Acute Ischemic Stroke Associated with COVID-19 in a Pediatric Patient: A Case Report

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Abstract
COVID-19, caused by novel coronavirus SARS-CoV-2, which seemed to have unaffected the children in the initial period of the pandemic, now has targeted the pediatric population with varied clinical manifestations; the pathophysiology is still under exploration. Neurological presentations are being increasingly reported in both adults and children. We present a case of ischemic stroke in a 12-year-old COVID-19 patient with seizure, right hemiparesis, and dysarthria.

Introduction
Current COVID-19 status in the world is reported to be 154 million cases with 3 million deaths worldwide at the time of writing this article. Clinical presentations in children range from asymptomatic or mild to the life-threatening multisystem inflammatory syndrome in children that can present at any time during the course of the illness but commonly at 1–6 weeks after infection [1]. There have been case reports of neurological presentations including transverse myelitis, encephalitis, and stroke presentations in the setting of an acute COVID-19 infection in children [2, 3]. The causal effect of COVID-19 in these presentations is still under review.

Case Report
A 12-year-old boy with normal development was brought to our facility with a history of focal status epilepticus (in the form of staring look and speech arrest) lasting for nearly 30 min followed by progressive weakness on the right side of his body. On admission, he was drowsy, afebrile with blood oxygen saturation of 98%, a heart rate of 95 bpm, and blood pressure 148/96 mm Hg. The patient had a right-sided upper motor neuron type seventh cranial-nerve palsy, right dense hemiplegia, brisk deep tendon reflexes, and extensor plantar response on the right. His pupils were normal, and there were no signs of meningeal irritation. There was a positive family history of COVID-19 in his maternal aunt a week ago (the aunt stayed with the family), while his parents had tested positive a day earlier. The child was also obese and had history of documented high blood pressure readings over the past 5 years, which had been managed conservatively. There was family history of Sjogrens syndrome in the mother who had been on treatment with hydroxychloroquine and colchicine.
His preliminary lab investigations were normal including blood counts, PT, PTT, liver and renal functions, CRP, and procalcitonin. Nasopharyngeal COVID-19 polymerase chain reaction was positive. Brain CT performed showed hyperdense MCA sign with a thrombus in the M1 segment of the left middle cerebral artery (shown in Fig. 1a). CT angiography showed mild narrowing of the intracranial portion of the left ICA with severe narrowing of the whole M1 segment of left MCA and severe focal stenosis at the origin of the superior M2 segment of the left MCA (shown in Fig. 1b). He was admitted to the PICU and started on aspirin 150 mg and levetiracetam and initiated on neuroprotective measures with regular monitoring of GCS. The child continued to be stable on room air, and blood pressure readings continued to be in the normal range.

Thrombolytic treatment or anticoagulation measures were ruled out after discussion with an interventional neuroradiologist in view of the extensive arteriopathy findings involving the intracranial vasculature. His cardiac workup including ECG and echocardiography was normal. After an initial stabilization, MRA brain was done. MRI brain (DWI) showed severe variable narrowing of both ICA and MCA, suggestive of vasculitis. The patient’s stroke workup including viral markers; lipid profile; thrombophilia screening; autoimmune workup including lupus anticoagulant, ds DNA, p-ANCA, and c-ANCA; rheumatoid factor; and complement levels were negative. The child underwent abdominal ultrasonography to rule out renal causes of hypertension, which was reported normal.

Clinical and laboratory findings did not fulfill criteria for multisystem inflammatory syndrome in children, given the absence of fever and negative inflammatory markers (D-dimer [0.5 μg/mL FEU], serum interleukin-6 [25.5 pg/mL], C-reactive protein [2.7 mg/dL], and white cell count [14,800 per mm3]). His SARS-CoV-2 anti IgG antibodies level was reported less than 3.8 AU/mL. Consent for the CSF study could not be obtained.

In view of the extensive arteriopathy findings, he was started on a 3-day course of intravenous methylprednisolone followed by a tapering course of oral steroids. He also received 2 g/kg of IV immunoglobulins. By day 5 of hospital stay, he was also started on rehabilitation.

He underwent a total of 10 days of inpatient rehabilitation and was discharged home on aspirin 75 mg daily. At the time of discharge, he had dense right hemiparesis with mixed aphasia and dysarthria. When seen on last follow-up 3 months later, the child was yet to recover from his right dense hemiplegia, with improvement noted in his speech.

Discussion

SARS-CoV-2 is reported to have a 76 times increase (95% CI: 2.3–25.2) in risk of resulting in a stroke in comparison with other seasonal viral infections in adults [4]. Pathophysiology of acute ischemic stroke in COVID-19 is hypothesized as virus-mediated potentiation of a prothrombotic and proinflammatory state via endothelial...
cell disruption and clotting cascade activation [5]. Also, proposed are direct viral-induced endotheliitis or endotheliopathy, potentially leading to angiopathic thrombosis, with viral particles reported to have been isolated from the endothelium of various tissues, including brain tissue [6, 7].

Interestingly COVID-19-associated strokes are noted to have a particular profile, characterized clinically by poor NIHSS and a poor outcome and radiologically by large artery occlusion and multiple arterial territory involvement. Increased incidence of cryptogenic stroke (patients with no identified typical causes of stroke) has also been reported [8].

This clinical profile was also seen in our patient. Postinfectious cerebral arteritis causing childhood large-vessel occlusion stroke is known to occur in the setting of numerous viral infections. Here, the classical radiological finding is of variable unilateral involvement of the intracranial ICA, MCA, or ACA in the absence of systemic disease, described as “focal cerebral arteriopathy” (FCA) [9].

Based on the imaging findings, FCA was considered in our patient as history and the labs had ruled out possibility of thrombosis as the stroke etiology. FCA following COVID-19 was also recently reported in a child whose nasopharyngeal and CSF samples tested positive too [10].

Our case had documented hypertension preceding the acute presentation as well as a family history of autoimmune disease in the mother. It is possible that these acted as risk factors for the stroke associated with COVID-19.

The findings described in this report suggest that COVID-19 infection could potentially trigger systemic postinfectious arteritis with CNS vascular involvement, especially in those pediatric patients with underlying comorbidities like obesity and hypertension. Thus, COVID-19 needs to be considered as an important association or risk factor for pediatric stroke.

Statement of Ethics

Written informed consent by the patient’s parents to publish the case and any accompanied images was obtained. Ethical approval is not required according to DHA committee policies.

Conflict of Interest Statement

The authors declared no conflict of interest.

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Author Contributions

S.V., G.A.K., P.K., and N.P. contributed to the conception and design of the study. S.V. contributed to drafting the text and preparing the figures. All the authors have access to all the data in the study. S.V. and P.K. have accessed and verified all the data in the study.

Data Availability Statement

All data generated or analyzed during this case report are included in this article. Further inquiries can be directed to the corresponding author.

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