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CASE REPORT

Acute stroke showing cerebral infarcts and microbleeds in a 31-year-old man with COVID-19 pneumonia

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Introduction

A 31-year-old man presented with COVID-19 pneumonia and required mechanical ventilation. Subsequently, he developed a left total anterior circulation stroke clinically while on ventilatory support in the critical care unit. His magnetic resonance imaging scan of the brain revealed acute infarcts in the right occipital and left fronto-parietal regions, and multiple microbleeds scattered in various vascular territories both within infarcted and non-infarcted areas. This suggested a COVID-19-induced cytokine storm and procoagulant state as plausible causes of thromboembolism and ischaemic stroke. However, owing to the clustered nature of the

Case report

A 31-year-old man of mixed white British-Egyptian ethnicity presented to the emergency department with an 8-day history of fever, cough, worsening shortness of breath and headaches. His only medical history was ulcerative colitis for which he was on a reducing course of steroid, and his prednisolone 5 mg once daily regimen was coincidentally stopped 10 days before hospital admission. There was no other significant medical and family history. He was in full-time employment and married with a young family.

On presentation, his respiration rate was 40/minute, saturating 96% on 4 litres of oxygen, temperature was 38 °C, blood pressure 113/70 mmHg, and his heart rate was 112 beats/minute and regular in rhythm. His electrocardiogram showed sinus tachycardia. His chest X-ray showed bilateral pneumonic consolidation. His blood results were deranged and the peak values were: white blood cells 29.9×10^9/litre, platelets 923×10^9/litre, C-reactive protein 449 mg/litre, procalcitonin 13.66 ng/ml, ferritin 870 µg/litre, prothrombin time 22.2 s, activated partial thromboplastin time 40.2 s, fibrinogen 9.26 g/litre, D-dimer 58 551 ng/ml, troponin 236 ng/litre.

He was started on antibiotics (piperacillin/tazobactam and clarithromycin), and enoxaparin 40 mg once daily for venous thromboembolism prophylaxis. His nasal and throat swab detected severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) deoxyribonucleic acid (RNA) by polymerase chain reaction. He became progressively hypoxic, required increasing amounts of oxygen and was intubated and mechanically ventilated on day 7 of admission in the critical care unit.

On day 13, it was noted that he had right-sided facial droop, right arm weakness (power=0/5), right leg weakness (3/5), clonus, aphasia and right-sided neglect, with a National Institutes of Health Stroke Scale (NIHSS) score of 23. A left hemispheric total anterior circulation stroke was diagnosed clinically. His computed tomography head scan suggested a left distal middle cerebral artery territory acute infarction, and aspirin 300 mg once daily was started. He was extubated on day 20 and had magnetic resonance imaging of the head and magnetic resonance angiography of the head and neck on day 21. While the magnetic resonance angiography of his circle of Willis and neck vessels was normal and ruled out dissection, magnetic resonance imaging of the brain revealed acute infarcts in the right occipital and left fronto-parietal regions (Figure 1) and multiple microbleeds in various vascular territories, not only within infarcted but also clustered and scattered in non-infarcted areas (Figure 2).

He was moved to the stroke unit for rehabilitation on day 24. Further monitoring and investigations revealed no atrial fibrillation, normal transthoracic echocardiogram, and negative antiphospholipid and lupus anticoagulant screen. He received standard medical care and multidisciplinary rehabilitation in the stroke unit. He had mild dysphasia and right sided hemiparesis but was able to walk independently (modified Rankin score 3). He made a very good recovery (NIHSS of 6), and on day 39, he was discharged home on clopidogrel, atorvastatin and mesalazine.

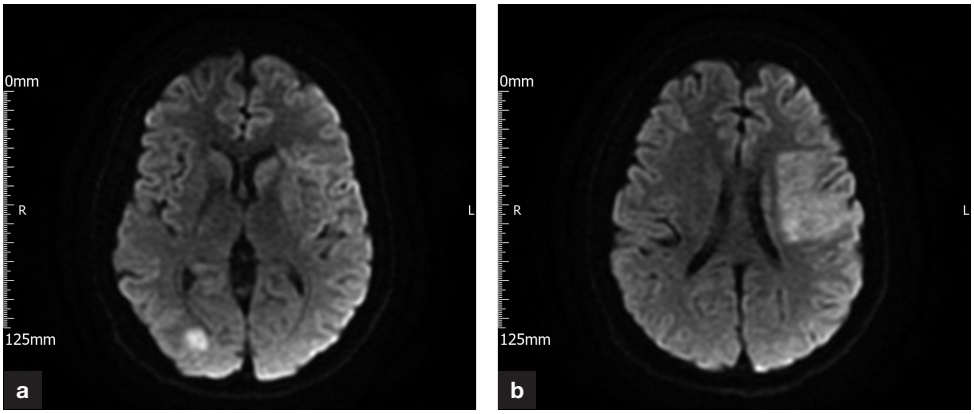

Figure 1. Magnetic resonance diffusion-weighted imaging showing acute infarcts in (a) the right occipital and (b) left fronto-parietal regions.

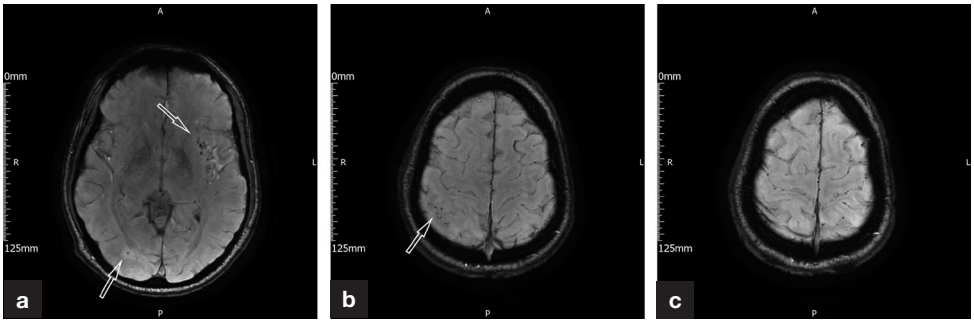

Figure 2. Magnetic resonance susceptibility-weighted angiography showing multiple microbleeds in various vascular territories, not only (a) within infarcted but also (b) clustered and (c) scattered in non-infarcted areas.

acute microbleeds, the authors hypothesise that this was COVID-19-induced endothelial dysfunction, possibly by direct invasion of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Additionally, a significantly elevated troponin level suggested myocardial injury such as myocarditis and possible cardio-embolism causing bi-hemispheric large vessel infarcts in different vascular territories, although the transthoracic echocardiogram was normal. He made good progress and was able to walk independently (modified Rankin score 3) on discharge after 6 weeks in hospital.

Discussion

In the Wuhan case series of 214 patients with COVID-19, the incidence of stroke was 2.8%, and the mean age was 52.7 years (Mao et al, 2020). Five patients were reported aged 33–49 years who presented with single territory, large-vessel stroke and diagnosed with COVID-19, three of whom had traditional risk factors for stroke (Oxley et al, 2020).

To the best of the authors' knowledge, this patient is the youngest COVID-19-related stroke patient reported to date. The temporal sequence of COVID-19 pneumonia and subsequent stroke in this patient with no stroke risk factors suggested COVID-19 disease as the aetiology of his stroke. The markedly elevated levels of inflammatory markers and coagulopathy suggested COVID-19-induced cytokine storm and hypercoagulopathy as plausible causes of thromboembolism and cerebral infarction (Valderrama et al, 2020). Although the significantly elevated troponin level suggested myocardial injury such as myocarditis and possible cardio-embolism causing bi-hemispheric large vessel infarcts in different vascular territories (Valderrama et al, 2020), his echocardiogram was normal.

In this case, the presence of multiple microbleeds scattered in various cerebral vascular territories is intriguing. Cerebral microbleeds result from red blood cell leakage from arterioles and capillaries (Wilson et al, 2019). Indeed, endothelial dysfunction in various vascular beds has been described in patients with COVID-19 (Varga et al, 2020). The

Learning points

- COVID-19-induced cytokine storm, inflammatory response and procoagulant state may cause thromboembolism and ischaemic stroke in young patients.
- The clustered nature of acute microbleeds could suggest COVID-19-induced endothelial dysfunction, possibly by direct invasion of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).
- In patients with COVID-19, a significantly elevated troponin level may suggest myocardial injury such as myocarditis and possible cardio-embolism causing bi-hemispheric large vessel infarcts in different vascular territories.
- The outcome of severe stroke in very young adult patients with COVID-19 may be favourable.

authors hypothesise that acute microbleeds are the result of COVID-19-induced endothelial dysfunction, possibly by direct viral invasion (Valderrama et al, 2020; Varga et al, 2020). Although clotting dysfunction could theoretically have caused the microbleeds, their clustered nature suggests direct invasion of SARS-CoV-2 as a more plausible explanation (Valderrama et al, 2020; Varga et al, 2020).

More recently, unusual microbleeds have been reported in the brain magnetic resonance imaging scans of patients with COVID-19 patients (Fitsiori et al, 2020). The postulated mechanisms include thrombotic microangiopathy related to direct or indirect damage by SARS-CoV-2 on the endothelium of the brain's vessels, and mechanisms similar to the hypoxaemia seen with a blood–brain barrier injury (Fitsiori et al, 2020). Furthermore, a suspected mechanism of SARS-CoV-2-induced vasculitis or endotheliitis has also been reported (Hanafi et al, 2020). Although not widely available, an imaging technique termed black-blood magnetic resonance imaging could be used to help in the diagnosis of possible viral-induced cerebral vasculitis (Shah et al, 2015).

This case of the youngest patient with COVID-19-related stroke reported in the literature to date illustrates that COVID-19 can cause not only multiple large vessel cerebral infarcts but also acute microbleeds in various cerebral vascular territories. Furthermore, the outcome may be favourable in very young COVID-19 stroke patients.

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