admission to the Medical HDU.

The patient was received in Medical HDU in a drowsy state (not oriented) and on repeated examination, vitals were as noted: Pulse- 66 beats/minute, Blood Pressure- 130/80 mmHg, and respiratory rate- 24 breaths/minute. The abdomen was examined to be flat with the umbilicus centrally placed and inverted, with the lower edge of the liver palpable 1 cm below the costal margin with moderate tenderness in right hypochondrium, no splenomegaly appreciated, signs of free fluid present with positive shifting dullness. Pupils were found to be equally reactive to light bilaterally.

The patient was shifted to Medical ICU on 20th October 2022 with the Laboratory findings described in Table 1 and being treated along the lines of Fulminant Liver Failure. The progressive fluctuations in hemoglobin levels, Total Leukocyte count, Platelets count, and electrolyte levels since before and during admission in the ICU are tabulated in Table 1.

The patient was subjected to the treatment regimen, which included Meropenem 1 gm IV x TDS, Risek 40 mg IV x OD, N-acetylcysteine 150 mg/kg in 5 divided doses Loading dose of 150mg/kg in 100ml 5% dextrose water over 15 minutes with the maintenance dose of 12.5 mg/kg/hour over 4 hours and third dose of 6.25 mg/kg/hour over 16 hours, Mannitol 200 ml IV stat then 100 ml IV x OD (3 days) and syrup Duphalac 30 ml BD

The patient tested positive for Dengue IgM Antibody and an Ultrasound of the whole abdomen was concurrently performed on 22nd October, with the findings as follows-

- Liver - Normal in size measuring 15.1 cm with irregular outline and decreased parenchymal echogenicity. The portal vein was 1.0 cm, while the intrahepatic duct and vessels showed no abnormality. No focal mass was visualized.
- Gall-bladder - A thick, hypoechoic wall measuring 1.0 cm was conceived. There were no mass or calculi apprehended, and the common bile duct was found to be 0.4 cm in diameter. The findings were denoted as acute acalculous cholecystitis.
- No abnormal finding was reported in the pancreas and spleen.
- Kidneys - Bilaterally normal in size, shape, and position. Bilaterally, renal parenchymal changes were observed.
- General - Gross ascites was evident, bilateral gross pleural effusion secondary to lung collapse.

The patient became tachypnic and tachycardic with drop in GCS due to which patient was electively intubated on 21st October 2022. The patient gradually developed scrotal swelling which was evaluated by the Urology Department on 26th October 2022. The department commented on the patient having generalized body swelling which was predisposed to scrotal swelling. The patient was currently on a mechanical ventilator and required only scrotal support and elevation for relief. However, he developed an abnormal breathing rhythm which was found secondary to blockage of the endotracheal tube with blood clots signifying massive internal hemorrhage. 4 packs of Fresh Frozen Plasma (FFP), 6 packs of platelets, and 1 bag of Packed Cell Volume (PCV) was transfused to combat the deteriorating hemodynamics of the patient.

The patient succumbed to the disease at 10:18 A.M. on 27th October secondary to cardiopulmonary arrest as a complication of acute and subacute liver failure.

## Discussion

Dengue is typically reported to the clinical setting with a history of high grade fever, and drastically depleting platelets. Plasma leakage is also a usual finding and its progress manifests as either compensated, or uncompensated shock. The shock syndrome may confer lethality by causing multi-organ failure or death. The term 'Expanded Dengue Syndrome' amalgamates the findings exacerbating from the usual clinical picture and manifesting as an unusual presentation [9].

Liver involvement is prevalent among people infected with Dengue virus, most commonly founded in the form of elevated transaminase levels. Escalating levels of serum glutamic-oxaloacetic transaminase and serum glutamic-pyruvic transaminase are in corollary to disease severity and are indirectly proportional to platelet counts [10]. Concomitant complains of abdominal pain, anorexia, nausea and vomiting are strong indicators of liver involvement in a diagnosed dengue patient [11].

A myriad of factors contributes towards liver involvement constituting direct damage and loss of hepatocytes, and indirect damage mediated by the host immune system which jeopardizes vascular and circulatory integrity and may also exhibit metabolic dysfunction such as acidosis and hypoxia [12]. Certain chemokines such as Interleukin 17 and Interleukin 10 (IL-17, IL-10) are also implicated in cases of severe hepatic involvement in the absence of prominent fluid leakage and endothelial damage, where immune mediators are expected to be involved [13].

According to a study conducted by Jayaratne et al., the presentation of abdominal pain, vomiting, clinical fluid accumulation, and mucosal bleeding was persistently high in Dengue patients who developed severe disease. Laboratory parameters including a mean Platelet count < 20,000/mm, Aspartate Transaminase Levels > 45 IU, and lymphocytes < 1500 were significantly associated with severe disease [14].

## Conclusions

Our case emphasizes the lethality of Dengue fever and its complications when the case is brought into clinical attention once hepatic encephalopathy has developed. Infection by Dengue Virus was proven practically days after signs and symptoms developed which was significantly contributory factor towards the poor outcome in this patient. Fulminant Hepatic Failure ensued with significant capillary leak and overt bleeding which manifested acutely before the patient expired.

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