## **Case Report**

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# Fatal dengue encephalitis in a recruit: lessons learnt

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#### **ABSTRACT**

Dengue infections may present within a widely variable spectrum of clinical manifestations. However, neurologic complications in general are rare and unusual. A 19 yrs old healthy male army recruit was brought to a service hospital in South India in a state of unresponsiveness, following 12 km route march. Despite aggressive and prompt management, his condition progressively deteriorated and he finally passed away about 10 hrs after reporting to the hospital. The final cause of death was acute dengue encephalitis with raised intracranial pressure. Epidemio-clinicopathological correlation in this case led to the conclusion that vigorous exertion with a hyper-metabolic state of fever in a setting of encephalitis led to metabolic injury, multi-organ failure, cerebral edema and intracranial hemorrhage. Encephalitis following dengue virus (DENV) infection is a rare phenomenon with the incidence ranging from 0.5% to 6.2%. Neurological features associated with DENV were first reported by Sanguansermsri et al in 1976. The rare neurologic presentations reported with DENV infection are transverse myelitis, acute encephalomyelitis, myositis, and gullain barre syndrome. As encephalitis caused by DENV mimics that caused by other pathogens it should always be kept in mind while managing encephalitis of unknown origin. Medical officers should maintain a high index of suspicion of DENV encephalitis. Training of medical officers; therefore, needs to be undertaken with regular refresher cadres, besides equipping of all peripheral facilities with rapid diagnostic kits for dengue. The same will ensure prompt detection of cases and timely referral to higher medical centres in chain. The instant case reflects an important, potentially fatal, complication of dengue. Pathophysiology of DENV encephalitis needs to be elucidated on priority through research involving all stakeholders.

Keywords: Dengue, Encephalitis, Neurotropic

#### **INTRODUCTION**

Dengue is a public health problem of international concern and is endemic in more than 100 countries; with about 2.5 billion people at risk of infection, 50 million infections and 24,000 fatalities every year. There are four circulating antigenically distinct serotypes of the dengue virus (DENV 1,2,3,4). A fifth serotype (DENV 5) has also been reported, which has been confirmed recently in forest canopies of South East Asia. Dengue infections

may present within a widely variable spectrum of clinical manifestations including asymptomatic infection, non-specific febrile illness, classical dengue syndrome, dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). However, neurologic complications in general are rare and unusual. Dengue infection is classified into two forms i.e. dengue fever and severe dengue. Neurological dengue is classified as a form of severe dengue.

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Encephalopathy is a rare though well-known neurological complication of dengue infection.<sup>3</sup> Deaths following dengue infection amongst members of the Armed Forces are rare. This is because of regular epidemiological investigation, timely notification to higher echelons (unlike in the civil sector where dengue is not a notifiable disease), early diagnosis and treatment; in addition to implementation of preventive measures comprising source reduction, insecticidal spray and personal protective measures on a war footing. A fatal case of dengue infection is reported here. This case is unique as the fatality was not due to effects of thrombocytopenia followed by haemorrhage; but encephalitis which in itself is rare in dengue; and is reported only as sporadic cases in the world.

#### CASE REPORT

A 19 years old male army recruit with no known comorbidities was brought to a service hospital in South India a state of unresponsiveness. He was having high grade fever with rigors and chills for last two days associated with headache and vomiting. He had participated in 12 km route march on the same morning following which he felt extreme weakness along with giddiness. He was then initially taken to unit M I room where he was initially managed as a case of heat stroke; with intravenous fluids and was then brought to the service hospital the same day. He was normotensive, with tachypnoea and a GCS of 9/15; deteriorating to 5/15 within 15 min of arrival at the hospital.

He had decerebrate posturing while being taken up for urgent non-contrast computed tomography (NCCT) head. NCCT showed bilateral hypodensity of thalamus and 01 hypertense lesion in Right thalamus. In view of high suspicion of cerebral venous thrombosis and viral encephalitis he was taken up for and urgent magnetic resonance imaging, magnetic resonance angiography and magnetic resonance venography brain which showed extensive involvement of B/I temporal midbrain, and cerebellum with raised intracranial pressure with impending herniation. He was immediately taken up for decompression craniectomy. He had cardiorespiratory arrest while being transferred to operating theater for the However, he was resuscitated surgery. decompression craniectomy was performed operatively, he continued to have poor sensorium along with unstable hemodynamic parameters.

The initial investigations showed hemoglobin – 17.3, total leucocyte count - 8900, platelet counts of 1.06L with mixed transaminitis (bilirubin: 1.1/0.3, serum glutamic-oxaloacetic transaminase or serum glutamic pyruvic transaminase -814/418, serum alkaline phosphatase -86), azotemia (BUN: 20 mg%, creatinine: 3.1 mg%) and deranged coagulation parameters (prothrombin time or international normalized ratio: 46.0/3.68, PTTK 96.0/28/0). All viral markers like HBV, HCV, HAV and HEV were negative. Immunochromatographic test and peripheral

blood smears for malaria was negative. Serum NS1Ag for dengue was positive.

The patient was started on I/V antibiotics, dexamathesone, mannitiol and put on ventilator support. However, his condition progressively deteriorated and he finally passed away about 10 hrs after reporting to the hospital.

Salient gross autopsy findings included oedematous brain with tense dura, large clot in infracerebellar area with tonsillar herniation and hemorrhagic transformation of thalamus and brain, cerebellum and pons. The important histopathological findings were noted in the form of congested alveolar capillaries and cerebral oedema with hemorrhages in thalamus, midbrain and cerebellum. The final cause of death was acute dengue encephalitis with raised intracranial pressure with tonsillar herniation.

#### **DISCUSSION**

Dengue has re-emerged as a grave public health challenge over the past few years due to rapid unplanned urbanisation coupled with poor sanitation and improper waste disposal facilities. It is one of the major causes of undifferentiated fever. Complicated dengue mostly presents as haemorrrhagic form, following a decrease in platelet counts.

Epidemio-clinico-pathological correlation in this case led to the conclusion that vigorous exertion with a hypermetabolic state of fever in a setting of encephalitis led to metabolic injury resulting in multi-organ failure as evidenced by deranged laboratory parameters, cerebral edema with intracranial hemorrhage in mid brain, thalamus, pons and cerebellum resulting in increased intracranial pressure and tonsillar herniation.

The dengue virus is basically thought of as a nonneurotropic virus and neurovirulent properties of DENV are not very comprehensible. Encephalitis following DENV infection is a rare phenomenon with the incidence ranging from 0.5% to 6.2%.4 Neurological features associated with DENV were first reported by Sanguansermsri et al in 1976.<sup>5</sup> The rare neurologic presentations reported with DENV infection are transverse myelitis, acute encephalomyelitis, myositis, and Gullain Barre syndrome. 6 The exact pathophysiology of how DENV acts on the nervous system is not clear. It is suggested that neurological symptoms are secondary to systemic manifestation i.e. encephalopathy. These symptoms may result as a complex interplay of hepatic failure (hepatic encephalopathy), cerebral hypoperfusion (shock), cerebral oedema (vascular leak), deranged electrolytes and intracranial bleeding coagulopathy, as a consequence of liver failure.<sup>7</sup> Dengue encephalitis with thrombocytopenia-induced intracerebral bleeding has not been reported. Another possible mechanism is by direct neuronal infiltration. This theory is gaining ground as DENV and dengue IgM antibodies has been found in cerebrospinal fluid of encephalopathy; thereby suggesting that DENV is capable of crossing the blood brain barrier. DENV belongs to the Flaviviridae family as do *Japanese encephalitis* virus and *West Nile* viruses which are notoriously known for causing outbreaks of encephalitis. Hence, DENV too causing direct neuronal injury is a real possibility. However, the same is subject to further research. The cause effect relation can be proved only on demonstration of DENV in the brain of patients in whom no other discernible cause of encephalopathy can be elicited.

Table 1: Neurological complications pertaining to DENV infection.

Neurotropic effect of virus	Systemic complications of infection	Post-infectious
Encephalitis	Encephalopathy	Encephalomyelitis
Meningitis	Stroke	Optic neuritis
Myositis	Hypokalemic paralysis	Guillain barre syndrome
Myelitis		

Neurological features pertaining to DENV-5 have been classified into three categories (Table 1).9 Though prognosis for dengue encephalitis is generally good, the present case could not be salvaged. The case became complicated with time due to liver and kidney failure along with deranged coagulation profile with intracranial haemorrhage and tonsillar herniation. As a favourable outcome in DENV encephalitis depends upon early diagnosis and aggressive management, timely reporting of patients to the nearest medical outfit in case of any febrile illness needs to be emphasised. Troops should be deployed in units in buddy pairs wherein the buddies should be encouraged to inspect each other for raised body temperature, rash or any other lesion in the body; and bring the affected buddy to medical care immediately.

As encephalitis caused by DENV mimics that caused by other pathogens such as malarial parasite, meningococci, JE virus, herpes virus, mycobacteria, toxoplasma, and HIV, it should always be kept at the back of the mind while formulating a differential diagnosis for encephalitis of unknown origin; especially in dengue endemic zones. Medical Officers should maintain a high index of suspicion of DENV encephalitis. Training of medical officers; especially those deployed in the periphery, therefore, needs to be undertaken with regular refresher cadres. Equipping of all peripheral facilities manned by medical officers including regimental aid posts and medical aid posts with rapid diagnostic kits for dengue is recommended in view of the ever increasing cases of dengue in the armed forces. The same will ensure prompt detection of cases and timely referral to higher medical centres in chain.

The instant case presented with altered sensorium and no classical features of dengue such as rash, hypotension or haemoorrhagic manifestations were noted. This unusual presentation brings home the point that that dengue should be considered in all patients presenting with encephalitis in dengue endemic zones, regardless of the presence or absence of classical signs and symptoms of DENV infection.

As of now, the aetiopathogenesis of DENV is still shrouded in obscurity. Further prospective multi-centre studies involving epidemiological, virological and radiological assessment are required. The same will help in formulating a concrete management policy against DENV encephalitis.

#### **CONCLUSION**

The instant case reflects an important, potentially fatal, though rare complication of dengue and highlights the importance of considering DENV encephalitis as a possibility in endemic settings. Pathophysiology of DENV encephalitis needs to be elucidated on priority through research involving all stakeholders. The same would provide valuable epidemiological data, which will help in better understanding of the dynamics of DENV transmission with better management strategies, besides providing help in preventing occurrence of potential dengue epidemics.

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