Encephalitis Due to Dengue Virus Infection Mimicking Japanese B Encephalitis: Two Case Reports

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Abstract

Dengue virus induced encephalitis is a very rare entity and its full clinico-radiological profile is still unknown. We here report two cases of dengue encephalitis from Eastern India. The first one is a 20 year old female and the second one is a 13 year old boy. Both of them presented with altered consciousness and seizures. Blood and CSF study for dengue IgM were positive. MRI of brain showed T2 hyperintensity in the Thalami along with similar changes in other parts of the brain. Both patients responded to conservative therapy but residual neurological deficit were variably present. Relevant literature pertaining to dengue encephalitis have also been discussed.

Introduction

Dengue virus is a vector-borne ssRNA flavivirus causing periodic epidemics in tropical countries. Especially in India, in the recent years, dengue infection has become quite common and has caused a number of outbreaks during the high mosquito breeding seasons.1 Also, in the recent years in India, along with these outbreaks, atypical features of dengue infection have become quite common.2 Dengue is not primarily known to be a neurotropic virus. But recently, a few cases of central nervous system affection in dengue infection have been reported.3 These neurotropic features may or may not coincide with the other more classical clinical features of the virus. Hence, a high degree of clinical suspicion is needed to diagnose this rare complication of dengue. We here report two such rare manifestations from Eastern India.

The Case Reports

Case 1

A 20 year old female from Howrah, West Bengal presented with low grade fever for three days and altered consciousness for one day. She had no skin rash, body ache, joint pain or any symptoms pertaining to any other system. On examination, there was no neck rigidity, pupils were equally reactive and plantar responses were flexor. Blood pressure was 100/60 mm of Hg with pulse of 110/min. Her Glasgow coma scale score at admission was 11. Other systemic examinations were normal. After admission, an initial CT scan was normal and CSF study showed 12 cells/cmm (all mononuclear) with a protein level of 70 mg/dl (N: 15—45). She had three episodes of generalized tonic-clonic seizures (GTCS) after admission, which were controlled with levetiracetam. Initial laboratory tests revealed hemoglobin of 15.2 gm/dl (Hct.: 48), total leukocyte count (TLC) of 8000/cmm and platelet...
count of 130000/cmm. Blood urea and electrolytes were normal. HIV, Hepatitis B, C and CMV serologies were negative. Malaria antigen test was negative. Liver function test showed normal bilirubin with SGOT 120 IU/L and SGPT 98 IU/L. However, on the next day, repeat blood counts showed a platelet count of 70000/cmm. Then, a dengue NS1 test was done which was positive.

MRI brain with contrast showed (Figure 1) bilateral T2 hyperintensities in thalami along with similar hyperintensities in cerebellum. The affected areas showed marked restriction of diffusion. After 7 days from the start of fever, a dengue IgM assay was sent from blood as well as the CSF. Both of these came positive. RT-PCR from CSF for Japanese B encephalitis virus was negative. In the meantime, the patient was given supportive management only. Her platelet count started to improve after 4th day of admission and GCS score also improved by the 6th day.

The patient was discharged after two weeks. Her only complaint then was profound fatigue. At 5 months' follow up, there is no residual neurodeficit or memory impairment. But the generalized fatigue was still present and she was being maintained on levetiracetam.

Case 2

A 13 year old boy from Hooghli, West Bengal, presented with acute onset headache followed by unconsciousness for two days. He had no history of fever to start with but at the time of admission, he had a temperature of 100ºF. There was slight neck rigidity and rigidity of lower limbs at presentation. There was no bleeding manifestation. Blood pressure was 90/60 mm of Hg. There were no abnormalities in the other systems on examination. His GCS score was 6. Initial CSF study showed 50 cells/cmm (all mononuclear) with normal sugar, chloride and ADA levels and CSF protein level of 90 mg/dl. His initial laboratory tests showed hemoglobin of 13 gm/dl (Hct.: 43), TLC 9000/cmm and platelet count of 130000/cmm. Urea, electrolytes, liver function test and viral serologies were all normal. Blood and urine culture were negative. After admission, the patient gradually developed high fever (102—104ºF) along with left sided focal seizures. Malaria antigen test was negative. MRI scan of brain showed (Figure 2) T2 hyperintensity in right thalamus and right fronto-parietal cortex. Both areas showed diffusion restriction. Blood for dengue IgM was sent which came positive. Dengue IgM from CSF was also positive. CSF RT-PCR for Jap-B and PCR for HSV were negative.

For this patient, the platelet count decreased only slightly up to 100000/cmm on the 5th day before recovering quickly. The haematocrit increased up to 50 on the 4th day. However, the unconscious state persisted for three weeks. The seizures were also difficult to control and required triple drug therapy with levetiracetam, sodium valproate and clobazam. After recovery, the patient had residual rigidity of lower limbs and occasional urinary incontinence. At two months' follow up, these problems, along with memory loss, were persisting.

In both of these cases, actual dengue viral isolation from CSF could not be attempted due to lack of facilities. But based on the available test results, they were diagnosed as encephalitis due to dengue virus infection.

Discussion

Encephalopathy and/or encephalitis due to dengue virus infection are very rare. The presenting manifestations are protean and range from headache, drowsiness, neck rigidity, hyperreflexia to seizures and coma. These manifestations along with fever may occur in a number of conditions and hence, dengue virus and/or its serological identification from both blood and CSF are needed for confirmation. This neurological complication of dengue is more commonly reported in children and adolescents.

In a study from Vietnam, out of a series of patients with CNS infection, only about 4% were due to dengue. Thus, even in endemic regions, dengue is a rare cause of encephalitis. This rarity, along with lack of other typical clinical features, often delay the diagnosis. Out of those diagnosed with dengue encephalitis in the Vietnam study, 57% had no characteristic clinical feature of dengue at admission. In both of our cases too, the initial features of dengue like body ache, rash or high fever were absent. Thus, clinical
diagnosis or even suspicion of dengue encephalitis is often delayed.

The pathogenesis of dengue induced cerebral dysfunction is still unknown. While dengue is primarily not a neurotropic virus, the isolation of the virus and its antibodies from CSF point to CNS invasion. Non-encephalitic causes of CNS dysfunction like liver failure, cerebral edema etc. are also important causes of altered consciousness in dengue infection. The outcome and long-term sequelae of dengue encephalitis is usually favourable with most authors reporting significant recovery. However, residual deficits, like our cases, are also seen.

Some viral encephalitic syndromes have characteristic MRI brain changes which can help in a presumptive diagnosis. In Japanese B encephalitis, the characteristic changes are T2 hyper intensities in thalami, basal ganglia and cerebellum. Since the entity of dengue encephalitis is a newly described intensity, the characteristic MRI changes have not yet been standardized. Some authors have described globus pallidus hyperintensity. Others have described JE-like hyper-intensity in thalami and cerebellum. In some cases, no changes were found. In our cases, we found thalamus involvement along with cerebellum in one and high parietal cortex in the other. Rarely, dengue encephalitis has been documented to cause extensive T2 hyperintensities in thalami, brainstem and cortical white matter. Thus, no particular region of the brain is preferentially involved.

Since Geographical locations like ours are endemic for both JE virus and dengue virus infection, such similarity in MRI changes may create a dilemma and viral isolation from the CNS remains the only way for differentiation. PCR or viral culture from CSF has better specificity. But for clinical purposes, such tests are not always available. Hence viral serology (IgM) from CSF is a good surrogate marker. Also, as our case shows, presence of raised haematocrit and/or low platelet count in a febrile encephalopathy should prompt a search for dengue infection.

Although both the viral infections have no definite treatment, but differentiation is important to prognosticate the patients. Clinical experience with dengue encephalitis is much less compared to JE. But dengue encephalitis has much better prognosis.

**Conclusion**

As dengue virus infection is becoming a wider public health problem in India, clinicians should be aware of the potentially serious neurological manifestations of the virus and its imaging similarity with Japanese encephalitis B.

**References**