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CLINICAL BRIEF

Unusual Involvement of Basal Ganglia and Dentate Nucleus in Children with Acute Encephalopathy with COVID-19

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Abstract
Children account for 1% to 5% of diagnosed COVID-19 infection with relatively mild presentation compared to adults. The frequency of neurological involvement in acute COVID-19 infection in children is unclear. COVID-19 is also considered to be a neurotropic virus, but so far, in the pediatric age group, very few cases with involvement of basal ganglia and no case of dentate nucleus involvement have been reported in the literature. The present paper reports two cases of acute encephalopathy with COVID-19, the first case with basal ganglia involvement and the second with dentate nucleus involvement. Both cases required aggressive management and had complete neurological recovery on follow-up. Hence, these cases are reported to make everyone aware of the neurological presentation with atypical neuroimaging finding of acute COVID-19 infection in the pediatric age group; timely management improves the outcome.

Keywords Acute COVID-19 · Dentate nucleus · Basal ganglia · Encephalopathy

Introduction

Children account for 1% to 5% of the diagnosed COVID-19 infection with relatively mild presentation compared to adults [1]. The neurological manifestations in adults include mild symptoms like anosmia, headache, dizziness, depression, and severe symptoms of encephalopathy, encephalitis, seizures, acute transverse myelitis, Guillain–Barré syndrome (GBS), stroke and cerebral edema. The frequency of neurological involvement in acute COVID-19 infection in children is unclear [2]. There is growing urgency to understand the pathological basis of neurological changes associated with SARS-CoV-2 infection, as this has been associated with disease severity and ongoing neurocognitive symptoms [3].

Two cases of acute encephalopathy with COVID-19 are reported here, the first with involvement of basal ganglia in an 18-mo-old boy and the second with dentate nucleus involvement in a 2-y-old boy. COVID-19 is also considered to be a neurotropic virus, but so far, in the pediatric age group, very few cases with involvement of basal ganglia and no case of dentate nucleus involvement have been reported in the literature.

Case Reports

Case 1: An 18-mo-old boy presented with 5-d history of high-grade fever, lethargy, and depressed sensorium. He had multiple episodes of seizures with altered sensorium and required intubation and ventilator support due to a low Glasgow Coma Scale (GCS) of 5/15. He was in a state of decompensated shock and required fluid resuscitation and inotropic support. The COVID-19 reverse transcriptase–polymerase chain reaction (RT-PCR) was positive. His mother was also COVID-19 RT-PCR positive 1 wk ago. Computerized tomography (CT) of the chest showed ground-glass opacity with a CT severity score of 7/25. A complete hemogram revealed mild anemia with normal WBC and platelet counts. Inflammatory markers were elevated [C-reactive protein (CRP) 86 mg/dL (0–6), ferritin 327 ng/dL (13.7–78.8), LDH 693.2 IU/L (150–300), D-dimer 128.3 ng/mL (0–500), NT-proBNP 2590 pg/mL (0–100), CPK- MB 30 U/L (0–24)]. EEG was suggestive of bilateral cortical slowing, MRI brain showed involvement of bilateral lentiform nuclei and hippocampi with cerebral

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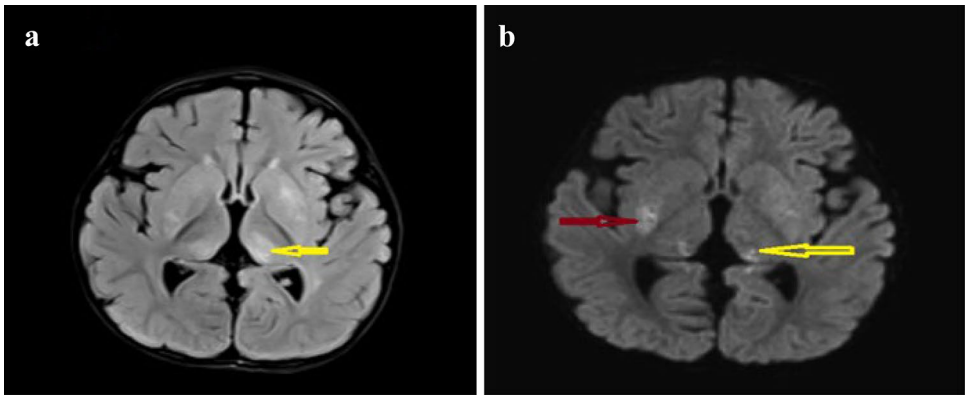

Fig. 1 **(a, b)** MRI images of case 1 showing putamen (*red arrow*) and thalamus (*yellow arrow*) hyperintensity in DWI axial imaging. *DWI* Diffusion weighted

edema (Fig. 1a and b). Cerebrospinal fluid (CSF) had normal sugar, protein and cell count. CSF pan neurotropic virus panel was negative. He was treated with antibiotics, remdesivir, and antiseizure medications (fosphenytoin, levetiracetam, phenobarbitone and midazolam infusion). He received intravenous immunoglobulin (IVIG) 2 g/kg and methylprednisolone pulse dose as his inflammatory markers were raised. Subsequently, his inflammatory markers were decreased. Antiseizure medications were tapered and he was weaned off from ventilator support. On follow-up after 3 mo, the child had normal neurological status, and repeat MRI Brain showed the normal study.

Case 2: A 2 y old boy presented with 3-d history of fever and progressive lower limb weakness associated with gait abnormality. On admission his vital signs were normal and higher mental functions were normal. Neurological examination showed hypotonia with a power of 3/5 and absent deep tendon reflexes in both lower limbs. His COVID-19 RT-PCR was positive. A complete hemogram revealed the normal study. Inflammatory markers were normal (CRP 0.3 mg/L, LDH 284 U/L, D-dimer 88 ng/mL, ferritin 108 ng/mL). Nerve conduction velocity suggested pure motor axonal neuropathy. MRI brain showed hyperintensities in the medulla oblongata and the dentate nucleus of the cerebellum (Fig. 2a and b). The child was treated with Inj IVIG (2 g/kg) along with a pulse dose of methylprednisolone for 5 d. CSF studies were normal. CSF pan neurotropic panel was negative. Subsequently, lower limb power improved. On follow-up after 2 mo, the child had normal neurological status, and repeat MRI Brain showed reversal of dentate nucleus hyperintensity.

Discussion

The mechanism by which COVID -19 affects the brain is not known. Direct brain infection or autoimmune process may be present as the virus binds the surface spike protein to the human angiotensin-converting enzyme 2 receptors (ACE-2). ACE-2 is present in the brain vascular endothelium; vascular process with clotting and infraction may be possible [4]. Neuroinflammatory response leads to blood–brain

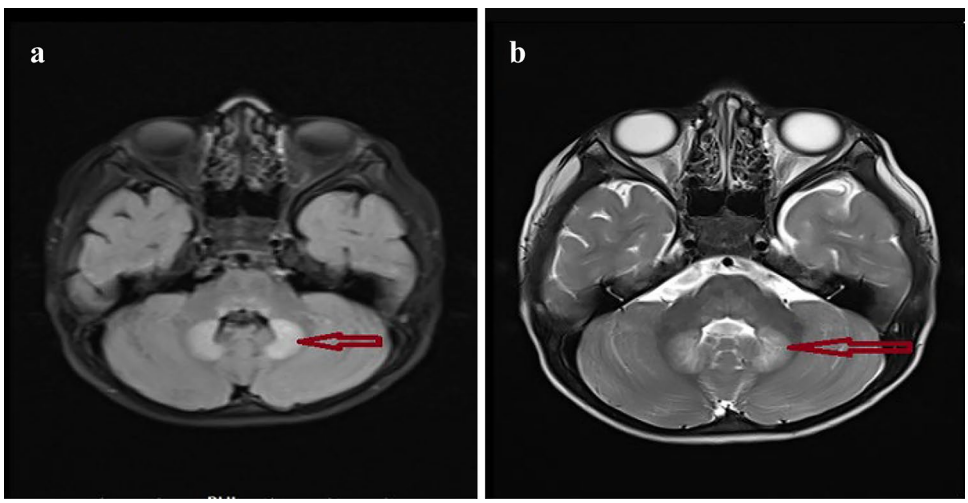

Fig. 2 MRI images of case 2 showing dentate nucleus (*red arrow*) hyperintensity in **(a)** FLAIR and **(b)** T2W axial imaging. *FLAIR* Fluid-attenuated inversion recovery, *T2W* T2 weighted

barrier breakdown, postinfectious immune dysregulation, and/or secondary injury from the complications of systemic inflammation or other non-CNS organ failure [5].

Gürkas et al. in Turkey reported that among 312 pediatric patients, 21.15% had neurologic symptoms. Of this, 14% had a headache, but no patient reported encephalitis [6]. On the contrary, the present two cases presented with neurological symptoms and encephalopathy.

LaRovere et al. reported life-threatening neurologic conditions in acute COVID-19 in children that includes severe encephalopathy, acute ischemic or hemorrhagic stroke, acute central nervous system infection, acute demyelinating encephalomyelitis, acute fulminant cerebral edema and GBS [7]. Acute encephalopathy has been reported in the pediatric population that has characteristic imaging features that are symmetrical, multifocal lesions with thalamic involvement [8]. Bilateral thalami damage is often a distinctive feature in acute necrotizing encephalitis. The absence of hemorrhage seems to be associated with a better outcome. In the present case there was an involvement of bilateral lentiform nuclei and hippocampi but without haemorrhage.

Al-Dalahmah et al. in their case report of adults describe autopsy finding suggestive of association of COVID-19 with marked neuronophagia involving inferior olives and dentate nuclei [9]. Similarly, the present case had dentate nuclei involvement on MRI brain.

Conclusion

The above cases are reported to make everyone aware of the atypical neuroimaging findings of acute encephalopathy with COVID-19 in the pediatric age group; timely management improves the outcome.

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Declarations

Conflict of Interest None.

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