Case Report

Thalamic Stroke associated with SARS-CoV-2 Infection: A Case Report

Karla Romero*, Jeremy Eckes MD[1], Kester Nedd MD[2], George Michel MD[3], George Yatzkan MD[4]

***Corresponding Author: Dr. Karla Romero,** 7031 SW 62nd Ave, South Miami, FL 33143.

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Abstract

***Background**: Protocol management of primary stroke prevention and acute stroke management in patients with SARS-COV-2 has not been well established.*

Case presentation: In this case, we describe a 58-year-old Hispanic male who was infected with SARS-COV-2 and developed an acute thalamic stroke. We discuss the pathophysiology of SARS-COV-2 which results in an increase in hypercoagulable status and the importance of stroke prevention in high-risk patient populations. Primary prevention of stroke is focused on identifying risk factors and modifying their risk by advising lifestyle changes and/or medication management. The importance of the evaluation is discussed after the patient has obtained a positive test for SARS-COV-2 with their primary care physician as to any risk-reducing measures that can be taken.

***Conclusion**: Acute treatment of stroke aims to revascularize with intravenous thrombolysis if indicated. However, before administration of intravenous thrombolysis in a SARS-COV-2 patient further consideration should be taken due to their increased risk of bleeding.*

***Keywords**: covid-19, stroke, thrombolysis.*

Background

Severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) as the name suggests was initially thought to only cause a respiratory illness. However, some reports have been published of patients with ischemic strokes in the setting of coronavirus disease 2019 (SARS-COV-2). The mechanisms of how SARS-CoV-2 results in blood clots and large-vessel stroke needs to be defined as it has therapeutic implications. SARS-CoV-2 enters the bloodstream by breaching the blood-air barrier via the lung capillary adjacent to the alveolus, then attaches to the angiotensin-converting enzyme II receptors on the endothelial cells. Once SARS-CoV-2 enters the bloodstream, a cascade of events unfolds including accumulation of angiotensin II, reactive oxygen species, endothelial dysfunction, oxidation of beta 2 glycoproteins 1, the formation of antiphospholipid antibody complexes promoting platelet aggregation, coagulation cascade, the formation of cross-linked fibrin blood clots, leading to pulmonary emboli (PE) and large-vessel strokes seen on angiographic imaging studies **(**1-2**)**.

In this case, we describe a 58-year-old Hispanic male who was infected with SARS-COV-2 manifesting right-sided hypoesthesia and hemiplegia. He was diagnosed with left side thalamic stroke. Sensorimotor stroke is characterized by weakness and numbness of the face, arm, and leg on one side of the body in the absence of cortical signs. It is responsible for 15 to 20 percent of lacunar syndromes. Lacunar infarcts are small (0.2 to 15 mm in diameter) noncortical infarcts caused by occlusion of a single penetrating branch of a large cerebral artery **(**3**)**.

These branches arise at acute angles from the large arteries of the circle of Willis, the stem of the middle cerebral artery (MCA), or the basilar artery. The ultimately terminal rather than anastomotic nature of these vessels is a factor explaining the predisposition to lacunar infarction. The etiology is associated with endothelial dysfunction and disruption of the associated blood-brain barrier. Sensorimotor strokes arise from infarcts involving the posterolateral thalamus and posterior limb of the internal capsule. Theoretically, penetrating arteries from the posterior cerebral artery (PCA) supply the thalamus and the internal capsule is supplied from the lenticulostriate branches of the MCA. The diagnostic tests used to confirm or exclude the clinical suspicion of a lacunar stroke are CT scan, MRI, and diffusion-weighted imaging. Vascular imaging (CTA or MRA) can be performed at the same time as brain imaging (CT or MRI) to exclude occlusion of the parent feeding artery, a condition that can mimic a lacunar infarct **(**4-6**)**. The best available evidence suggests that intravenous alteplase is beneficial for patients with lacunar stroke. For secondary prevention, intensive medical treatment is recommended including antihypertensive, antiplatelet, and statin therapy **(**4-6**)**.

Case Presentation

A 58-year-old male presented to the Emergency Department experiencing two days of shortness of breath, fever, dry cough, diarrhea, headache, fatigue, and right-side body numbness, he tested positive for SARS-COV-2. Previous medical records were notable for hypertension and dyslipidemia, taking aspirin 81 mg, hydrochlorothiazide 25 mg, and lisinopril 10 mg daily. The initial physical examination was remarkable for a blood pressure of 140/80 mmHg, heart rate of 79 bpm, oxygen saturation of 97%, respiratory rate of 18 rpm, and temperature of 102 F (38.8 C). The cardiovascular examination was unremarkable. The pulmonary examination revealed bilateral rales. The neurological examination was notable for the focal weakness of the right upper and lower extremity, focal right-sided hypoesthesia to light touch positive right-sided Babinski sign, positive pronator drifts on the right-side. Although, vibration with proprioception intact. NIHSS score of 3. Physical examination was otherwise unremarkable. Laboratories tests were ordered and revealed an elevated white blood cell count of 11,000 with neutrophils of 89% and lymphocytes of 6.3% and an elevated CRP of 15 mg/dl.

As shown in Figure 1, brain CT revealed well-rounded focal hypodensity within the left basal ganglia, which may be representative of a lacunar infarct, with a high clinical suspicion of acute ischemic stroke. MRI of the brain revealed late acute to early subacute left thalamic infarct without hemorrhagic conversion (figure 2). CT angiogram of the head (figure 3) revealed normal intracranial imaging.

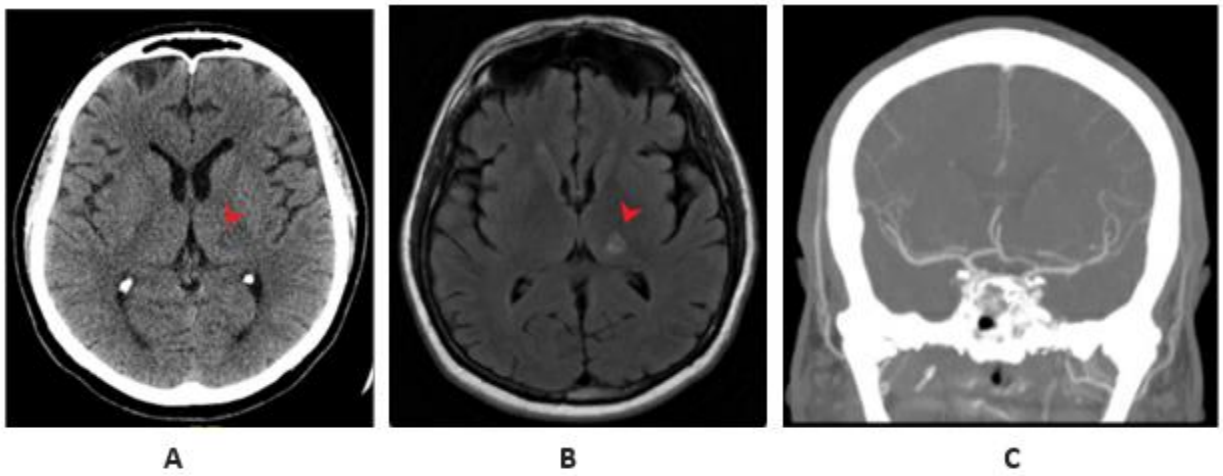

Fig. 1 (A) Brain CT showing focal well-rounded hypodensity within the left basal ganglia (white arrow). (B) MRI of the brain showing late acute to early subacute left thalamic infarct without hemorrhagic conversion (white arrow). (C) CT angiogram of the head showing normal intracranial imaging.

Chest x rays showed patchy bilateral interstitial and/or alveolar infiltrate in the setting of known COVID-19 pneumonia, possible small pleural effusion. CT scan chest revealed bilateral infiltrative process most prominent in the lung bases with air bronchogram most like multifocal viral pneumonia. Doppler carotid US showed a small plaque at the right carotid bulb without stenosis or significant obstruction. Transthoracic echocardiogram revealed normal left ventricle size, no atrial septal defect, and normal global systolic left ventricular function with an ejection fraction of 60%.

The patient was admitted to the intensive care unit and treated with Remdesivir 100 mg IV once daily for 5 days, Solu-Medrol 40 mg twice daily, aspirin 81 mg once daily, Enoxaparin 40 mg SQ twice daily, Lisinopril 40 mg once daily, Tocilizumab 400 mg IV once, atorvastatin 40 mg once daily and convalescent plasma. After stabilization, the patient was admitted to the floor with persistent right-sided hypoesthesia and right-side weakness. After physical therapy, the patient improved and was discharged with apixaban 2.5 mg, aspirin 81 mg, and gabapentin 100 mg.

Discussion and Conclusion

The pathophysiology of SARS-COV-2 leading to cerebrovascular events is not fully understood. However, the autopsies of patients with SARS-COV-2 have shown the presence of the virus in the endothelial capillary cells in the brain. Viral CNS access is likely to occur by infecting the blood-brain barrier endothelial cells, the blood-CSF barrier epithelial cells, or using inflammatory cells as a decoy. It has been well established that cerebrovascular endothelial cells express ACE-II receptors. SARS-COV-2 binds to these receptors, resulting in a cytokine storm leading to a hypercoagulable state in patients **(**1,2**)**. Patients with SARS-COV-2 show elevated D-dimer levels, activated platelets which increase the propensity to cerebrovascular events **(**7-9**)**. The incidence of acute ischemic stroke in SARS-COV-2 patients ranges from 0.9% to 2.7%. Stroke severity in SARS-COV-2 patients is typically at least moderate (NIHSS score 19±8), with a high prevalence of 40.9% of large vessel occlusion. The mortality rate is 38% **(**10**)**.

SARS-COV-2 infection may lead to a prothrombotic state. This is supported by high fibrinogen and d-dimer levels in patients who are SARS-COV-2 positive. Medical literature has reported a small but significant proportion of acute ischemic stroke patients. At the initial presentation, 24 % had no acute respiratory symptoms. Chest radiograph or computed tomography scans showed characteristic findings for possible pneumonia before testing for SARS-COV-2. The mean age of these patients with AIS was 63±13.1 years, with commonly observed cardiovascular risk factors. The duration of AIS from the onset of SARS-COV-2 symptoms was 10±8 days, suggesting a delay in presentation. This coincides with the

current postulation that patients with severe SARS-COV-2 symptoms may develop an early hyper inflammation state from cytokine storm followed by a prothrombotic condition often complicated by venous and arterial thromboembolism **(**11-14**)**.

Elevated biomarkers such as D-dimer, fibrinogen, and factor VII provide further evidence of a prothrombotic state **(**11-15**)**. Clinicians should consider thrombotic sequelae such as stroke may be seen in both early and late phases of the infection **(**15,16**)**. Patients with concomitant SARS-COV-2 suffered more severe strokes, with a higher NIHSS score, a greater proportion of large vessel occlusion, and higher hospital mortality **(**3**)**. In the Department of Neurology Union Hospital, Tongji Medical College of Wuhan in China, out of 219 patients with SARS-COV-2, 10 (4.6%) developed acute ischemic stroke and 1 (0.5%) had an intracerebral hemorrhage. SARS-COV-2 with new onset of cerebrovascular disease were significantly older, more likely to present with severe SARS-COV-2, and were more likely to have cardiovascular risk factors, including hypertension, diabetes mellitus, and medical history of cerebrovascular disease. Also, they were more likely to have increased inflammatory response and hypercoagulable status as evidenced by reactive protein C and D-dimer. These findings suggested that SARS-COV-2 positive elderly patients have a higher risk of developing the cerebrovascular disease **(**17**)**. Studies have shown that SARS-COV-2 infection can accelerate the progression of acute stroke **(**18-19**)**. The current treatment of SARS-COV-2 should be part of the standard treatment of these patients, such as Remdesivir, tocilizumab, and convalescent plasma, although the respiratory symptoms are not severe **(**1,2**)**.

Primary prevention of strokes focuses on identifying risk factors and modifying them by suggesting changes in lifestyle and/or medication management. High blood pressure impacts both ischemic and hemorrhagic stroke. Current guidelines recommend treating hypertension with lifestyle and medical therapy to achieve a blood pressure of <130/80 mm Hg. Diabetes mellitus is an independent risk factor for stroke. A glycated hemoglobin goal of less than 7% is recommended to reduce the risk of stroke. Active smoking increases stroke risk by 2 to 4 times. Smoking cessation is recommended to reduce the risk of stroke. Patients who have tested positive for SARS-COV-2 should be encouraged to consult with their primary care physician for an assessment because of their increased risk of developing a stroke secondary to SARS-COV-2 **(**19**)**.

The acute management of the lacunar infarction is revascularization. Within 4.5 hours of symptom onset, patients should receive alteplase (IV thrombolysis) therapy when indicated. Administration of thrombolysis IV to a patient positive for SARS-COV-2 should be considered due to the increased risk that these patients develop disseminated intravascular coagulation (DIC) and the possibility of

presenting in a hypercoagulable state. Current guidelines for ordering tests recommend glucose levels before administration. However, a detailed assessment of patients with SARS-COV-2 is required before the decision on intravenous thrombolysis to determine the benefit-risk ratio. This includes a coagulation profile (PT, INF, APTT, fibrinogen), a platelet profile, a renal and hepatic function profile **(**20**)**.

The infection with SARS-COV-2 manifests itself under different medical conditions, the CNS is certainly a vulnerable target for the virus. There are several mechanisms involved in stroke and SARS-COV-2, including hypercoagulable state and disseminated intravascular coagulation (DIC). Further case-control studies will be required to establish whether SARS-COV-2 is either causal or coincidental in these patients. However, there seems to be a correlation between patients with SARS-COV-2 and presenting in a hypercoagulable state. When assessing patients with neurological symptoms, consideration should be given to their SARS-COV-2 status. Diagnostic testing should include a comprehensive neurological evaluation and images. Further diagnostic tests including a coagulation profile, platelet count, renal and hepatic function profile, should be performed to determine the benefit-risk ratio for intravenous thrombolysis treatment in patients with a stroke who experience SARS-COV-2. Also, establish primary and secondary prevention in patients with both conditions due to the increased risk of embolism. Further evidence is needed from larger studies.

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Ethics approval and consent to participate

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Consent for publication

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Competing interests

The author declares no competing interests concerning the publication of this article.

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