



# Successful Treatment of a COVID 19-Associated Multisystem Thrombotic Event in a Young Patient in a Neurocritical Care Unit

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## Abstract

This case report describes a young patient with no comorbidities, who presented with two systemic thrombotic events within 24 hours of admission. She presented with a right middle cerebral artery territory infarct and developed an inferior wall myocardial infarction soon after. The hypotension was refractory to inotropes and required emergency intra-aortic balloon pump insertion. She was evaluated for prothrombotic states and other causes of stroke in young. However, the workup for the same was negative. Coronavirus disease-2019 immunoglobulin G antibody titer and inflammatory markers were found to be extremely elevated, which suggested recent severe infection. This case report throws light on the multidisciplinary management of thrombotic events, most probably secondary to coronavirus infection.

## Keywords

- ▶ COVID-19
- ▶ ischemic stroke
- ▶ myocardial infarction

## Introduction

Although the coronavirus disease 2019 (COVID-19) has been essentially known to affect the lungs, this disease has caused multiple thromboembolic complications.<sup>1-3</sup> COVID-19 has been frequently described as a prothrombotic state with raised D-dimer levels.<sup>4</sup> The increased incidence of these catastrophic events suggested that there is a pressing need to upgrade diagnostic strategies and thromboprophylaxis in ambulatory COVID-19 patients.<sup>1</sup> We report a riveting case report of the successful treatment and rehabilitation of a young female with two consecutive thrombotic events within 24 hours of admission, likely following an asymptomatic COVID-19 infection.

## Case Report

A 35-year-old female with no significant past medical history presented to the emergency room 4 hours after the onset of

stroke with complaints of sudden onset left-sided weakness and left upper limb focal seizures, preceded by headache and vomiting.

She was hemodynamically stable with a Glasgow coma scale of E4V5M6. She had left hemiparesis, upper motor neuron facial palsy, and extensor plantar reflex. Computed tomography (CT) brain (plain) revealed an acute right middle cerebral artery (MCA) territory infarct (▶**Fig. 1**), but carotid and lower limb venous doppler were normal. Digital subtraction angiography revealed high-grade stenosis in the right internal carotid artery (ICA), distal to the bifurcation of common carotid artery (▶**Fig. 2**). Since there was good flow in the ICA and decreased flow only in the M3 segment of right MCA, she was managed conservatively (tab. aspirin 150 mg, tab. clopidogrel 75 mg, tab. atorvastatin 40 mg). Antiepileptic therapy was initiated with levetiracetam.

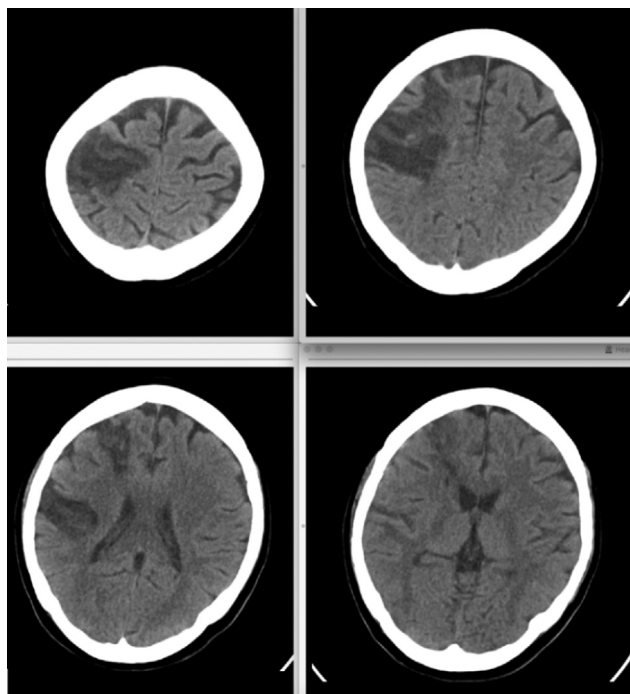
The initial investigations, electrocardiography (ECG), and two-dimensional echocardiography (2D ECHO; ejection

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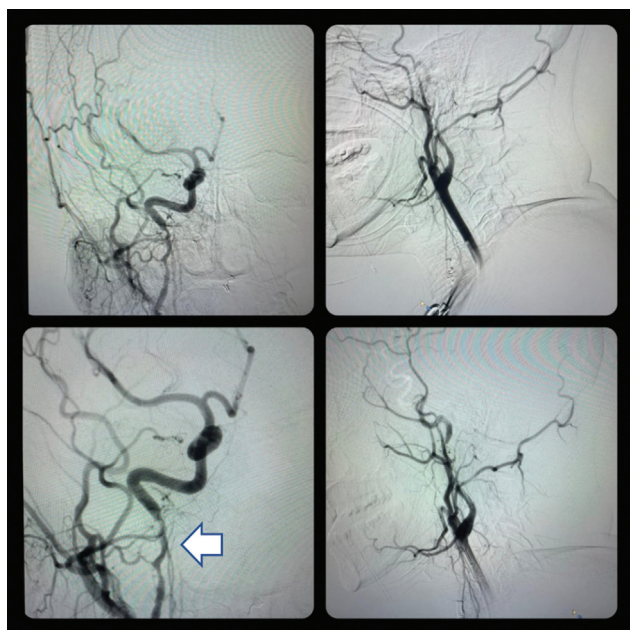
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**Fig. 1** Computed tomography brain (plain) showing acute right middle cerebral artery infarct.

fraction [EF] 58%) were normal. The stroke in young workup, including autoimmune stroke workup, was negative.

She developed persistent hypotension, desaturation, focal seizures and a drop in Glasgow coma scale the following morning. ECG and 2D ECHO (EF 45%) were suggestive of an inferior wall myocardial infarction (MI). Noradrenaline, adrenaline, and dopamine were initiated in succession to maintain mean arterial pressure (MAP) 60 to 80 mm Hg and



**Fig. 2** Digital subtraction angiography study demonstrating upper right cervical internal carotid artery narrowing with irregularity of its wall. Poor flow in the M3 segment of right middle cerebral artery territory with contrast stasis.

tracheal intubation was done. Due to refractory hypotension, bedside intra-aortic balloon pump (IABP) insertion was done immediately as per the cardiologist's advice. The treatment was initiated with heparin infusion, which was titrated based on activated clotting time (institutional protocol) levels done 4th hourly with a target of more than 200 second. The patient had systemic thrombosis and was started on dual antiplatelets and statins only 24 hours before the MI occurred.

The primary aim was to stabilize her as she had severe hypotension (systolic blood pressure of 30 mm Hg). In view of continuous left focal seizures, electroencephalogram was done that showed continuous discharges. Hence, antiepileptics were escalated (inj. levetiracetam, inj. sodium valproate, and tab. clobazam). We were unable to take her for per cutaneous transluminal coronary angioplasty due to her hemodynamic instability and ventilator dependency. Serial 2D ECHOs (EF averaging 40%) and refractory hypotension were in favor of cardiogenic shock. Coronary angiogram done on day 7 was normal.

Though the COVID-19 reverse-transcription polymerase chain reaction done on day 3 was negative, her COVID-19 immunoglobulin G (IgG) titer was unusually high at 10417.6 AU/ mL with elevated inflammatory markers and D-dimer, indicating severe recent infection. However, her coagulation profile was normal.

The trachea was extubated on day 9. IABP support was gradually titrated and it was weaned off on day 13. As the stroke was subcortical with no mass effect, heparin was used to treat both MI and stroke. Repeat CT brain (plain) on day 14 showed no further changes. She required minimal noradrenaline until day 30 to maintain MAP 60 to 80 mm Hg. The patient was hospitalized for 49 days. She had significant neurological improvement, which was noted during her monthly follow-up and she is able to walk with support.

## Discussion

Although the severe acute respiratory syndrome coronavirus 2 virus affects the lungs primarily, there have been numerous reports of thromboembolic complications.<sup>1-3</sup> As a practice, critical COVID-19 patients receive thromboprophylaxis. However, there is a significant incidence of thrombotic complications, frequently pulmonary embolism. Prolonged prothrombin time and activated partial thromboplastin time have been identified as prognostic markers.<sup>3</sup>

Acute coronary events, associated with elevated cardiac troponin, are seen in around 1.1% and acute ischemic strokes in 2.5% of the population infected with COVID-19,<sup>1,5</sup> leading to increased rates of mechanical ventilation and mortality.<sup>6,7</sup>

Various mechanisms have been postulated. It could occur due to direct viral insult or indirect offense by vessel wall inflammation as explained by the Virchow's triad. The principal disease process is the interaction between the virus binding to the angiotensin-converting enzyme-2 (ACE-2) receptor and its effect on the renin-angiotensin-aldosterone system, host immune response, underlying comorbidities, and the cytokine release. There is downregulation of ACE-2

receptor activity and therefore there is piling up of angiotensin II causing vasoconstriction, proinflammatory and profibrotic states. M1 macrophages are triggered leading to release of interleukin (IL)-1 $\beta$  and IL-6 and hence endotheliitis. Due to type-1 respiratory failure, there is an imbalance between the myocardial oxygen supply and demand. COVID-19 is often described as a systemic inflammatory response syndrome with high levels of circulating cytokines.<sup>8</sup>

Following two doses of ChAdOx1 vaccination, the mean level of IgG antibodies was  $80.0 \pm 70.1$  BAU/mL in people who were not previously infected compared with  $155 \pm 61.2$  BAU/mL in people without previous COVID-19 infection.<sup>9</sup> Even though our patient was asymptomatic, she had unusually high IgG COVID-19 antibodies that were highly suggestive of a recent asymptomatic COVID-19 infection. Elevated inflammatory markers further supported the diagnosis. She received her second dose of ChAdOx 1 vaccination, 2 months before presentation to the hospital with no history of previous COVID-19 infection.

With other causes of stroke in young ruled out, the cause of stroke in our patient is likely COVID-19 infection. Although the pathogenesis remains unclear, COVID-19 can present as a prothrombotic state. This case report showcases systemic thrombotic events in a young patient probably secondary to antecedent COVID-19 infection, with high antibody titers.

#### Conflict of Interest

None declared.

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