

Role of imaging in neonatal Chikungunya encephalitis acquired by vertical transmission

Namrita Sachdev¹, Yashvant Singh², Shivani Gupta³

From ¹Consultant and Associate Professor, ²Senior Radiologist, ³Senior Resident, Department of Radiodiagnosis, PGIMER and Dr. Ram Manohar Lohia Hospital, New Delhi, India

Correspondence to: Dr. Yashvant Singh, D II/91, West Kidwai Nagar, New Delhi - 110 023, India. E-mail: y_ashvant@yahoo.com

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ABSTRACT

Background: Chikungunya is a viral infection which usually manifests as fever, rash, and arthralgia. Neurological complications are rare but are increasingly seen in children and adults in endemic countries like India. Vertical transmission is seen in neonates with mothers who have been infected with the virus in the antenatal period. **Objective:** The objective of the study was to identify the essential role of imaging in the workup of these neonates, especially magnetic resonance imaging (MRI). **Methods:** A retrospective descriptive analysis of 10 neonates presenting with hypoactivity, maculopapular rash, and fever progressing to generalized seizures, and apnea suggestive of encephalitis was done. Chikungunya was confirmed by serum IgM CHICK enzyme-linked immune sorbent assay. Imaging evaluation included neurosonogram, computed tomography, and MRI with diffusion-weighted sequence with follow-up imaging at 1–3 months. **Results:** All the neonates had encephalopathy (100%) with or without seizures and perioral rashes. Cerebrospinal fluid showed mononuclear pleocytosis, raised protein or hypoglycorrhachia in 75% cases. Bacterial markers including cultures were negative. MRI showed features of viral encephalitis involving frontoparietal subcortical and deep white matter and corpus callosum with restricted diffusion. Neurocognitive outcomes in these neonates revealed neurodevelopmental delays for which follow-up MRI imaging was important, revealing reversal in diffusion changes, cystic encephalomalacia, and diffuse cerebral atrophy. **Conclusion:** In countries like India, experiencing annual outbreaks of Chikungunya infections radiologists must be familiar with the neuroimaging features and its possible sequelae.

Key words: Chikungunya, Diffusion-weighted magnetic resonance imaging, Encephalitis, Neonatal, Vertical

Chikungunya virus (CHIKV) is an insect-borne virus, of the genus, alphavirus that is transmitted to humans by virus-carrying Aedes mosquitoes [1]. In India, CHIKV was first isolated in Calcutta in 1963, with several seasonal outbreaks in India since then [2].

CHIKV infection typically induces a self-limiting arthritis except in immuno-compromised patients and newborns where it can be a serious disease. Mother to child perinatal transmission can occur when intrapartum maternal viremia leads to severe neonatal infection [3]. Clinico-radiological evaluation with cerebrospinal fluid (CSF), blood cultures, and magnetic resonance imaging (MRI) play a key role in the diagnosis and prognosis of these neonates. MRI with diffusion-weighted sequences shows non-specific viral encephalitis imaging picture; however, the demyelinating changes involving white matter with diffusion restriction is a usual feature. We conduct this study to highlight the importance of neuroimaging in the management and follow-up of neonates diagnosed as having Chikungunya encephalitis.

METHODS

A retrospective descriptive analysis was done for 10 neonates of Chikungunya encephalitis born of mother's with Chikungunya in

the past 2 weeks before delivery, was referred to the Department of Radiodiagnosis, at a tertiary care hospital, Delhi, from August 2016 to September 2016 for the MRI evaluation.

Diagnosis of Chikungunya was made with NIV CHIK IgM enzyme-linked immune sorbent assay in serum samples of neonates who presented with symptoms of fever, lethargy refusal to feed, and peri-oral rash. Vertical transmission was confirmed by the antenatal clinical history of Chikungunya symptoms in mothers 1 week before delivery and serology real-time polymerase chain reaction analysis in newborns and mothers.

MRI evaluation included T1, T2, fluid-attenuated inversion recovery (FLAIR), diffusion-weighted imaging (DWI), gradient echo, and post-contrast images. Neurosonogram was done in one child and computed tomography (CT) scan in another. Follow-up MRI was done at 1 month or 3 months depending on the clinical evaluation of neurodevelopmental delay.

RESULTS

All 10 (100%) cases presented with lethargy and refusal of feeds within 1st week of postnatal life, 8 (80%) presented with fever while 5 (50%) cases presented with seizures. Encephalopathy was predominant in all the cases, and the duration of encephalopathy

was variable lasting for 10–15 days. A total of 9 (90%) cases had peri-oral rashes. Pigmentary changes had an acrofacial distribution beginning 3–4 days after fever in the peri-oral region leading to the characteristic “brownie-nose” pigmentation. There was no mortality, and at the time of discharge, neurological examination showed hypotonia in all the cases.

Laboratory investigations showed thrombocytopenia in 90% of the cases, with leukopenia in 30% cases. C-reactive protein was raised in 6 neonates while CSF showed mononuclear pleocytosis, raised protein, or hypoglycorrhachia in 75% cases. Bacterial markers including cultures were negative.

All the neonates also had some imaging evaluations which included neurosonogram and MRI. Changes on sonography were seen in one case while the rest of the patients were normal. CT scan was done in one case followed by MRI wherein, 2 neonates (20%) did not show any abnormality on MRI. Rest of the 8 cases (80%) showed bilateral supratentorial involvement of the frontal, parietal, and occipital lobes. Infratentorial compartment with cerebellum and brain stem was not involved. T2 and FLAIR hyperintensities, diffuse (70% cases) as well as discrete in appearance (10% cases), were

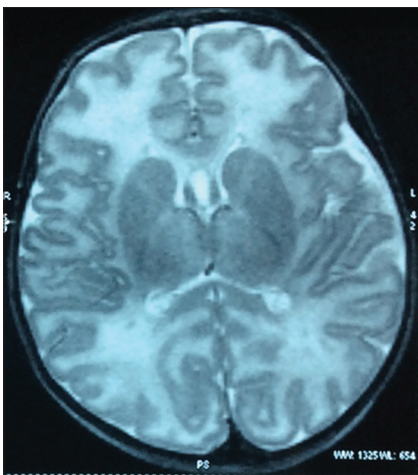


Figure 1: Axial T2-weighted image demonstrates bilateral symmetrical hyperintensities affecting frontal and parietal lobes

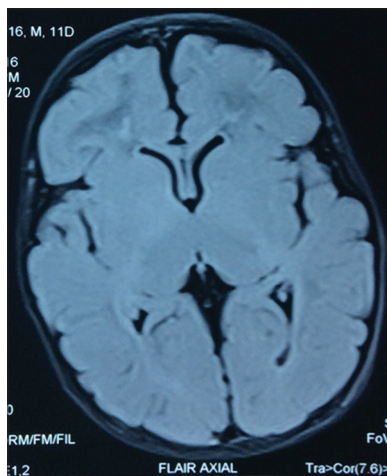


Figure 2: Fluid-attenuated inversion recovery axial image of a 20-day-old neonate shows discrete foci of hyperintensities in bilateral frontal lobes

seen in the subcortical and deep white matter in the periventricular location, with sparing of the U-fibers (Figs. 1 and 2).

Involvement of the peritrigonal areas and perirolandic fissures with centrum semiovale was also seen (Fig. 3a and b). Diffusion restriction was a prominent feature which was patchy in nature, seen in 60% of cases. Diffusion restriction was seen involving the rostrum and splenium of corpus callosum with normal apparent diffusion coefficient images.

Hemorrhage with blooming on gradient sequences was absent. Post-contrast images were normal in all the cases (Fig. 4 a-d).

Follow-up MRI showed changes with a significant reversal in the diffusion restriction after 1 month. Cystic encephalomalacia with ventricular dilatation and reduction in the white matter volume was seen in 3 months follow-up scan in two neonates (20%) (Fig. 5a and b). Diffuse cerebral atrophy also was seen on follow-up in two patients (20%) (Fig. 6). Neuro sonogram revealed bilateral heteroechoic areas in frontal lobes in one neonate and was normal in the rest. Plain CT was done in one

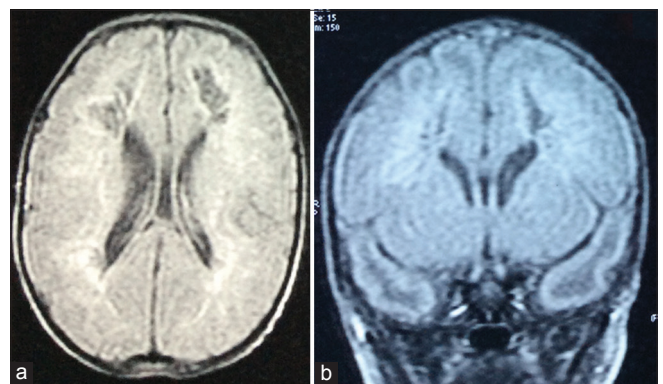


Figure 3: (a) Fluid-attenuated inversion recovery axial section in a 20-day-old neonate shows altered signal intensity areas in bilateral frontoparietal peri-ventricular region and deep white matter. (b) Corresponding coronal section of Fig. 3a

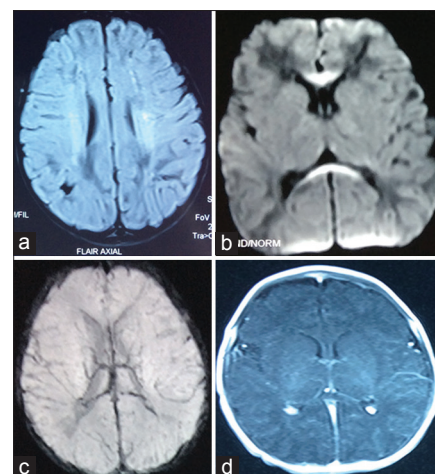


Figure 4: (a) Fluid-attenuated inversion recovery axial image shows typical hyperintensities involving peri-ventricular deep white matter and centrum semiovale in a 15-day-old neonate. (b) Diffusion restriction image of same patient shown in Fig. 4a involving rostrum and splenium of corpus callosum. (c) Susceptibility weighted image of the same patient shown in Fig. 4a, shows no evidence of hemorrhage. (d) Post-contrast T1-weighted image of the same patient shown in Fig. 4a, shows no contrast enhancements

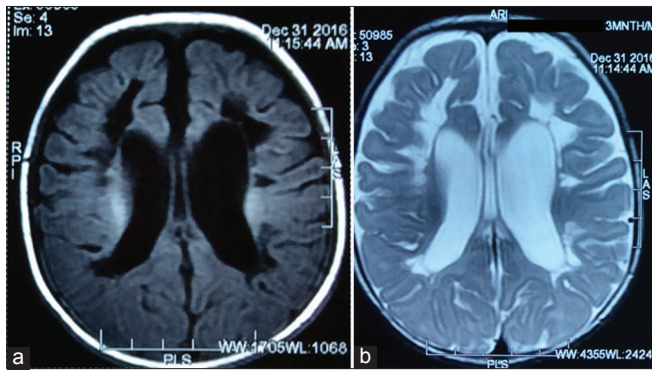


Figure 5: (a) 3 months follow-up scan in a patient of Chikungunya encephalitis shows cystic encephalomalacia with ventricular dilatation on fluid-attenuated inversion recovery axial. (b) Corresponding T2-weighted images of the same patient shown in Fig. 5a

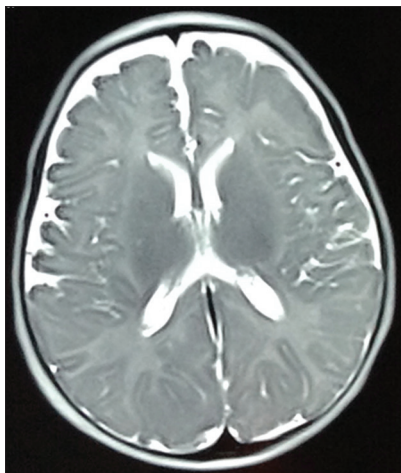


Figure 6: 3 months follow-up scan in a patient of Chikungunya encephalitis shows diffuse cerebral atrophy on axial T2-weighted image

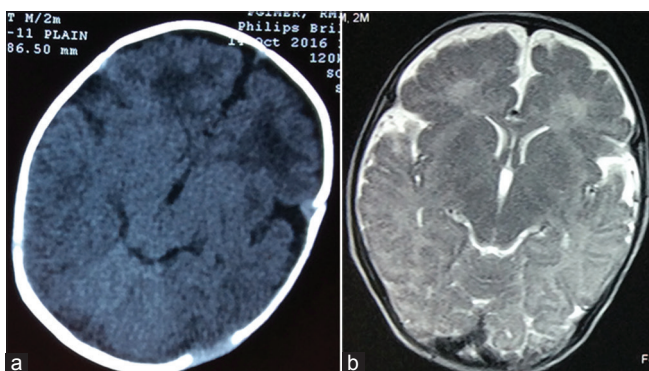


Figure 7: (a) Axial computed tomography in a 2-month-old child revealed bilateral frontal lobe hypodensities. (b) Corresponding axial T2 magnetic resonance imaging of the patient shown in Fig. 7a appear as patchy white matter hyperintensities

neonate and showed frontal lobe hypodensities consistent with white matter changes on MRI (Fig. 7a and b).

DISCUSSION

There have been few reports of detailed neuroimaging findings for neuro Chikungunya, especially in children and neonates. In the Le Reunion outbreak in 2005–2006, the most distinctive feature

on MRI was that lesions were seen exclusively in the white matter and consisted of areas of reversible diffusion restriction [3]. Follow-up MRI on those with persistent disabilities revealed extensive white matter degeneration.

In a series of 30 children reported from the same area [4,5], radiological findings showed positive neurosonogram in 2 neonates with periventricular hypoechoogenicity. In MRI study in children over 1 month, there was an increased T2 signal in periventricular white matter and bilateral centrum semiovale. DWIs were normal. On the other hand, the four neonates showed characteristic areas of diffusion restriction in bilateral centrum semiovale, anterior and posterior corpus callosum, posterior limb of internal capsule, and optic radiation. There were diffusion changes in parietal, frontal, and temporal white matter. Hemorrhage was reported in 2 neonates evidenced by a high signal on T1 in periventricular white matter and cerebellum. Follow-up MRI obtained after 6 months showed bilateral cavitations in frontoparietal white matter with atrophy in 2 cases

Encephalitis due to Chikungunya vertical transmission reported from Brazil exhibited similar DWI hyperintensity involving subcortical areas and corpus callosum [6]. Ali *et al.* reported restricted diffusion in 7 of 14 patients infected with West Nile Virus [7]. Immune-mediated perivascular demyelination could be the cause for cytotoxic edema. The appearance of vasogenic edema seen at this stage is seen as hyperintensity on T2. Hence, the restricted diffusion precedes the signal abnormalities on T2 and is also known to resolve before the changes are seen on T2 [7,8].

Besides, this leukoencephalitis pattern on MRI in Chikungunya has a predilection for frontal and parietal regions with the involvement of corpus callosum [9]. The MR appearance using DWI is closely related to the pathologic changes that occur after viral infections. Acute inflammatory lymphocytic infiltration and perivascular cuffing are responsible for cytotoxic edema that reflects as diffusion restriction. In the subacute stage, as the inflammatory vasculitis regresses so does the diffusion restriction [10]. The presence of perivascular lymphocytic infiltrates with demyelination is non-specific and common to all viral infections [11].

With regard to neurological outcome, cytotoxic edema suggests a more fulminant change with poor prognosis and vasogenic edema more mild change with better prognosis. The transient ischemia seen does not imply the neuronal death [7]. The neurological outcome of Chikungunya encephalitis is varied ranging from mild ocular, behavioral, and postural deficiencies to severe cerebral palsy [3]. Therefore, the MRI features on follow-up range from subcortical atrophy to cystic encephalomalacia of periventricular white matter.

Long-term follow-up of a minimum of 2 years is required for confirmed cases of CHIKV infection acquired congenitally or during the neonatal period to assess long-term sequelae from a neurologic and psychomotor perspective [12]. Neuroimaging follow-up MRI is, therefore, a must in these cases.

CONCLUSION

Encephalitis is the most common neurological presentation in the Chikungunya infected neonates after mother to child transmission.

Neuroimaging is essential with MRI with DWI being the primary imaging modality. DWI images may show changes before signal intensity changes on T2 images. DWI can also be used to prognosticate the disease. Long-term MRI imaging is important in neonates who have neurodevelopmental delays.

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