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Coronavirus Positive Patients Presenting with Stroke-Like Symptoms

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Several studies from Wuhan, China have reported neurological manifestations in patients who tested positive for coronavirus disease 2019 (COVID-19). One study reported 214 COVID-19 positive patients, out of which 41.1% had severe infection. 5.7% of patients with severe infection had acute cerebrovascular disease.¹ Another study looked at 221 COVID-19 positive patients, out of which 5% had ischemic infarcts and 0.5% had cerebral hemorrhage.² A recent study from Mount Sinai Hospital in New York reported five cases of cerebral infarcts due to large vessel occlusion in patients who tested positive for COVID-19. Several mechanisms such as vascular endothelium dysfunction and pro-inflammatory responses which can accelerate atherosclerosis and enhance coagulopathy have been proposed as potential causes for ischemic infarcts.³

Studies seem to demonstrate a relationship between COVID-19 and stroke, however further investigation is needed. This paper presents a series of patients who presented with stroke and other neurological disorders to our stroke center in Philadelphia and were found to be

COVID-19 positive. The goal is to identify risk factors and potential mechanisms of stroke etiologies for this subset of patients. We reviewed various stroke patterns, lab values, and risk factors in this subset.

Results

The patients in this case series presented to our center from April 2020 to June 2020. The total number of stroke codes called during this time period was 127. Out of the 127 stroke codes, 2 stroke codes were called on patients who were COVID-19 positive and have been reported in our series. Seven of the stroke patients in our series were direct transfers from another hospital. The remaining two patients presented to our emergency department with symptoms lasting more than twenty four hours and therefore no stroke code was called. Most of the patients in our series were transfers from surrounding hospitals and outside the window for tPA. The high rate of outside hospital transfers seen in our case series is most likely due to higher acuity of these patients who had medical complications secondary to COVID-19 along with stroke.

Seventeen patients presented with stroke-like symptoms and tested positive for COVID-19 upon arrival to our hospital (Table 1). Three patients were diagnosed as seizures, two patients had subarachnoid hemorrhage (SAH), and one patient had a venous infarct. Of the remaining eleven patients, ten patients had ischemic infarcts as seen on MRI and one patient had a central retinal artery occlusion (CRAO) secondary to occlusive thrombus in the right internal carotid artery. Out of the ten patients who had imaging-confirmed ischemic strokes, five were due to large vessel occlusion, four were presumed embolic strokes, and one was a subcortical lacunar infarct thought to be related to small vessel disease. Three of the stroke patients were found to have evidence of atherosclerotic disease as seen on CTA/MRA head/neck imaging. Out of the two patients with SAH, one of them was found to have a posterior communicating artery aneurysm.

All patients in our series were admitted for further work up. At the end of the hospital stay, three of the stroke patients were discharged directly to home as they did not meet any rehabilitation needs. Three others required either skilled nursing or rehabilitation facilities.

In the time period from April 2020 to June 2020, we had 15 deaths in our ischemic stroke patients. Out of this, 5 deaths (33 %) occurred in the stroke patients who were found to be COVID-19 positive.

Fig. 1.

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Table 1. Clinical Characteristics of Covid Positive Patients who presented with Stroke-Like Symptoms

Patient	Age	Sex	Medical History	Diagnosis	Initial NIHSS	Stroke Pattern	Vascular Territory Involved	IV-tPA	Thrombectomy	Atherosclerosis in Stroke Territory	Antithrombotic Agent	Covid-19 Symptoms	WBC (per mm3)	Platelet (B/L)	INR	D-dimer (ng/ml)	Disposition	Cause of Death
1	55	M	HTN	Ischemic Stroke	2	Embolic	Anterior and Posterior Circulation	No	No	No	Aspirin	Sore throat, Fever, Cough, SOB	5.7	303	1.1	3.93	Skilled Nursing Facility	N/A
2	78	F	CAD s/p Stent, PAD, DM2	Ischemic Stroke	Unknown	Embolic	Anterior and Posterior Circulation	No	No	No	None due to thrombocytopenia	SOB	11.4	69	1.3	7147	Death	Respiratory Failure, DIC
3	72	M	Stroke, CHF	Ischemic Stroke	12	Embolic	Left MCA	No	No	Yes	Aspirin	SOB	12.7	167	1.3	3486	Death	Respiratory Failure, Septic Shock
4	73	M	HTN, DM2	Ischemic Stroke	23	Large Vessel Intracranial Occlusion (Right M1)	Right MCA	No	No	Yes	Aspirin	SOB	20.4	238	1	2043	Death	Respiratory Failure, Septic Shock
5	62	M	HTN, DM2	Ischemic Stroke	Unknown	Large Vessel Intracranial Occlusion (Right M1)	Right MCA	No	No	No	Aspirin	Cough, SOB	8.9	212	1.1	524	Skilled Nursing Facility	N/A
6	48	M	HLD	Ischemic Stroke	23	Large Vessel Intracranial Occlusion (Left M1)	Left MCA	Yes	Yes	No	Aspirin	None	7.2	237	1.1	6383	Home	N/A
7	64	F	HTN	Ischemic Stroke	4	Embolic	Posterior and Anterior Circulation	No	No	No	Aspirin	Cough, SOB	6	457	1.1	419	Home	N/A
8	51	M	CAD, HTN	Ischemic Stroke	15	Large Vessel Intracranial Occlusion (Right ICA)	Right MCA	No	Yes	No	Aspirin + Clopidogrel	SOB	5.8	273	1.4	2476	Death	Respiratory Failure, Septic Shock
9	70	F	None	Ischemic Stroke	Unknown	Large Vessel Intracranial Occlusion (Right M1, A1)	Right MCA and ACA	No	Yes	No	None due to risk of hemorrhagic conversion	SOB, Fever	10	483	1.3	11559	Death	Respiratory Failure, Septic Shock
10	59	M	HTN, Smoker	Ischemic Stroke	1	Large Vessel Extracranial Occlusion (Right ICA)	Right Central Retinal Artery	No	No	No	Rivaroxaban	Sore throat	7.6	327	1.3	450	Home	N/A
11 N/A	83	F	DM2, HTN	Ischemic Stroke	8	Small Vessel Disease	Posterior Circulation	No	No	Yes	Aspirin + Apixaban	Cough, SOB	2.5	133	1.2	282	Acute	Rehabilitation
12	54	M	HTN	Venous Infarction due to Cerebral Venous Sinus Thrombosis	Unknown	N/A	N/A	N/A	N/A	N/A	N/A	Cough, SOB	13.4	372	1	5748	Death	Obstructive Hydrocephalus, ICP Crisis, Respiratory Failure
13	62	F	HTN, HLD	Seizure	N/A	N/A	N/A	N/A	N/A	N/A	N/A	None	13	312	1	1075	Home	N/A
14	50	M	HTN, HIV, CKD, Stroke	Seizure	N/A	N/A	N/A	N/A	N/A	N/A	N/A	None	3.9	231	1	5619	Death	Respiratory Failure
15	62	F	Stroke, Seizures	Seizure	N/A	N/A	N/A	N/A	N/A	N/A	N/A	None	12.9	340	1.2	706	Death	Respiratory Failure
16	38	F	None	Subarachoid Hemorrhage	N/A	Posterior Communicating Artery Aneurysm	N/A	N/A	N/A	N/A	N/A	Cough, SOB	Not collected	396	1.1	971	Home	N/A
17	63	M	None	Subarachoid Hemorrhage	N/A	N/A	N/A	N/A	N/A	N/A	N/A	SOB, Fever	6.6	188	1	408	Death	Respiratory Failure, Septic Shock

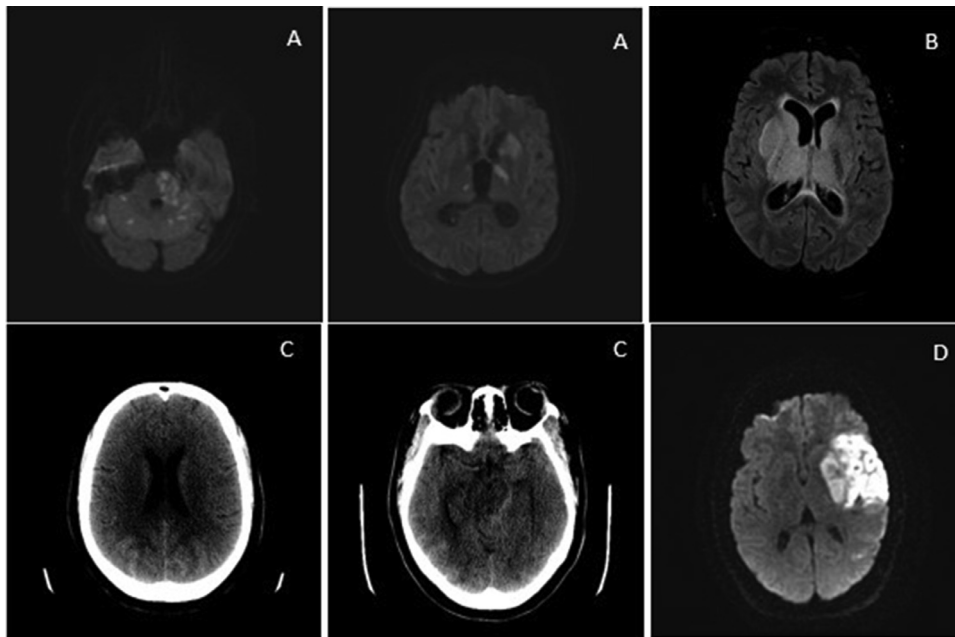


Fig. 1. A. Patient 1: Ischemic stroke, DWI sequence showing embolic stroke pattern in the anterior and posterior circulations. B. Patient 12: Venous infarctions, FLAIR sequence of MRI brain showing bilateral hyper intensities. C. Patient 16 SAH, CT HEAD SHOWING SAH in the left ambient cistern, quadrigeminal plate cistern and bilateral parieto-occipital lobes. D. Patient 6: Large vessel ischemic infarct, DWI sequence with diffusion restriction in the left MCA territory.

Conclusion

COVID-19 positive patients who presented with acute stroke-like symptoms were found to have a variety of neurologic diagnoses including seizures, cerebral venous sinus thrombosis, arterial ischemic stroke, and subarachnoid hemorrhage.

Three patients presented with seizure. There have been several case studies of COVID-19 causing hyponatremia.⁵ Patient 13 was found to have hypovolemic hyponatremia with a sodium of 106 mmol/L. Several mechanisms have been proposed, one of them being that the virus binds to angiotensin-converting enzyme receptors.⁶ This can lead to renal excretion of these electrolytes. We believe that the seizure was triggered by the low sodium levels. Patient 15 had a history of seizures and chronic infarcts, while patient 14 only had a history of chronic infarcts. We believe these patients presented in status epilepticus in the setting of COVID-19 infections lowering their seizure thresholds and causing metabolic derangements.

The majority of our stroke patients had either large vessel occlusion infarcts or scattered, multi-territorial infarcts, suggestive of a proximal embolic source. Workup of these patients did not identify any embolic source, however this could suggest an underlying pro-inflammatory condition related to COVID-19 infection causing accelerated atherosclerosis or a hypercoagulable state. These patients did also have traditional risk factors for stroke such as hypertension, dyslipidemia, and diabetes, however; making it difficult to determine a single mechanism of stroke in COVID-19 patients. Anterior circulation infarcts were more common than posterior circulation infarcts. There

was no predilection to any particular age group in our cohort.

As evident from [Table 1](#), five patients with ischemic stroke died. The cause of death for the stroke patients was primarily due to COVID-19 related respiratory failure and septic shock rather than complications of stroke. A recent study revealed that D-dimer is commonly elevated in patients with COVID-19 and that it can be a marker for disease severity with a higher risk of mortality.⁴ In our study population, patients who died had significantly elevated D-dimers and a more complicated hospital course compared to survivors. Patient 12 was diagnosed with extensive cerebral venous sinus thrombosis which led to ICP crisis, respiratory failure, and ultimately, death. Interestingly, patient 6 in our series had an elevated D-dimer but a good outcome which may have been secondary to his age and treatment with both IV-tPA and mechanical thrombectomy. It is also worth mentioning that two patients with ischemic strokes and one patient with central retinal artery occlusion improved to a degree that allowed discharge directly to home rather than rehabilitation facility.

Most of the stroke patients were placed on an antiplatelet agent; the role of anticoagulation in the management of this patient population requires further investigation.

Declaration of Competing Interest

None.

Disclosures

None.

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