CASE REPORT

Unmasking atypical dengue: A case of multi-organ failure and acute coronary syndrome

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Abstract

This case report discusses a rare and challenging presentation of dengue haemorrhagic fever (DHF) in a 62-year-old male, complicated by acute coronary syndrome (ACS) and multi-organ failure (MOF). The patient was initially afebrile, presented with respiratory symptoms, and was diagnosed with non-ST elevation myocardial infarction (NSTEMI) and cardiogenic shock. Dengue serology confirmed a secondary dengue infection with profound thrombocytopenia, respiratory failure, and cardiogenic shock. Coronary angiography revealed triple-vessel disease, prompting consideration of coronary artery bypass grafting (CABG). However, owing to severe dengue-related complications, a multidisciplinary team deferred surgery in favour of medical management, leading to gradual haemodynamic recovery. This case underscores the importance of recognising atypical dengue presentations, especially in endemic regions, and highlights the complex interplay between dengue and pre-existing coronary artery disease in acute coronary syndrome (ACS). Prompt diagnosis, multidisciplinary collaboration, and individualised management are crucial for improving the outcomes in severe dengue cases with cardiac involvement.

Keywords: Dengue haemorrhagic fever, Acute coronary syndrome, Multi-organ failure, Cardiogenic shock, Thrombocytopenia, Coronary artery disease, Multidisciplinary management.

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Introduction

Dengue fever, a prevalent mosquito-borne viral illness in tropical and subtropical regions, presents with a range of symptoms, from mild fever to severe manifestations, such as dengue haemorrhagic fever (DHF) and dengue shock syndrome.[1-4] While DHF classically involves bleeding, thrombocytopenia, and plasma leakage, atypical presentations with multi-organ involvement are increasingly recognised.[5] Although rare, cardiac complications, ranging from electrocardiographic changes and arrhythmias to myocarditis, pericarditis and heart failure, can occur.[2,6] Acute coronary syndrome (ACS), characterised by reduced blood flow to the heart, is an uncommon but serious complication of dengue.[6]

The pathophysiology linking dengue to ACS is not completely understood; however, potential mechanisms include endothelial dysfunction, platelet activation, and cytokine storm, leading to plaque rupture or coronary vasospasm. Multi-organ failure (MOF), a life-threatening condition affecting multiple organ systems, can complicate severe dengue infections. The pathogenesis of MOF in dengue probably involves a complex interplay of factors including direct viral damage, immune dysregulation, and microvascular dysfunction. This can lead to a cascade of events, resulting in organ dysfunction and ultimately failure.[5] Early recognition and aggressive management are crucial for improving the outcomes of patients with dengue-associated MOF.

This report presents a rare case of DHF complicated by both ACS and MOF. The aim is to highlight the unusual cardiac and multi-systemic manifestations of dengue and emphasise the importance of considering these complications in patients with severe dengue, particularly those presenting with atypical symptoms. This report also underscores the need for further research to elucidate the underlying mechanisms and optimal management strategies for these rare but serious complications.[3] By presenting this case, we hope to raise awareness among healthcare professionals about the potential for severe and atypical presentation of dengue fever, ultimately leading to improved patient care and outcomes. Early identification and prompt treatment of these complications are essential to minimise the morbidity and mortality associated with severe dengue infections.

Case Report

The case was first seen at Shifa International Hospital, Islamabad, Pakistan, on September 5, 2024. A 62-year-old male patient with diabetes mellitus and thalassemia.

Presented to the emergency room with a two-day history of fever, cough, and generalised weakness. He initially

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sought care at a local hospital where he received a provisional diagnosis of respiratory infection and was treated with intravenous antibiotics (details unavailable). The patient was on steroids for unknown reasons. However, his symptoms persisted and his condition continued to deteriorate. Therefore, the family decided to shift him to Shifa Hospital.

On arrival in the emergency room, he exhibited shortness of breath with a respiratory rate of 25b/min, oxygen saturation of 91% on room air, pulse 110, blood pressure 83/65, Glasgow Coma Scale (GCS)15/15, and was afebrile. He was initially placed on oxygen via a face mask at 5 L/min, followed by a BiPAP support with 15 litres of oxygen. A right femoral central venous pressure (CVP) line was inserted, and Norepinephrine infusion was initiated to support his blood pressure. After initial management, his blood pressure improved, but he remained tachycardic and tachypnoeic. His initial laboratory workup showed elevated cardiac enzyme levels (TropI 22,820), and an initial echocardiogram revealed severe left ventricular failure with an ejection fraction of 25-30%. The patient was subsequently diagnosed with NSTEMI, cardiogenic shock, and respiratory failure secondary to pulmonary oedema. The cardiology team advised starting acute coronary syndrome protocol which include aspirin, Ticagrelor, Rovista, I/V Heparin bolus, and infusion. The patient received intravenous Furosemide for pulmonary oedema. IV Tanzo (Piperacillin and Tanzobactam) was started empirically after taking blood for CS. He also received stress dose steroids. After initial management, the patient was shifted to a medical step-down unit for further management.

Coronary angiography done on the second day of admission revealed triple-vessel coronary artery disease with a critical left main stenosis. The cardiology team advised emergency CABG. Cardiothoracic surgery department was informed. On the fourth day of admission, the patient was transferred from the medical step-down unit to the surgical step-down unit. His haemodynamic status continued to deteriorate, requiring triple inotropic support with Vasopressin, Norepinephrine, and Dobutamine. Finally, an intra-aortic balloon pump (IABP) was placed in the surgical step-down unit to provide haemodynamic support before CABG. On the fifth day of his admission, pre-operative anaesthesia evaluation revealed a declining platelet count, dropping from 257k on admission to 36k, raising concerns about heparin-induced thrombocytopenia (HIT) or dengue-induced thrombocytopenia, given the endemic nature of dengue in the region. A haematology consultation was sought, and based on their advice, dengue serology and HIT (heparin-induced thrombocytopenia) testing were performed. Platelet factor 4 (PF-4) IgG antibodies for HIT were negative. However, the dengue rapid NS1 antigen and IgG were positive, whereas IgM was weakly positive. Subsequent platelet ELISA immunosorbent assay returned positive results. Positive

Table: Serial laboratory investigations during hospital stay.

Parameter	Day 1	Day 3	Day 4	Day 8	Day 9	Day 11	Day 12	Day 14	Day 17	Day 20	Day 24
Haemoglobin (g/dL)	9.3	9.5	8.8	6.5	8.9	8.2	8.4	7.3	10.3	10.0	10.2
Haematocrit (%)	30.7	29.7	27.2	20.8	28.3	27.4	27.0	23.9	30.3	32.7	33.8
Total leukocyte count (/µL)	9070	18210	9910	18100	17660	21640	21600	15000	12150	9840	8010
Platelet count (/µL)	257000	207000	53000	58000	38000	86000	75000	74000	93000	108000	108000
Urea (mg/dL)	59.9	115.6	115.6	59	75	75	100	117	102.7	72.0	–
Creatinine (mg/dL)	1.50	1.78	1.67	0.86	1.07	1.06	1.01	1.00	1.09	0.79	–
BUN (mg/dL)	28	54	54	28	35	35	47	55	48	34	–
AST (U/L)	222	–	1221	407	258	110	146	101	48	37	–
ALT (U/L)	102	–	791	516	176	200	138	149	86	48	–
ALP (U/L)	66	–	243	205	169	158	296	332	218	147	–
Total bilirubin (mg/dL)	0.71	–	1.75	2.07	1.72	1.25	1.23	1.81	1.36	1.45	–
Direct bilirubin (mg/dL)	0.38	–	1.49	1.36	0.97	0.81	0.40	1.28	0.83	0.94	–
GGT (U/L)	107	–	950	461	336	–	–	–	203	149	–
Prothrombin time (sec)	14.9	–	12.5	11.2	12.0	14.7	–	–	–	–	–
APTT (sec)	29.6	–	107.9	30.1	–	28.9	–	–	–	–	–
INR	1.37	–	1.15	1.04	1.11	1.35	–	–	–	–	–
Sodium (mEq/L)	137	135	135	156	150	146	139	143	155	151	–
Potassium (mEq/L)	4.7	4.0	3.3	3.4	4.1	3.9	3.8	3.6	3.6	3.4	–
Bicarbonate (mEq/L)	16	19	24	30	27	27	29	23	29	27	–
Troponin-I (pg/mL)	22820	–	–	–	–	–	–	–	–	–	–
CK-MB (ng/mL)	129.2	59.3	41.0	–	–	–	–	–	–	–	–
Dengue NS1 antigen	Positive	–	–	–	–	–	–	–	–	–	Negative
Dengue IgM antibody	Positive	–	–	–	–	–					Negative

Values shown are serial laboratory measurements obtained during hospitalisation.

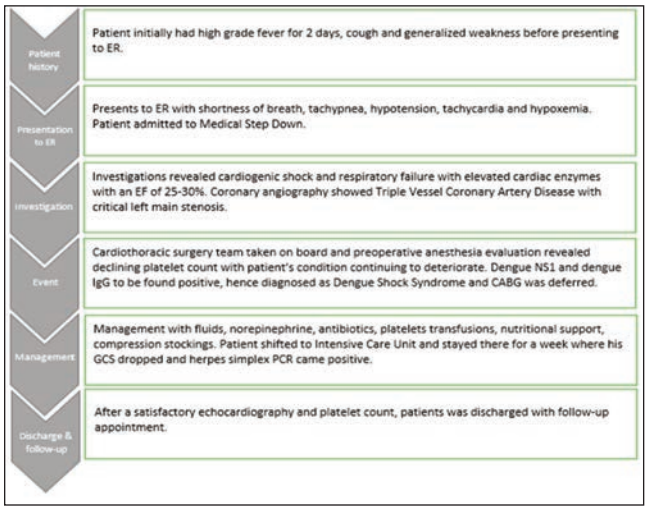

Figure: Case summary.

IgG with weakly positive IgM suggests either a late phase of primary dengue infection or, more likely, a secondary dengue infection where IgG levels rise rapidly and persist for a longer duration. A graphical summary of the case is presented in Figure and investigations are presented in Table.

Upon confirmation of dengue infection as the cause of thrombocytopenia and multi-organ dysfunction, including deranged liver function tests, elevated creatinine, respiratory insufficiency requiring BiPAP support, and cardiogenic shock requiring inotropic support and IABP, a multidisciplinary team (MDT) meeting was called to assess the surgical risk. The meeting involved consultants from anaesthesiology, intensive care, cardiology, cardiac surgery, infectious disease, and haematology. The multidisciplinary team (MDT) agreed that considering the patient's current condition, proceeding with cardiac surgical revascularisation would carry a very high risk. Instead, they recommended focussing on medical management as a safer option. This plan was discussed with the family who understood the situation and supported the decision. The patient was transferred to the intensive care unit for medical management. On the seventh day of hospitalisation, the patient developed irritability and restlessness, followed by a drop in GCS to 12/15. A neurological consultation was conducted, and based on their advice, a lumbar puncture and a CT brain scan were performed. The CT scan result was unremarkable, but the cerebrospinal fluid (CSF) tested positive for herpes simplex PCR. The patient was started on Acyclovir to treat herpes encephalitis.

On the eighth day of hospitalisation, the intra-aortic balloon pump (IABP) was removed, and the patient was successfully weaned off inotropic support by the 13th day. Throughout hospitalisation, blood cultures remained negative, although urine cultures revealed Candida albicans. The patient was treated with multiple empirical antibiotics to prevent any superimposed bacterial infections. Additionally, the patient received multiple blood and A blood product transfusions, particularly platelet transfusions. His overall condition showed significant improvement on subsequent days. Finally, he was able to be moved from the medical ICU to the floor and was discharged from the hospital. His total ICU stay was 10 days and hospital stay was 23 days. Upon discharge, the patient was prescribed insulin, Carvedilol, Frusemide, Atorvastatin, Clopidogrel, Acyclovir, and Aspirin. Follow-up over the next three months showed no significant clinical complaints.

Discussion

This case highlights a rare and challenging presentation of dengue haemorrhagic fever complicated by acute coronary syndrome and multi-organ failure.[5] Several atypical features distinguished this case from the typical presentation of DHF. First, the patient was afebrile in the emergency room, masking the underlying dengue infection. Although fever is a hallmark of dengue, afebrile presentations, particularly in the critical phase, have rarely been reported. This atypical presentation can delay diagnosis and appropriate management, as observed in this case. This case underscores the importance of considering dengue haemorrhagic fever in patients presenting with atypical symptoms even in the absence of fever. This emphasises the need for heightened clinical suspicion and prompt diagnostic testing in endemic regions to prevent delays in critical care management.

Second, the patient's initial symptoms were predominantly respiratory, with shortness of breath and hypoxia as the primary complaints. Although respiratory involvement can occur in dengue, it is usually a later manifestation, often secondary to plasma leakage and pulmonary oedema. The prominence of the respiratory symptoms in this case further obscured the diagnosis of DHF.

Third, cardiac involvement was evident only through elevated cardiac enzyme levels and echocardiographic findings of left ventricular dysfunction. Subsequent angiography revealed triple-vessel coronary artery disease, suggesting ACS as a contributing factor to cardiac compromise. Although cardiac manifestations can occur in dengue, ranging from arrhythmias to myocarditis, the presence of significant coronary artery disease adds another layer of complexity. The interplay between dengue infection and pre-existing coronary artery disease in the development of ACS warrants further investigation.[6] While this case presents compelling evidence for the complexity

of diagnosing DHF with cardiac involvement, it is important to consider alternative explanations. Elevated cardiac enzymes and left ventricular dysfunction could potentially be attributed to the stress of severe dengue infection itself, rather than underlying coronary artery disease. Furthermore, the angiographic findings of triple-vessel disease may have been incidental and not directly related to the acute presentation, as chronic coronary artery disease can occur without causing acute symptoms.

Finally, the decision to postpone coronary artery bypass graft surgery due to the patient's severe dengue and multi-organ failure likely averted a potentially fatal outcome. This case highlights the need for a comprehensive approach to patient assessment that considers both acute and chronic cardiovascular conditions. Further research into the mechanisms by which dengue infection may exacerbate or unmask the underlying coronary artery disease could provide valuable insights for clinical management. The challenge of differentiating between cardiac complications directly caused by dengue infection and those resulting from pre-existing coronary artery disease underscores the importance of thorough diagnostic evaluation and individualised treatment strategies in complex cases. Surgery in the setting of active dengue infection, particularly with thrombocytopenia and multi-organ dysfunction, carries a high risk of bleeding and other complications.[4,7] The interplay between acute dengue infection and chronic coronary artery disease presents a complex clinical scenario that requires careful consideration of the risks and benefits of the various management strategies. Clinicians should remain vigilant for the potential cardiac manifestations of dengue fever, which may mimic or exacerbate the symptoms of pre-existing coronary artery disease. Close monitoring of coagulation parameters, organ function, and cardiac biomarkers is essential for guiding treatment decisions and determining the optimal timing of surgical interventions in patients with concurrent dengue infection and cardiovascular disease. In this case, the multidisciplinary approach enabled a comprehensive assessment and balanced decision regarding surgical intervention. This case highlights the critical importance of a multidisciplinary approach for managing complex clinical scenarios involving acute dengue infection and chronic coronary artery disease. This underscores the need for careful risk-benefit analysis and close monitoring of patients to optimise treatment outcomes in such challenging situations.

Conclusion

This case underscores the importance of considering dengue infection in patients presenting with atypical symptoms, particularly in endemic regions. The absence of fever, predominance of respiratory symptoms, and presence of significant coronary artery disease masked the underlying dengue infection, delaying appropriate management. The decision to postpone CABG surgery likely prevented fatal outcomes. A high index of suspicion for dengue in patients presenting with unexplained multi-organ failure, even in the absence of classical symptoms, is crucial.

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