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Original Research Article

Role of MRI in Evaluation of Neurological Manifestations of Dengue Fever - Prospective Study

Yashas Ullas L[1], Krutagni Adwait Mehta[2], Revanth R. B[3], Bukke Ravindra Naik[4], Aluru Venkata Sai Nikhilendra Reddy[5], Vinay Patel[6]

1) Senior resident, Department of Radio-diagnosis
2) Junior Resident, Department of Medicine
3) Junior Resident, Department of Radio-diagnosis,
4) Assistant professor, Department of Radio-diagnosis,
5) Junior Resident, Department of Radio-diagnosis,
6) Junior Resident, Department of Medicine

Corresponding Author : Dr. Bukke Ravindra Naik
Assistant professor, Department of Radio-diagnosis

ABSTRACT

Background: One of the most common arboviral illnesses is dengue fever. It's the second-leading cause of acute febrile sickness among tourists. The dengue virus is a flaviviridae virus with a single-stranded, non-segmented ribonucleic acid (RNA) genome. Dengue fever is caused by four separate serotypes (DENV-1, 2, 3, & 4) each has its own set of infectious characteristics. Dengue fever has spread over 128 countries, placing more than 2.5 billion people at risk each year.

Materials and Methods: This study was a prospective study done at a teaching hospital and included 60 serologically confirmed dengue patients who had brain MRI done after presenting with neurological symptoms during a 12-month period. IgM antibody against dengue antibody in the blood and/or dengue antigen (NS1) in the serum were used to determine if a patient had dengue encephalopathy or encephalitis in addition to the signs and symptoms of acute encephalitic illness. Patients who had typhus, malaria, scrub, leptospirosis, Chikungunya, Japanese encephalitis (JE) virus, or Herpes simplex virus (HSV) encephalitis were not included in the research.

Results: There were 60 patients in this research (35 males and 25 women, with an average age of 31.2 years and a range of 5–80 years). Fourteen of the patients (23 percent) were children (under the age of 18), while the rest were adults.

Conclusion: MRI is a useful tool for determining the extent of brain involvement in dengue. Although the symptoms are not fully specific to dengue, when combined with serological tests and CSF analysis, they can aid in reducing the number of potential diagnoses. The decisive underlying pathologic process in the case of dengue fever can be identified by the radiologist using a pattern-based approach to brain MRI interpretation in conjunction with the patient's clinical data.

KEYWORDS

Dengue, Encephalitis, MRI, Hemorrhagic Infarct, Meningoencephalitis.

INTRODUCTION

Dengue fever is the world's fastest-growing tropical illness and one of the most common arboviral diseases. It's the second-leading cause of acute febrile sickness among visitors1. Dengue fever is caused by four different serotypes (DENV-1, 2, 3, and 4) that have different infectious outcomes (asymptomatic to severe hemorrhagic fever). Dengue fever is found in 128 countries, posing a threat to about 2.5 billion people each year. According to some estimates, 400 million individuals have the infection each year,

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with 96 million having clinical relevance. In around 2.5 percent of instances, all sick people die. In recent years, dengue fever has been related to neurological symptoms, although the actual incidence rates are unknown.[2].

In 1976, neurological manifestations were first described as uncommon dengue infection symptoms; in recent years, their incidence rates have ranged from 0.5 to 20%. In 25 nations covering virtually all of the continents, neurological symptoms have been seen in adults from 3 months to 60 years of age. High body temperature, a greater hematocrit, thrombocytopenia, rash, and liver failure are all different risk factors for neurological problems[3].

Neurological manifestations were first documented in 1976 as uncommon dengue symptoms; in subsequent years, The incidence rate has varied from 0.5 to 20%. Neurological indications have been observed in 25 countries, covering almost the whole globe.

Dengue virus neurotropism in the human host was once thought to be an opportunistic trait. However, an increasing body of data suggests that the virus is directly neurovirulent. Miagostovich et al. discovered that the virus is highly neurotropic in Aedes aegypti by analysing viral proteins, ribonucleic acid (RNA), and immunoglobulins in the central nervous system (CNS). The DENV-2 and DENV-3 serotypes are mostly linked to neurological problems[4].

Encephalitis is a serious symptom of dengue fever that can manifest itself within any of the three illness groups. The criteria for diagnosing dengue encephalitis are as follows[5]. Neuroimaging for dengue encephalitis has conflicting outcomes, with normal findings in the majority of patients[6,7].

When abnormal neuroimaging data are evident, MRI has an advantage over cranial computed tomography (CT) in diagnosing brain lesions in dengue encephalitis.[8] The exact MRI features characterizations of dengue encephalitis are yet unclear. The majority of patients receive just symptomatic alleviation as a result of their treatment. The vast majority of people recover completely.

The results of magnetic resonance imaging (MRI) of the brain have been documented in several case reports and studies, with a broad variety of outcomes. In this study, We examined the MRI brain scan results of dengue patients who had tested positive for the virus by serology and had encephalitis on the basis of clinical suspicion.

MATERIAL AND METHODS

In this prospective study, 60 serologically positive dengue patients who had neurological symptoms and underwent a brain MRI at a tertiary care teaching hospital over the course of a year were included. IgM antibody against dengue antibody in the blood and/or dengue antigen (NS1) in the serum were used to determine whether a patient had dengue encephalopathy or encephalitis in addition to the signs and symptoms of acute encephalitic disease. Patients with encephalitis caused by typhus, malaria, scrub, leptospirosis, Chikungunya, the JE virus, or the Herpes simplex virus (HSV) were not included in the study.

Clinical Evaluation

A complete clinical assessment was given to all of the patients. Fever, headache, nausea, vomiting, seizures (number of episodes and seizure type) and other features of dengue were all recorded. Vital signs of the patients were also recorded To measure the state of consciousness, the Glasgow Coma Scale was utilised (GCS). A general systemic examination was performed on all of the patients. All patients were given a complete neurological examination to the degree practicable. A fundus examination was performed on all individuals to determine if they had papilledema. Sensation and cerebellar symptoms were also investigated.

Laboratory Investigation

Haemoglobin, haematocrit, total and differential white blood cell counts, coagulation profile (platelet count, prothrombin time, activated partial thromboplastin time), blood sugar, blood ammonia, blood urea nitrogen, serum creatinine, bilirubin, transaminases, sodium, potassium, chloride, and calcium levels were all measured in all patients. A chest X-ray, an electrocardiogram, and an abdominal ultrasound were

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also conducted. The cerebral fluid (CSF) of those with a platelet count of at least 40,000/mm3 was tested for cells, sugar, and proteins. The serum of all patients was tested for IgM antibodies to dengue virus and antigen (NS1). JE was ruled out by a negative CSF IgM ELISA, whereas Leptospira and Chikungunya were ruled out by a negative serum IgM ELISA. A peripheral blood smear as well as a rapid malaria parasite dual antigen test were performed.

MRI

The 2D axial T2 and FLAIR sequences for the brain, the pre- and postcontrast T1-FS sequence, diffusion weighted images (DWI), and susceptibility weighted images were among the MRI sequences used (SWI). A single-shot fast spin-echo echoplanar sequence with sensitising gradients in all three orthogonal planes and a b value of 1000 s/mm2 was used to create the diffusion weighted images. The slice thickness used to create the 2D sequences was 4 mm, while the 3D sequences used a slice thickness of 0.9 mm. Unless gadolinium-based contrast agents were contraindicated in the patient, intravenous gadolinium (Gd-DTPA) was administered at a dosage of 0.1 mmol/kg of body weight for postcontrast sequences.

RESULTS

There were 60 patients in this research (35 males and 25 women, with an average age of 31.2 years and a range of 5–80 years). Fourteen of the patients (23 percent) were children (under the age of 18), while the rest were adults.

Patients are classified according to WHO guidelines.

Seven people were classified as having dengue fever without symptoms, ten as having dengue fever with symptoms, and the rest as having severe dengue.

Indication for MRI

Thirty-five patients had an MRI for changed sensorium with seizures, whereas twelve patients had an MRI for altered sensorium with seizures. Other patients had MRI for a severe headache that had started suddenly.

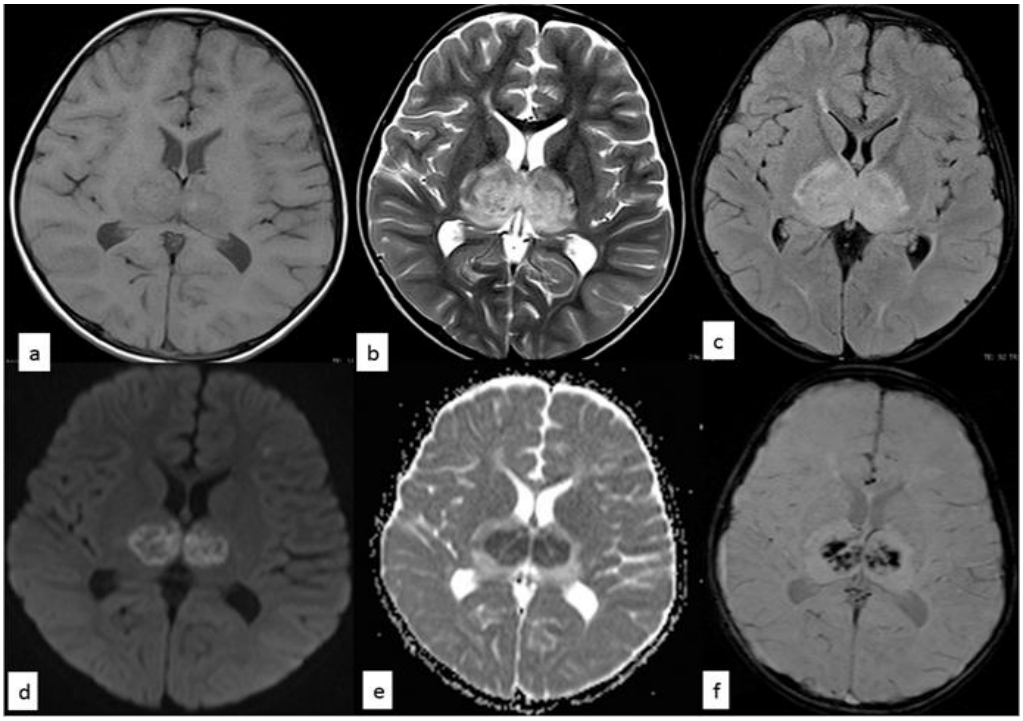

Figure 1: showing encephalitis pattern- Symmetrical T1 hypointense with few interspersed areas of hyperintense foci (a), T2/FLAIR hyperintensities in bilateral thalami (b, c) showing restricted diffusion on DWI (d,e) and blooming on SWI (f).

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MRI findings

Twenty-one of the sixty patients had no notable abnormalities on MRI. The remaining 39 patients were all aberrant in some way. The imaging results are described using a pattern recognition method.

Encephalitis pattern

In 18 of the 39 instances with a positive MRI result, an MRI anomaly connected to an encephalitic pattern was found. When the basal ganglia, thalami, cerebellar structures, brainstem, cortical grey or subcortical white matter were impacted alone or in combination, the diagnosis was evaluated. The basal ganglia, thalami, cerebellar regions, and brainstem were all connected in five of the individuals. The basal ganglia, thalami, brainstem, and cerebellum were all implicated in the three individuals, as well as the cortex and subcortical white matter. Four instances had isolated cerebellar involvement. All of the patient's structures had T2/FLAIR hyperintensity and T1 hypointensity, suggesting that their signal intensity (SI) had altered.

Real diffusion restriction with hypointensity was observed in every instance on similar apparent diffusion coefficient (ADC) maps in the regions with changed SI. In 13 of the cases, there was sporadic bleeding in the vicinity of the changed SI. In Figure 1.

Encephalopathy pattern

While one patient exhibited white matter structures (periventricular, fronto-parietal deep and subcortical white matter, as well as the corpus callosum) but no cerebral edoema, four patients displayed extensive cerebral edoema and aberrant S.I in bilateral hippocampi. These characteristics are consistent with seizure-induced encephalopathic alterations.

Acute disseminated encephalomyelitis

In the bilateral periventricular and fronto-parietal white matter of five individuals, there were multifocal, asymmetrical, non-enhancing, fluffy T2/FLAIR hyperintensities, which may indicate ADEM. There is no indication that the brainstem, cerebellum, or ganglio-thalamic complexes are involved in any of the cases. True diffusion restriction was absent in one of these patients, but the lesions had increased mean diffusivity and appeared bright on both diffusion weighted imaging (b = 1000) and the ADC map in the other two cases. In the third case, the lesions had increased mean diffusivity and appeared bright on both diffusion weighted imaging (b = 1000) and the ADC map.

Hemorrhagic pattern

11 of the 39 patients with a positive MRI exhibited intracranial macro-, micro-, or both haemorrhages. In this group, hemorrhagic encephalitis is not present. This group only includes those who have experienced an isolated intracranial bleed. There was thrombocytopenia in all nine patients (20,000/mm3 in eight and 30,000/mm3 in two). On susceptibility weighted imaging (SWI) sequences, four patients showed a number of punctate foci of micro-hemorrhages dispersed throughout both cerebral and cerebellar hemispheres as well as the brainstem. Right frontal intra-parenchymal hematoma in both the cerebral and cerebellar hemispheres of two of the patients was present, along with multifocal micro-hemorrhages in the basal ganglia, thalami, and both of the hemispheres. Isolated intra-parenchymal haemorrhage was seen in the left parietal and frontal regions of the remaining individuals.

Outcome of the cases

19 out of the 60 trial participants who had the acute episode had a favourable outcome and were sent home in quite good health. Ten of the 26 patients passed away at the hospital. Ten patients were conscious and oriented but still had deficits, whereas six patients were released with diminished sensorium (GCS > 12). (four with hemiparesis, four with swallowing difficulty requiring nasogastric

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feeding, and two with truncal ataxia). 18 of the 21 patients with normal MRIs had a good prognosis, whereas three had a bad prognosis.

DISCUSSION

Dengue virus comes in four different forms (DENV-1 to DENV-4). Dengue fever symptoms include fever, headache, rashes, and hemorrhagic signs. According to popular thinking, dengue disease is a non-neurotropic virus[9]. The serotypes DEN2 and DEN3 have been connected to neurological symptoms the most[10] .Dengue encephalitis has been documented by Solomon et al. and Borawake et al., both from India[10]. Conversely, there is hardly any recent study on dengue encephalitis in adult Indian patients.

Headaches, convulsions, and altered consciousness are all symptoms of dengue encephalitis[11]. Less than half of encephalitis patients had indications of dengue fever, such as myalgias, rash, and bleeding[12]. As a result, Solomon et al. recommend that all encephalitic people in endemic areas be tested for dengue fever, regardless of whether they have classical symptoms or not. Our patient had no signs or symptoms of dengue fever, such as rashes or low blood pressure.[13].

Dengue encephalitis is defined by fever, immediate signs of cerebral involvement, anti-dengue IgM antibodies, or dengue genomic material in the blood and/or cerebrospinal fluid, and the lack of other viral encephalopathy and encephalitis causes[14]. Varathraj has established standards for dengue encephalitis as well. Our patient had a fever, seizures, and sensorium changes, and we discovered dengue-IgM in his blood. In this patient, we also conducted appropriate testing to rule out other causes of encephalitis. As a consequence, our patient satisfied the criteria for dengue encephalitis.

Nonspecific MRI abnormalities characterise dengue encephalitis, which can also be found in Japanese and herpes encephalitis. A serological test can help differentiate it from other kinds of viral encephalitis in difficult settings. Clinical signs of chikungunya encephalitis are similar to those of dengue encephalitis[16-19]. Chikungunya encephalitis is characterised by T2-weighted hyperintense white matter lesions with restricted diffusion.

CONCLUSIONS

The results of this study suggest that dengue encephalitis should be considered in the differential diagnosis of fever with altered sensorium, particularly in nations like India. Early signs of dengue infection in the brain can be found with an MRI scan. In combination with serological tests and CSF studies, it can help reduce the number of possible differential diagnoses. A thorough method will be used to diagnose the condition, and relevant clinical and MRI data will also be helpful.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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DISCLAIMERS

The opinions expressed in this article are the authors' personal views and do not represent that of their affiliated organizations, employers, or associations.

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DATA AVAILABILITY STATEMENT

Not Applicable

HIGHLIGHTS OF THE STUDY

• This research aids in the identification of imaging aspects of dengue fever neurological symptoms, as well as the early diagnosis and treatment of patients.
• The numerous patterns of dengue virus neurological presentation are described in this paper.
• We looked at how clinical symptoms of dengue fever associated with lab findings and imaging characteristics.
• This research found that MRI had an advantage over CT in diagnosing dengue encephalitis.

AUTHOR CONTRIBUTIONS

YUL conceived the review idea. KAM & RBB conducted the literature search. YUL & BRN prepared the first draft of the manuscript. ANR reviewed, edited, and revised the manuscript substantially on the key intellectual content. YUL & VP finalized and approved the current version agreed to be accountable for accuracy and integrity and decided to submit the manuscript to Trends in Medical Research.

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