Case report

DENGUE WITH SICKLE CELL ANAEMIA ASSOCIATED WITH ACUTE LIVER FAILURE: A CASE REPORT

ABSTRACT

Aim: Dengue fever is a major health risk in endemic regions, and its complications can be severe in individuals with underlying haematological conditions like sickle cell anaemia (SCD). SCD increases the risk of Vaso-occlusive crises, haemolysis, and multi-organ dysfunction, which can be exacerbated by dengue's endothelial damage. This case highlights the rare and complex interaction between SCD and dengue fever, particularly the severe hepatic complications due to co-existing illness, emphasizing the need for specialized treatment strategies.

Case Presentation: A female patient from Chikkaballapur, Karnataka, India, with sickle cell anaemia (SCD), presented with dengue shock syndrome and severe hepatic complications. She experienced fever, shock, and liver dysfunction, worsened by both dengue and SCD. Diagnostic challenges arose due to overlapping symptoms. Management included careful hydration, pain control, and transfusion therapy, with close monitoring.

Conclusions: This case demonstrates the complexities of managing patients with both SCD and dengue fever. The interaction between dengue-induced endothelial damage and SCD can lead to severe complications, including organ failure and death. Timely intervention, close monitoring, and a multidisciplinary approach are essential for improving outcomes. This case underscores the need for specific treatment guidelines for managing dengue in SCD patients to reduce morbidity and mortality.

KEYWORD: Sickle cell disease (SCD), Dengue shock syndrome, Dengue infection, Acute liver failure

INTRODUCTION

Dengue fever is a mosquito borne tropical infection caused by flavivirus and transmitted by *Aedes aegypti and Aedes albopictus.* Over the past 60 years, the prevalence of strains and the severity of the disease have significantly increased, contributing to the complexity of the epidemiology of dengue fever in India.[1] Worldwide dengue affects 390 million individuals annually.[2]

Sickle cell anaemia is the result of substitution of valine for glutamine at position sixth in the beta chain of haemoglobin.[3] India has the highest disease frequency in South Asia with approximately 20 million SCD patients.[4]

Patients with sickle cell disease (SCD) who visit undeveloped tropical nations have a significant risk of developing malaria, bacterial infections and sickle cell-associated Vaso

occlusive crises.[5] Endothelial dysfunction is known to happen in SCD but there is no sufficient evidence that the dengue virus replicates in endothelial cells. Dengue fever triggers the sickling process by exacerbating endothelial dysfunction in sickle cell disease (SCD) patients, which is the primary identified cause of organ dysfunction.[6] The permeability of the vascular endothelial layer can increase due to either erythrocyte sickling or DENV infection by inflicting the Vascular endothelial cells damage. This can result in the release of cytokines, plasma leakage, and severe shock. Based on these results, we hypothesize that endothelial cells play a crucial role in exacerbating the severity of the disease.[2]

We present a unique case of a female SCD patient who was admitted to Aster CMI Hospital, Bengaluru with dengue fever leading to dengue shock syndrome associated with sickle cell crisis, and she eventually passed away from fatal hepatic complications resulting from accelerated severe endothelial dysfunction, which was caused by comorbidities and dengue infection.

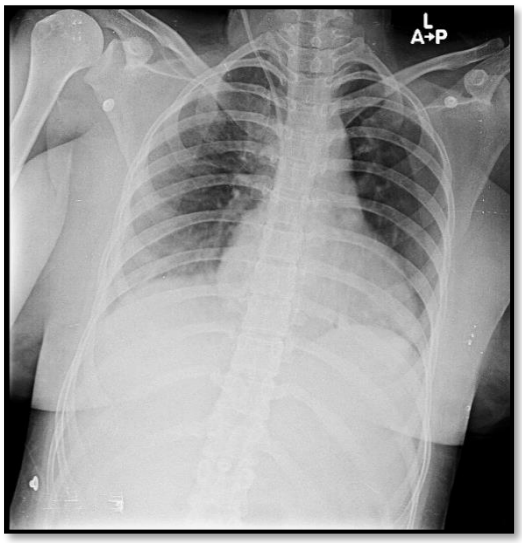
PRESENTATION OF CASE:

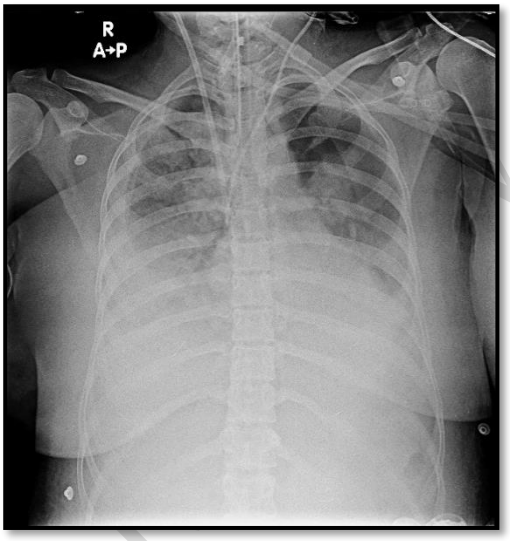
A 23-year-old female patient who was originally from Chikkaballapura, Karnataka, presented with the history of abdominal pain and multiple episodes of vomiting for 2 days. vomiting is non bilious, non-blood stained, non-projectile, containing food particles. Evaluation outside shows dengue NS1+, platelets- 46k, Liver Function Test deranged, found to have hypotension, started on Noradrenaline and was referred to Aster CMI Hospital for further management. Familial history of sickle cell anaemia was found but was not checked for the patient. History of jaundice during her childhood was found and history of dengue deaths among 2 siblings.

The patient presented with above complaints at Aster CMI Hospital. On clinical examination CNS-conscious, oriented and obeying commands. Pallor and icterus were positive associated with cold extremities and rashes all over the body. BP- 90/60mmHg, Heart Rate- 134bpm, Respiratory Rate- 24cpm, SPO_2- 94%, CVS- S1, S2 heard, RS- Bilateral air entry (+) no added sounds, P/A- soft, diffused tenderness, Temperature-97^0F, necessary investigations were done at ER.

In view of hypotension, patient required inotropic support and was shifted to MICU. Patient was administered with INJ CEFTRIAXONE 1GM IV Q12H for 4 days, INJ DOXYCYCLINE 100MG IV Q12H for 4 days then escalated it to INJ MEROPENEM 1GM IV Q8H for another 3 days, INJ PANTOPRAZOLE 40MG IV Q24H, INJ EMESET 4MG IV Q12H, INJ PARACETAMOL 500MG IV Q6H, INJ NERVIEJN 1AMP IV Q24H and other supportive measures. Liver function test report shows hyperbilirubinemia with elevated SGOT/SGPT-1770/1022, hence medical gastroenterology opinion was sought, suggested N- ACETYL CYSTEINE infusion 2GM in 100ML DEXTROSE 5% over 30 minutes to prevent acute liver failure. Patients report shows decreasing hemoglobin levels and high INR- 2.58sec. Repeated platelet count tests showed thrombocytopenia and ABG showed metabolic acidosis. USG A/P shows mildly altered echo texture of liver, reactive Gall bladder wall edema, isoechoic solid soft tissue in the splenic fossa which revealed Atrophic spleen, moderate ascites and bilateral mild pleural effusion (RT>LT). On day 2, hematology opinion was sought in view of thrombocytopenia, suggested sickling test which revealed positive sickle cell crisis, hence added INJ THIAMINE 200MG IV Q12H and INJ DEXAMTHASONE 8MG IV Q8H to treat painful occlusive events associated with SCD. On day 3, patient was intubated and mechanically ventilated in view of restlessness and respiratory distress. Patient developed severe epistaxis; hence ENT opinion was taken, suggested anterior nasal packing with foley's

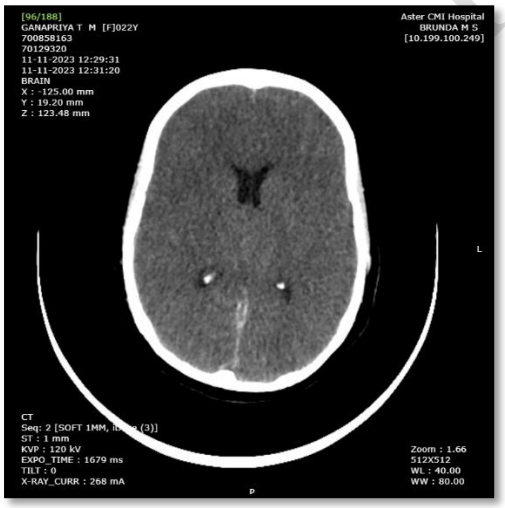
to cauterize bleeding points which was done on day 3 in operation theatre under general anesthesia. Infectious disease specialist opinion was sought in view of atypical dengue fever symptoms, which confirmed the presence of dengue shock syndrome. There are some features of secondary HLH (+)- markedly high serum ferritin-63350, LDH-3137 and markedly low initial fibrinogen- 47.2. multiple units of PRBC, SDP and FFP was transfused throughout the stay in the MICU. One cycle of exchange blood transfusion was done on day 4.

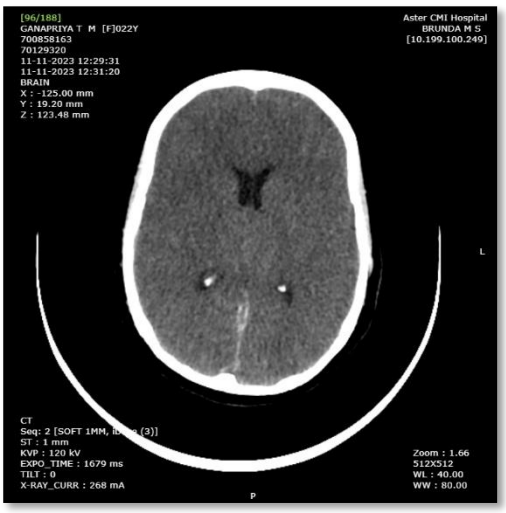




CHEST X RAY OF DAY 1
suggestive of mild haziness noted at bilateral lower lung Zone

CHEST X RAY OF DAY 5
suggestive of mild interval increase in the haziness noted at bilateral lower and mid lung





ONCO CT BRAIN: Diffuse cerebral edema with bilateral uncal herniation and tonsillar herniation. Features are suggestive of hypoxic ischemic encephalopathy, could be due to sickle crisis

Onco-CT revealed: extravasation of contrast in the nasopharynx or oropharynx, diffuse bulky and edematous pancreas with multiple non enhancing areas in the pancreas with few peri pancreatic lymph nodes, diffuse consolidation with confluent patchy ground glass opacities in the B/L lung parenchyma predominantly in the lower lobes, right moderate and left mild pleural effusion, hyperdense polypoidal lesion in the left maxillary sinus, calcified and atrophic spleen.

Hemoglobin continued to drop, in spite of no further nasal bleed or no melena or other external bleeds. On day 5, hematology review was done, suggested bone marrow biopsy and steroid administration. Nephrology opinion was taken in view of acute kidney injury, advised SOS hemodialysis. In view of fixed and dilated pupils, CT brain was done – diffuse cerebral edema with B/L uncal herniation and tonsillar herniation, features are suggestive of ischemic encephalopathy, could be due to sickle crisis. Patient was continued on ventilation and high ionotropic support in view of low GCS E1V1M1 and persistent hypotension. One cycle of sustained low-efficiency dialysis (SLED) was done on day 5 in view of high serum ammonia. Patient attenders were clearly explained about the critical condition of the patient and the grave prognosis of the disease. Patient's condition started to deteriorate progressively despite optimal medical management and vasopressor infusions was increased to maximum. Patient had a cardiac arrest at 5:30pm and CPR was initiated and it lasted for more 30minutes. Patient's ECG was done which showed a flat line and she succumbed to her death on day 6 at 6:10pm.

DISCUSSION

Dengue fever is a prevalent cause of fever in developing countries and is regarded as one of the most significant viral infections transmitted by arthropods. It impacts human health, quality of life, and can contribute to mortality.[12] Around 80% of dengue infections are asymptomatic, while less than 20% of those infected show clinical symptoms, and 2.5% result in death each year.[13]

Sickle cell anaemia (SCA), an autosomal recessive disorder, is caused by the substitution of valine for glutamic acid at the position of the beta-globin gene.[14] Although the mechanical fragility and vaso-occlusive characteristics of sickled erythrocytes have long been identified as key factors in the pathophysiology of SCA, recent evidence indicates that oxidative damage plays a crucial role in driving vascular complications. [15]

Severe dengue is known to develop in people with chronic diseases such as sickle cell disease (SCD), hypotension, diabetes, ischemic heart disease, and alcohol consumption. However, there is a lack of research on dengue in people with SCD. [7,8] The following conditions must be met for considering as severe dengue: severe bleeding, significant organ involvement, particularly the liver (AST or ALT levels greater than 1000), severe plasma leakage that might cause dengue shock syndrome and fluid accumulation with respiratory distress. impaired consciousness in the central nervous system, the heart, and other organs.[9] Although the precise pathophysiology of dengue-related liver damage is unknown, vascular leakage and hypoxia have been demonstrated to play an important role.[7,8] At admission, our patient presented with history of abdominal pain and multiple episodes of vomiting for 2 days, outside evaluation showed dengueNS1 positive and later on, a clinical picture resembling severe dengue. Liver function test report shows hyperbilirubinemia with elevated AST/ALT- 1770/1022. Haematology opinion was sought in view of thrombocytopenia, suggested sickling test which revealed positive sickle cell crisis. However, it turned out that our patient actually had sickle cell trait (SCT), which was previously not diagnosed.

There is poor clinical outcome for dengue infection in sickle cell anaemia (HbSS). Studies already conducted indicate that individuals with a relatively moderate genotype (haemoglobin SC - HbSC) may be at a higher risk of fatal dengue, while the precise incidence and magnitude of risk remain unknown.[10]

We believe that our patient's liver failure was caused by the predisposition of endothelial damage in SCD and dengue, which ultimately led to the most severe form of sickle hepatopathy, known as Sickle cell intrahepatic cholestasis (SCIC), which is ultimately fatal. The endothelium was directly harmed by dengue replication, which resulted in inflammation and coagulopathy, leading to sickling, increased plasma leak, and severe shock. Patients with SCD associated with dengue infection have been shown to have a mortality rate of approximately 50% within 24 hours.[11] Our patient survived for 6 days despite early ICU admission and treatment initiation, and transfusions.

CONCLUSION

Dengue infection is known to cause multi-organ dysfunction. Acute degeneration may be exacerbated by coexisting, previously undetected illnesses such as sickle cell trait. A high index of clinical suspicion aids in early detection of comorbidities, and careful observation helps in the proper management of complicated dengue cases. Since a large portion of the world's SCD population is from our nation and dengue epidemics are annual event, hence developing guidelines for the treatment of dengue-associated complications in SCD is becoming more and more crucial.

Disclaimer (Artificial intelligence)

Option 1:

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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