Case report

Dengue encephalitis: A rare presentation of dengue fever

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Abstract

The prevalence of dengue fever in South Asian countries has been increasing for the last few years including Sri Lanka. Dengue encephalitis is an unusual and severe manifestation of dengue fever, with only a few cases being reported worldwide. This uncommon manifestation of dengue fever gives rise to many diagnostic dilemmas, thus challenging the treating physicians. Here, we report a case of dengue fever complicated with encephalitis with the typical magnetic resonance imaging (MRI) features. This report highlights the importance of considering dengue fever in patients presenting with fever and neurological manifestations.

Keywords: Dengue fever, Encephalitis, Double Doughnut sign

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Introduction

Dengue fever is one of the leading infectious diseases in Sri Lanka with increased morbidity and mortality. Approximately 37000 diagnosed cases were reported from all over the island during the first five months of the year 2023.1

Dengue virus is a Flavivirus, transmitted through the bite of an infected Aedes aegypti mosquito. Among the four virus serotypes, DEN-2 and DEN-3 are the serotypes commonly involved in neurological complications including dengue encephalitis [2]. A study which was conducted in India revealed that the dengue virus carries a prevalence of 5% among all the causative agents causing acute encephalitis [3].

Dengue fever can cause a spectrum of diseases which vary from undifferentiated fever to dengue shock syndrome and expanded dengue syndrome. The expanded dengue syndrome can give rise to serious consequences involving several organs including the brain, heart, liver and kidneys. Dengue encephalitis is one such serious manifestation [4].

This unusual, sinister manifestation of dengue can give rise to various diagnostic challenges. Hence, it is important to know dengue as an etiological agent for encephalitis.

Case Presentation

A 28-year-old lady, with a history of first trimester (T1) miscarriage 2 years back, was initially admitted to District General Hospital Dambulla, with high grade, intermittent fever for three days and vaginal bleeding for 2 days. She had a period of amenorrhoea for eight weeks. She was found to be complicated with another T1 miscarriage for the second time upon admission. Evacuation of retained products was done and she was transferred to National Hospital, Kandy due to ongoing high-grade fever and gradual onset of reduced responsiveness.
There was no history of fits nor urinary, gastrointestinal, or respiratory symptoms. There were no features of underlying connective tissue disorders or a history of arterial or venous thrombosis. Family members denied any psychotic episodes, high-risk sexual behaviour, tattooing, intravenous drug abuse, or previous blood transfusions.

On examination, she was drowsy with a Glasgow coma scale of 10/15 (E-4, V-1, M-5). Pupils were bilaterally equal and reactive to light. There was no neck stiffness. She was febrile and tachycardic with pulse rate of 120 beats per minute. The blood pressure was 140/80 mmHg. She had a right sided gaze palsy with bilateral spastic limbs with exaggerated reflexes (Right > Left). Plantar reflex was equivocal. There were no signs of underlying connective tissue disorders. No organomegaly was detected in the abdominal examination. The rest of the system examination was normal.

Non-contrast computed tomography (CT) of brain revealed an early infarction in the parietal lobe. The transvaginal scan was normal with no retained products. Full blood count revealed relative leukopenia (white blood cells - 3.52 × 10⁹/L) and thrombocytopenia (platelets - 113 × 10⁹/L). Haemoglobin was normal. C reactive protein (CRP) was 4.8mg/dl. Dengue NS 1 antigen, which was done at the local hospital was positive. Dengue encephalitis was considered as one of our major differential diagnoses with the given history and NS1 positivity. The possibility of a young stroke with cerebral venous sinus thrombosis or arterial thrombosis secondary to antiphospholipid syndrome was also highly considered given the background history of recurrent T1 miscarriages and NCCT brain report. The other differentials considered were thrombotic thrombocytopenic purpura, autoimmune and other infectious encephalitis. Initially, she was empirically managed with intravenous (IV) ceftriaxone 2g twice per day and IV acyclovir 500mg 8 hourly. However, contrast enhanced computed tomography (CECT) of brain did not reveal any features of cerebral venous sinus thrombosis.

Blood picture revealed recent evidence of viral infection with thrombocytopenia. There was no evidence of microangiopathic haemolytic anaemia. Dengue IgM antibody was also positive with negative IgG, confirming primary dengue infection. Liver functions were de-arranged with mild transaminitis. Erythrocyte sedimentation rate was 27mm/hour. Antinuclear antibody (ANA) was negative. Renal functions were normal. There was no growth in blood culture. Serologies for Epstein-barr virus, Cytomegalovirus and Varicella virus were negative.

Cerebrospinal fluid (CSF) analysis didn’t show any pleocytosis. Protein level was slightly elevated 68(8-32) with normal sugar levels. CSF culture for bacterial organisms were negative with negative serology for herpes simplex virus1, 2 and Japanese Encephalitis virus. However, Dengue RNA was not detected in CSF.

The absence of CSF pleocytosis with haematological evidence of thrombocytopenia with leukopenia prompted us to consider the possibilities of acute demyelinating encephalomyelitis (ADEM) secondary to dengue infection or dengue encephalitis. She was started on IV Methyl prednisolone 1g daily with IV Immunoglobulins in a dose of 0.4g/kg/day due to the suspicion of ADEM and withheld after confirmation of Dengue Encephalitis. Magnetic resonance imaging (MRI) of the brain revealed microhaemorrhages in bilateral thalami, cerebellum and bilateral posterior internal capsule which is highly suggestive of Dengue Encephalitis (Double Doughnut sign). [Figure 1][8]. Serology positivity for dengue and positive MRI features, confirmed the diagnosis of dengue encephalitis. IV Immunoglobulin was then withheld and prednisolone was tailed off. She was then offered physiotherapy with supportive care.

Her neurological deficits markedly improved with an improvement of GCS to 12 after two weeks of hospital stay. She was referred to a rehabilitation center for speech and physiotherapy upon discharge.

Figure 1: T1 low T2 FLAIR high signal intensities with micro haemorrhages in bilateral thalami (indicated with orange arrows) and cerebellar hemisphere (indicated with green arrows) and involvement of posterior limbs of bilateral internal capsule (indicated with yellow arrows) suggestive of dengue encephalitis]
Dengue is a vector borne viral infection that spreads from mosquitoes to people. It is more common in tropical and subtropical climates. Dengue virus (serotypes DEN-1, 2, 3, 4) is a Flavivirus, which is transmitted through the bite of an infected Aedes aegypti mosquito. As per the census of the World Health Organization (WHO), the number of dengue cases has increased to nearly nine times in the last two decades [2].

DEN-2 and DEN-3 are the serotypes commonly involved in neurological complications with central nervous system (CNS), peripheral nervous system (PNS) and ophthalmic involvement. The involvement of CNS can manifest as ischemic/haemorrhagic stroke, encephalitis, ADEM and transverse myelitis. Peripheral nervous system manifestations are long thoracic nerve palsy, abducens nerve palsy, facial palsy, brachial neuritis and Guillain-Barre syndrome. Ophthalmic involvement can give rise to maculopathy, optic neuropathy, and subconjunctival and vitreous haemorrhages [5].

An Indian study which was conducted from 2014-2017 revealed that the dengue virus carries a prevalence of 5% among all the aetiologies causing acute encephalitis syndrome (AES) [3].

Direct viral invasion in the CNS, possibly as a result of the blood brain barrier disruption, is the proposed pathogenesis for neural involvement. Additionally, autoimmune reactions and metabolic variations have also been established, which further worsen the neurological manifestations [5].

The main diagnostic criteria for dengue encephalitis are high grade fever, acute signs of cerebral involvement, presence of anti-dengue IgM antibodies or dengue genomic material in the serum and/or cerebrospinal fluid, exclusion of other causes of viral encephalitis and positive imaging with MRI brain. Normal cellularity in CSF can be seen in 75% of cases of dengue encephalitis [6].

Clinical and laboratory parameters such as higher mean body temperature, rash, increase in haematocrit, thrombocytopenia, and liver dysfunction are independent predictors of neurologic complications [7].

MRI is the preferred mode of imaging. Although the findings are often non-specific, commonly affected sites are the thalamus and basal ganglia, followed by the cerebral cortex and cerebellar hemispheres. Focal haemorrhages and post contrast enhancement are the most common findings [8].

Management is mainly supportive with adequate hydration with intravenous fluids, antipyretics for fever, seizures control with anti-epileptic drugs, and transfusion of blood products (if required). Raised intracranial pressure can be treated with head elevation, mannitol, and steroids. The prognosis in dengue encephalitis is good, although the mortality can range up to 3.7% [8].

Conclusion

Dengue encephalitis is a rare and unusual manifestation that can cause significant morbidity and mortality. Even though it is a rare manifestation, nowadays it is an emerging problem in South Asian countries that needs a high degree of suspicion and prompt treatment for acute encephalitis which is suggested by the Indian study showing 5% of prevalence among all the aetiology causing acute encephalitis syndrome.

Consent

Informed written consent was taken from the patient for writing his case report and publishing clinical images.

References


