Case Report: Right Hemispheric Neuroimaging Abnormalities in a Patient with Dengue Encephalopathy

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Abstract. Dengue encephalitis and dengue encephalopathy are frequent neurological complications of systemic dengue virus infection. Neuroimaging is normal in approximately 50% of patients. Common imaging abnormalities involve periventricular structures, including the basal ganglion, thalamus, and periventricular white matter. We describe an unusual case of dengue encephalopathy with unilateral imaging abnormalities involving the right cerebral hemisphere and mimicking the involvement of the right middle cerebral artery.

INTRODUCTION

Dengue virus is a single-stranded RNA arbovirus, which belongs to the family Flaviviridae and genus Flavivirus. Four serotypes of the dengue virus (DEN-1, DEN-2, DEN-3, and DEN-4) cause clinical manifestations in a majority of the cases.¹

According to the current estimate, there are approximately 390 million dengue infections every year. Dengue is endemic in more than 100 countries,² and approximately 3.9 billion people in 128 countries are at risk of infection by dengue viruses. Approximately, 500,000 dengue patients need hospitalization every year, and approximately, 2.5% of these patients result in mortality.^{2,3} According to the World Health Organization, Americas, Southeast Asia, and Western Pacific regions are the worst affected parts of the world.^{3,4}

In dengue-endemic areas, dengue encephalitis and dengue encephalopathy are frequently encountered neurological complications of systemic dengue viral infection.⁵ Both these complications are clinically characterized by an impaired consciousness. In dengue encephalitis, dengue virus antibody or antigen (IgM, RNA, or nonstructural protein 1 [NS1]) is identified in the cerebrospinal fluid. But this is not the case in dengue encephalopathy, in which routine cerebrospinal fluid is frequently normal.^{6,7} In addition, there are several other pathologies such as ischemic and hemorrhagic stroke, subdural hematoma, cerebral venous thrombosis, and acute disseminated encephalomyelitis that can severely affect the brain.^{6,8,9}

In this report, we present a case of dengue encephalopathy due to unusual imaging abnormalities.

CASE REPORT

A 32-year-old man presented with 2 days of fever and altered sensorium headache. He had no history of diabetes, hypertension, or any cardiac disease. On general examination, he was afebrile with normal pulse rate and blood pressure. On neurological examination, he had impaired consciousness. His Glasgow Coma Scale score was 11 (E3V3M5). A detailed examination of his mental status could not be carried out because of altered sensorium. Cranial nerve examination, including fundus examination was normal. There was no apparent focal neurological deficit, however, formal muscle

power assessment could not be performed because of depressed sensorium. There were no signs of meningeal irritation. A laboratory work-up revealed normal urinalysis, haemoglobin of 12.7 g/dL, total leucocyte count of 13,600 cells/mm³, and platelet count 160,000/mm³. Liver function tests revealed mild elevation in serum glutamic pyruvic transaminase levels (71.8 IU/L). Blood sugar, renal functions, and blood electrolytes were normal. C-reactive protein was 107.56 (N 0–6 mg/L). Serum vitamin B12 and folic acid levels were 83 pg/mL (normal range: 187–883) and 3.4 nmol/mL (normal range: 7–46), respectively. Dengue IgM test in serum was markedly positive but dengue virus serum NS-1 antigen test was negative. Human immunodeficiency virus, Hepatitis C, and Hepatitis B virus virology were negative. Cerebrospinal fluid analysis revealed 10 cells (all lymphocytes) with normal sugar and protein levels. Dengue IgM antibody was not detected in cerebrospinal fluid. Dengue polymerase chain reaction and NS-1 antigen test in cerebrospinal fluid were not performed. Gram's staining, acid-fast bacilli, and India ink preparation were negative. Cerebrospinal fluid virology for Japanese encephalitis, enterovirus, herpes simplex virus-1, and varicella zoster virus were also negative. Computed tomography of the brain revealed an ill-defined hypodense area. Contrast administration revealed gyral enhancement in right temporoparietal region (Figure 1). Magnetic resonance imaging of the brain revealed restricted diffusion in right basal ganglia and occipital region. Contrast-enhanced magnetic resonance imaging revealed gyral enhancement in the right cerebral hemisphere (Figure 2). A magnetic resonance angiogram and magnetic resonance venography were normal. Cardiac examination was also normal. The patient was treated with vitamin B12 and folic acid supplementation and other symptomatic treatment in the form of intravenous fluid and paracetamol. The patient was fully conscious after 5 days and was discharged on day 10 without any focal neurological deficit. At the time of discharge, we did not repeat blood laboratory parameters and magnetic resonance imaging.

DISCUSSION

Our case of dengue encephalopathy demonstrated an unusual imaging picture. The imaging abnormalities involved right cerebral hemisphere and mimicked the involvement of right middle cerebral artery. However, angiography was normal.

In dengue encephalitis and dengue encephalopathy, neuroimaging may be normal in more than 50% of the patients.¹⁰ However, imaging abnormalities, if present, usually involve

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FIGURE 1. (A) Non-contrast computed tomography scan head showing sulcal effacement and ill-defined hypodensity on the right side (B) post contrast image showing gyral enhancement in the right temporoparietal region. This figure appears in color at www.ajtmh.org.

periventricular structures such as basal ganglion, thalamus, and periventricular white matter.¹¹ Common magnetic resonance imaging abnormalities are hyperintensities in bilateral cerebral parenchyma, including basal ganglia, detected in T2 and fluid-attenuated inversion recovery sequences.¹²

In our case, it is difficult to explain the cause of unilateral imaging abnormalities in our patient that mimicked middle cerebral artery infarct but without any focal deficit. Dengue-induced central nervous system vasculitis, acute disseminated encephalomyelitis, and ischemic involvement of the cortex can produce changes in unilateral hemispheric imaging.^{13,14} The possibility of dengue-mediated central vasculitis seems to be remote given the normal magnetic resonance angiography.¹⁵ Dengue myocarditis leading to the transient thromboembolic phenomenon is a possible explanation for unilateral hemispheric ischemic involvement.¹⁶

Encephalopathy is presumed to be caused by many metabolic abnormalities frequently associated with dengue virus

infection. The possible pathogenetic mechanisms resulting in dengue encephalopathy include shock syndrome, electrolyte abnormalities, concurrent bacterial infection, acute liver or renal failure, dyspnea due to lung dysfunctions, cerebral edema due to capillary leakage, and coagulopathies leading to bleeding disorders. Dengue infection cause cytokine storm and complement activation, which result in endothelial dysfunction and blood–brain barrier dysfunction.^{17–19} Low platelet counts and coagulopathies may result in cerebral bleed.²⁰ We believe that in our case, the low levels of serum vitamin B12 and folic acid levels could have triggered altered sensorium. In addition, we noted increased inflammatory cells in cerebrospinal fluid, indicating an encephalitic process.

Dengue virus is closely related to other flaviviruses such as Japanese encephalitis virus and Zika virus. Serological cross-reactivity among the different flaviviruses viruses make serological test less reliable for the diagnosis of flavivirus infections in endemic areas (such as in India), where many flaviviruses

FIGURE 2. T2 and fluid-attenuated inversion recovery (FLAIR) (A and B) images showing signal intensity alteration involving right hemisphere and basal ganglia, respectively. (C) diffusion-weighted magnetic resonance imaging (DWI) image showing restricted diffusion in right basal ganglia and occipital region. (D) Post contrast T1 image showing gyral enhancement.

co-circulate.²¹ Viral isolation is an accurate method to achieve a confirmed diagnosis. The demonstration of IgM or high levels of IgG in serum specimen taken from a suspected patient suggests probable dengue.²²

The dengue diagnosis was based only on positive IgM. This is not rigorous enough because false-positive IgM results are not uncommon. The diagnosis of dengue virus infection is considered confirmed if virus particle, the viral genome or NS1 antigen, is detected in the examined specimen. A sero-conversion to IgM or IgG positivity or 4-fold increase in the IgG/IgM antibody titer in paired sera also indicates confirmed diagnosis of dengue virus infection. Our patient had dengue encephalopathy as he fulfilled the diagnostic criteria. He had febrile encephalopathy and serum dengue IgM antibodies as demonstrated in serum. In addition, other possible causes of febrile encephalopathy were excluded.^{7,23,24}

In conclusion, hemispheric imaging abnormalities can be encountered in a patient with dengue encephalopathy.

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