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Case Report

COVID-19 related vascular complications in a pediatric patient: A case report☆

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ABSTRACT

The novel coronavirus infection (COVID-19) caused by the SARS-CoV-2 virus is a relatively recent infection that has resulted in a global pandemic, appearing first at the end of 2019. While initially presenting as a predominantly respiratory disease, with a classical picture of fever, dry cough, dyspnea and, in some cases anosmia and ageusia, recent cases have shown increasingly atypical and more systemic manifestation of the disease. A precise understanding of the extent and pathophysiology of COVID-19 remains underway to this day, particularly concerning its behavior in the pediatric population. Moreover, there has been an increasing number of COVID-19 reports with neurological complications and manifestations, prompting inquiry into neuroinvasion. Postulations include indirect invasion through a surge of inflammatory mediators "cytokine storm" and subsequent widespread endothelial injury; and direct neural tropism. We report the case of a previously healthy 12-year-old male presenting with acute right-sided hemiparesis, new-onset seizures and a generalized petechial rash. Laboratory tests revealed elevated inflammatory markers and radiological investigations confirmed an evolving left middle cerebral artery (MCA) infarct and large vessel vasculitis. Testing for SARS-CoV-2 infection was positive.

Introduction

COVID-19 is a primarily respiratory illness that has first been documented in December of 2019 [1] and has since resulted in a still ongoing global pandemic, with over 250 million reported cases thus far [2]. While the conditions behind its emergence remain a matter of speculation and investigation, it was rapidly established that the causative pathogen is a virus, structurally similar to that implicated in severe acute respiratory distress syndrome (SARS) [1]. While several molecular tests have been devised for the detection of SARS-CoV-2 infection, polymerase chain reaction (PCR) testing remains the gold standard and most widely used [1,4]; where a sample is obtained from either the nasal cavity or nasopharynx and undergoes a chain of enzymatic reactions which serve to am-

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plify the viral genome. Radiological studies have also been employed to evaluate the direct effects on the virus on the lung parenchyma; resulting in a viral-like pattern of bilateral peripheral patchy areas of consolidations on conventional radiography and a characteristic ground-glass pattern on computed tomography (CT) [5]. While largely thought of as a respiratory disease, COVID-19 infection has shown a propensity to involve other organ systems as well, namely the vascular and neurological systems [6,7] – leading to thromboembolic events, such as myocardial, pulmonary and cerebral infarctions and, in some patients, hemorrhagic events. It has also resulted in a variety of neurological complications from meningitis and infarcts to vasculitis-like diseases [8,9]. We report an unusual case of a pediatric patient with an atypical presentation of COVID-19.

Case presentation

A previously healthy 12-year-old male presented with acute right-sided hemiparesis, associated with profuse sweating, grunting and unresponsiveness. The episode persisted for thirty minutes before the patient was brought in to the emergency department. History was negative for fever, flu-like symptoms or recent travel; however, it was significant for positive sick contact with COVID-19 patients. Physical examination revealed expressive aphasia, right upper extremity weakness and brisk reflexes. A non-enhanced contrast brain CT was initially performed and showed a dense MCA (Fig. 1) along with subtle hypoattenuation and loss of grey-white matter differentiation across its territory, leading to a diagnosis of a hyperacute evolving left MCA infarct. CT angiography further confirmed the presence of a 20mm long thrombus in the M1 branch of the left MCA, in addition to stenosis at the origin of its M2 segment and left intracranial internal carotid artery (ICA) (Fig. 1). Laboratory investigations revealed leukocytosis, elevated inflammatory markers and a positive COVID-19 PCR test. The patient was admitted under pediatric neurology with the impression of acute non-hemorrhagic stroke and status epilepticus. He was started on 150mg of oral aspirin and 125mg of intravenous phenytoin and investigated for underlying cardiac or renal causes; all of which turned out negative. On the second day of admission, the patient developed a generalized petechial rash (Fig. 2). In light of this clinical development and his presentation, a contrast-enhanced magnetic resonance imaging (MRI) of the brain was performed. It revealed acute ischemic changes involving the left MCA territory (Fig. 3) and circumferential segmental thickening and increased signal intensities of the left ICA wall (Figs. 4 and 5), in keeping with a diagnosis of central nervous system vasculitis. A battery of vasculitis-related tests ensued; C and P-antineutrophil cytoplasmic antibodies (ANCA), C3 and C4 complement factor deficiencies, methylenetetrahydrofolate reductase (MTHFR) deficiency and rheumatoid factor were all negative; whereas interleukin 6 (IL-6) levels were elevated. On that basis, a 3-day course of IV methylprednisolone was commenced, followed by a 2-day course of IV immunoglobulins (IVIg). On the sixth day of admission, he was started on a tapering course of steroids and switched to intravenous levetiracetam. The patient continued to test positive for SARS-CoV-2 throughout his hospital admission. While this case was encountered during a time where the Beta variant was dominant in the United Arab Emirates (UAE), followed closely by Delta; this patient's particular strain was not pursued. His vaccination status was not disclosed either; however, it is speculated that this patient may not have been vaccinated against SARS-CoV-2, as he presented 2 months prior to the official approval of COVID-19 vaccine use in children between the ages of 12 to 15 in the UAE. With continued clinical and functional improvement, the patient was discharged 2 weeks later on a 6-month course of low dose oral Aspirin and levetiracetam. As well as scheduled follow up with speech and physical therapy.

Discussion

COVID-19 is a novel infectious disease caused by the SARS-CoV-2 virus. It was first documented in Wuhan, China in December, 2019 [1,3]. It has since spread beyond, resulting in a global pandemic that remains changing until today. COVID-

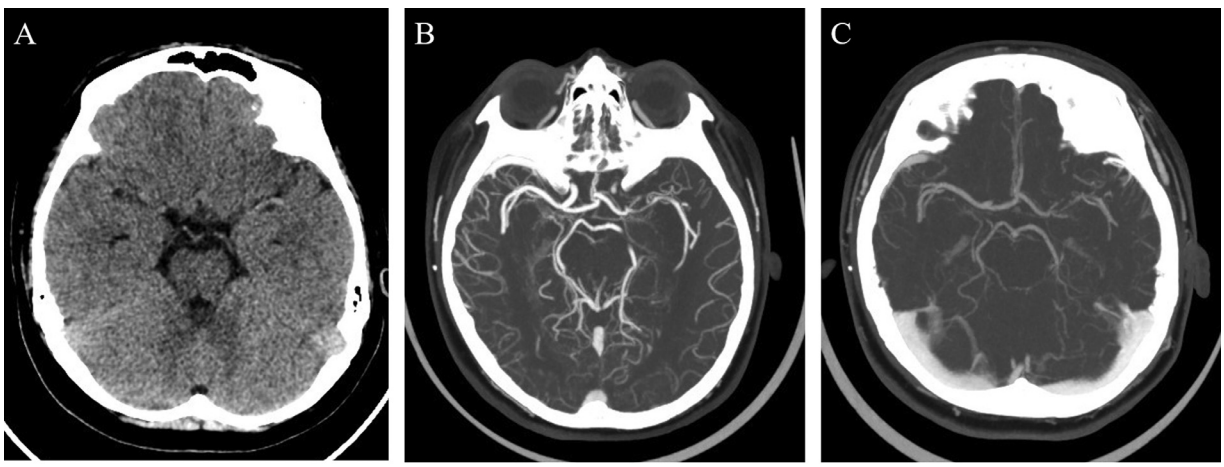

Fig. 1 – Axial CT images of the brain revealing a relatively dense left middle cerebral artery (MCA) on unenhanced images (A). CT angiography reveals severe narrowing and stenosis involving the left ICA and the M1 segment of the left MCA (B, C).

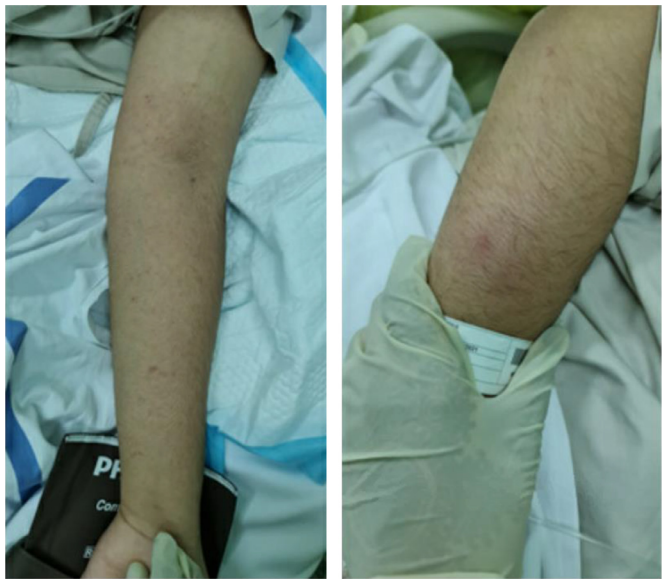

Fig. 2 – Newly seen generalized petechial rash 1 day following admission.

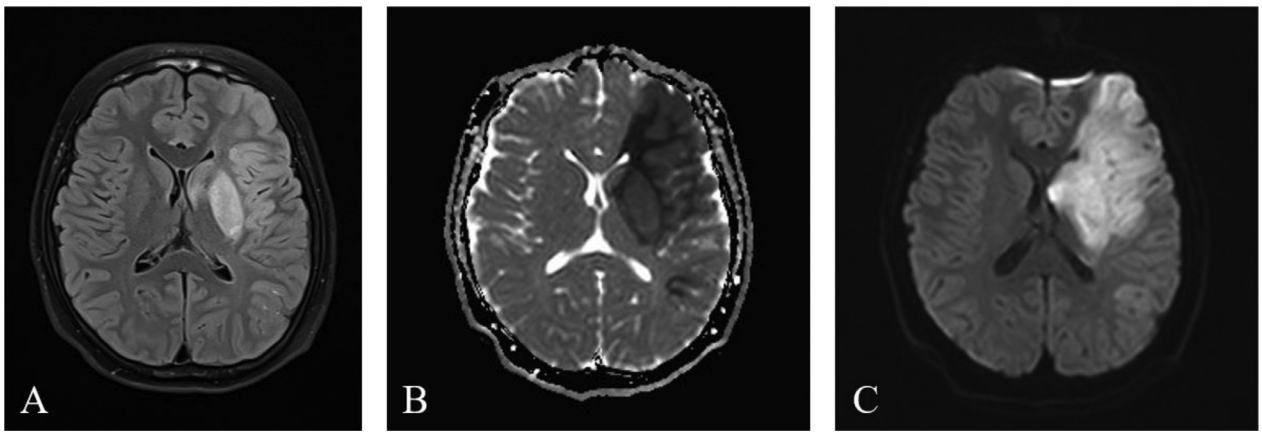

Fig. 3 – Acute infarction involving the left MCA territory and basal ganglia; seen as increased signal intensity on fluid inversion recovery (FLAIR) (A) with corresponding changes on diffusion weighted sequences, showing low signal on ADC (B) and high signal in DWI (C).

19 was initially assumed to be a primarily respiratory illness with a clinical picture ranging from a complete absence of symptoms to cardiopulmonary collapse; however, an increasing number of atypical cases suggests a wider spectrum of involvement. Several studies have highlighted the neurotropic tendencies of SARS-CoV-2, supplemented by case reports of patients developing predominantly neurological complications such as encephalopathy [10], large-vessel occlusion [11,12], Guillain-Barré syndrome [13,14,17] and reversible cranial nerve injuries [14]. While the mechanism by which this occurs remains largely speculative, a few studies have been able to demonstrate the virus' propensity to affect nervous tissue [16,18]; either through an amplified aberrant immune response, known as a "cytokine storm" or direct invasion of neuronal tissue [15]. COVID-19 is caused by the SARS-CoV-2 virus, a positive-sense, single-stranded RNA virus. Its structure comprises of the following glycoproteins: spike (S), envelope (E), membrane (M) and nucleocapsid (N); the latter encloses the viral genome, while the former 3 make up the viral envelope and facilitate its entry into cells and hijacking of their replication mechanisms. The spike glycoprotein especially does so by attaching to angiotensin converting enzyme 2 (ACE2) receptors, which are expressed on epithelial cells lining the lungs, intestines, brain, kidneys and blood vessels. SARS-CoV-2 gains entry through respiratory droplets and establishes initial contact through the nasal epithelial cells. Due to a limited immune response to infected nasal epithelial cells, the virus is able to go undetected early in its course [16,19]. Some studies have postulated transneuronal viral entry to the central nervous system through the olfactory nerve, which was believed to explain anosmia in COVID-19 patients [16,18,19]. Other studies involving animal and cellular models of the blood brain barrier (BBB) have established a transcellular pathway of invasion. An increased permeability of the BBB,

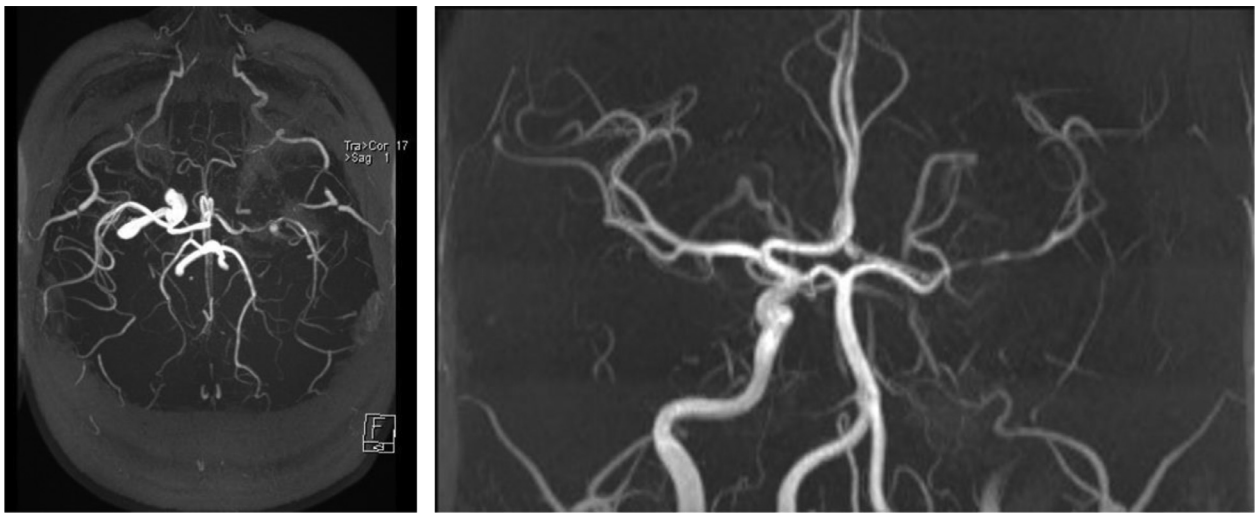

Fig. 4 – Circle of Willis MIP reconstructions revealing moderate to severe stenosis involving the entirety of the left ICA and extending to the MCA; namely its M1 segment and origin on its M2 segment.

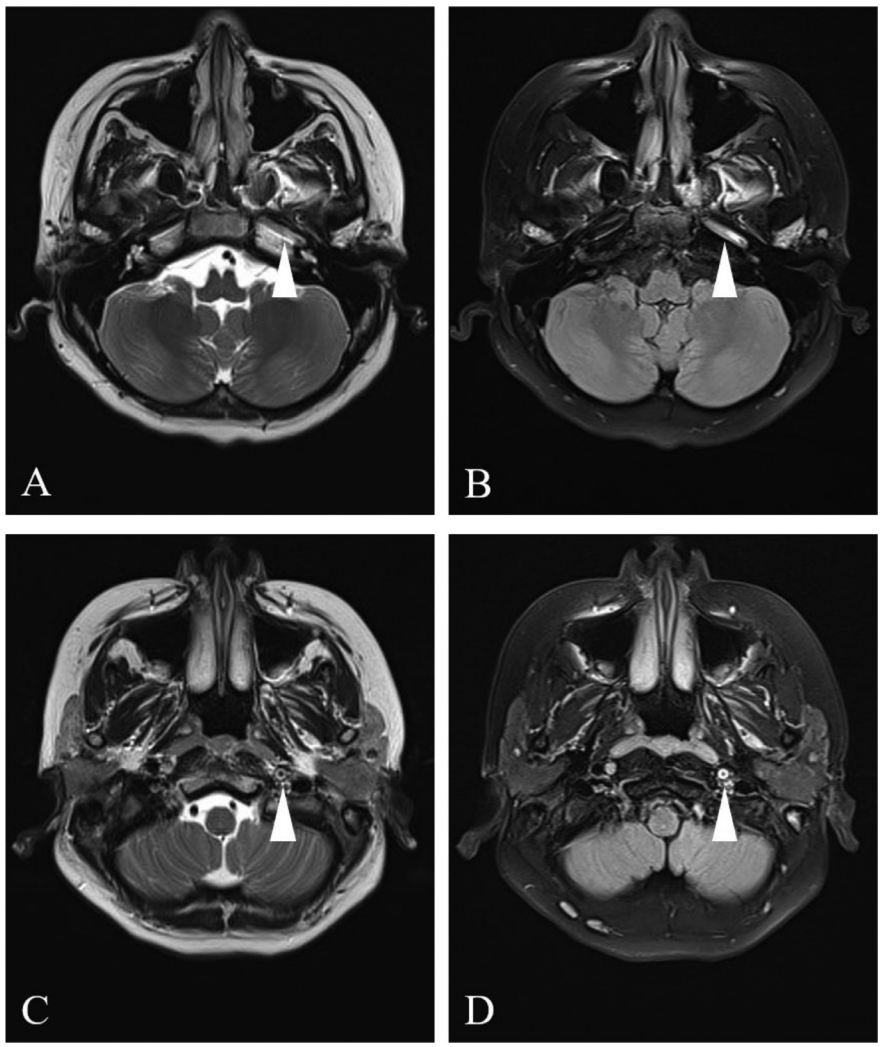

Fig. 5 – The left ICA (arrowhead) demonstrating circumferential wall thickening and hyperintensity on pre-contrast T2WI (A, C) and FLAIR (B, D).

as a consequence to the "cytokine storm" seen in COVID-19 infections and implicating especially IL-6, was seen with detectable viral replication at the basement membrane epithelial cells [16,18,19].

Conclusion

The understanding of the pathophysiology and scope of COVID-19 is constantly changing and appears to be much wider than previously thought, with particular tropism towards the vascular and neurological systems. Hypothesized mechanisms by which it achieves so include direct tissue invasion or as a consequence of an aggravated systemic inflammatory response, ultimately leading to widespread endothelial wall injury and inflammation. Its varied neurological manifestations have been a subject of numerous case reports and research papers, and remains an area of active interest. A deeper understanding of its neuro-invasive mechanisms is essential in deriving guidelines to treat and prevent neurological complications associated with COVID-19.

Patient consent

Given the patient is a minor, consent for the documentation and publication of this case has been obtained from their legal guardian accompanying her at the time. The information provided about this patient will maintain their anonymity and honor their privacy.

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