MRI features in dengue encephalitis: A case series in South Indian tertiary care hospital

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Abstract
Dengue virus, a RNA virus of family Flaviviridae is considered non-neurotropic. Increasing studies and case reports reveal neurological manifestations of dengue virus. In our case series, we have evaluated magnetic resonance imaging (MRI) findings of 3 patients with dengue fever diagnosed by positive dengue NS1 antigen with neurological symptoms, which revealed nonspecific imaging features of dengue encephalitis in two cases and dengue meningoencephalitis in one case. Autopsy findings are also correlated in 2 patients who succumbed to their disease. This case series underlines the consideration of dengue encephalitis in patients of dengue fever with neurological symptoms and relevant imaging findings.

Key words: Cerebral edema; dengue fever; hemorrhagic infarct; meningoencephalitis

Introduction
RNA virus of family Flaviviridae that spreads by Aedes mosquitoes is responsible for dengue fever.1,2 Approximately 2.5 billion people are at risk primarily in the densely populated areas of tropical and subtropical countries, with an estimated infection load of 50 million worldwide annually. According to the World Health Organization (WHO), India is considered as endemicity category A, in which dengue is a major public health problem. Presentations in symptomatic patients include undifferentiated viral fever, dengue fever, and dengue hemorrhagic fever. Expanded dengue spectrum includes unusual manifestations including neurological, hepatic, renal, and other isolated organ involvement.3

Dengue virus is considered as a non-neurotropic virus.2 However, increasing number of studies and case reports of central nervous involvement (CNS) involvement are being reported.1,3-6 The CNS manifestations can be attributed to three factors (a) neurotropic effect, (b) secondary to systemic manifestation, and (c) postinfectious sequelae including immune-mediated reactions.1,6-7 Findings of magnetic resonance imaging (MRI) of the brain have been reported in several case reports and studies,2,8-14 with a variable spectrum of findings.

In this series, we have evaluated MRI brain findings of serologically proven patients of dengue with clinical suspicion of encephalitis, with autopsy correlation done in 2 patients who succumbed to their illness.

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Case Reports

Case 1
A 44-year-old female presented with 3-days history of fever with chills and headache. On the third day of the fever, she presented with features of altered sensorium, drowsiness, and slurred speech. Her pulse rate was 108/min and blood pressure (BP) 110/76 mmHg. Clinical examination revealed neck rigidity and Glasgow coma scale (GCS) of E4V1 M6 (11/15). Urgent noncontrast computed tomography (NCCT) was done, which was normal. It was followed by cerebrospinal fluid (CSF) study, which revealed the possibility of viral meningitis. Her routine haemogram showed lymphocytosis. She was detected to be positive for NS1 Antigen test for Dengue.

Contrast-enhanced MRI brain was done on the fifth day of the fever to rule out dengue meningoencephalitis. MRI brain revealed bilateral symmetrical fluid-attenuated inversion recovery (FLAIR) and T2 hyperintensities in thalami, Pons, and upper half of medulla, which were iso to hypointense on T1-weighted images and showed mild-to-moderate heterogeneous enhancement on contrast administration. These areas showed restriction on diffusion weighted imaging (DWI). No blooming was seen on gradient recovery echo sequence (GRE). Similar FLAIR and T2 hyperintensities were also seen in the deep white matter of the left frontal lobe, bilateral temporal lobes in periventricular locations, and bilateral corona radiata, which did not show restriction of diffusion on DWI or blooming on GRE sequence [Figure 1]. A diagnosis of dengue encephalitis was offered. Patient was treated conservatively for 1 week, and was discharged on day 10 after complete recovery.

Case 2
A 19-year-old male was brought to the emergency department with a history of sudden and progressive deterioration of consciousness with associated vomiting and unsteady gait. There was preceding history of fever for 2 days with chills, rigor, and intermittent headache. His urgent dengue serological test was positive.

On examination at the emergency department, he was found unresponsive with heart rate 140/min, BP 210/110, and GCS E1V1M2 (4/15). Pupils were bilaterally constricted with sluggish response to light. The patient also had decerebrate posturing. He was intubated and urgent NCCT head was done which revealed diffuse cerebral edema, bilateral symmetrical hypodensity in bilateral thalami, temporal lobe, mid brain, cerebellum, and tonsilar herniation [Figure 2]. Urgent CEMRI was also done which revealed FLAIR and T2 hyperintensities in both thalami, bilateral temporal lobes, pons, midbrain, and bilateral cerebellar hemispheres. Corresponding areas were iso to hypointense on T1 weighted images. The areas of altered signal intensity in the bilateral thalami showed restriction of diffusion on diffusion weighted imaging (DWI) and loss of signal on GRE sequence. MRI also revealed diffuse cerebral edema and herniation of cerebellar tonsils as seen on NCCT. Postcontrast images show peripheral enhancement around hypointense area in thalamus [Figure 3]. CEMRA and CEMRV did not reveal any significant abnormality. Considering his lab investigations and clinical symptoms, diagnosis of dengue encephalitis was given.

Figure 1 (A-E): Axial FLAIR images show bilateral symmetrical hyperintensities in thalami, Pons and left temporal lobe (A and B). DWI and ADC images shows restriction on diffusion (C and D). Post contrast image show peripheral enhancement in bilateral thalami (E)

Figure 2 (A-D): NCCT head demonstrating diffuse cerebral oedema (A). Bilateral symmetrical hypodensity in thalami with focal hyperdensity in left thalamus (B). Hypodensity in bilateral temporal lobe, mid brain, cerebellum and tonsillar herniation (C and D)
The patient underwent emergency decompressive craniectomy for herniation. He had an intraoperative cardiac arrest from which he was revived after cardiopulmonary resuscitation. Postoperatively, he again developed cardiac arrest and succumbed to his illness.

Postmortem cranial findings revealed areas of hemorrhage in the thalamus with marked Oedema of the surrounding brain parenchyma and tonsillar herniation.

Case 3
A 40-year-old male presented at the emergency department with a history of fever, vomiting, unstable gait, and giddiness of 1-day duration. On examination, his pupils were sluggishly reactive with decreased movements and extensor plantar reflex. Patient was put on ventilator due to progressive drowsiness and hypoventilation. He later developed seizures. Serological and hematological evaluations revealed dengue NS1 positivity with raised hematocrit.

He was referred for urgent MRI. CEMRI brain revealed bilateral symmetrical areas of altered signal intensity involving both thalami, pons, and midbrain, which were hyperintense on FLAIR and T2 and hypointense on T1-weighted sequence. These areas showed patchy enhancement on contrast administration. Restriction of diffusion was seen in pontine lesion. No blooming on GRE was seen. Meningeal enhancement was present on the surface of mid brain and pons [Figure 4]. Patient was offered a diagnosis of dengue meningoencephalitis.

He continued to have seizures and developed refractory hypotension. Despite rigorous resuscitative measures, the patient could not be saved.

Postmortem examination of mid brain, pons, medulla, cerebellum, cerebral cortex, and dura showed diffuse edema. Hemorrhagic areas in the frontal lobe seen which revealed subarachnoid haemorrhage with congested dilated capillaries [Figure 5].

Discussion
Dengue virus is a single-stranded RNA virus of Flaviviridae family. There are four distinct but closely related serotypes of dengue virus – DEN1, DEN2, DEN3, and DEN4. Recovery from infection provides lifelong immunity from that particular serotype. However, cross immunity to other serotypes is partial and temporary. Subsequent infection from other serotypes may lead to severe dengue infection. Neurological involvement in dengue infection was first reported in 1976. Common presentations were in the form of headache, altered sensorium, papilledema, neck rigidity, or seizures. Dengue can involve the brain in the form of encephalopathy or encephalitis. Encephalitis occurs due to direct neurological invasion by virus causing inflammation of brain parenchyma. On imaging, focal abnormalities are suggestive of encephalitis rather than encephalopathy. Encephalopathy is usually secondary to multisystem derangement such as encephalitis, hepatic failure, shock, coagulopathy, and bacterial infections. It presents as diffuse involvement of brain without any specific findings on imaging.\(^{[6,12]}\)
Our case series described findings similar to various case reports and studies in the past.\cite{2,5,9,11,12} We predominantly reported diffuse cerebral oedema, bilateral symmetrical FLAIR and T2 hyperintensities in thalami, pons, and medulla with heterogenous or peripheral enhancement on contrast administration, with few of these areas showed restriction on diffusion and petechial hemorrhages. Our findings were comparable to cases described by Bhoi et al.,\cite{2} Souren et al.,\cite{5} and Jayaseelan et al.,\cite{11} where they reported T2 and FLAIR hyperintensity in the thalamus and cerebral hemisphere, centrum semiioval, and corpus callosum. Restriction on diffusion similar to our case series was also described by Bhoi et al.\cite{2} Pal et al.\cite{5} reported diffuse cerebral edema similar to our cases. Borawake et al.\cite{9} mentioned petechial hemorrhages in his case series, which was also described in our cases. We also had one case with meningeal enhancement.

MRI findings in dengue encephalitis are mostly nonspecific, and these findings can be seen in Japanese and herpes encephalitis. In difficult cases, serological examination is helpful in differentiating it from other viral encephalitis. Chikungunya encephalitis also presents with clinical presentations similar to dengue encephalitis. However, Chikungunya encephalitis shows T2-weighted hyperintense white matter lesions with restricted diffusion.\cite{10}

**Conclusion**

High degree of suspicion of dengue encephalitis should be kept in a patient of dengue fever with neurological symptoms. MRI features are contributory to the diagnosis as they correlate well with autopsy findings.

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**Conflicts of interest**
There are no conflicts of interest.

**References**