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# Massive Ischemic Strokes in a Young Patient With Severe Coronavirus Disease 2019 Pneumonia

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**Abstract**

Stroke is an identified sequela of severe coronavirus disease 2019 (COVID-19) infection. While the pathophysiology remains poorly understood, endothelial dysfunction and intravascular thrombosis secondary to sepsis-induced hypercoagulability likely increase the risk of stroke. This report describes the rare case of an otherwise healthy 42-year-old male who developed large bilateral ischemic infarcts during admission for severe hypoxemic respiratory failure secondary to COVID pneumonia. This report adds to scarce literature describing massive cerebrovascular injury in COVID patients and emphasizes the importance of increased clinical suspicion for stroke in patients who exhibit acute change in mental status or motor function, as well as rapid clinical deterioration.

**Keywords**

COVID, stroke, pneumonia, bilateral, hypercoagulable, CVA, infarct

## Introduction

Stroke, among other neurological complications, has been identified as a sequela of severe coronavirus disease 2019 (COVID-19) infection. While the pathophysiology remains poorly understood, endothelial dysfunction and intravascular thrombosis secondary to sepsis-induced hypercoagulability are likely contributory.[1] This report details a rare case of a healthy 42-year-old male with hypertension who developed large bilateral ischemic infarcts, during admission for severe hypoxemic respiratory failure secondary to COVID infection. This report adds to scarce literature on massive cerebrovascular injury in COVID patients, with limited comorbidity, and emphasizes the importance of increased clinical suspicion for stroke in patients who exhibit acute change in mental status or motor function as well as rapid clinical deterioration.

## Case Presentation

The patient was a 42-year-old male with previous hypertension who presented with a 5-day history of shortness of breath, subjective fever, chills, and an occasional cough productive of clear sputum. Associated symptoms included generalized bone pain, intermittent headache, watery diarrhea, anorexia, and a home temperature recording of 105 °F. Review of systems was negative for chest pain, abdominal pain, numbness, tingling, or weakness. There was no history of pulmonary embolism (PE), deep vein thrombosis, or recent travel. The patient denied use of tobacco or drugs.

On arrival, vitals were as follows: temperature: 38.6 °C, heart rate: 109 beats per minute, respiratory rate 39 breaths per minute, $SpO_2$: 57, blood pressure: 132/66 mm Hg. The patient was dyspneic and unable to speak in full sentences. On examination, breath sounds were equal, with symmetrical chest wall expansion. Cardiovascular examination showed regular rhythm, with strong and symmetrical peripheral pulses. Albeit distressed, the patient was alert and oriented, with no focal neurological deficits.

Initial workup included a chest X-ray, which revealed scattered bilateral airspace opacities. Pertinent laboratory values were as follows: sodium: 120 mEq/L (L), potassium: 4 mEq/L, blood urea nitrogen: 21 mg/dL (H), and creatinine: 1.1 mg/dL (H); white blood cell: 13 900/μL (H), neutrophil %: 89.4 (H), and lymphocyte %: 5.5 (L); hemoglobin: 13.3 g/dL, platelets: 250 000/μL; and Dimer 2.74 (H), C-reactive protein: 29.32 mg/dL (H), ferritin: 826.30 ng/mL (H), lactate

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dehydrogenase: 1883 U/L (H), interleukin-6: 224.35 pg/mL (H), and troponin <0.019 (ng/mL). RT-PCR (reverse transcriptase-polymerase chain reaction) nasopharyngeal swab returned positive for COVID.

The patient was managed on nonrebreather mask and nasal cannula; he received ceftriaxone, azithromycin, hydroxychloroquine, tocilizumab, and was enrolled in the ongoing remdesivir trial. After developing severe hypoxia on day 2 with oxygen saturation to the 60s off his nonrebreather mask, which he had removed, he was rapidly intubated. He had hypotension post-intubation which required vasopressor therapy; however, no overt shock was demonstrated. Lactate remained below 2.5, post intubation and serum creatinine remained below 0.8 mg/dL. Troponinemia worsened (0.194-0.682 ng/mL), and due to concern for acute PE, a heparin drip was initiated. The patient's hospital course would continue with fluctuating hypoxia on ventilation while receiving heparin (intravenous), sedatives, and occasionally paralytics. He was continuously febrile and required pressor support for suboptimal blood pressures. Duplex study revealed no deep vein thrombosis in lower extremities and transthoracic echocardiography was without intracavitary thrombus.

On the morning of day 6, physical examination revealed diminished pupillary reflexes and mid-dilated pupils without corneal or oculocephalic reflexes, which persisted after withdrawing sedation. Computed tomography (CT) head revealed large ischemic infarcts involving bilateral occipital, left parietal, right temporal, and right frontal lobes with downward herniation into basal cisterns (Figure 1). CT chest with angiography disclosed extensive multifocal dense ground-glass opacities in the lungs without PE. Taking the patient's clinical deterioration, and severity of radiographic findings into consideration, no further workup was pursued. The patient was pronounced dead the following day.

## Discussion

Neurological manifestations are now being recognized as sequelae of severe COVID-19 infection. A study of COVID-infected patients in Wuhan, China, found 36.4% of their studied cohort to have neurological symptoms including dizziness, headache, ageusia, anosmia, and stroke.[2] While stroke occurred in 2.8% of the 214 patients reviewed in that study, the incidence of stroke occurred more frequently in patients defined as having severe infection (5.7% vs 0.8%), suggesting that risk of stroke is directly correlated with severity of disease.[2]

Literature describing the characteristic stroke associated with COVID is limited. Despite several cases of young patients who developed large-vessel occlusion, early literature suggests that COVID stroke occurs more commonly in elderly patients with comorbidities including hypertension, diabetes, obesity, and heart disease.[1,3] Similar to our patient, stroke in COVID has been associated with large-vessel occlusion occurring 1 to 3 weeks after symptom onset. Additionally, some reports suggest increased stroke incidence in males compared with females.[4,5] This needs to be investigated further. As seen in our patient, COVID patients who developed stroke have had elevated D-dimer, ferritin, LDH, and troponins when compared with stroke patients without COVID.[4,5]

Several types of strokes including venous sinus thrombosis, subarachnoid hemorrhage, intracerebral bleeds, and ischemic strokes have all been reported as a complication of COVID infection.[6] To date, ischemic stroke has been the most frequently reported.[6] Investigations surrounding the mechanism of cerebral ischemia in COVID patients are ongoing. Early literature has suggested several mechanisms.

First, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is thought to cause an endotheliopathy as well as a prothrombotic state, with release of inflammatory cytokines and upregulation of tissue factor and thrombin causing platelet activation.[5] SARS-CoV-2 virus infects cells via an angiotensin converting enzyme-2 (ACE2) receptor found in lung, heart, kidney, brain, and vascular tissues.[3] Increased receptor occupation by SARS-CoV-2 is thought to cause ACE2 receptor downregulation and decreased cleavage of angiotensin 2 (vasoconstrictor) to angiotensin 1-7 (vasodilator), increasing risk of vessel occlusion and cerebrovascular events.[3] Additionally, studies have described patients who developed bilateral ischemic infarcts and, on hematologic investigation, had workup suggestive of an acquired and transient thrombophilia (ie, antiphospholipid syndrome).[4] Last, patients with severe COVID sepsis requiring ventilation in the intensive care unit are more prone to episodes of prolonged hypotension and fluctuations in blood pressure causing posterior reversible encephalopathy syndrome, arrhythmias, and cardiac arrest.[4] These mechanisms all increase likelihood of cerebral hypoperfusion.

Our patient illustrates the difficulties in monitoring neurological functions in severe COVID disease. He became suddenly agitated on the third day of admission (day 8 of his illness), which was followed by respiratory failure requiring endotracheal intubation and sedation. He then, at one point, sustained massive bilateral ischemic stroke in both anterior and posterior circulations, as his underlying pneumonia progressed, with cerebral edema and downward herniation. This was likely due to intravascular thrombosis, as there was no deep venous clot in lower extremities by ultrasound and no cardiac thrombus by transthoracic echocardiogram.

Our patient experienced his stroke within the 9-day period, from onset of COVID symptoms, that some authors described.[7-9] Other authors have reported large-vessel stroke in young COVID patients with limited risk factors; however, the stroke usually occurred at the onset of COVID illness before patients presented to the hospital and involved

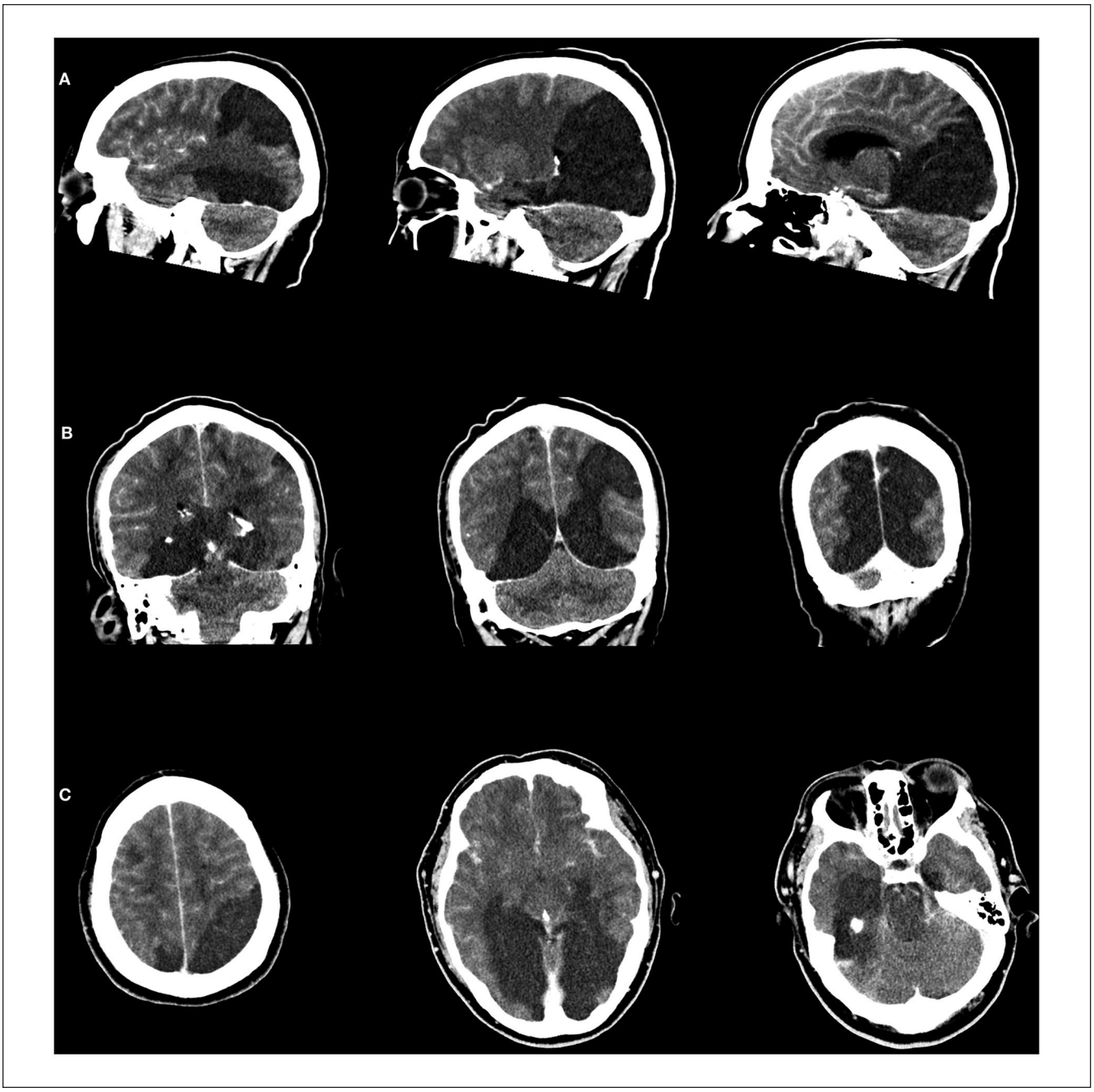


**Figure 1.** Computed tomography (CT) head without contrast showing large regions of low density involving bilateral occipital, left parietal, right temporal, and right frontal lobes representing ischemic infarctions. There is evidence of global brain edema, with effacement of basal cisterns and cerebral sulci: (A) sagittal, (B) coronal, and (C) axial; CT head without contrast done immediately after CT chest with contrast; lingering effects of contrast (diffuse sulcal hyper-density) appear in images above.

one vascular territory.[8] Malignant edema has complicated stroke in other patients, at times requiring hemicraniectomy,[9] but this occurred again with unilateral infarcts. The closest case to ours was a 40-year-old woman who presented with severe COVID pneumonia and diabetic ketoacidosis, was intubated, and expired on day 7 of her illness; CT revealed massive right middle cerebral artery infarct with midline shift and downward herniation.[10] Our patient is unusual in that he developed massive bilateral ischemic infarcts in several vascular territories, with herniation, likely contributing to his demise. Indeed, autopsy reports in other patients have showed neuro-inflammatory changes in the brainstem as the most common finding, with no evidence of direct central nervous system damage.[11]

Diagnosing acute stroke in COVID patients requiring ventilation is challenging, as use of sedatives can complicate evaluation of mental status and neurologic function. Additionally, the need for patient isolation makes thorough and frequent patient monitoring more difficult. Clinical trials investigating the efficacy of prophylactic anticoagulation are ongoing. To date, studies seem to suggest that patients are at risk for stroke even while on anticoagulation. For this reason, a structured and efficient method to neurologically evaluate patients with severe COVID is needed. For now, clinicians should have increased suspicion for stroke in patients with severe disease who exhibit change in motor function, mental status, and or rapid clinical deterioration.

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## Ethics Approval

Our institution does not require ethical approval for reporting individual cases.

## Informed Consent

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