

# Acute upper limb ischemia as the first manifestation in a patient with COVID-19

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## ABSTRACT

Coronavirus disease-19 (COVID-19) first emerged in December 2019 in China and rapidly spread worldwide. Although various studies have reported that COVID-19 is associated with a hypercoagulable state and thrombotic complications in critically ill patients, there are few case reports on thrombotic events as one of the presenting symptoms. We report a case of acute upper extremity ischemia as the initial clinical presentation of a patient with COVID-19. (*J Vasc Surg Cases and Innovative Techniques* 2020;6:674-7.)

**Keywords:** Coronavirus; COVID-19; Acute limb ischemia; Anticoagulation; Hypercoagulable state

The novel coronavirus first emerged in December 2019 in China and is now classified as a pandemic. According to a report from the Chinese Center for Disease Control and Prevention, up to 19% of the confirmed cases in China were classified as severe or critical.<sup>1</sup> Despite coronavirus disease-19 (COVID-19) being initially a respiratory infection, multiple case reports globally have demonstrated various complications, including cardiovascular complications, liver failure, and renal insufficiency.<sup>2-7</sup> Studies have revealed markedly elevated D-dimer and fibrinogen degradation product in this group of patients, which suggests that this infection can lead to procoagulant states and thrombotic events.<sup>8,9</sup> In appraising the current body of literature, a number of studies have described the link between critically ill patients with COVID-19 and hypercoagulable states. However, there are few reports that highlight acute thrombotic events at initial presentation. We believe that clinicians should be aware of the possibility of acute thrombotic events being one of the initial symptoms of this infection. In this report, we describe an unusual case of a patient who presented with acute unilateral upper extremity ischemia and was diagnosed with COVID-19.

Consent was obtained from the patient for publication.

## CASE REPORT

The patient is a 67-year-old man with no significant medical history who presented to the emergency room with a chief complaint of worsening right hand and forearm pain. He also reported mild shortness of breath and cough for 3 days. His distal forearm and hand were cold and mottled with motor and sensory loss on physical examination (Fig 1). His axillary pulse was palpable; however, his brachial, radial, and ulnar pulses were absent. His laboratory tests were only remarkable for leukocytosis and elevated D-dimer. A computed tomography angiogram of the chest and right arm showed extensive patchy ground-glass opacities throughout bilateral lungs and an occlusion of the brachial artery at the level of the midhumerus with no reconstitution of any vessels distally (Fig 2). A rapid polymerase chain reaction test for COVID-19 confirmed active infection. Anticoagulation was initiated and he was taken to the operating room for emergent revascularization.

Upon exploration, the brachial, radial, and ulnar arteries were completely thrombosed. Embolectomies were performed via incisions at the antecubital fossa and the wrist. The arteries were noted to be healthy with no appreciable atherosclerotic disease. A significant amount of dark, acute-appearing thrombus was retrieved. Palpable pulses were achieved; however, the digits still seemed to be ischemic. Therefore, thrombolysis was performed by injecting alteplase directly into the radial and ulnar arteries. Palpable brachial, radial, and ulnar pulses as well as Doppler signal of the palmar arch were present at completion. Forearm and hand fasciotomies were performed and the muscles were all viable. The patient remained intubated and recovered in the intensive care unit (ICU).

Postoperatively, the patient maintained palpable radial and ulnar pulses on full anticoagulation; however, three digits remained nonviable. The remaining digits were viable along with the palm and forearm (Fig 3). A workup for hypercoagulability and source of embolism was performed (Table). The only positive test was the lupus anticoagulant panel. However, the patient was on a direct thrombin inhibitor when the test was sent, which can affect the reliability of these results. During the

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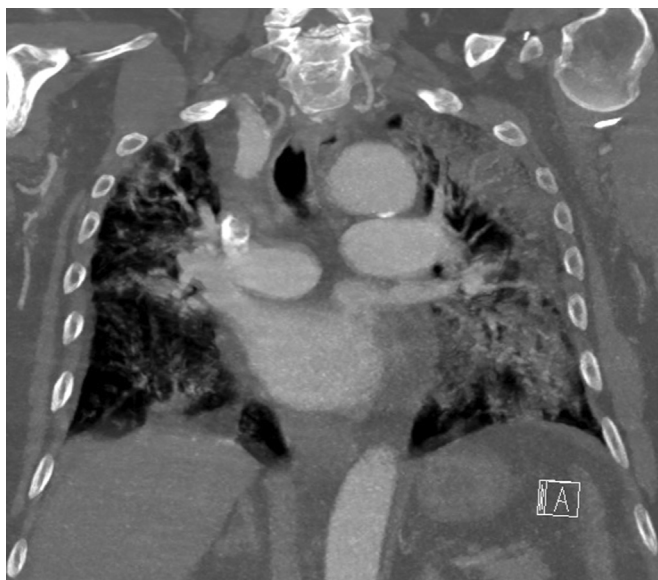
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**Fig 1.** Clinical presentation of the upper extremity acute limb ischemia. Palmar view with discoloration of the hand and digits.



**Fig 2.** Diagnostic images. Computed tomography scan of the chest demonstrating extensive peripheral patchy ground-glass opacities throughout bilateral lungs.

course of hospitalization, he was diagnosed with subsegmental pulmonary embolism. This event may have occurred during a 3-day period when anticoagulation was held owing to concerns of gastrointestinal bleeding.

Two months after surgery, the patient had well-demarcated dry gangrene of his first, fourth, and fifth digits with preserved motor and sensory function of his hand. At the time of publication, the patient remained on full anticoagulation with the plan to discontinue it after 3 months to allow further workup for hypercoagulability.

## DISCUSSION

The current body of literature has been focused on the severe to critical cases of COVID-19 and their association with hypercoagulability and risk of thrombotic events. Tan et al found that the critically ill cases had substantially elevated clot waveform analysis parameters, which indicates hypercoagulability.<sup>10</sup> Klok et al<sup>11</sup> presented a



**Fig 3.** Postoperative examination. Palmar view of the hand showing three nonviable digits.

31% incidence of thrombotic complications in (ICU) patients with COVID-19, demonstrating that the infection may predispose patients to both venous and arterial thrombosis. Zhang et al<sup>12</sup> reported seven cases of patients in the ICU with COVID-19 who subsequently developed marked cyanosis and gangrene of the digits. Our case is unique because the patient presented with acute limb ischemia as an initial symptom of COVID-19, unlike those who were already admitted to the ICU and subsequently developed thrombotic events.

There was no discernible cause of in-situ thrombosis in this case other than COVID-19 infection. Our patient demonstrates that thrombotic events can be one of the early presenting symptoms. Li et al<sup>13</sup> postulated that around 7 to 14 days after the onset of symptoms, the virus starts a second attack, which leads to developing a hypercoagulable state. However, our case speculates that, regardless of the severity or duration of symptoms, COVID-19 can lead to a hypercoagulable state.

The pathophysiology of thrombotic events in the context of COVID-19 is not completely understood. Recent studies have focused on outlining the mechanism of microthrombotic lesions. Currently, there are no studies on the pathogenesis of thrombosis in

**Table.** Hypercoagulable and embolic workup: Various tests performed to identify the cause of this patient's acute limb ischemia

Test	Result
Lupus anticoagulant panel	Positive
Homocysteine level	Normal
Anticardiolipin antibodies	Negative
Factor V Leiden mutation	Negative
Serotonin assay	Negative
Antithrombin 3 activity	Normal
Protein C activity	Normal
Protein S activity	Normal
Echocardiogram	Negative for patent foramen ovale
Electrocardiogram	Negative for arrhythmia

medium-sized vessels, as seen in our patient. A potential contributing factor found in our patient is the presence of antiphospholipid antibodies vs a cytokine storm. Our patient had elevated levels of anticardiolipin IgM antibodies and a positive lupus anticoagulant panel, along with elevated levels of fibrinogen and D-dimer. Previous studies have reported the possibility of developing antiphospholipid antibodies after viral infections. A recent case report by Zhang et al<sup>14</sup> also observed the presence of anticardiolipin antibodies along with elevated levels of fibrinogen and D-dimer in three ICU patients with limb ischemia.

Owing to the acuity and severity of ischemia, our patient required emergent surgery. The postoperative anticoagulant treatment the patient received was a therapeutic intravenous unfractionated heparin infusion, which was then switched to argatroban owing to concerns of developing heparin-induced thrombocytopenia.

There is currently no consensus on anticoagulating patients with COVID-19 prophylactically to prevent arterial thrombotic events. The current pharmacological anticoagulant therapy recommendations for COVID-19 cases are focused on venous thromboembolism prophylaxis, but it is recommended that these guidelines should be considered and applied to arterial thrombotic prophylaxis.<sup>15</sup> The World Health Organization recommends only prophylactic doses of low-molecular-weight heparin daily or subcutaneous unfractionated heparin twice daily for venous thromboembolism prophylaxis in critically ill patients with COVID-19.<sup>15,16</sup> Tang et al<sup>17</sup> showed that anticoagulant treatment with low-molecular-weight heparin is associated with a better prognosis in cases of severe COVID-19 with an elevated D-dimer and a sepsis-induced coagulopathy score of 4 or greater.<sup>17</sup> Given the potential benefit of antithrombotic therapy, some hospital systems have implemented protocols that treat

critically ill patients with COVID-19 with empiric full anticoagulation.

Data regarding the role of pharmacologic prophylaxis for asymptomatic or mild COVID-19 cases in quarantine are limited. One may consider prescribing a prophylactic dosage of anticoagulation for patients with COVID-19 who are not hospitalized, in effort to prevent thrombotic events.

## CONCLUSIONS

Acute thrombotic events are a serious and potentially life-threatening complication associated with patients with COVID-19. Providers must be vigilant in identifying these events and initiate appropriate treatment. Further studies on the use of empiric anticoagulation on select patients with COVID-19 are warranted.

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