Vessel wall imaging in COVID-19 associated carotid atherothrombosis and stroke: a case report and literature review

Journal of Central Nervous System Disease
Volume 14: 1–4

DOI: 10.1177/11795735221112589

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ABSTRACT

COVID-19 associated neurological syndromes, including acute ischemic stroke, pose a challenge to treating physicians. The role of MRI in aiding diagnosis and further management is indispensable. The advent of new MRI sequences such as vessel wall imaging (VWI) allows an avenue in which these patients could be better investigated and treated. We describe our experience in managing a patient with COVID-19 associated atherothrombosis and stroke, focusing on the VWI imaging findings.

KEYWORDS: COVID-19, Magnetic resonance imaging (MRI), Vessel wall imaging (VWI), Acute ischemic stroke (AIS), Imaging

RECEIVED: March 7, 2022. **ACCEPTED:** June 10, 2022.

TYPE: Case Report

DECLARATION OF CONFLICTING INTERESTS: The author declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

FUNDING: The authors received no financial support for the research, authorship, and/or publication of this article.

ETHICAL APPROVAL: Our institution does not require ethical board approval for the publication of single case studies.

INFORMED CONSENT: Informed written consent was obtained from the patient for the publication of this manuscript.

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Introduction

Coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been shown to affect a multitude of organ systems. This includes the neurological system, with many groups documenting the associated neurological syndromes associated with COVID-19.[1,2] Inevitably, the investigation and work-up of affected patients, particularly via imaging, would also need to evolve to provide an accurate diagnosis and the best care possible. We describe a patient with COVID-19 associated carotid atherothrombosis and stroke, whom was managed in our institution, as well as the vessel wall imaging (VWI) findings via magnetic resonance imaging (MRI) using our protocol.[3]

Case presentation

A 60-year-old man, a chronic smoker with background history of hypertension and dyslipidemia was referred to us from the low risk COVID-19 quarantine center for further management of COVID-19 infection Category 4. The patient reported a history of 'stroke-like' symptoms with mild weakness on the right side three months previously, which resolved. At the time, the patient did not seek medical attention. He was not vaccinated and presented with an upper respiratory tract infection after contact with recently infected family members. COVID-19 infection was confirmed with nasopharyngeal sample polymerase chain reaction (PCR). Upon presentation to us, he was at day seven of illness with complaints of generalized lethargy, reduced oral intake as well as worsening cough and dyspnea; requiring increasing oxygenation – initially via nasal cannula three litres, eventually requiring face mask five litres. On examination, the patient's Glasgow Coma Scale (GCS) was full. He was dehydrated with a blood pressure of 110/70 mmHg, pulse rate being regular with moderately reduced volume at 95 beats per minute (bpm), afebrile and tachypnoeic at 24 breaths per minute. Oxygen saturation was 90% with nasal cannula three litres. There was evidence of fine bibasal crepitations on lung examination but systemic examination including neurological, was unremarkable. The full blood count showed total white cells of 11.1 × 10^3μ/L with low absolute lymphocytes of 0.3 × 10^3μ/L, haemoglobin of 13.2 g/dL, and platelet of 172 × 10^3μ/L. There was biochemical evidence of acute kidney injury with urea of 12.3 mmol/L and creatinine of 81 μmol/L on a background of normal kidney function. C-reactive protein was elevated at 39 mg/L (normal range < 5) with a D-dimer of 1134 ng/ml (normal range <500). Arterial blood gas on 5-litre oxygen showed normal pH of 7.45, acceptable oxygen level with PaO2 of 80 mmHg coupled with

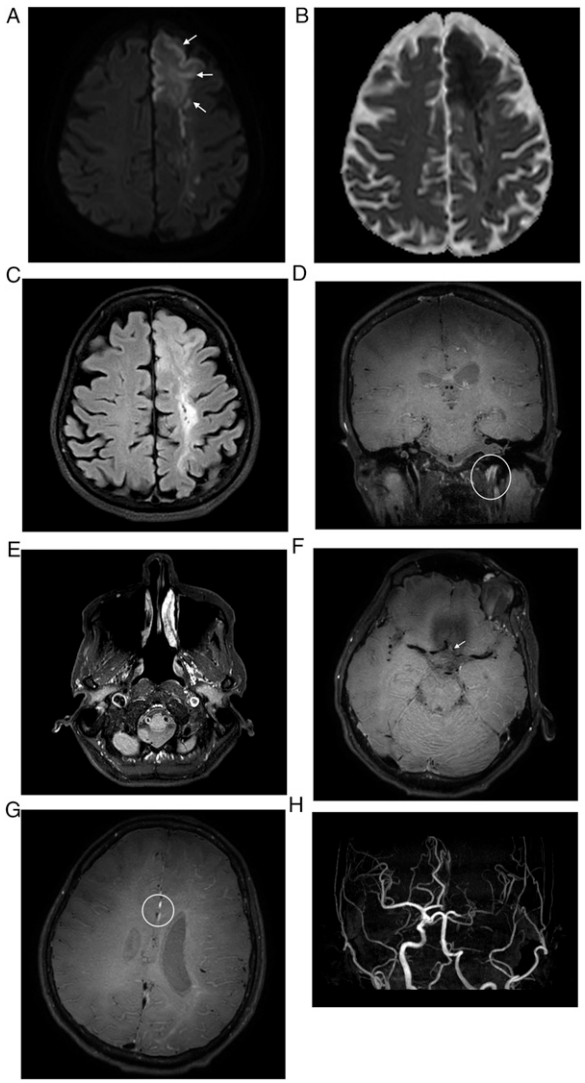

Figure 1. A & B – Axial MRI images, on the diffusion weighted imaging (DWI) and apparent diffusion coefficient (ADC) sequences show restricted diffusion involving mainly the left anterior cerebral artery (ACA) territory (white arrows). Also note presence of internal watershed acute infarcts. C – Axial FLAIR image showing corresponding hyperintensity of the involved left ACA territory. Also note internal watershed hyperintensity of varying ages, mostly acute. D – Post gadolinium vessel wall imaging (black-blood sequence) MRI image, in coronal section, showing enhancement and thickening of the wall of the left internal carotid artery (ICA) (white circle), compared to the right. Also note inhomogeneity of the luminal hypointensity, indicative of slow/stagnant blood flow. E – Post gadolinium vessel wall imaging (black-blood sequence) MRI image, in axial section, showing circumferential vessel wall thickening and enhancement of the left carotid artery, as well as luminal stenosis. F – Post gadolinium vessel wall imaging (black-blood sequence) MRI image, in axial section, showing enhancement of the left ACA A1 segment (white arrow). G – Post gadolinium vessel wall imaging (black-blood sequence) MRI image, in axial section, showing intraluminal hyperintensity of the distal left ACA (white circle), indicative of slow/stagnant flow. Note that the normal distal right ACA adjacent to it exhibits normal intraluminal hypointensity consistent with normal flow. H – Time of flight MRA image showing loss of signal intensity of the left internal carotid artery (ICA), with faint signal intensities of the left ACA and middle cerebral artery (MCA).

evidence of hyperventilation with pCO2 of 29 mmHg. Chest radiograph showed subtle bilateral peripheral airspace opacities (L>R) at the lower zones. The patient was started on intravenous (IV) fluids, IV dexamethasone of 8 mg once daily and subcutaneous enoxaparin 40 mg daily for venous thrombosis prophylaxis. The admission had been uneventful; however, on day 10 of illness, he developed an acute onset of right-sided hemiparesis with expressive dysphasia. GCS was E4V3M5; confused, inconsistent in obeying commands with neurological examination revealing dense hemiparesis on the right upper and lower limbs, with a power of 0/5. The patient also had right hemisensory loss with normal tone and reflexes as well as evidence of upgoing plantar reflex. Pupils were equal with no evidence of gaze preference or hemianopia. The National Institutes of Health stroke scale (NIHSS) was 18 out of 42, in keeping with moderate to severe stroke. Blood pressure was 130/80 mmHg, with a regular pulse rate at 70-bpm and oxygen saturation of 98% on nasal cannula 3 litres. The blood test showed total white cells of $4.3 \times 10^3\mu/L$ with low absolute lymphocytes of $0.2 \times 10^3\mu/L$, with an increasing trend of CRP and D-dimer with values at 161.5 mg/L 1553 ng/mL respectively. An electrocardiogram showed sinus rhythm with biphasic T wave over the lateral anteroseptal leads. Urgent acute stroke MRI, as per our institution's protocol, revealed an acute internal watershed zone infarct and a predominantly anterior cerebral artery (ACA) territory acute infarct on the DWI/ADC map. Magnetic resonance angiography (MRA) showed loss of signal intensity of the left internal carotid artery (ICA), with faint signal intensities of the left ACA and middle cerebral artery (MCA). No blooming artefacts to suggest hemorrhage were noted on susceptibility weighted imaging (SWI). Post gadolinium vessel wall imaging via black-blood sequence demonstrated circumferential vessel wall enhancement of the left ACA and ICA. Some segments of the involved vessels also showed luminal hyperintensity [Figure 1].

We decided to proceed with mechanical thrombectomy, however, after thorough discussion, the family members were not keen on pursuing further intervention and opted for conservative medical management. The patient's condition deteriorated 36 hours following the stroke; a further decrease in mentation with poorly reactive pupils were noted, suggestive of stroke progression. The patient eventually succumbed to his illness on day 13 (day 2 post stroke) of the COVID-19 infection.

Discussion

Among the many neurological syndromes associated with COVID-19, acute ischemic stroke (AIS) appears to be one of the more commonly reported.[4] This creates the perception of AIS being more common in those inflicted with COVID-19. Lobanova et al.[5] in their analysis of 27676 patients from 54 healthcare facilities found that in those with COVID-19, 1.3%

developed AIS, as opposed to 1.0% in those not diagnosed to have COVID-19. Additionally, a larger proportion of cardiovascular risk factors was noted in COVID-19 associated AIS patients. Based on their cohort, they concluded that AIS in COVID-19 was infrequent, and that the risk of being discharged to other destinations than home, or death, was increased 2-fold, in COVID-19 patients developing AIS. The pathophysiological mechanism bringing about the cardiovascular events, including AIS, is still at this point non-confirmatory. However, few postulations have been put forth. One of it being the binding of the SARS-CoV-2 on the human angiotensin-converting enzyme 2 (ACE2) receptor, which is highly expressed in the endothelium.[6,7] This in turn mediates vessel wall inflammation, atherosclerosis, and oxidative stress. An overwhelming immune response to the infection is also shown to propagate systemic inflammation, associated coagulopathy, and local endotheliitis – which may also explain the occurrence of cardiovascular events in these patients.[8,9] Our patient gave a history of 'stroke-like' symptoms with weakness on the right side three months prior to presenting to our institution, which resolved spontaneously. This episode was never investigated, hence there was no objective evidence to say that this patient had already had an AIS, or abnormal brain imaging findings to support his predisposition to the AIS that he had at the time of admisson, while being treated for COVID-19 infection. However, factoring in the stage of infection at which he presented to us, coupled with his underlying metabolic condition, it is certainly possible that the COVID-19 infection is at least partly contributory, if not causative, to the development of this patient's AIS, as well as the left carotid atherothrombosis. Multiple studies have described the cross sectional imaging findings of COVID-19 patients with neurological syndromes,[10,11] particularly via MRI, but studies describing the vessel wall imaging (VWI) findings have been scarce.[12,13] One of the biggest cohort described to date is by Uginet et al[14] in which 34 older patients with COVID-19 encephalopathy were noted to have circumferential vessel wall enhancement in 85% (29/34), located in the intracranial vertebral and basilar arteries. However, they also noted that on the MRA, no associated stenosis was seen – to which they concluded was evidence of endotheliitis and an inflammatory origin. On the contrary, Guggenberger et al[15] argued that the reported VWI findings by Uginet et al were also possibly due to enhancement associated with intracranial vasa vasorum, developing with advancing age, seen in their own cohort with no clinical or laboratory features of vasculitis. Another study by Mazzacane et al[16] reported concentric vessel wall thickening and enhancement of the involved arterial territories, with associated stenosis and/or occlusion on MRA and cerebral angiography, of patients with COVID-19 deemed to have cryptogenic stroke. We feel that VWI findings that are seen in patients with COVID-19 associated neurological syndromes do not definitively confirm causality, nor do they exclude in total the contributory role of COVID-19 infection in the pathophysiology. More studies are needed in order to confirm or refute the VWI findings seen in this group of patients. The vessel wall imaging findings in our patient were circumferential vessel wall enhancement of the left ACA and ICA, suggestive of an inflammatory process, with some segments of the involved vessels showing luminal hyperintensity, suggestive of slow/stagnant flow, or total occlusion. Circumferential vessel wall thickening and enhancement is most typically seen in vasculitis, but to a lesser degree in intracranial atherosclerosis. The typical VWI MRI findings in intracranial atherosclerosis is eccentric vessel wall thickening and enhancement, with positive remodeling and unchanged vessel diameter; uncommonly, negative remodeling can also be seen.[17] On the MRA, stenosis of these involved vessels were also noted. The parenchymal changes on the DWI/ADC map, consistent with acute infarct, further supports the diagnosis. Our patient's VWI MRI findings echo those by Mazzacane et al. This certainly makes for an intriguing argument, as to whether the cross sectional imaging findings, particularly those seen on VWI, are attributable at least partly to the COVID-19 infection. Based on the available literature so far, and our limited experience, we are not able to discredit this theory entirely, nor can we confirm causality.

Conclusion

COVID-19 associated neurological syndromes definitely pose a challenge to the treating physicians. The availability of cross sectional imaging, in particular MRI, certainly helps in the diagnosis and management of these patients. The understanding of the VWI findings of these patients is still in its infancy, and more studies are needed to best understand and utilize those findings, in order to provide the best care possible.

Author contributions

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