American Journal of Internal Medicine
2024, Vol. 12, No. 6, pp. 125-130
https://doi.org/10.11648/j.ajim.20241206.14

Case Report

The Neurological and Hemorrhagic Faces of Dengue: A Case of Encephalitis with Upper GI Bleed

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Abstract

Dengue fever is a mosquito-borne viral infection caused by the dengue virus, belonging to the Flavivirus genus and primarily transmitted by Aedes mosquitoes. It is prevalent in tropical and sub-tropical regions, affecting millions of people globally each year. The World Health Organization (WHO) estimates that about 390 million dengue infections occur annually, with approximately 96 million manifesting clinically. The epidemiology of dengue is influenced by several factors, including climate change, urbanization, and globalization, which facilitate the spread of the vector and the virus. While the typical presentation of dengue includes high-grade fever, headache, myalgia, arthralgia, and rash, the disease can escalate to more severe forms, such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). These severe forms can lead to life-threatening complications, necessitating prompt recognition and intervention. DHF is characterized by plasma leakage, thrombocytopenia, and hemorrhagic manifestations, which can culminate in significant morbidity and mortality. The pathophysiology underlying these severe manifestations is complex and involves the interplay of the virus, host immune response, and genetic predisposition. Additionally, neurological involvement, such as dengue encephalitis, and gastrointestinal (GI) complications, such as upper GI bleeding, are rare but increasingly recognized complications. This case report describes the clinical course of a young adult male who initially presented with typical dengue symptoms but developed severe complications during hospitalization. His clinical course included the development of dengue encephalitis and upper GI bleeding, both of which were primarily driven by plasma leakage and dengue hemorrhagic fever. Through this case, we aim to shed light on the atypical manifestations of dengue fever and the importance of early recognition and management of these complications.

Keywords

Dengue, Flavivirus, Aedes, Rash, Plasma Leakage, Dengue Encephalitis, Upper GI Bleeding, Myalgia, Fever, Hem-concentration, Thrombocytopenia

1. Introduction

Dengue fever is a significant global health challenge, particularly in tropical and subtropical regions, where it poses a substantial burden on healthcare systems. The disease is caused by the dengue virus, which is transmitted primarily by Aedes mosquitoes, particularly Aedes aegypti and Aedes albopictus. Typically, dengue fever presents with a classic triad of high-grade fever, severe headache, and musculoskeletal pain [1]. Other symptoms may include retro-orbital pain,

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Received: 30 November 2024; **Accepted:** 11 December 2024; **Published:** 27 December 2024

myalgia, rash, and gastrointestinal disturbances. While most cases are self-limiting and resolve within a week, some patients progress to severe forms of the disease, including dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). DHF is characterized by plasma leakage, leading to hem-concentration, thrombocytopenia, and bleeding tendencies [2]. These severe manifestations can lead to significant morbidity and mortality, particularly in children and individuals with underlying health conditions.

Neurological complications related to dengue fever are uncommon but increasingly recognized. Dengue encephalitis can present with a range of neurological symptoms, including confusion, seizures, and focal neurological deficits [3]. The pathophysiology of dengue-associated neurological involvement remains poorly understood but is thought to involve both direct viral effects and immune-mediated mechanisms.

Gastrointestinal complications, such as upper GI bleeding, are also serious concerns in severe dengue cases. The bleeding may arise from a combination of thrombocytopenia, hepatic dysfunction, and increased vascular permeability due to plasma leakage. Upper GI bleeding can present as hematemesis or melena, necessitating urgent intervention to manage potential hypovolemic shock and other severe complications. Overall, the management of dengue or dengue related complications is purely symptomatic [4]. After a prolonged hospital stay of about 20 days, the patient was eventually discharged with no residual signs of ailment. (Though the weakness persists for a certain amount of time just like any other viral illness)

2. Case Presentation

A 25 years old un-married male presented in emergency room of a tertiary care hospital with the presenting complaints of high grade fever along with severe body aches and occasional nausea & vomiting for last 4 days. The patient denied having any significant comorbidities. He was in his usual state of health 4 days back when he started having high grade fever which was intermittent in nature, documented at 102-103 F associated with mild rigors & chills and severe body aches, having no significant aggravating factors but got relieved after taking anti-pyretic. He denied having any unprotected intercourse, history of contact (Tuberculosis), and animal exposure, use of any illicit drugs, recent travel, and consumption of unhygienic food or self-medications. He had 3-4 episodes of vomiting at home containing partially digested food particles with no passage of blood & mucus.

The patient was having temperature of 100 Fahrenheit, blood pressure was 120/80 mm HG, respiratory rate of 18 breaths per minute and pulse rate of 75 (regularly regular). On examination, a young man of an average built lies comfortably in bed with no obvious distress or irritability. The overall examination was unremarkable and the patient was admitted for further management and workup.

The baseline investigations were ordered which showed leucopenia along with thrombocytopenia in CBC plus mild derangement of liver function tests which is as follows while all the other investigations were unremarkable including RFTs, CRP, S/E, Urine complete examination, malarial parasite, cultures. Since, the onset of symptoms was within 5 days, NS-1 antigen for dengue was sent which came out to be positive.

Table 1. *Investigations at presentation.*

Parameters	Patient's values	Normal range
Hemoglobin g/dl	12.5	13.5-17.5
WBC cells/uL	4000	4500-11,000
Platelets	80,000	150-450
MCV (fl)	85	80-100
MCH (pg)	27.0	27-31
RDW (%)	13.5	11.5-14.5
ALT	150	10-40
AST	200	10-40
ALP	120	30-120
Direct Bilirubin	0.5	0-0.3
Indirect Bilirubin	1.0	0.1-1.0
Albumin	3.0	3.5-5.0
Hematocrit%	40	40-50

The patient was isolated afterwards and was being managed with IV fluids, anti-emetics and anti-pyretic since the management of dengue break bone fever is purely symptomatic. At the third day of admission, the patient's condition got deteriorated as he developed drowsiness and altered state of consciousness for which he was shifted to M-ICU. The CBC done at that time showed raised hematocrit confirming the presence of dengue leak. In most of the cases, the 7th day of illness decides the course of disease i-e whether the patient is going to get recovered or development of complications as in this very care. The investigations done at that time are as follows:

Table 2. Investigations at 3rd day of admission.

Parameter	Patient's value	Normal range	Clinical significance
Hemoglobin	14.5	13.5-17.5	Hem-concentration due to plasma leakage
Hematocrit	48	40-50	Indicating plasma leakage
Platelet count	50,000	150-450	Severe thrombocytopenia, hall mark of DHF
WBC count	2500	4500-11000	Leukopenia, common in leak phase
Albumin	2.5	3.5-5.0	Low, indicating leak
Prothrombin time	16	11-14	Prolonged, indicating coagulation dysfunction
Serum creatinine	1.2	0.6-1.2	May be elevated due to hypo perfusion

Following the shifting to M-ICU, CT Brain (plain) of the patient was done which showed signs of cerebral edema

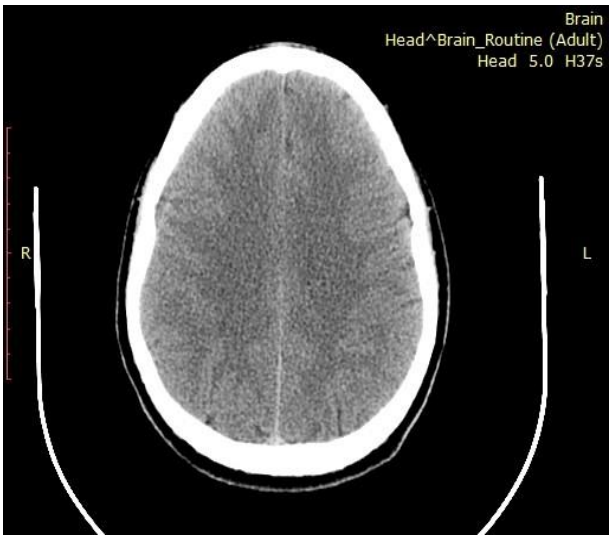

Figure 1. CT Brain showing Cerebral Edema.

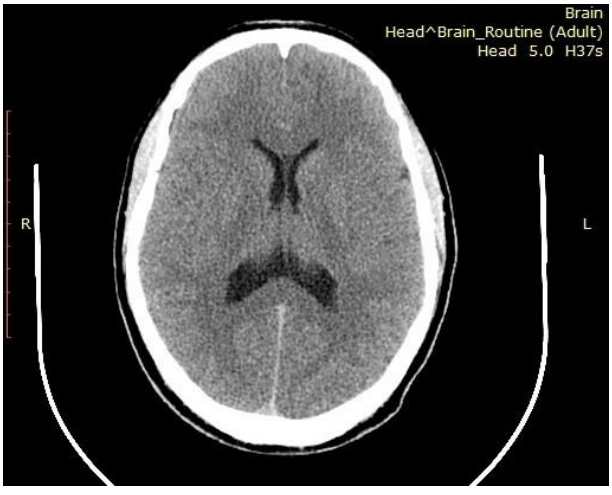

Figure 2. Ventricular compression secondary to Cerebral Edema.

Figure 3. Manifesting Cerebral Edema.

Followed by the lumbar puncture report which came out to be:

Table 3. Lumbar puncture.

Parameters	Patient's value	Normal range
Opening pressure	18	10-20
Color	Clear	Clear
White blood cells	20	0-5
RBCs	2	0
Lymphocytes%	85	60-79
Protein	70	15-45
Glucose	65	40-70
Gram stain	Negative	Negative
AFB	Negative	Negative

The lumbar puncture report was highly suggestive of Dengue Encephalitis after which the patient was put on IV Dexamethasone 8 mg every 6 hourly along with a stat shot of 200 ml IV Mannitol and 100 ml IV Mannitol every 8 hourly afterwards. The Herpes Simplex PCR, CSF culture and AFB smear was all negative. At 8th day of admission, the patient developed concurrent episodes of melena. Since the patient was not having any history of viral hepatitis or alcohol intake, the patient was put on Omeprazole continuous infusion at the rate of 8 mg/hr. The vitals and hemoglobin count was measured continuously which showed no significant drop in hemoglobin concentration. However, prophylactically he was transfused two units of FFPs prior to upper GI endoscopy. The report is as follows:

Findings:

1) *Esophagus*:

No abnormalities were noted. No evidence of varices or active bleeding.

2) Stomach:

Gastric Mucosa: Diffuse erythema and petechial hemorrhages were observed, consistent with hemorrhagic gastritis secondary to dengue.

Antrum: Multiple areas of mucosal oozing were noted.

Active Bleeding: Present in the gastric antrum with slow oozing from the mucosa. No large ulcers or visible vessels.

3) Duodenum:

Mild inflammation was seen in the first part of the duodenum (duodenitis).

No active bleeding or ulcers identified.

Figure 4. *Upper GI Endoscopy showing Duodenal erosions leading to Upper GI Bleed.*

The patient was managed on high dose of PPIs and 2 table spoons of Sucralfate syrup afterwards. On 15th day, the patient's GCS started to improve and he was discharged on 20th day of admission with 15/15 GCS and called for follow up.

3. Discussion

Dengue fever is a viral illness caused by the dengue virus, primarily transmitted to humans through the bites of infected Aedes mosquitoes, particularly Aedes aegypti and Aedes albopictus [5]. It is prevalent in tropical and subtropical climates, especially in urban and semi-urban areas. Symptoms typically appear 4 to 10 days after being bitten and can range from mild to severe [6]. Common symptoms include high fever, severe headaches, pain behind the eyes, joint and muscle pain, fatigue, nausea, vomiting, skin rash, and mild bleeding, such as nosebleeds or gum bleeding. In some cases, dengue can progress to severe dengue, characterized by severe abdominal pain, persistent vomiting, rapid breathing, bleeding, fatigue, and decreased platelet count [7]. Diagnosis is primarily clinical, supported by laboratory tests, including the dengue NS1 antigen test, serology for IgM and IgG antibodies, and RT-PCR for viral RNA detection in the early stages [8]. The illness generally follows a three-phase course: the febrile phase lasts 2 to 7 days, followed by a critical phase that can present severe complications, and finally a recovery phase that may last 2 to 3 days. Most cases of dengue fever are self-limiting and resolve within a week, but severe cases can lead to life-threatening complications if not managed promptly, making timely medical attention essential, especially for patients exhibiting signs of severe dengue [9].

Dengue fever can lead to several complications, particularly in cases of severe dengue, also known as dengue hemorrhagic fever or dengue shock syndrome [10]. These complications can be life-threatening and require immediate medical attention.

1) *Hemorrhagic Manifestations*: Patients may experience bleeding from the gums, nose, or gastrointestinal tract, which can lead to significant blood loss.
2) *Shock*: Severe dengue can cause a sudden drop in blood pressure (dengue shock syndrome), leading to inadequate blood flow to vital organs. This condition can be fatal if not treated quickly.
3) *Organ Impairment*: The liver can become enlarged and may show signs of dysfunction, while other organs, such as the heart and kidneys, can also be affected.
4) *Fluid Accumulation*: Patients may develop pleural effusion (fluid in the chest cavity) or ascites (fluid accumulation in the abdomen), contributing to respiratory distress and abdominal discomfort [11].
5) *Severe Neurological Complications*: In rare cases, dengue can lead to neurological issues, such as encephalitis or seizures [12].
6) *Acute Respiratory Distress Syndrome (ARDS)*: This serious condition can develop due to fluid overload or complications from bleeding, leading to severe respiratory failure.
7) *Mortality*: Although most cases of dengue are mild, severe dengue can result in death, particularly in high-risk populations such as children and individuals with pre-existing health conditions.

Warning signs in dengue fever indicate a progression towards severe dengue, requiring immediate medical attention.

These warning signs typically occur after the initial fever has subsided, usually around days 3 to 7 of the illness [13]. Key warning signs include:

1) *Severe Abdominal Pain*: Persistent and intense pain in the abdominal area, which may indicate complications such as bleeding or organ impairment.
2) *Persistent Vomiting*: Frequent vomiting that does not subside, which can lead to dehydration and complicate the patient's condition.
3) *Rapid Breathing*: Increased respiratory rate may indicate fluid accumulation in the lungs or shock.
4) *Bleeding*: Signs of bleeding, such as bleeding gums, nosebleeds, or blood in vomit or stool, can suggest severe dengue and require urgent evaluation.
5) *Fatigue and Restlessness*: A sudden change in energy levels, including increased fatigue or irritability, can signal deterioration.
6) *Decreased Platelet Count*: A significant drop in platelet levels, which can be monitored through blood tests, is a key indicator of severe dengue.
7) *Fluid Accumulation*: Symptoms of fluid overload, such as swelling in the abdomen or extremities, may indicate serious complications.
8) *Shock Symptoms*: Signs of shock include cold or clammy skin, rapid pulse, and low blood pressure, which require immediate medical intervention.

In dengue, blood product transfusion is typically reserved for specific indications, given the risks associated with transfusion and the dynamic nature of dengue [14]. Here are the indications for transfusing different blood products:

1) *Packed Red Blood Cells (PRBCs)*
   a. *Significant bleeding*: When there's clinically significant bleeding (e.g., upper GI bleed or severe mucosal bleeding).
   b. *Symptomatic anemia*: If anemia is symptomatic or if hemoglobin levels fall below a critical threshold (often <7-8 g/dL, depending on the patient's condition).
   c. *Hemodynamic instability* due to blood loss that does not improve with fluid resuscitation.
2) *Platelets*
   a. *Severe thrombocytopenia with active bleeding*: Platelet transfusions are generally considered if platelet count is <10,000/μL, even in the absence of bleeding, due to high risk of spontaneous bleeding.
   b. *Active bleeding with platelet count <30,000/μL.*
   c. *Prior to invasive procedures*: If the patient requires an invasive procedure (e.g., lumbar puncture, central line placement), platelet transfusion may be indicated to reduce bleeding risk.
3) *Fresh Frozen Plasma (FFP)*
   a. *Coagulopathy with active bleeding*: If the patient has bleeding with evidence of coagulopathy (elevated PT/INR), FFP may be indicated.
   b. *Severe liver involvement*: FFP may be considered in cases of dengue with liver impairment, resulting in coagulopathy and active bleeding.
   c. *Preparation for procedures*: FFP may also be considered before invasive procedures in patients with coagulopathy.
4) *Cryoprecipitate*

Fibrinogen <100 mg/dL with bleeding: In cases where there is bleeding, and fibrinogen levels are low, cryoprecipitate can be given to support clotting.

4. Conclusion

In conclusion, this case report underscores the importance of recognizing atypical presentations of dengue fever, such as dengue encephalitis and upper gastrointestinal bleeding. By highlighting these uncommon manifestations, we emphasize the need for healthcare providers to maintain a high index of suspicion for dengue in patients presenting with unexpected symptoms, especially in endemic regions. Timely diagnosis and appropriate management are crucial for preventing severe complications and improving patient outcomes. This case not only contributes to the growing body of literature on dengue fever but also serves as a reminder of the disease's diverse clinical spectrum, reinforcing the necessity for continued vigilance and education in the face of evolving infectious diseases.

Abbreviations

DHF	Dengue Hemorrhagic Fever
DSS	Dengue Shock Syndrome
FFPs	Fresh Frozen Plasma
MCV	Mean Corpuscular Volume
MCH	Mean Corpuscular Hemoglobin
RDW	Red Cell Distribution Width
AFB	Acid Fast Bacilli

Patient's Consent

Informed consent was obtained from the patient.

Authors Contributions

Waqar Hafeez: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing

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Conflicts of Interest

The authors declare no conflicts of interest.

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