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Focal Cerebral Arteriopathy in a COVID-19 Pediatric Patient

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Summary statement:

We present a case of focal cerebral arteriopathy and ischemic stroke in a pediatric COVID-19 patient presenting with seizure, right hemiparesis, and dysarthria with positive for SARS-CoV2 virus both from nasopharyngeal swab and cerebral spinal fluid.

Introduction

The neuroinvasive mechanism of SARS-CoV-2 is not fully understood. SARS-CoV-2 may enter the central nervous system (CNS) hematogenously, with other proposed routes, including the olfactory and trigeminal nerves, cerebral spinal fluid (CSF), and the lymphatic system (1). Neurologic manifestations in COVID-19 pediatric patients have uncommonly been reported. We report a presumptive case of ischemic stroke due to focal cerebral arteriopathy (FCA) associated with COVID-19.

Case Presentation

Previously healthy 12 year-old-boy with a new onset of generalized seizures, initially treated with diazepam. Shortly after, he developed right-sided hemiparesis and dysarthria. There was no previous history of fever, cough, shortness of breath, skin rash, hemoglobinopathy, or recent trauma. No one in his family had a known history of COVID-19 infection.

The diagnosis of COVID-19 was made by the presence of SARS-CoV2 viral nucleic acid through nasopharyngeal swab using 2019-Novel Coronavirus (2019-nCoV) real-time reverse transcriptase-polymerase chain reaction assay. Testing for the presence of SARS-CoV-2 viral nucleic acid in the CSF was also positive. Viral genome was extracted using a viral RNA kit (Roche®), using a multiplex one-step reverse transcriptase real-Time polymerase chain reaction (PCR), amplifying Covid19 E, N, and ORF1ab/RdRp genes. CSF bacterial culture showed no growth after three days, and tests for herpes simplex virus 1 and 2 and varicella-zoster virus PCR (QIAGEN GmbH, Hilden, Germany) were negative. Serum ferritin measured 86.7 ng/L, C-reactive protein measured 3 mg/L, and erythrocyte sedimentation rate measured 45 mm/h. CSF analysis demonstrated 21 mg/dL of protein, 62 mg/dL of glucose, 100 red

blood cells per mm³ (traumatic lumbar puncture), and no white blood cells. CSF opening pressure was 25 mm of H₂O. D-dimer was not obtained. Platelet count was 285 103/μL, prothrombin time was 12.1, international normalized ratio was 0.9, and partial thromboplastin time was 27 seconds. Antinuclear antibody was normal.

Lung low dose computed tomography was normal. Carotid color Doppler ultrasound and echocardiography were normal. Magnetic resonance imaging demonstrated findings consistent with acute infarction without microhemorrhages (**Figure 1a, b, and c**), along with focal irregular narrowing and banding of the proximal M1 segment of the left middle cerebral artery (MCA) with a slightly reduced distal flow (**Figure 1d**). High-resolution contrast-enhanced vessel wall imaging was not performed.

There were no symptoms of other systems involvement, cervical enlarged lymph nodes, cutaneous or mucosal rash, or redness. The patient had no respiratory abnormalities. The patient received conservative management. Upon discharge, the patient is still hemiparetic at home and undergoing rehabilitation.

Discussion

The major imaging findings in this patient are the presence of unilateral focal vasculopathy, characterized by focal irregular narrowing and banding of the proximal left middle cerebral artery associated with left basal ganglia and insula acute infarct. There are many potential differential considerations in a child with acute stroke, including FCA, arterial dissection, embolic or thrombotic stroke, cerebral vasculitis in the context of systemic disease (including Kawasaki disease), and genetic disorders with arteriopathy, among others. Our leading diagnosis is FCA, one of the most common causes of childhood arterial ischemic stroke, which is defined by Wintermark

et al. (2) as a "unifocal and unilateral stenosis/irregularity of the large intracranial arteries of the anterior circulation (distal internal carotid artery and/or its proximal branches)". Varicella zoster virus vasculopathy is a well-known cause of FCA. Other infectious agents less commonly associated with FCA include other herpesviruses, human immunodeficiency virus, parvovirus B19, influenza A, enteroviruses, and *Mycoplasma pneumoniae*.

Based on the patient's history and lack of thrombotic processes outside the CNS, embolic stroke, and dissection were considered less likely than FCA. Recent reports of an elevated immune response and an inflammatory syndrome have been reported in children with COVID-19 infection (3). There have been reports of typical vasculitis findings in other organ systems, including Kawasaki disease like presentations (4,5). There was no evidence to suggest a multisystem inflammatory syndrome or Kawasaki-like presentation, as the patient did not show any of the classical clinical physical findings. The lumbar puncture CSF was not inflammatory. To our knowledge Kawasaki-like illnesses do not manifest as FCA. The presence of SARS-CoV-2 material from the nasopharynx swab is evidence that the patient had COVID-19, and the presence of the virus in the CSF, although uncommon, further corroborates CNS involvement.

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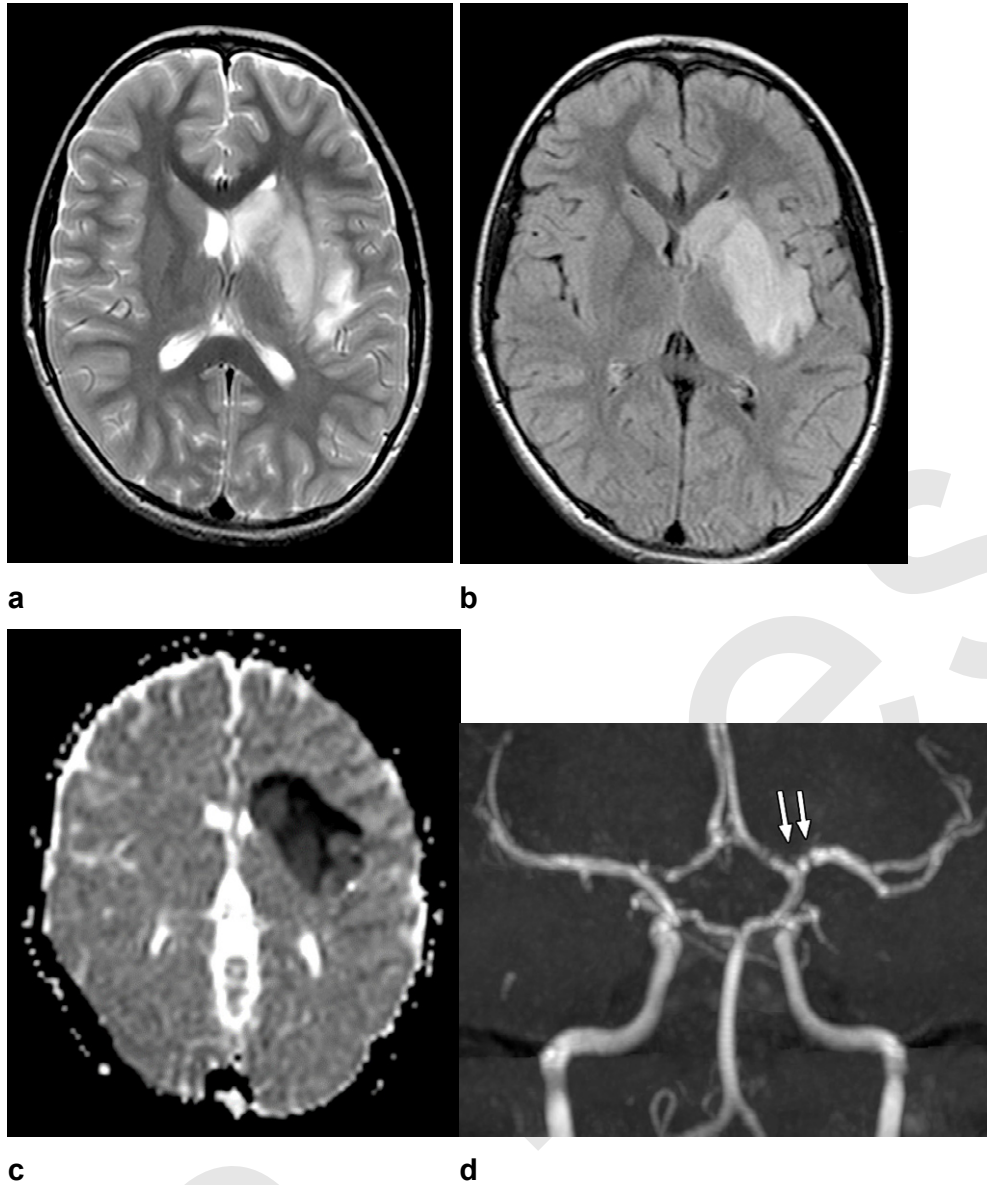


Figure 1: Axial T2-weighted (a) and FLAIR (b) Magnetic resonance imaging show diffuse hyperintense signal and edema of the caudate nucleus head, putamen, anterior limb of the internal capsule, and parts of external capsule and insula on the left side, with corresponding low values on the axial apparent diffusion coefficient map, in keeping with an acute infarct. Time-of-flight magnetic resonance angiography maximal intensity projection reformatted image demonstrates focal irregular narrowing and banding of the proximal left M1 segment of the middle cerebral artery with a slightly reduced distal flow in the middle cerebral artery.