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# Unusual Pattern of Arterial Macrothrombosis Causing Stroke in a Young Adult Recovered from COVID-19

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Coronavirus disease-19 (COVID-19) pandemic continues to grow all over the world. Neurological manifestations related to COVID-19, including acute ischemic stroke (AIS), have been reported in recent studies. In most of these, the patients are older, have multiple co-morbidities as risk factors for AIS and have developed a severe respiratory illness. Herein, we report a 36-year-old man with no significant past medical history who recently recovered from a mild COVID-19 infection and presented with unusual pattern of arterial macrothrombosis causing AIS. When the AIS happened, he had no COVID-19 related symptoms, had two negative screening tests for the infection and his chest CT was unremarkable.

**Key Words:** Coronavirus disease-19—COVID—Large Vessel Occlusion—Acute Ischemic Stroke—Young—Macrothrombosis—SARS-CoV-2 Infection

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## Introduction

Coronavirus disease-19 (COVID-19) pandemic continues to grow all over the world. Symptoms vary from none to mild common cold symptoms, fever, diarrhea, myalgia, and cough which can progress to acute respiratory distress syndrome, multisystem organ failure, and death. Neurological sequelae

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*Abbreviations:* COVID-19, Coronavirus disease-19; AIS, Acute Ischemic Stroke; PMH, Past Medical History; NIHSS, National Institutes of Health Stroke Scale; CT, Computed Tomography; CTA, CT Angiography; ASPECT, Alberta Stroke Program Early CT, MCA, Middle Cerebral Artery; ECA, External Carotid Artery; ICA, Internal Carotid Artery; LVO, Large Vessel Occlusion; PCR, Polymerase Chain Reaction; TICI, Thrombolysis in Cerebral Infarction

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have also been reported in addition to the pulmonary symptoms. Neurological symptoms range from mild headache, dizziness, and anosmia to more severe complications such as thrombotic stroke, a finding reported in 1–3% of patients.<sup>1,2</sup>

To date, several patients presenting with AIS during active COVID-19 infection have been reported. However, most of these patients had significant co-morbidities and established cardiovascular risk factors, making it difficult to confirm COVID-19 as the precipitating cause.<sup>3</sup> While coagulopathy and vascular endothelial dysfunction have been widely reported as a consequence of severe COVID-19 infection, these findings are proposed to be directly related to the severity of the respiratory illness,<sup>4</sup> and the prevalence of this prothrombotic state among milder or asymptomatic cases is not yet established.

Herein, we report an unusual pattern of arterial macrothrombosis presenting as large vessel stroke in a 36-year-old patient with no prior medical history (PMH) who had recently recovered from a mild COVID-19 infection. In addition to his lack of conventional stroke risk factors except for mildly elevated Hemoglobin A1c and elevated low-density lipoprotein (LDL) cholesterol, the case is unique in the temporal association of stroke occurring in the post-symptomatic phase of infection.

## Case Description

A previously healthy 36-year-old male who had recently recovered from a mild case of COVID-19 infection presented to the emergency department with acute onset of left hemiparesis, left visual hemi-neglect and dysarthria 10 hours after symptom onset. Ten days prior to this, he was diagnosed with COVID-19 via nasopharyngeal swab and reverse transcription polymerase chain reaction (rtPCR). At the time of COVID-19 diagnosis, his symptoms included mild fever, myalgias and three days of diarrhea. Prior to this, the patient had no significant PMH and was not taking any medications. Throughout his illness he never experienced any respiratory symptoms. The patient had complete resolution of his COVID-19 symptoms several days prior to admission for stroke symptoms. Furthermore, COVID-19 testing, via nasopharyngeal swab and PCR was performed at the presenting emergency department as well as at the accepting hospital and were all negative. Computed tomography of the head (CTH) and angiography (CTA) of head and neck showed a large sub-occlusive thrombus in the right common carotid bifurcation extending to both internal (ICA) and external carotid arteries (ECA). The patient was loaded with Aspirin 325mg, started on heparin infusion and transferred to our center for treatment.

Upon arrival, 12 h after symptom onset, he had right middle cerebral artery (MCA) syndrome with a National Institute of Health Stroke Scale (NIHSS) score, a measure of stroke severity based on neurological exam, of 12 (range 0–42).

At our center, CTA head and neck, CT perfusion of brain and CTH revealed a right MCA (anterior M2 segment) occlusion with significant perfusion mismatch in right MCA territory in addition to the CTA neck findings. He had an Alberta Stroke Program Early CT (ASPECT) score of 8 (range 0–10) on CTH. Given the disabling neurological symptoms with significant perfusion mismatch in the right MCA territory, the decision was made to proceed with mechanical thrombectomy.

In the cervical right common carotid angiogram, a large amount of sub-occlusive thrombus was noted in the right carotid bulb and proximal ICA with extension into the proximal right ECA (Fig. 1). A Walrus balloon guide catheter (Q'Apel Medical, Fremont, CA) was advanced under fluoroscopy via femoral arteriotomy to the distal common carotid artery and inflated to cause flow arrest. Direct aspiration was then performed using a large bore catheter positioned within the proximal ICA and carotid bulb clot. A large amount of clot was suctioned and subsequent angiogram demonstrated resolution of thrombus within the carotid bulb and proximal ICA. Of note, some thrombus was still present within the proximal ECA (Fig. 2). We then proceed with mechanical thrombectomy of the occluded right anterior M2 segment (Fig. 3). Following a total of three stent retrieval pulls using the Solitaire X



**Fig. 1.** Initial angiogram of the right Common carotid artery (lateral View) shows extensive sub-occlusive thrombus in both carotid bulb and proximal internal carotid artery (right arrow) and proximal external carotid artery (left head).

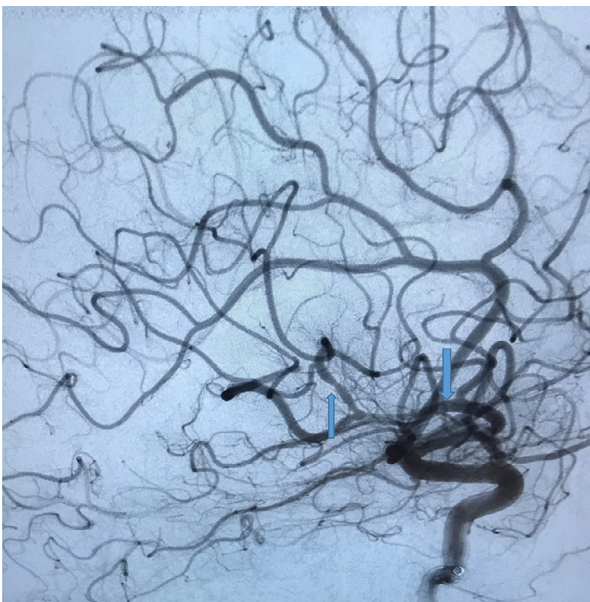


**Fig. 2.** Post thrombectomy angiogram of the right Common carotid artery (lateral View) shows complete resolution of the thrombus in carotid bulb and proximal internal carotid artery (right arrow) but thrombus still present in the proximal external carotid artery (left head).



**Fig. 3.** Angiogram of the right internal carotid artery (lateral View) shows complete occlusion of middle cerebral artery, anterior proximal M2 segment (down arrow).

4 mm x 40 mm (Medtronic Inc, Mansfield, Massachusetts, USA) in combination with aspiration through the large bore catheter, successful recanalization of the occlusion site was noted (Thrombolysis in Cerebral Infarction [TICI] score 3); however, mild vasospasm of the M3 branches was noted, possibly due to catheterization of the vessel (Fig. 4). Post-operatively the patient was transferred to the intensive care unit. A CTH was performed post



**Fig. 4.** Post thrombectomy angiogram of the right internal carotid artery (lateral View) shows complete recanalization of the anterior proximal M2 segment occlusion (down arrow); however, mild vasospasm of the M3 branches noted (up arrow).

procedure which did not show any intracerebral hemorrhage. Heparin drip and Aspirin 81 mg daily were continued due to the patient's massive thrombus and clinical hypercoagulable state associated with recent COVID-19 infection.

Given his recent COVID-19 infection history, a chest CT was performed which was unremarkable. Magnetic resonance imaging (MRI) of the brain was performed 24 h later which demonstrated a large acute infarct in the right MCA territory with only minor petechial bleed, despite complete recanalization. A full stroke workup, including electrocardiogram, telemetry during hospital admission, echocardiography, and blood work for evaluation of underlying inherited coagulation disorder were performed which were all unremarkable. In his transthoracic echocardiogram with bubble study, no right-to-left shunting was detected, ejection fraction was 65% and there was no evidence of left ventricular hypertrophy. However, his labs were notable for elevated CRP and D-Dimer, signifying a persistent procoagulant/proinflammatory state (Table 1). Patient's weight was 67.3 kg and body mass index was 23.3 kg/m<sup>2</sup>. He had no family or personal history of stroke and no history of tobacco use. The patient's neurological symptoms did not significantly improve during hospitalization and he was transferred to an acute rehabilitation unit (ARU) where he regained some strength in his previously flaccid left hemi-body. Modified Rankin Scale on discharge to ARU was 4.

## Discussion

AIS with COVID-19 infection has been recently reported in 1 to 30 days following onset of respiratory symptoms. Rate of stroke in COVID-19 patients is 1–3% depending on the severity of the COVID-19 illness.<sup>1–3,9,10</sup> Our patient characteristics and imaging findings were notable for the following aspects:

### Young Age

The majority of COVID-19 patients with large vessel stroke reported thus far were older with underlying comorbidities and conventional cardiovascular risk factors. Here, the patient's young age with no PMH supports the idea that his stroke might have been associated with his recent COVID-19 infection. Of the reported large vessel strokes, few were in young adults without any underlying cardiovascular risk factors, comorbidities or history of thrombophilia. Oxley T et al.<sup>5</sup> described five COVID-19 patients, aged 33–49 years old, with large vessel stroke. The proposed mechanisms for stroke in this group of patients include involvement of endothelial and neutrophil extracellular traps as well as coagulopathy.<sup>6,9</sup> Our patient is among the few reported cases who fall under this category given his young age, lack of comorbidities or cardiovascular risk factors except for mildly elevated

**Table 1.** *Laboratory Findings*

	Patient's Lab Results	Normal Ranges
White blood cell count per mm <sup>3</sup>	9740	5,000–10,000/mm <sup>3</sup>
Neutrophils	87%	45–75% of total white blood cells
Lymphocytes	8.5 %	18–45% of total white blood cells
Platelet count per mm <sup>3</sup>	569000	150 000–450 000/mm <sup>3</sup>
Hemoglobin g/dL	14.1	13.8–17.2 g/dL
Albumin g/dL	3.7	3.4–5.4 g/dL
Alanine aminotransferase U/L	40	7–55 U/L
Aspartate aminotransferase U/L	19	6–34 IU/L.
Lactate dehydrogenase U/L	232	140 U/L–280 U/L
Cardiac Troponin T ng/mL	<0.010	0–0.4 ng/mL
Prothrombin Time-sec	14.1	11.0–12.5 s
Activated partial thromboplastin time -sec	31.4	25–35 seconds
D-Dimer ng/ml	649	< 250 ng/mL
Ferritin ng/ml	420	20–250 ng/mL
C-reactive protein mg/L	11.7	< 10 mg/L
Homocysteine μmol/L	6.9	<15 μmol/L
Hemoglobin A1C	6.2 %	<5.7%
Low-Density Lipoprotein mg/dL	152	<129 mg/dL
drug screen test (blood)	Negative	
Activate protein C	Normal	
Factor V Leiden	Negative	
Factor 2 level	Normal	
Lupus Anticoagulant	Negative	
Blood Gas Findings on arrival		
PH	7.33	7.35–7.45
Pco2	40	35–45 mmHg,
Po2	110	80–100 mmHg,

Hemoglobin A1c and elevated LDL cholesterol, and his negative inherited thrombophilia screen.

#### *Mild COVID-19 infection*

There is strong evidence to support development of coagulation abnormalities and rise in procoagulant factors in patients with COVID-19 infection. However, these findings are reported far more in patients with severe pulmonary disease.<sup>6</sup> Our patient had completely recovered from COVID-19 symptoms at the time presentation and never manifested pulmonary symptoms or pathology on his chest CT, which might suggest the presence of coagulopathy and endothelial dysfunction even in the absence of severe disease. This may be attributable to viral involvement of the endothelium.<sup>7</sup>

#### *ECA involvement*

The common carotid artery angiogram of our patient showed an extensive amount of sub-occlusive thrombus in the carotid bulb with extension into the proximal internal carotid artery and ECA (Fig. 1) in addition to an MCA occlusion. Such extensive thrombus in the ECA occur uncommonly in AIS patients and were not reported in the prior COVID-19 patients with large vessel stroke.

#### *Negative COVID-19 status*

To date, all the reported large vessel strokes in young adults attributed to COVID-19 infection have been in patients with at least mild symptoms of COVID-19 infection with positive PCR at the time of stroke.<sup>8</sup> Our patient is different since he clinically recovered from his mild COVID-19 symptoms days prior to the stroke and had 2 negative PCR tests on the day stroke occurred. This finding is unique and may suggest a continued procoagulant state with endothelial involvement even after resolution of COVID-19 symptoms.

#### *Outcome*

Despite swift and successful recanalization in this patient with significant mismatch on perfusion imaging, he had a devastating prognosis and functional outcome. This is in line with the outcome of other young COVID-19 patients with large vessel stroke reported thus far displaying poor prognosis.<sup>5,9,10</sup> Delay in seeking care and subsequently delayed treatment due to fear and concerns about going to a hospital during the pandemic have been reported repeatedly and may have contributed to the poor outcome of these patients; however, re-occlusion of the recanalized vessels might have developed by the procoagulant state, an association that has already been

described with the virus.<sup>10</sup> In addition, significant neurological deficits with NIHSS score of 12 at presentation and presence of some established ischemic changes on initial head CT with ASPECT score of 8 are the other potential contributors to poor outcome in our patient.

In conclusion, we report a young adult with no underlying comorbidities who recently recovered from COVID-19 infection and presented with AIS due to multicentric large vessel occlusion. He had salvageable penumbra and underwent successful mechanical thrombectomy but infarcted nonetheless and unfortunately remained with poor functional outcome. Our patient had very mild COVID-19 related symptoms which had resolved at the time of stroke presentation, approximately ten days after his initial COVID-19 screening test. In addition, he had two negative PCR test on the day of admission for stroke. Although our understanding of COVID-19 pathophysiology in the CNS vasculature and its role in morbidity and mortality is still in its infancy, acquired thrombophilia and endothelial dysfunction have been proposed as the potential mechanisms of AIS in these patients. Our findings also suggest the possibility of a prolonged and continued procoagulant state even after resolution of symptoms from the infection, a characteristic which also potentiates the risk for re-occlusion of the recanalized vessels. The poor outcome of our patient may also be partially attributable to the delay in seeking appropriate care in light of the current climate of fear for the hospital. Lastly, our case had both intracranial and extracranial large vessel occlusion with an unusual pattern of macrothrombosis of the proximal ECA, not previously reported.

### Declaration of Competing Interest

APA reports the following: Consultant to Medtronic Neurovascular and Valencia Technologies WJM reports the following: consultant: Rebound Therapeutics, Viseon Imperative Care, Q'Apel, Medtronic, Stryker, Stream Biomedical, Spartan Micro; Investor: Cerebrotech, Endostream, Viseon, Rebound, Q'Apel, and Spartan Micro Other coauthors report no conflict of interest.

### Authors Roles

**Ashkan Mowla:** Responsible for study design, Literature review, Drafting of the initial manuscript, Critical revising for intellectual content; **Saman Sizardkhani:** Responsible for patient selection, Collection of clinical data and critical revising for intellectual content; **Maryam Sharifian Dorche:** Responsible for literature review, Drafting of the initial manuscript, Critical revising for intellectual content; **Prad Selvan:** Responsible for patient selection critical revising for intellectual content; **Benjamin A. Emanuel:** Responsible for critical

revising for intellectual content; **Matthew S. Tenser:** Responsible for critical revising for intellectual content; **Arun P. Amar:** Responsible for critical revising for intellectual content; **William J. Mack:** Responsible for critical revising for intellectual content

### Statement of Ethics

Subject has provided his informed consent for the creation of this manuscript with full knowledge that his clinical findings and treatment are utilized herein for educational and peer-reviewed publication purposes.

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