

## CASE REPORT

# Multisystem Complications of Dengue Encephalitis: Addressing Hemophagocytic Lymphohistiocytosis (HLH) – A Case Report

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### Abstract

Dengue encephalitis is uncommon, as neurological involvement is a rare complication of dengue fever. Neurological, hematological, and cardiac manifestations can occur, presenting a challenging clinical scenario. This report describes an elderly female with a decade-long history of type 2 diabetes mellitus who presented with dengue encephalitis, complicated by hemophagocytic lymphohistiocytosis (HLH) and cardiac arrhythmias. The initial symptoms led to a diagnosis of dengue encephalitis, confirmed by positive dengue IgM and MRI brain findings. Her condition subsequently deteriorated, necessitating recurrent hospitalizations and the development of both supraventricular and ventricular tachycardia, requiring advanced cardiac life support (ACLS). Despite intensive care and clinical stabilization, persistently elevated inflammatory markers, including elevated C-reactive protein (CRP), indicated ongoing systemic inflammation. This case highlights the complexities involved in managing severe dengue infection in elderly diabetic patients.

**Keywords:** Dengue encephalitis, Type 2 diabetes mellitus, Elderly female, Hemophagocytic Lymphohistiocytosis, Intensive care

### Introduction

Dengue fever (DF) is an infectious disease caused by the dengue virus, which is transmitted by striped *Aedes* mosquito. Most cases resolve spontaneously in about a week with no complications. However older adults, pregnant women, diabetics, and patients with renal failure have an increased risk of severe disease, which may even lead to death.<sup>1</sup> Severe dengue, the most common arboviral infection in humans, is linked to both generalized vascular leak syndrome and hemorrhagic illness. It's unclear how significant dengue is as a contributor to neurological disorders. Regardless of

whether they exhibit additional symptoms of the disease, patients with encephalitis in dengue-endemic areas should be evaluated for this infection.<sup>2</sup> In DF, the presence of warning signs increases the risk of serious disease and can lead to dengue shock syndrome. Mechanisms of thrombocytopenia in DF include hemophagocytic lymphohistiocytosis (HLH).<sup>3</sup>

### Case Presentation

An elderly female, aged 74 years, with a 10-year history of type 2 diabetes mellitus (T2DM), presented at the hospital on June 6, 2024 with a five-day history of fever, altered mental status, an episode of vomiting,

reduced appetite, generalized weakness, neck stiffness, and diminished breath sounds. Given her constellation of symptoms, initial clinical evaluations and laboratory investigations pointed towards dengue encephalitis. This diagnosis was confirmed by a positive dengue IgM test, indicating active infection, alongside MRI brain, which revealed T2 hyperintensity in left frontal lobe without diffusion restriction, chronic mild cerebral atrophy with small vessel ischemic changes. These MRI brain results suggested chronic brain structural changes, possibly exacerbated by her long-standing diabetes, and indicated prior ischemic damage.

Complicating her diagnosis, the patient developed hemophagocytic lymphohistiocytosis (HLH), a rare, life-threatening condition caused by excessive immune system activation, commonly triggered by infections such as dengue. The diagnosis of HLH was supported by the presence of systemic inflammatory response syndrome (SIRS), evidenced by persistent high fever, malaise, myalgia, tachycardia, tachypnoea and leucocytosis indicative of a widespread inflammatory process. The uncontrolled inflammatory response, likely a direct result of the dengue infection triggering HLH, led to the patient's rapidly deteriorating clinical status. The patient had a fever of  $\geq 38.5^{\circ}\text{C}$  (Table 1) and the blood test findings are elaborated in Table 2. Although there was no splenomegaly and no evidence of hemophagocytosis in the bone marrow, the patient met the diagnostic criteria for HLH (Table 1).

**Table 1:** The diagnosis of HLH can be established if five out of eight criteria below is fulfilled<sup>3</sup>

SI No	Diagnosis of HLH Criteria
1	Fever of $\geq 38.5^{\circ}\text{C}$
2	Splenomegaly
3	Cytopenias (affecting $\geq 2$ lineages in the peripheral blood): Hemoglobin $< 90$ g/L (in infants $< 4$ weeks: hemoglobin $< 100$ g/L), Platelets $< 100,000/\mu\text{L}$ , - Neutrophils $< 1000/\mu\text{L}$
4	Hypertriglyceridemia and/or hypofibrinogenemia: - Fasting triglycerides $\geq 265$ mg/dL, Fibrinogen $\leq 1.5$ g/L
5	Hemophagocytosis in bone marrow, spleen, or lymph nodes
6	Low or absent NK-cell activity
7	Ferritin $\geq 500$ $\mu\text{g/L}$
8	Soluble CD25 $\geq 2400$ U/L

Supportive clinical criteria include neurologic symptoms and cerebrospinal fluid pleocytosis, conjugated hyperbilirubinemia, transaminitis, hypoalbuminemia, and hyponatremia.

### Patient profile

Blood test Parameters	Range
Hemoglobin	7.8 g/dL (12-16)
Platelets	12,000 cells/cu mm (150,000-410,000)
Total Count (WBC)	7740 cells/cu mm (4000-10,000)
Fasting Triglycerides	220 mg/dL ( $< 150$ )
Fibrinogen	109.5 mg/dL (200-400)
Ferritin	$> 10,000$ ng/mL (11.1-264)
Bilirubin	0.84 mg/dL (0.2-1.3)
ALT (Alanine Aminotransferase)	652 IU/L (14-36)
AST (Aspartate Aminotransferase)	336 IU/ L (0-35)
Albumin	3.2 g/dL (3.5-5.0)
Sodium	135 mEq/L (136-145)

Given the severity of her condition, she was admitted to the intensive care unit (ICU) for immediate stabilization. Her initial treatment regimen consisted of Thiamine 100 mg three times daily, to prevent complications such as Wernicke's encephalopathy, especially in critically ill patients; Pantoprazole 40 mg once daily, administered before food to manage gastric acidity and prevent stress ulcers; and Dexamethasone 4 mg twice daily, a corticosteroid to manage inflammation. Following this comprehensive treatment, the patient's condition stabilized, and she was transferred from the ICU to the general ward before being discharged on June 11, 2024. Close follow-up was advised due to the complexity of her condition.

However, her recovery was short-lived. On June 24, 2024, she was readmitted to the hospital with symptoms of altered consciousness, fever, and neck stiffness. These alarming signs raised concerns for a possible recurrence or continuation of central nervous system involvement, such as encephalitis or meningitis. A lumbar puncture was promptly performed to rule out central nervous system infections, but the results were normal, effectively ruling out common causes like bacterial or viral meningitis. Despite this, due to the evidence of systemic inflammation, neck stiffness, and after consultation with

the neurology team, she was treated with antibiotics to address a suspected febrile illness, though no specific infectious etiology was identified at that time. As her condition deteriorated, especially her mental status, she was shifted to the ICU on June 28, 2024.

In the ICU, the patient's condition worsened, culminating in severe cardiac complications. On July 2, 2024, she developed supraventricular tachycardia (SVT), a rapid heart rhythm originating above the ventricles. The SVT episode was managed successfully with Adenosine (6 mg). However, shortly after this, she experienced a more critical and dangerous arrhythmia-ventricular tachycardia (VT). Immediate action was taken, and a biphasic shock of 200 J was delivered through a defibrillator, restoring the patient's normal heart rhythm. In addition, advanced cardiac life support (ACLS) was initiated.

After several days of careful management in the ICU, the patient's condition began to stabilize. She was successfully weaned off mechanical ventilation, marking a significant step in her recovery. Her hemodynamic status stabilized, was transferred back to the general ward. Despite these improvements, signs of ongoing systemic inflammation persisted. On July 4, 2024, her C-reactive protein (CRP) level was found significantly elevated at 67.313 mg/L, indicative of an active inflammatory process. By July 5, her CRP levels had further increased to 93.069 mg/L, signaling a worsening inflammatory response. The surge in CRP, combined with the patient's known history of HLH and SIRS, suggested that the underlying inflammatory process, potentially related to her dengue infection and immune dysregulation, was still active. Gradually, the patient improved with continuous monitoring and physiotherapy, making a near complete recovery. The patient was discharged from the hospital to continue recovering at home.

## Discussion

The course of illness in this patient diagnosed with dengue underscores the importance of intensive care, advanced cardiac interventions, and continuous monitoring to manage potential complications. The interplay between infectious, inflammatory, and cardiac complications necessitates a multidisciplinary approach, with close attention to the patient's evolving clinical status. The rising inflammatory markers toward the end of her hospital stay further emphasize the need for continued

follow-up and potential adjustments in the treatment plan to address the underlying immune dysregulation that may persist despite apparent clinical stabilization.

Initial clinical assessments and laboratory tests suggested that the patient had dengue encephalitis, a dangerous but rare side effect of dengue infection, based on her constellation of symptoms.<sup>2</sup> HLH, an uncommon and sometimes fatal illness brought on by excessive immune system activation and frequently brought on by viruses like dengue, complicated the patient's diagnosis.<sup>3</sup> The patient satisfied the diagnostic requirements for HLH even though there was no splenomegaly or indication of hemophagocytosis in the bone marrow.<sup>4</sup>

Supraventricular tachycardia (SVT), a fast heartbeat that starts above the ventricles, occurred in the patient. Adenosine effectively treated the SVT episode; nevertheless, she soon developed ventricular tachycardia, a more serious and severe arrhythmia.<sup>5</sup> At 67.313 mg/L, her CRP level was discovered to be considerably higher, suggesting an active inflammatory process. One day later, her CRP levels had risen to 93.069 mg/L once more, indicating a deteriorating inflammatory response. The patient's known history of HLH and SIRS, along with the spike in CRP, indicated that the underlying inflammatory process possibly brought on by her dengue illness and immunological dysregulation was still going strong. With constant observation and physical treatment, the patient gradually recovered and made a full recovery.<sup>6</sup>

This case underscores the intricate challenges of managing severe dengue infection, particularly in elderly patients with underlying comorbidities such as type 2 diabetes mellitus. The progression from dengue encephalitis to HLH and cardiac arrhythmias highlights the critical need for early diagnosis and a proactive, multidisciplinary approach to care. Given the complex interplay of infectious, inflammatory, and cardiovascular factors, timely interventions are essential to mitigate complications and improve patient outcomes.

Furthermore, this case reinforces the significance of continuous monitoring and individualized treatment plans, especially for high-risk patients. The occurrence of life-threatening arrhythmias necessitated ACLS measures, underscoring the importance of rapid response protocols in managing severe dengue complications. Persistent systemic inflammation despite clinical

stabilization suggests that long-term follow-up and immune regulation strategies should be integrated into post-hospitalization care.

By documenting this case, we highlight the necessity for heightened awareness among healthcare professionals regarding atypical and severe manifestations of dengue. Strengthening surveillance, improving supportive care strategies, and fostering interdisciplinary collaboration can contribute to better patient survival rates and long-term recovery.

### Conflict of Interest

No

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Nil

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