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Case Report

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Dengue fever leading to acute dengue hemorrhagic leukoencephalitis: A case report

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ABSTRACT

Rationale: Dengue fever is a prevalent tropical infectious disease that has a broad panorama of presentations from mild febrile illness to life-threatening manifestations in the form of dengue hemorrhagic fever and dengue shock syndrome.

Patient's concerns: A 20-year-old male presented with a 2-day history of fever, multiple episodes of vomiting, and altered sensorium.

Diagnosis: Dengue fever leading to acute hemorrhagic leukoencephalitis.

Interventions: Multiple transfusions of single donor platelets, intravenous methylprednisolone, intravenous immunoglobulin, anti-seizure prophylaxis, and broad-spectrum antibiotics.

Outcomes: Repeat brain magnetic resonance imaging showed resolution of lesions. The patient was subsequently discharged from the hospital in a healthy state.

Lessons: This report helps us to gain a better understanding of the patient's presentation, which will help to improve the timely recognition and prevention of this rare devastating presentation.

KEYWORDS: Dengue hemorrhagic fever; Dengue shock syndrome; Neurological manifestations; Hemorrhagic leukoencephalitis

1. Introduction

Dengue fever caused by an arbovirus is a widespread tropical infectious disease. The infection has a wide spectrum of presentations, ranging from mild fever to life-threatening conditions such as dengue hemorrhagic fever and dengue shock syndrome. Dengue hemorrhagic fever and dengue shock syndrome can present as a disaster of events secondary to vascular leak and hemorrhage, cerebral hypoperfusion, cerebral edema, and multisystem organ dysfunction[1]. Neurological manifestations are rare and have been observed only in 1%-3% of patients. Mechanisms resulting in neurological involvement include direct central nervous system viral invasion, autoimmunity, metabolic disturbances, and hemorrhagic disorders. Here we reported a 20-year-old patient diagnosed with dengue fever leading to acute hemorrhagic-leukoencephalitis.

2. Case report

Informed consent was obtained from the patient. The ethical approval has been obtained from the Ethical Committee of the Armed Forces Medical College.

A 20-year-old male, with no known comorbidity, presented with a 2 d history of fever and multiple episodes of vomiting and diarrhea. The next day, the patient developed an altered sensorium. An urgent head contrast-enhanced computed tomography scan was

Significance

Dengue fever leading to acute hemorrhagic leukoencephalitis is an uncommon complication. This report helps us to gain a better understanding of the patient presentation, which will help to improve the timely recognition and prevention of this rare devastating presentation.

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done, which showed cerebral edema and extensive demyelination. Blood investigations showed thrombocytopenia (platelet count: 40 000/cm^3, normal:150 000 to 450 000/cm^3), transaminitis (aspartate transaminase: 240 IU/L, normal: 8 to 33 IU/L), alanine transaminase: (257 IU/L, normal: 4 to 36 IU/L), raised creatinine (1.4 mg/dL, normal: 0.7 to 1.2 mg/dL), and positivity for dengue NS1Ag and IgM and IgG antibodies. Additionally, there was negative serology for scrub typhus, normal titers for enteric fever, and absence of visualization of malaria parasite on both thick and thin smears. Brain magnetic resonance imaging (MRI) revealed bilateral changes in cerebral hemispheres, cerebellar hemispheres, thalami, and brain stem with associated mass effect, and punctuate foci of hemorrhage within the white matter (Figure 1). MAC ELISA for dengue was positive, and dengue IgM and IgG antibodies were found in cerebrospinal fluid. Ultrasound of the abdomen showed mild to moderate ascites and bilateral pleural effusion. No features of papilloedema were found on fundoscopy. The patient was diagnosed to have dengue fever with dengue hemorrhagic leukoencephalopathy with multi-organ dysfunction syndrome.

The patient was managed with multiple transfusions of single donor platelets, intravenous methylprednisolone 1g *o.d.*, and intravenous immunoglobulin (IVIG) is given at the dose of 2 g/kg over 5 d. Other treatments included mannitol to reduce intracranial pressure, anti-seizure prophylaxis in the form of levetiracetam, broad-spectrum antibiotics, and routine care of a bedbound patient. Subsequently, transaminitis, creatinine, and thrombocytopenia started improving. On day 5, the patient showed improvement in sensorium. Repeat MRI brain showed resolution in previously seen altered signal intensity lesions in the tegmentum of the pons, bilateral cerebellar hemispheres, and vermis. Also, the punctate foci of hemorrhage seen within the white matter changes showed partial resolution, along with a reduction in the mass effect in the posterior fossa. The patient subsequently showed improvement in the symptoms and was discharged from the hospital.

3. Discussion

Dengue virus is a single-stranded RNA virus that belongs to the Flavivirus family. It is classified into four serotypes. Although, neurological manifestations of dengue infection are rare but can be seen most commonly with serotypes 2 and 3 or with reinfection with these serotypes. Neurological manifestations of dengue fever are classified into 3 categories[2]. The first category includes manifestations like encephalitis, meningitis, and myelitis which are related to the neurotrophic effect of the virus[3-5]. The second category includes post-infectious complications like encephalomyelitis, acute inflammatory demyelinating polyradiculoneuropathy, and optic neuritis. The third category includes systemic complications like stroke, encephalopathy, and delirium[6,7].

There are scanty case reports of dengue encephalitis. In these cases, most patients were presented with seizures episode, altered sensorium, or severe headaches. Additionally, the typical symptoms of dengue may present in 50% of dengue encephalitis patients. Therefore, intensivists must employ a high index of suspicion to distinguish this treatable entity. Imaging performs a complementary role in corroborating the final recognition of encephalitis diagnosis along with biochemical reports and clinical presentation. MRI findings are diverse. Haemorrhages diffuse cerebral edema, focal abnormalities involving the globuspallidus, the hippocampus, the thalamus, and the internal capsule can be found, with hyperintense lesions visualized in MRI. The involvement of the temporal lobe, hippocampus, pons, midbrain, bilateral gangliocapsular location, and spinal cord on MRI has been described in various case reports. MRI findings are usually nonspecific, and therefore common etiologies of viral encephalitis like Japanese encephalitis and herpes virus must be considered in the differential diagnosis[8]. Cerebrospinal fluid picture is required to finalize the etiological virus because most of the time it becomes strenuous to differentiate dengue hemorrhagic encephalitis

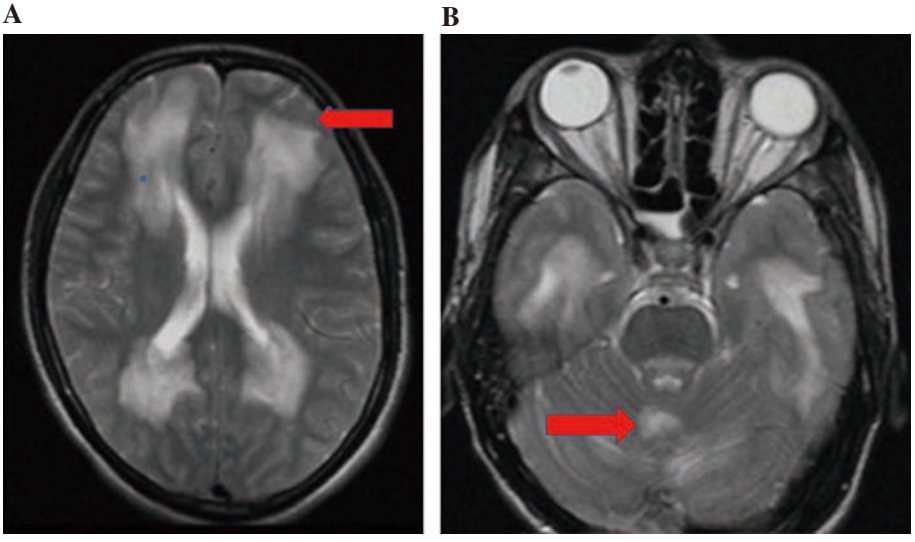

Figure 1. T2WI brain magnetic resonance imaging of a 20-year-old male. A: Hyperintensities in the subcortical areas (red arrow); B: Involvement of the tectum of the pons and cerebellum and deep white matter (red arrow).

from other viral aetiologies solely based on MRI findings.

Studies showed 5%-30% of patients who present with neurological complications lead to fatal consequences. Treatment is mainly supportive and includes the administration of steroids and IVIG. Steroids act by inhibiting Fc-receptor-mediated platelet phagocytosis and by reducing anti-platelet antibody synthesis. IVIG in the treatment of various autoimmune diseases is well established as an immunomodulator despite not a well-established mechanism of action. However, some studies did not show any mortality benefit of IVIG in dengue patients. The author emphasizes the importance of conduct of further trials and larger studies to find out the efficacy of IVIG in such patients.

To sum up, dengue fever leading to acute hemorrhagic leukoencephalitis is an uncommon complication. This report helps us to gain a better understanding of the patient presentation, which will help to improve the timely recognition and prevention of this rare devastating presentation.

Conflict of interest statement

The authors report no conflict of interest.

Authors' contributions

A.G. and P.D.D. collected and curated the data; S.S., S.K.N., and D.D. contributed to writing the manuscript; All authors read and approved the final manuscript.

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