

COVID-19 and a Mysterious Case of Transient Cerebral Arteriopathy

Sir,

COVID-19 infection and neurological involvement are a well-known association by now! However, the presentation of a patient with catastrophic neurological involvement while in the convalescent phase is rare. We report such a case where a young man had a high antibody titer against COVID-19 and faced the consequence of a reversible cerebral arteriopathy.

A 20-year-old man with no known medical illness was apparently asymptomatic. He had a mild cough and generalized weakness for 4 days before his presentation to us with fever and altered sensorium. He was not on any drug and had no history of toxin exposure. His urine for routine toxin screen was negative. At emergency room (ER), his Glasgow Coma Scale (GCS) was 13/15 with normal pupillary reaction, normal brain stem reflexes, and had no definite lateralizing sign. He had a pulse rate of 110/min, a temperature of 100 °Fahrenheit, blood pressure of 140/90 mm of Hg, and SpO₂ of 90% in room air.

Immediately postadmission, he had convulsive status-epilepticus requiring airway protection and ventilator support. He regained his sensorium the next day (GCS was 14/15), and we withdrew him from ventilator support 1 day after ictus. However, the immediate next day morning (the third day of admission) he had a sudden gaze preference towards the right with the decreased movement of the left side of the body. He had an National Institutes of Health Stroke Scale (NIHSS) of 8 and was detected to have an acute infarct at the right parietal-temporal region.

He improved gradually with rehabilitation and was left with residual expressive aphasia and left hemiparesis on the fourth day postadmission. From the seventh day, he started walking with minimal support and on follow-up 2 weeks later, he was completely asymptomatic.

The cartridge-based nucleic acid amplification test (CBNAAT) for COVID-19 was positive on the day of presentation (he had not done any test earlier and was yet to be vaccinated for COVID-19 infection). His *reverse transcription*-polymerase chain reaction (RT PCR) for COVID-19 was however negative. There was evidence of reticulonodular opacities in the CT scan of the chest as seen in the COVID-19 infection suggestive of basal pneumonitis. The IgG for COVID-19 was very high (2529 AU/mL), C-reactive protein (CRP) was 20 mg/L, fibrinogen level was 6 gm/L, IL-6 level was 200 pg/mL, D-Dimer was 0.3 mg/L, and the rest coagulation parameters were within normal limits. His initial computed tomography (CT) scan of the brain was noncontributory, but an magnetic resonance imaging (MRI) of the brain on the day of new deterioration (third day of admission) revealed an acute infarct in the right middle cerebral artery (MCA) territory

involving the right parietal-temporal region [Figure 1a-d]. Contrast-enhanced MR angiography showed abrupt tapering in supra-clinoid segments of bilateral internal carotid arteries (ICA) with attenuated M1 segments of bilateral middle cerebral arteries (MCA) giving rise to a moyamoya-like picture; however, without abnormal collaterals [Figure 2a-c]. The findings were more pronounced on the right side. To get a better glimpse of the pathophysiology of intracranial vessels, we did a cerebral digital subtraction angiogram (DSA) one day later. DSA revealed minimal narrowing in the supra-clinoid segment of the right ICA [Figure 3a-d]; however, the left ICA and bilateral middle cerebral arteries were normal in caliber [Figure 3a-h]. Bilateral vertebral artery and external carotid artery injections were normal as well.

A detailed stroke workup including cardiac evaluation (including transthoracic echocardiogram (TTE) and 24 h, Holter monitoring) and vasculitis markers (including markers for anti-phospholipid antibody syndrome) were unremarkable.

At ER, during status epilepticus, we administered 4 mg of lorazepam and loaded him with 1.5 gm of sodium valproate. He received standard care of COVID-19 infection.

On the day of new-onset deterioration (third day of admission), injection fosphenytoin 1.5 gm was loaded and

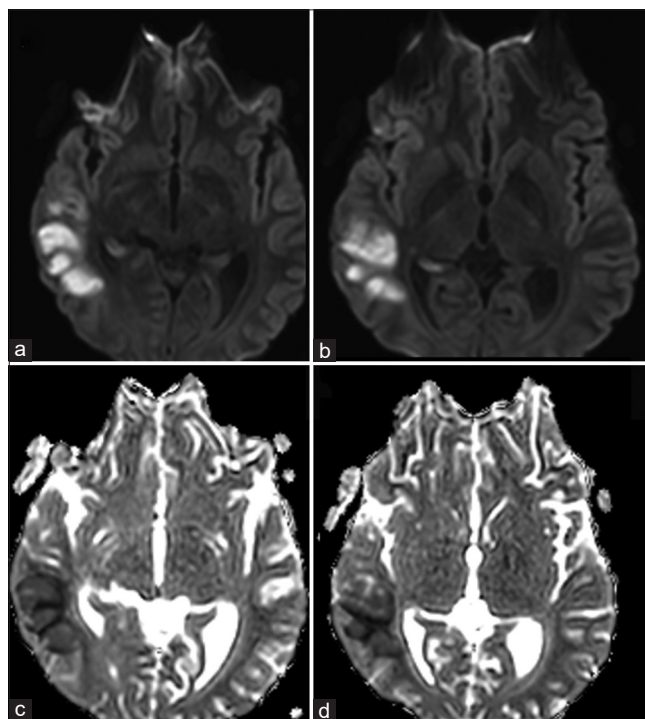


Figure 1: (a) and (b) Axial DWI trace images and (c) and (d) corresponding ADC maps showing acute infarct in the right middle cerebral artery territory involving the right parietal-temporal region

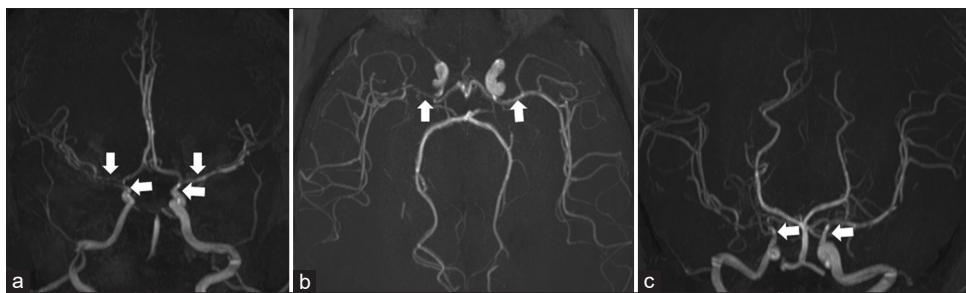


Figure 2: (a-c) Coronal, axial, and coronal oblique maximum intensity projection (MIP) images of contrast-enhanced MR angiography images showing abrupt tapering in supra-clinoid segments of bilateral internal carotid arteries (ICA) with attenuated M1 segments of bilateral middle cerebral arteries (MCA) giving rise to a Moyamoya disease like picture; however, with no abnormal collaterals

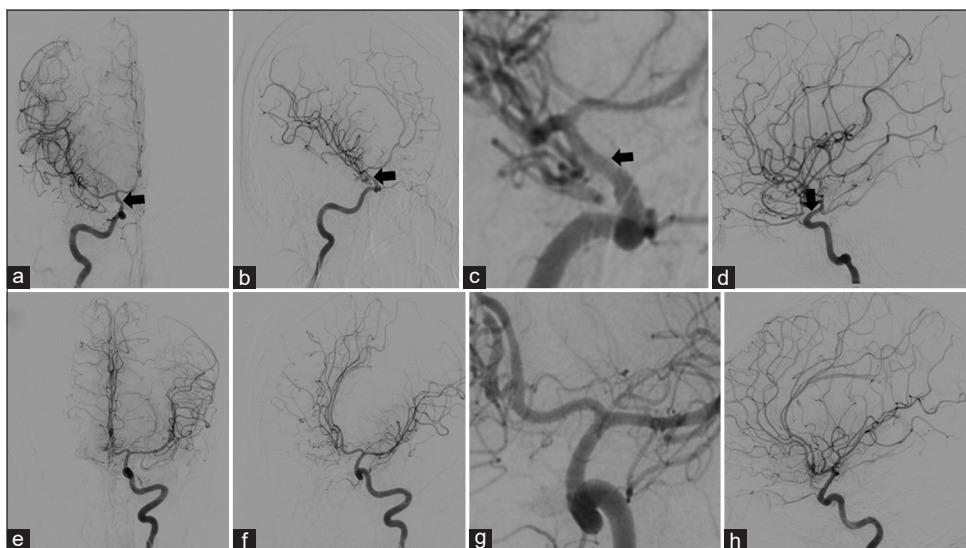


Figure 3: Digital subtraction angiogram images. (a-d) Anteroposterior, right anterior oblique, magnified right anterior oblique, and lateral projection of right internal carotid artery injection showing a minimal narrowing in the right internal carotid artery. However, the rest of the right internal carotid artery, right anterior and middle cerebral artery and their branches are normal. (e-h) Anteroposterior, right anterior oblique, magnified right anterior oblique, and lateral projection of left internal carotid art

continued (150 mg thrice daily) in suspicion of another episode of seizure along with sodium valproate (500 mg thrice daily). When a stroke was detected (same day), we loaded him with aspirin 325 mg and atorvastatin 80 mg and continued clopidogrel and aspirin combination of 75 mg each along with high dose atorvastatin because of intracranial large vessel disease. He was also on injection of enoxaparin 40 mg subcutaneously once daily as prophylaxis for deep vein thrombosis (He was later continued with dual antiplatelet and apixaban 2.5 mg twice daily).

A diagnostic cerebrospinal fluid study was within normal limits (including the infective markers). We increased the steroid from an initial 6 mg of dexamethasone once daily to dexamethasone 8 mg thrice daily in dread of vasculitis. However, once intracranial vasoconstriction got reversed quickly and the CSF study was found to be noncontributory, we tapered off the steroid within 2 weeks of its initiation.

So, our patient had an asymptomatic infection and was in the convalescent phase when he presented to us with a

life-threatening neurological symptom. On the background of COVID-19 infection, he presented with seizure, cortical infarct along with the evidence of reversible vasoconstriction of multiple large intracranial arteries. Although MRA can overestimate vasoconstriction, it is unlikely that the contrast-enhanced MRA, would overestimate narrowing to this extent, that too on both sides. Hence, we can conclude, there was a rapid reversal of the vasoconstriction in our case. Now, very high COVID-19 antibody and raised inflammatory markers (high CRP, fibrinogen, IL-6 level) hinted that this transient vasoconstriction of intracranial large vessels was likely because of the vessel wall inflammation. This inflammation had probably responded to the steroid. The vessel wall imaging during the MRI could have been more informative but was not possible in our setting because of some technical reasons. The other possibility in this setting would have been reversible cerebral vasoconstriction syndrome (RCVS). Mansoor *et al.*^[1] have reported RCVS in COVID-19 infection. However, rapid reversal of vasoconstriction within a day as

documented by serial MRA and DSA is unlikely, and it does not report such quick reversibility of the vasoconstriction in literature. Viruses like varicella-zoster virus (VZV) or cytomegalovirus (CMV) are known to be associated with transient arteriopathy.^[2-5] An alternative explanation of the etiology for stroke in our case could be a similar type of transient cerebral arteriopathy in association with COVID-19 infection. We consider transient cerebral arteriopathy and not small microthrombi or emboli as the cause of stroke in our case because we could not get evidence of thrombus in any imaging, though there was a considerable area of transient vasoconstriction.

To the best of our knowledge, no one has had reported COVID-19–induced transient and reversible CNS arteriopathy presenting as a moyamoya-like angiographic picture. Although COVID-19–associated CNS vasculitis is in the literature,^[6] the transient and reversible nature of arteriopathy has not been established. The association is difficult to prove but based on the clinic-radiological evidence, we can say that COVID-19 infection can present with transient cerebral arteriopathy, like VZV or CMV infection. It is yet not clear whether this focal cerebral arteriopathy is idiopathic or is precipitated by active viral infection.^[7] As VZV and CMV associated with vasculitis can be treated with steroids,^[8] we also followed the same regimen. We added antithrombotic medications and statins to the treatment regimen to prevent further strokes and antiepileptic drugs to prevent further episodes of seizure.

We will await more supporting literature or guidelines to handle such COVID-19–related complications. Though they present with life-threatening neurological events, COVID-19 related symptoms may be mild, or the patient may be asymptomatic from the infection.

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Conflicts of interest

There are no conflicts of interest.

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