

CASE REPORT

Ischaemic stroke as the presenting feature of COVID-19: a series of three cases from Qatar

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Abstract

Most cases of stroke associated with coronavirus disease 2019 (COVID-19) occur during the course of a characteristic COVID-19 respiratory illness. We report three patients where the presenting feature of COVID-19 was stroke. Two patients had no respiratory symptoms throughout their clinical course. In each case, COVID-19 was confirmed by a reverse transcription polymerase chain reaction (RT-PCR) test and the diagnosis of ischaemic stroke by brain imaging. The patients were relatively young (40, 45 and 50 years). None had a prior history of cerebrovascular events. Stroke risk factors were absent in one, limited to overweight and smoking in another but more prominent in the third patient. Two patients had large vessel occlusion and elevated D-dimer levels. Multiple infarcts were seen in two patients. Clinicians should consider the possibility of COVID-19 in patients presenting with stroke and conversely consider investigating for stroke if a patient with COVID-19, even if mildly ill, develops acute neurological symptoms.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It typically presents with respiratory symptoms, but many systems can be involved [1]. A retrospective analysis of hospital patients in Wuhan, China conducted early in the pandemic showed a wide range of neurological complications including central and peripheral nervous system manifestations and skeletal muscular injury [2]. Since then, neurological and neuropsychiatric features, including stroke, have been increasingly recognized [3]. A study from New York reported that 0.9% of hospitalized patients with COVID-19 suffered a radiologically proven ischaemic stroke [4]. An earlier study from China reported a higher incidence of stroke (4.6%) [5]. In the New York study, the median age of the

stroke patients was 62.5 years and the median time between onset of first COVID-19 symptoms and stroke was 10 days [4].

We report three cases seen in Qatar where stroke was the presenting feature of COVID-19. All three patients were taken by ambulance to the Emergency Department of a major hospital, with a tertiary stroke centre, in Doha, the capital of Qatar. The time between the onset of neurological symptoms and arrival at hospital was no more than a few hours. In all cases COVID-19 was diagnosed by a reverse transcription polymerase chain reaction (RT-PCR) test and stroke was confirmed by brain imaging. Clinical features are summarized in Table 1 and below. One patient was diagnosed with diabetes and hypertension during his admission (case 3). Risk factors for stroke were absent in another (case 2) and limited to smoking and overweight in

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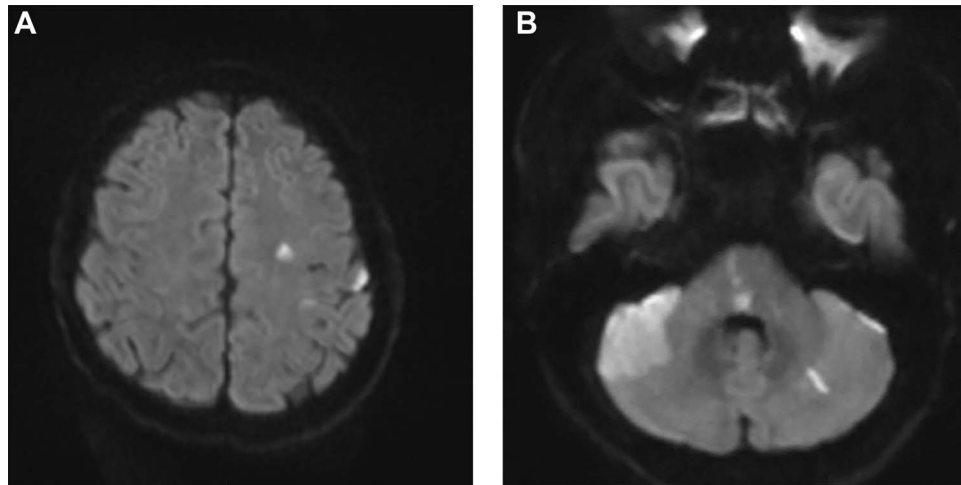


Figure 1: A: DWI axial image with three small restricted diffusion in left MCA territory. B: Axial DWI showing acute strokes in right cerebellum, pons and left cerebellum.

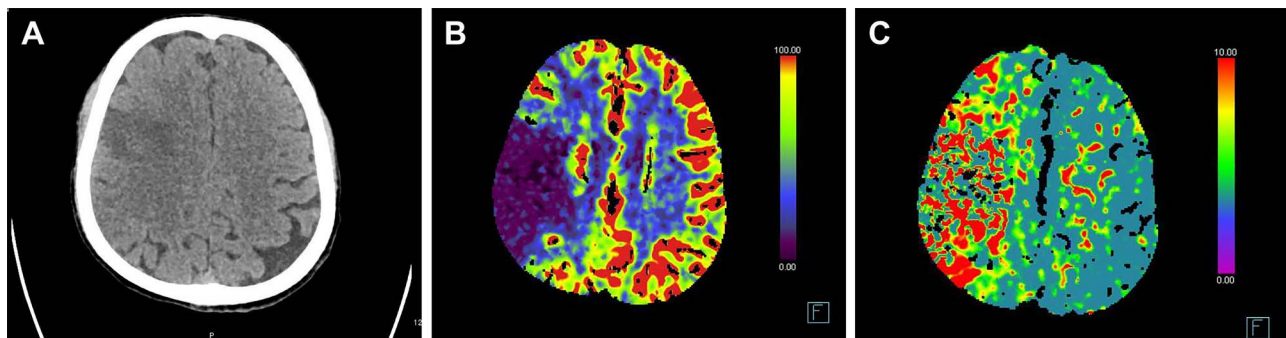


Figure 2: A: CT Scan showing right MCA hypodensity. B and C: CT Perfusion scan showing decreased cerebral blood flow and increased mean transit time indicating right MCA stroke.

the third (case 1). All three patients had normal echocardiograms and electrocardiograms (ECGs) showed no significant abnormalities. All received comprehensive care from the multidisciplinary stroke team. None received thrombolysis or thrombectomy. All three patients had neuropsychiatric features and two received input from the psychiatric consultation-liaison team (Table 1).

CASE REPORTS

Case 1

A 45-year-old man presented with a sudden onset of generalized tonic-clonic seizures, dysarthria, right-sided facial weakness, weakness of the left side of the body and confusion. He had a recent COVID-19 exposure. On admission, a COVID-19 PRC test was positive. Computer tomography (CT) brain showed a right posterior cerebral artery (PCA) territory infarct. CT angiogram showed occluded P2 segment of right PCA and absent non-opacified intracranial right vertebral artery. Subsequent magnetic resonance imaging (MRI) confirmed the right-sided PCA infarct but showed additional right pontine paramedian, left cerebellar, right superior cerebellar artery (SCA) and left-sided middle cerebral artery (MCA) territory acute infarcts (see Fig. 1). He required intubation and treatment for COVID-19 and aspiration pneumonia. Subsequently he experienced a prolonged period of delirium. His clinical course was marked by multiple generalized tonic-clonic seizures that required treatment with levetiracetam.

Case 2

A 50-year-old man was admitted following sudden onset of left-sided weakness, confusion and agitation. He had decreased level of consciousness, left hemianopia, left upper and lower limb weakness and sensory loss. CT showed a right MCA territory acute infarct (see Fig. 2), right proximal internal carotid artery (ICA) severe stenosis and severe stenosis/occlusion of M2 branches of right MCA. He had no respiratory symptoms, but chest X-ray showed bilateral apical pulmonary ground glass opacities. He tested positive for COVID-19 (PRC test). He developed a pulmonary embolism 3 weeks post-admission. MRI brain performed on Day 54 confirmed the right MCA distribution stroke with subacute extension. His clinical course was complicated by delirium.

Case 3

A 40-year-old man presented with a sudden onset facial drooping, slurred speech, left arm weakness, confusion and focal facial seizures. A week earlier, he had tested positive for COVID-19 but was asymptomatic other than having a mild fever. CT brain showed a hypodense lesion in the right frontal region suggestive of small acute infarct. MRI brain showed multiple small acute frontal strokes (see Fig. 3) with focal meningeal enhancement suggestive of an underlying vasculitis. Subsequent MRI showed another infarct in the posterior limb of the internal capsule. He was commenced on levetiracetam for focal seizures. At presentation he has been diagnosed with diabetes and hypertension which were brought under control with treatment.

Table 1: Clinical details of the three cases

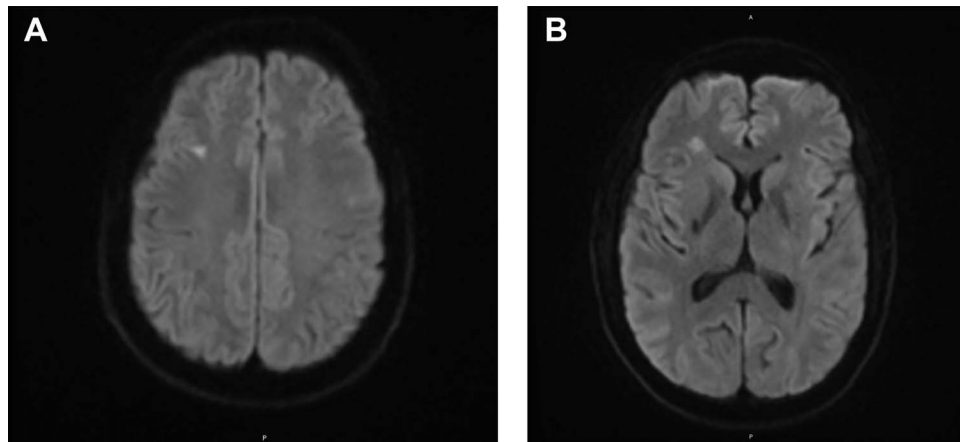
| | Case 1 | Case 2 | Case 3 |
|---|--|--|--|
| Age (years) | 45 | 50 | 40 |
| BMI (kg/m ²) | 27.0 | 24.5 | 30.5 |
| Smoking status | Smoker | Non-smoker | Non-smoker |
| Other stroke risk factors ¹ | Nil | Nil | Diabetes and hypertension diagnosed on admission |
| Neuropsychiatric features | Impaired memory and orientation, visual hallucinations, labile mood, agitation and disturbed sleep during course of admission ² | Impaired memory and orientation, agitation and disturbed sleep during course of admission ² | Confusion and drowsiness prior to admission |
| COVID respiratory disease | Pneumonia | No respiratory symptoms (bilateral apical pulmonary ground glass opacities seen on chest x-ray) | No respiratory symptoms (mild pyrexia for several days prior to stroke) |
| Site of infarct on brain imaging | Right pontine paramedian, left cerebellar, right PCA, right SCA and left MCA territory infarcts. | Right MCA territory infarct. Subsequent subacute stroke size expansion. | Multiple small infarcts in right frontal lobe. Subsequent new acute lacunar infarct in posterior limb of right internal capsule. |
| Intensive care unit required | Yes (intubated) | Yes (not intubated) | No |
| D-dimer level (around appearance of stroke symptoms) (normal: 0.00–0.44 mg/L) | 0.90 | 11.62 | Not measured |
| Other imaging | | Subsequent pulmonary embolus | |
| Treatment | Atorvastatin ³ Aspirin Enoxaparin Levetiracetam ⁴ | Atorvastatin ³ Aspirin Enoxaparin Rivaroxaban Baclofen | Atorvastatin ³ Aspirin Enoxaparin Levetiracetam ⁴ |
| Stroke outcome | Receiving inpatient rehabilitation | Receiving inpatient rehabilitation | Full recovery. Discharged home |

¹Other stroke risk factors refers to any of the following: atrial fibrillation, diabetes, hypertension, hyperlipidaemia or past history of stroke, transient ischaemic attack or myocardial infarction.

²Case 1 and 2 received additional input from the consultation-liaison psychiatry team to assist with the management of delirium and behavioural disturbance.

³For secondary stroke prevention.

⁴To treat seizures.



Figures 3A and 3B: FLAIR axial image. Two small right frontal subcortical T2 hyperintensities, one seen in A and the second in B.

DISCUSSION

Most cases of stroke associated with COVID-19 occur during the course of a characteristic COVID-19 respiratory illness [4]. The three cases we report are unusual in several regards. First, in all three cases the presenting feature that led to admission was stroke. Furthermore, prior to the onset of stroke symptoms,

symptoms of COVID-19 were absent in two cases (case 1 and 2) and restricted to a mild fever in the remaining patient (case 3). Stroke has previously been reported to be the presenting feature of COVID-19 [6]. Second, two patients (case 2 and 3) had no respiratory symptoms throughout their clinical course. Third, the patients were relatively young being aged between 40 and 50 years. This partly reflects the demographics of Qatar; nearly

90% of the population are foreign workers and the median age of the population is 32 years [7]. Nevertheless, other countries are recognizing that younger patients with COVID-19 can suffer strokes [8, 9].

We cannot prove the strokes were causally linked to COVID-19 but the young age, the absent/limited risk factors for stroke in two cases (cases 1 and 2) and the close temporal association of stroke and a positive COVID-19 PCR test are highly suggestive. Potential mechanisms for ischemic strokes in COVID-19 patients include a hypercoagulable state, vasculitis and cardiomyopathy [10]. Hypercoagulability reflects elevated plasma prothrombotic factors including von Willebrand factor (vWF), factor VIII, D-dimer, fibrinogen and anionic phospholipids and increased inflammatory cytokines (cytokine storm) [11]. Data are conflicting regarding whether anti-phospholipid antibodies (aPLs) also play a role in COVID-19 coagulopathy [12, 13]. Case 1 and case 2 involved large vessel occlusion. This could reflect in situ thrombosis but embolization due to hypercoagulability state or from an intracardiac thrombus is more probable [10]. The elevated D-dimer level in these two patients is consistent with hypercoagulability and may reflect the effect of pro-inflammatory cytokines. Hypercoagulability may have implications for offering more aggressive anticoagulant treatment for ischaemic stroke but needs to be balanced against potential risk of bleeding. The brain imaging in case 3 suggested multiple acute infarcts secondary to vasculitis.

In summary, ischaemic stroke can be the presenting feature of COVID-19. This can occur in young otherwise healthy individuals and in the absence of COVID-19 respiratory symptoms. Consequently, the possibility of COVID-19 infection needs to be considered in patients who present with stroke. The corollary is that investigations for stroke need to be considered in patients with COVID-19 illness, even if mild, who develop acute neurological symptoms [9]. These recommendations apply to young as well as older patients.

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Nil.

CONFLICT OF INTEREST STATEMENT

P.M.H. reports personal fees from Janssen, Lundbeck, Otsuka, NewBridge Pharmaceuticals and Sunovion, outside the submitted work. The other authors report no conflicts of interest.

ETHICAL APPROVAL

Ethical approval to report these cases was obtained from the Medical Research Center at Hamad Medical Corporation (MRC-04-20-831).

CONSENT

Written informed consent was obtained from two patients and next of kin for the third patient who was unable to give consent.

GUARANTOR

Dr Yousaf Iqbal.

AUTHOR CONTRIBUTIONS

All authors have been involved in all stages of the preparation of this case report and they have all read and approved the final version of this report.

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