Case Report

Left Subclavian Arterial Thrombosis Presenting as Acute Limb Ischemia in a COVID-19 Patient – An Extreme Rarity

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a viral respiratory disease; therefore, it has been primarily treated as a severe respiratory infection worldwide. However, the peak of the pandemic has exposed several cases marked by manifestations of venous and arterial thrombosis. A substantial number of patients have displayed coagulation abnormalities mimicking other systemic coagulopathies associated with severe infections, often disguised as venous and arterial thromboembolic complications.[1]

CASE PRESENTATION

A 52-year-old male presented to our COVID-19 treatment facility with a dry cough and sore throat on admission. National Early Warning Score was 0 on admission. The patient did not have a history of diabetes, smoking, tobacco chewing, or atherosclerosis cardiovascular disease. He was COVID-19 positive as detected by reverse transcription polymerase chain reaction. He was prescribed azithromycin 500 mg once daily. Laboratory investigations revealed negative D-dimer levels of <200 ng/ml, negative antinuclear antibody (ANA) levels, fibrinogen levels of 210 mg/dL, serum ferritin levels of 189 ng/ml, prothrombin time of 12.8 s, hemoglobin level of 12.7 g/dL, and normal platelet count. On the 7th day of admission, he developed sudden onset of left upper limb claudication, absent pulsation of the axillary, brachial, and radial arteries of the left arm, and pale middle and index fingers. However, no cyanosis was observed. Electrocardiography showed sinus rhythm, normal PR interval, and QRSd with QTc of 0.40 s with no evidence of chamber hypertrophy or dilation. Two-dimensional echocardiography was unremarkable. Laboratory investigations indicated normal D-dimer, ANA, fibrinogen, serum ferritin and hemoglobin levels, prothrombin time, and platelet count. Chest and neck X-ray and subsequent chest computed tomography (CT) ruled out thoracic outlet syndrome. Transthoracic echocardiography confirmed the absence of patent foramen ovale, thereby ruling out the possibility of paradoxical embolism. However, chest X-ray confirmed right lower lobe pneumonia [Figure 1]. Urgent CT angiography of the aortic arch and left arm revealed a large thrombus of 8 cm extending from the origin of the left subclavian artery to the axillary artery [Figure 2a and b]. In view of the onset of acute limb ischemia within 6 h, it

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was elected to thrombolyze the patient with 500,000 U of intravenous bolus of streptokinase tapered to 100,000 U/h as continuous infusion for 24 h after ruling out contraindications for the same. The patient also received aspirin 300 mg, clopidogrel 300 mg, and atorvastatin 80 mg orally.

In view of clinical improvement in the form of significant pain relief and return of brisk pulses at the left wrist for >24 h, CT angiography of the left subclavian artery was repeated after 24 h which demonstrated almost complete (80%) resolution of the thrombus [Figure 3] with thrombolysis in myocardial infarction (TIMI) III distal flow in the radial artery and TIMI II flow in the distal ulna artery. Administration of low-molecular heparin 0.6 mg twice daily for 7 days 6 h after extended thrombolysis was initiated, and dual antiplatelet and statin therapy were continued as prescribed earlier. The patient did not experience any bleeding complications during the course of his treatment. Red color of the hand was observed postthrombolysis. After the 7th day, pneumonia resolved [Figure 4]. Furthermore, CT angiography confirmed complete recanalization of subclavian, axillary, radial, and ulna arteries without residual plaque or thrombus [Figure 5a and b]. After the 14th day, the nasal swab for COVID-19 was repeated which was negative. The patient was discharged as per the Indian Council of Medical Research Protocol for COVID-19 management.

### Discussion

COVID-19 may predispose patients to thrombotic disease, both in the venous and arterial circulations due to a spectrum of misleading complications, such as excessive inflammation, platelet activation, coagulopathy, endothelial dysfunction, and stasis. Several justifications have been set forth to explain the association between COVID-19 and thrombotic disease. First, direct effects of COVID-19 or indirect effects of the infection such as critical condition and hypoxia may predispose patients to thrombotic events. Second, investigational therapies for treating COVID-19 may display adverse drug–drug interactions with antiplatelet agents and anticoagulants. Third, viruses are able to activate the coagulation system as seen in human immunodeficiency virus, dengue virus, and Ebola virus. Finally,

### Timeline

| Time                  | Event                                                                                                           |
|-----------------------|-----------------------------------------------------------------------------------------------------------------|
| Admission             | COVID-19–positive patient presented with dry cough and sore throat                                             |
| Day 7 postadmission   | Patient developed sudden onset of left upper limb claudication, absent pulsation of the axillary, brachial, and radial arteries of left arm, and pale middle and index fingers |
|                       | Chest X-ray confirmed right lower lobe pneumonia                                                                |
|                       | Urgent CT angiography of the aortic arch and left arm revealed large thrombus of 8 (cm) extending from origin of the left subclavian artery to the axillary artery |
|                       | In view of onset of acute limb ischemia within 6 h, thrombolysis of the patient was planned                      |
| Day 8 postadmission   | CT angiography of the left subclavian artery revealed almost complete resolution of thrombus with TIMI III distal flow in the radial artery and TIMI II flow in the distal ulna artery |
|                       | Administration of low-molecular heparin 0.6 (mg) twice daily for 7 days 6 h after extended thrombolysis was initiated, and dual antiplatelet and statin therapy were continued |
|                       | Pneumonia resolved                                                                                                |
| Day 14 postadmission  | Nasal swab for COVID-19 was repeated which was negative                                                         |
|                       | The patient discharged as per the ICMR protocol for COVID-19 management                                           |

COVID: Coronavirus disease, CT: Computed tomography, TIMI: Thrombolysis in myocardial infarction, ICMR: Indian Council of Medical Research
inaccessibility or unavailability of resources along with social distancing norms may unfavorably affect care of COVID-19–negative patients presenting with thrombotic events. The most fitting example explanation for the association between COVID-19 and thrombotic disease is the widespread notion that antithrombotic agents confer increased risk for contracting COVID-19. This may unfortunately cause several such patients to abandon their anticoagulant or antiplatelet regimen.

The most distinctive hematological finding in COVID-19 patients with coagulopathy is increased D-dimer levels, modest decrease in platelet count, and prolonged thrombin time.[1] Normal levels of all the aforementioned hematological parameters highlight rarity of the present case. Nonetheless, regardless of hypercoagulable state, D-dimer level, or fibrinogen level, thrombotic events in COVID-19 patients pose a significant risk, especially to patients in critical condition.

Venous thrombosis in the lower limbs has been described by several investigators during the pandemic. Yet, there is a dearth of evidence describing arterial thrombosis in the upper limbs. Perini et al.[5] in a recent publication in the *Lancet* recall treating four COVID-19 patients presenting with acute limb ischemia. Interestingly and similar to the present case, none of the patients had atherosclerosis or pre-existing blood clotting disorders. One of these patients was a 37-year-old male with thrombosis at the level of the humeral artery bifurcation. After 2 days of unfractionated heparin administration, the acute limb ischemia resolved. However, to the best of our knowledge, the present case is the first ever case of subclavian artery thrombosis observed in a COVID-19–positive patient with normal D-dimers during
this global pandemic. The patient was successfully managed conservatively with systemic thrombolysis. The association between large-vessel thrombus in COVID-19 patients requires further investigations.

**Conclusion**

COVID-19 is more than a severe respiratory infection. It displays propensity to affect the vasculature of the lungs and multiple other organs. The subsequent acute life-threatening events and increased thrombotic risk necessitate adequate treatment with anticoagulants based on laboratory investigations along with monitoring with appropriate imaging modalities.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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