Stroke in a Child with Dengue Encephalopathy

Sir,

Dengue is a mosquito-borne viral disease caused by dengue virus that belongs to the genus *Flavivirus,* transmitted by two mosquito vectors, namely, *Aedes aegypti* and *Aedes albopictus.*[1] Dengue with or without warning signs, and severe dengue are the categories of disease under the WHO recent classification.[1] This recent clinical case definition had stated to consider all patients with neurological manifestations under severe dengue. Here, we describe the clinical presentation, neuroimaging findings, and management of a child with dengue encephalopathy manifesting with seizures and stroke. Neuroimaging had shown pontine bleed and watershed infarcts in this child.

A 29-month-old child was brought with high-grade fever of 6-day duration and multiple episodes of vomiting of 3-day duration. He had altered level of consciousness from the 5th day of illness and had developed multiple episodes of right focal motor seizures with secondary generalization without regaining consciousness. Seizures were controlled after the administration of benzodiazepines and phenytoin. Altered level of consciousness had persisted, and he was observed to have paucity of right-sided limb movements. There was an outbreak of dengue epidemic in their geographic area.

Length and weight of the child were <3rd centile for age. Temperature of 101°F, heart rate of 120/min, blood pressure of 95/41 mmHg, and respiratory rate of 38/min were documented on admission. Capillary refill time and oxygen saturation were normal. Glasgow coma score was 9/15. Tone was decreased in all four limbs and right hemiparesis was observed. Deep tendon reflexes were exaggerated and bilateral plantar responses were extensor.

Clinical syndrome and laboratory parameters of this child [summarized in Table 1] were highly suggestive of severe dengue. Magnetic resonance imaging of the brain [Figure 1 a-g] describes the radiological findings observed in our patient. Computerized tomography of the brain [Figure 1 h] showed hypodensity and swelling of the pons.

The child was managed with intravenous fluids as per the WHO protocol and maintenance doses of anticonvulsants. During the hospital stay, blood culture had grown nonfermenting Gram-negative *Bacillus* which was treated appropriately. His sensorium had gradually improved over next 2 weeks. At discharge, central hypotonia persisted but right hemiparesis had improved. Bilateral alternate convergent squint was observed. Follow-up assessment after 3 months had shown an alert and active child with normal speech and language. Bilateral alternate convergent squint persisted. Follow-up MRI brain findings are depicted [Figure 2 a-e].

"Dengue central nervous system (CNS) involvement refers to the presence of any one of the symptoms such as impaired consciousness, neck stiffness, focal neurological signs, or seizures with laboratory evidence."[2] Neurological complications reported in association with dengue are Guillain–Barre syndrome, rhabdomyolysis, and neuro-ophthalmic.[2] Criteria for severe dengue include plasma leakage resulting in shock, fluid accumulation, clinical evidence of severe bleeding or severe organ involvement such as elevated liver enzymes, CNS involvement, and heart or other organ involvement.[1]

Table 1: Summary of laboratory parameters

Laboratory parameters	Results
Activated partial thromboplastin time (s)	71.7 (27.6-42.4)
Prothrombin time (s)	13 (10-12.5)
Total leukocyte count (cells/mm^3)	26,300 (6000-17,500/mm^3)
Hemoglobin (g/dL)	10.5 (11-14)
Platelet count (cells/mm^3)	33,000 (150,000-400,000/mm^3)
Alanine aminotransferase (U/L)	321 (8-40 U/L)
Sodium (mmol/L)	134 (138-145)
Metabolic acidosis	Absent
Lowest platelet count during the course of illness (cells/mm^3)	16,000 (150,000-400,000/mm^3)
NS1 antigen	Positive
Dengue IgM antibody	Positive
Dengue IgG antibody	Negative
CSF analysis	
Cell count (cells/mm^3)	WBC-5, RBC-2
Protein (mg/dL)	38.4
Glucose (mg/dL)	47
Multiplex viral PCR (HSV 1, 2, adenovirus, cytomegalovirus, and Epstein-Barr virus)	Negative

NS1 = Nonstructural protein 1, Ig = Immunoglobulin, PCR = Polymerase chain reaction, WBC = White blood cell count, RBC = Red blood cell count, HSV = Herpes simplex virus,: CSF = Cerebrospinal fluid

Diagnosis of dengue encephalopathy in our case was based on the presence of clinical evidence of CNS involvement such as altered consciousness, seizures, focal neurological deficit, and laboratory evidence such as positivity for nonstructural protein 1 antigen and presence of dengue immunoglobulin (Ig) M antibody. Our patient also had documentation of elevated liver enzymes, intracranial bleed, and normal cerebrospinal fluid findings. Postulated mechanisms to explain the various CNS presentations in dengue are direct virus invasion, metabolic disturbances, capillary leak, shock, and immune mediated.[3]

Incidence of stroke in dengue has been reported as 0.26%, and reports of both ischemic stroke and hemorrhagic stroke exist.[4,5] Imaging findings described in patients with dengue are hyperintensity involving thalami, corpus callosum, centrum semiovale, cortex, basal ganglia, cerebral edema, hypoxic brain injury, focal lesions, meningeal enhancement, multiple hemorrhagic foci, watershed infarcts, cerebellar haemorrhage,

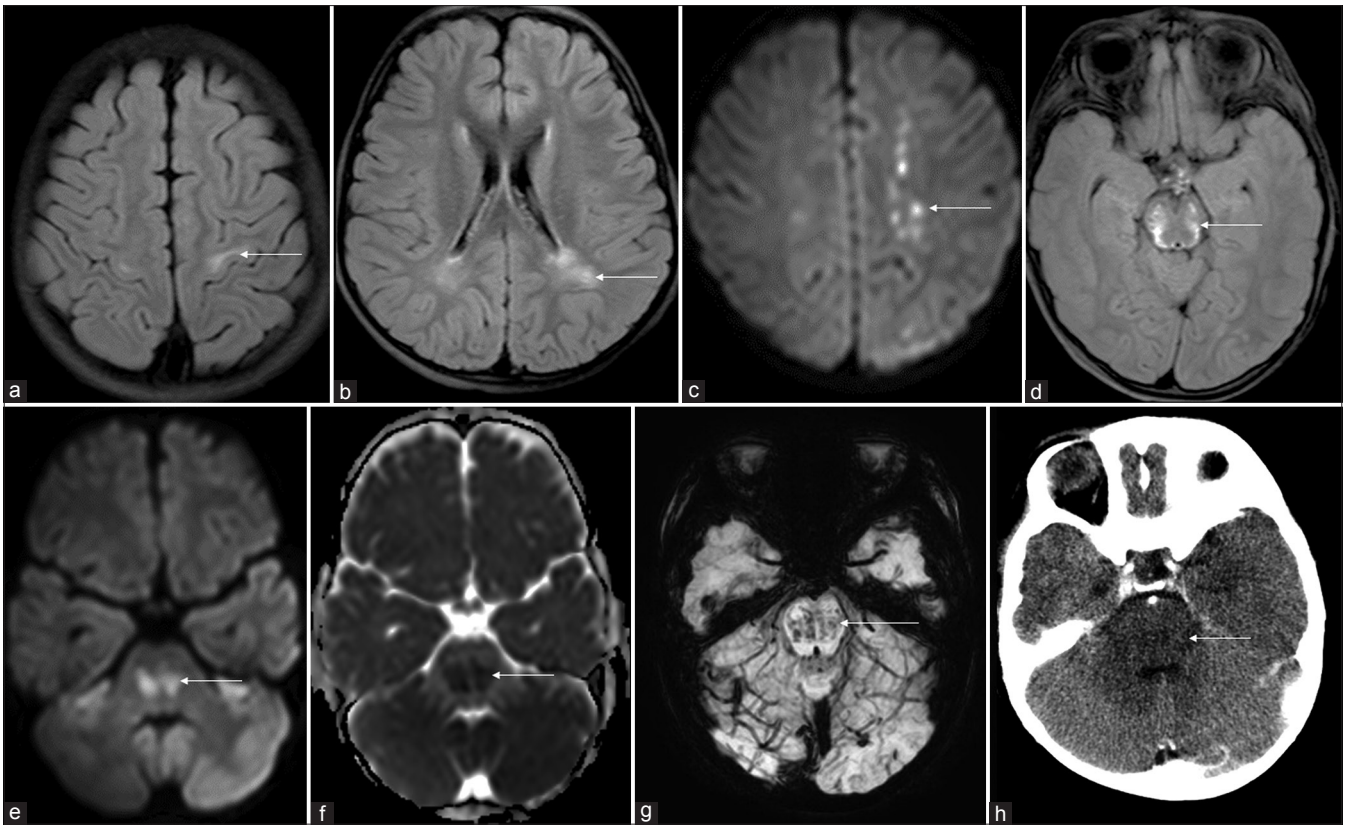

Figure 1: Magnetic resonance imaging fluid-attenuated inversion recovery axial images (a and b) bilateral white matter hyperintensities in the precentral gyrus and posterior periventricular region. Diffusion-weighted image (c) multiple foci of restriction in the left centrum semiovale. Fluid-attenuated inversion recovery axial image (d) symmetric midbrain hyperintensity. Diffusion-weighted image and apparent diffusion coefficient image at pontine level (e and f) restricted diffusion. Susceptibility-weighted image (g) hypointense foci in pons suggestive of bleed. Computerized tomography brain (h) hypodensity and swelling of the pons

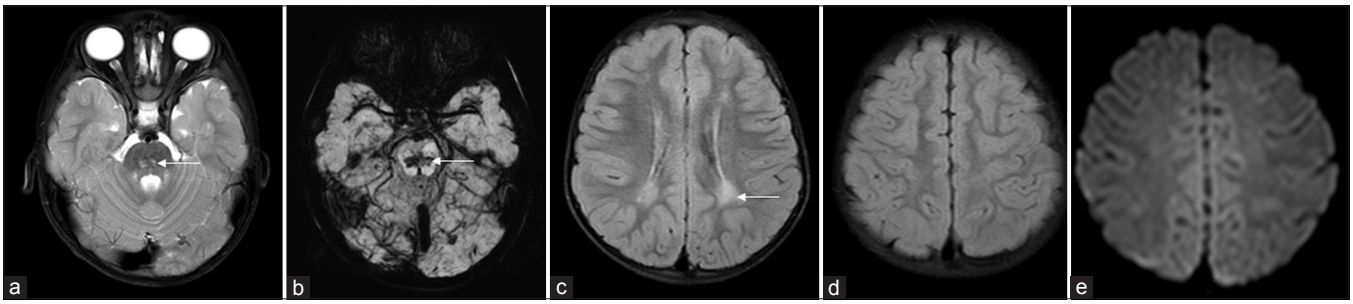

Figure 2: Follow-up magnetic resonance imaging T2 axial image (a) small persistent hyperintense foci in the pons. Susceptibility-weighted image (b) persisting hypointensity suggestive of hemosiderin deposits. Minimal persistent posterior periventricular hyperintensity is seen on fluid-attenuated inversion recovery axial image (c). Fluid-attenuated inversion recovery axial image and diffusion-weighted image at a higher level (d and e) complete resolution of findings

and obstructive hydrocephalus.[5-8] Pontine hemorrhage, subdural hematoma, subarachnoid bleed, and hemorrhage into pituitary adenoma have also been reported.[3,9-11]

Stroke in children is extremely rare. Watershed infarcts and pontine hemorrhage could possibly explain the neurological deficit in our case. This is the earliest reported age of presentation of dengue with stroke with a near complete neurological recovery. Ischemic stroke in dengue has been previously reported in elderly adults.[4,12,13] Ischemic stroke due to dengue-associated vasculopathy has also been reported in an 8-year-old child.[14]

Treatment in dengue encephalopathy is usually supportive. Intravenous methylprednisolone or immunoglobulins may be considered for immune-mediated encephalomyelitis and dengue-associated vasculopathy. Our patient was managed conservatively with adequate hydration, nutrition, anticonvulsants, and neurorehabilitation.

In conclusion, dengue-associated stroke is extremely rare in children. Stroke in dengue patients may be hemorrhagic or ischemic. Dengue should be enlisted as a cause of stroke in children from tropical countries with febrile encephalopathy and focal neurological deficits. Treatment is supportive and prognosis may be variable.

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Conflicts of interest

There are no conflicts of interest.

Sangeetha Yoganathan, Sniya Valsa Sudhakar[1], Leena Priyambada[2], Maya Thomas

Departments of Neurological Sciences, [1]Radiodiagnosis and [2]Pediatrics and Christian Medical College, Vellore, Tamil Nadu, India

Address for correspondence: Dr. Maya Thomas, Department of Neurological Sciences, Christian Medical College, Vellore - 632 004, Tamil Nadu, India.
E-mail: maya@cmcvellore.ac.in

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