



Clinical Observations

Pediatric Ischemic Stroke due to Dengue Vasculitis

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ABSTRACT

BACKGROUND: Dengue infection is an important arboviral infection in southeast Asia, especially in India. Neurological manifestations of dengue are increasingly recognized. **METHODS:** We report an ischemic stroke due to dengue vasculitis in an 8-year-old child. **PATIENT:** We present a girl with a short febrile illness followed by episodic severe headache, with gradually progressive hemiparesis and visual impairment. Her brain magnetic resonance imaging revealed multiple infarctions in the anterior and posterior circulation. The magnetic resonance angiogram revealed irregular narrowing of bilateral middle cerebral arteries, right anterior cerebral artery, left posterior cerebral, and bilateral vertebral arteries suggestive of vasculitis. Her dengue serology was strongly positive for immunoglobulin M with 68.9 panbio units. The rest of the evaluation for pediatric stroke was unremarkable. She was treated with intravenous followed by oral corticosteroids and recovered totally with resolution of vasculitis on magnetic resonance angiogram over the next 3 months. **CONCLUSION:** This child illustrates possible immune-mediated vasculitis caused by dengue infection which is rather a rare presentation in a child who subsequently recovered well. One should consider dengue in childhood strokes in endemic regions.

Keywords: dengue infection, vasculitis, ischemic stroke, child

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Introduction

Dengue infection is an important arboviral infection, reported more often in southeast Asia. In India, dengue is endemic with high frequency of outbreaks. The neurological manifestations of dengue infection include encephalitis, meningoencephalitis, Guillain-Barre syndrome, myelitis, and myositis.¹⁻³ There are a few reports of both hemorrhagic and ischemic stroke due to dengue hemorrhagic fever. We present a child with dengue vasculitis as the likely cause of ischemic stroke.

Patient Description

An 8-year-old girl presented with episodic severe headache for 10 days, with each lasting episode for 20 to 30 minutes with vomiting at the

peak of headache and relieved by analgesics. She had a short febrile illness for 5 days at the onset, and the headache continued even after the fever subsided. Her birth and developmental history were normal. Her general and neurological examinations were unremarkable. She received symptomatic therapy with analgesics. Two days later, she developed two episodes of transient left leg weakness followed arm weakness which improved spontaneously in few minutes. Routine hematological studies including platelet count were normal. Cranial computed tomography without contrast was normal. Magnetic resonance imaging (MRI) revealed cortical infarcts in the right frontal and parietal regions in the middle cerebral artery (MCA) territory on the diffusion weighted images (Fig 1A,B). The magnetic resonance angiography (MRA) revealed focal narrowing of both MCAs, the right anterior cerebral artery, the left posterior cerebral artery, and both vertebral arteries (Fig 1C).

The child developed visual blurring which deteriorated to significant visual impairment in both the eyes over 24 hours. Neurological examination revealed left hemiparesis with a power of 3 of 5 on the Medical Research Council scale. The fundoscopic examination was normal. Repeat MRI of the brain revealed new infarcts in left parietal and increase in size of right frontal and parietal regions (Fig 2A,B). MRA revealed multifocal irregular narrowing of M1 segment of bilateral MCA, V4 segment of vertebral arteries bilaterally and A1 segment of right anterior cerebral artery, and P1 segment of left posterior cerebral artery with increasing severity compared with the previous MRI (Fig 2C).

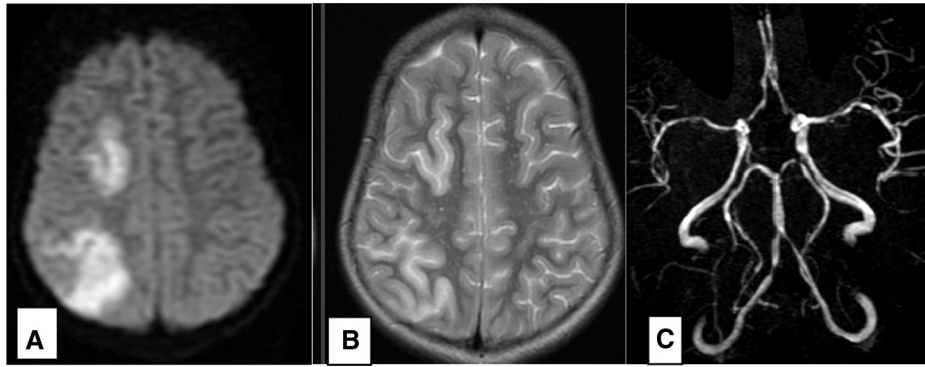
The child's blood counts, erythrocyte sedimentation rate, biochemical studies, renal and liver function tests were normal. Serum markers of

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**FIGURE 1.**

(A) Diffusion-weighted magnetic resonance imaging (B) T₂-weighted images on day 1 of stroke depicting right frontal and posterior parietal cortical infarcts in right middle cerebral artery (MCA) territory. (C) Magnetic resonance angiography depicting narrowing of both MCAs, right anterior cerebral artery, left posterior cerebral artery, and both vertebral arteries.

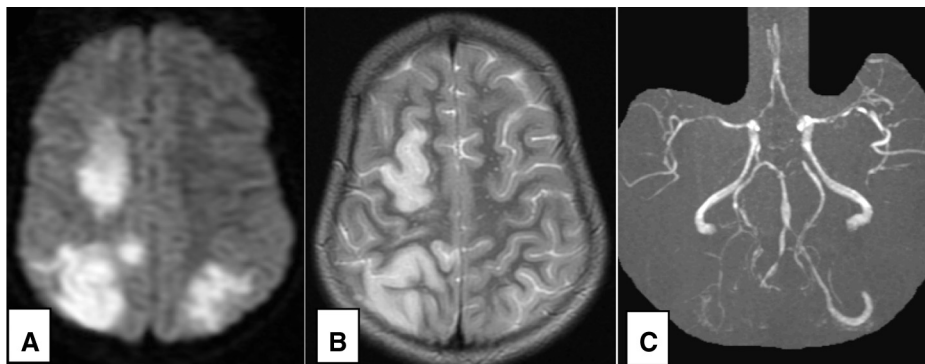
vasculitis including antinuclear antibody, double stranded DNA, rheumatoid factor, and C-reactive protein were unremarkable. Her protein C, S, and antithrombin III levels were normal. Serum homocysteine, lipid profile, thyroid profile, rheumatoid factor, and antistreptolysin-O titer were normal. Sickle cell test was negative by sodium meta bisulphite test. Her 2D echocardiogram and transesophageal echocardiogram were unremarkable. Cerebrospinal fluid analysis indicated protein of 27 mg%, glucose of 69 mg%, and white blood cell count of 6 with all lymphocytes, and polymerase chain reaction for tuberculosis and herpes simplex virus (1 and 2) was negative. Gram stain, Ziehl-Neelson, and fungal stains and cultures for organisms were negative. The dengue serology was strongly positive for IgM with 68.9 panbio units (negative <9, positive >11, equivocal 9-11 panbio units), and IgG was negative. PanBio test is an indirect enzyme-linked immunosorbent assay test for detection of antibodies against dengue antigen. Mantoux test was negative, and chest radiograph was normal. She was administered intravenous (IV) methylprednisolone pulse therapy for 5 days followed by oral corticosteroids for 2 weeks. Vision improved over the next 72 hours. Her left hemiparesis gradually improved, and she began attending school after 2 months. Brain MRI after 3 months revealed evolution of the brain lesions with encephalomalacia changes and normal caliber vessels on MRA, suggesting resolution of vasculitis (Fig 3A,B). At 1 year follow-up the child had no neurological deficits.

Discussion

Patients with dengue infection and stroke usually have intracerebral hemorrhage with accompanying thrombocytopenia and vasculopathy; ischemic infarcts are

uncommon.⁴⁻⁶ Liou et al.⁴ reported one individual with dengue infection with thrombocytopenia and ischemic stroke associated with progressive neurological deficits that improved subsequently. Mathew et al.⁵ reported three patients with dengue fever presenting with stroke. One patient had dengue hemorrhagic fever with hemiparesis, and MRI of the brain revealed multiple hemorrhagic foci in the left parietal and temporal lobe. The second patient had dengue fever followed by altered sensorium and quadriparesis. MRI revealed bilateral cerebellar hemorrhages, obstructive hydrocephalus, and multiple watershed infarctions. The third patient in this report had right parietal infarct. Thrombocytopenia was present in all the three patients and one patient died in this series.⁵ Dysarthria-clumsy hand syndrome were described with dengue infection.⁷

Results from a large multinational stroke registry with more than 600 children indicate that arteriopathy is the most common cause of strokes in children evident in 53% of pediatric strokes.⁸ There is an ongoing study to assess the association of vascular changes and infection in childhood stroke.⁹ We present a child with dengue vasculitis involving major intracranial vessels with angiographic evidence of focal irregular narrowing. Febrile illness with severe headache preceding the stroke in this child from endemic region for dengue fever and strongly positive dengue IgM in serum

**FIGURE 2.**

(A) Diffusion-weighted magnetic resonance imaging (B) T₂-weighted images on day 4 of stroke depicting ischemic infarcts in right frontal and bilateral parietal regions in the bilateral middle cerebral artery (MCA) territory. (C) Magnetic resonance angiography (MRA) depicting narrowing of both MCAs, the right anterior cerebral artery, the left posterior cerebral artery, basilar, and both vertebral arteries of increased severity compared with the MRA in Fig 1.

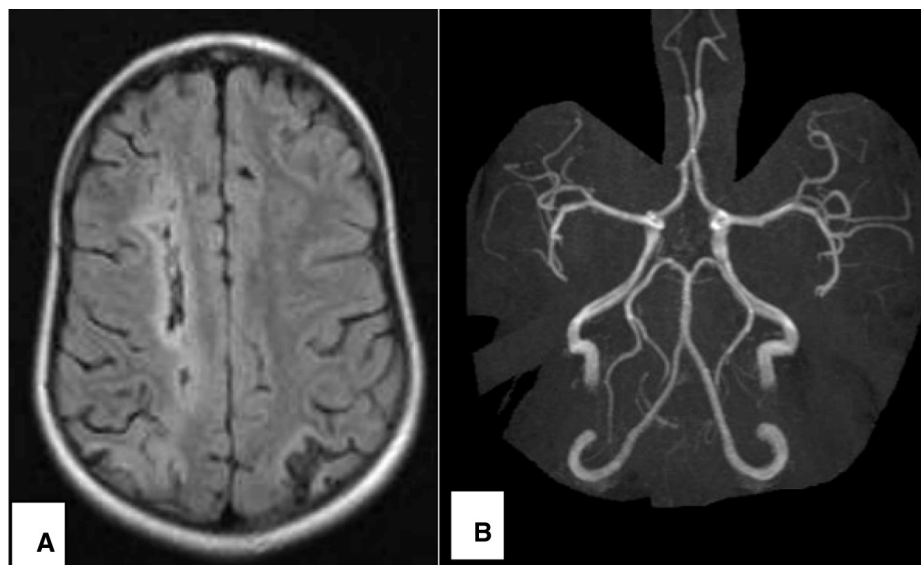


FIGURE 3.

Magnetic resonance imaging (fluid attenuated inversion recovery sequence 2 months after the stroke depicts (A) gliotic changes in the previous areas of cortical infarctions (B) the magnetic resonance angiography depicts total resolution of vasculitis and normal middle cerebral arteries, posterior cerebral artery, and vertebral arteries.

confirmed dengue infection. Thrombocytopenia was not documented in this child, perhaps because she was not evaluated during the initial part of her illness. She had progressive hemiparesis and visual impairment preceded by severe headache. The infarctions were probably due to vasculitis involving both anterior and posterior circulation vessels. Infective arteritis of intracranial vessels associated with coagulopathy has been suggested as the pathophysiological mechanism of hemorrhagic stroke in dengue infection.¹⁰ Dengue meningovascularitis has been postulated to be one of the mechanisms for ischemic stroke in patients with dengue infection.⁴ The most likely explanation of stroke in our patient could be immune-mediated arteritis because her stroke occurred after the fever subsided and responded well to IV and oral corticosteroids. The vasculitis completely resolved at the end of 3 months as evident by MRA.

Conclusion

This child exhibited a rare presentation of dengue infection associated immune-mediated vasculitis associated with ischemic stroke. She had multiple bilateral infarcts on MRI of the brain and multifocal narrowing on MRA. The child had good response to corticosteroids and experienced a complete clinical recovery.

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