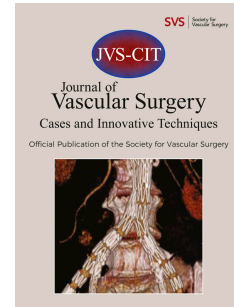


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Acute Upper Limb Ischemia as the First Manifestation in a Patient with COVID-19

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1 **Acute Upper Limb Ischemia as the First Manifestation in a Patient with COVID-19**

2

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18 **Classifications:** 1.2 acute ischemia thrombosis/embolism, 32 hypercoagulable states, 85.4
19 vascular medicine hypercoagulability therapy.

20 **Keywords:** coronavirus, COVID-19, acute limb ischemia, anticoagulation, hypercoagulable state

21 **Conflict of Interest:**

22 ¹⁻⁶.No conflict of interest.

1 **Abstract:**

2 Coronavirus disease 19 (COVID-19) first emerged in December 2019 in China and rapidly
3 spread worldwide. While various studies have reported that COVID-19 is associated with a
4 hypercoagulable state and thrombotic complications in critically ill patients, there are scant case
5 reports on thrombotic events as one of the presenting symptoms. We report a case of acute upper
6 extremity ischemia as the initial clinical presentation of a COVID-19 patient.

1 **Introduction:**

2 The novel coronavirus first emerged in December 2019 in China and is now classified as a
3 pandemic. According to a report from the Chinese Center for Disease Control and Prevention, up
4 to 19% of the confirmed cases in China were classified as severe or critical.¹ In spite of COVID-
5 19 being initially a respiratory infection, multiple case reports globally have demonstrated
6 various complications, including cardiovascular complications, liver failure, and renal
7 insufficiency.²⁻⁷ Studies have revealed markedly elevated D-dimer and fibrinogen degradation
8 product (FDP) in this group of patients, which suggest this infection can lead to procoagulant
9 states and thrombotic events.⁸⁻⁹ In appraising the current body of literature, a number of studies
10 have described the link between critically ill COVID-19 patients and hypercoagulable states.
11 However, there are scant reports that highlight acute thrombotic events at initial presentation. We
12 believe that clinicians should be aware of the possibility of acute thrombotic events being one of
13 the initial symptoms of this infection. In this report, we describe an unusual case of a patient who
14 presented with acute unilateral upper extremity ischemia who was diagnosed with COVID-19.

15
16 Consent was obtained from the patient for publication.

18 **Case Report:**

19 The patient is a 67-year-old male with no significant medical history that presented to the
20 emergency room with a chief complaint of worsening right hand and forearm pain. He also
21 reported mild shortness of breath and cough for three days. His distal forearm and hand were
22 cold and mottled with motor and sensory loss on physical examination (*Figure 1*). His axillary
23 pulse was palpable however his brachial, radial and ulnar pulses were absent. His laboratory tests

1 were only remarkable for leukocytosis and elevated D-dimer. A computed tomography
2 angiogram (CTA) of the chest and right arm showed extensive patchy ground-glass opacities
3 throughout bilateral lungs and an occlusion of the brachial artery at the level of the mid-humerus
4 with no reconstitution of any vessels distally (*Figure 2*). A rapid PCR test for COVID-19
5 confirmed active infection. Anticoagulation was initiated and he was taken to the operation room
6 for emergent revascularization. Upon exploration, the brachial, radial and ulnar arteries were
7 completely thrombosed. Embolectomies were performed via incisions at the antecubital fossa
8 and the wrist. The arteries were noted to be healthy with no appreciable atherosclerotic disease.
9 A significant amount of dark, acute appearing thrombus was retrieved. Palpable pulses were
10 achieved; however the digits still appeared ischemic. Therefore, thrombolysis was performed by
11 injecting alteplase directly into the radial and ulnar arteries. Palpable brachial, radial and ulnar
12 pulses as well as doppler signal of the palmar arch were present at completion. Forearm and hand
13 fasciotomies were performed and the muscles were all viable. The patient remained intubated
14 and recovered in the intensive care unit (ICU). Postoperatively, the patient maintained palpable
15 radial and ulnar pulses on full anticoagulation; however three digits remained non-viable. The
16 remaining digits were viable along with the palm and forearm (*Figure 3*). A work-up for
17 hypercoagulability and source of embolism was performed (*Table 1*). The only positive test was
18 the lupus anticoagulant panel. However, the patient was on a direct thrombin inhibitor when the
19 test was sent, which can affect the reliability of the results. During the course of hospitalization,
20 he was diagnosed with subsegmental pulmonary embolism. This may have occurred during a
21 three day period when anticoagulation was held due to concerns of gastrointestinal bleeding.
22 Two months after surgery, the patient had well demarcated dry gangrene of his 1st, 4th and 5th
23 digits with preserved motor and sensory function of his hand. At the time of publication, the

1 patient remained on full anticoagulation with the plan to discontinue it after 3 months to allow
2 further work-up for hypercoagulability.

3

4 **Discussion**

5 The current body of literature has been focused on the severe to critical cases of COVID-19 and
6 their association with hypercoagulability and risk of thrombotic events. Chuen et al. found that
7 the critically ill cases had substantially elevated clot waveform analysis (CWA) parameters,
8 which indicates hypercoagulability.¹⁰ Klok et al. presented a 31% incidence of thrombotic
9 complications in (ICU) patients with COVID-19 demonstrating that the infection may predispose
10 patients to both venous and arterial thrombosis.¹¹ Zhang et al. reported seven ICU cases of
11 COVID-19 patients who subsequently developed marked cyanosis and gangrene of the digits.¹²
12 Our case is unique as the patient presented with acute limb ischemia as an initial symptom of
13 COVID-19, unlike those who were already admitted to the ICU and subsequently developed
14 thrombotic events. There was no discernible cause of in-situ thrombosis in this case other than
15 COVID-19 infection. Our patient demonstrates that thrombotic events can be one of the early
16 presenting symptoms. Li et al. postulated that around 7-14 days after onset of symptoms, the
17 virus starts a second attack which leads to developing a hypercoagulable state.¹³ However, our
18 case speculates that regardless of the severity or duration of symptoms, COVID-19 can lead to a
19 hypercoagulable state.

20

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

1 seen in our patient. One potential contributing factor found in our patient is the presence of
2 antiphospholipid antibodies versus a cytokine storm. Our patient had elevated levels of
3 anticardiolipin IgM antibodies and a positive lupus anticoagulant panel, along with elevated
4 levels of fibrinogen and D-dimer. Previous studies have reported the possibility of developing
5 antiphospholipid antibodies following viral infections. A recent case report by Zhang et al. also
6 observed the presence of anticardiolipin antibodies along with elevated levels of fibrinogen and
7 D-dimer in three ICU patients with limb ischemia.¹⁴

8
9 Due to the acuity and severity of ischemia, our patient required emergent surgery. The post-
10 operative anticoagulant treatment the patient received was therapeutic intravenous unfractionated
11 heparin (UFH) infusion which was then switched to argatroban due to concerns of developing
12 heparin induced thrombocytopenia. There is currently no consensus on anticoagulating COVID-
13 19 patients prophylactically to prevent arterial thrombotic events. The current pharmacological
14 anticoagulant therapy recommendations for COVID-19 cases are focused on venous
15 thromboembolism (VTE) prophylaxis, but it is recommended that these guidelines should be
16 considered and applied to arterial thrombotic prophylaxis.¹⁵ The World Health Organization
17 (WHO) recommends only prophylactic doses of low molecular weight heparin (LMWH) daily or
18 subcutaneous UFH twice daily for VTE prophylaxis in critically ill COVID-19 patients.¹⁵⁻¹⁶
19 Tang et al. showed that anticoagulant treatment with LMWH is associated with better prognosis
20 in severe COVID-19 cases with elevated D-dimer and a sepsis-induced coagulopathy (SIC) score
21 ≥ 4 .¹⁷ Given the potential benefit of antithrombotic therapy, some hospital systems have
22 implemented protocols that treat critically ill COVID-19 patients with empiric full
23 anticoagulation.

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

5

6 **Conclusion**

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

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Legends

Figure 1. Clinical presentation of the upper extremity acute limb ischemia.

Palmar view with discoloration of the hand and digits.

Figure 2. Diagnostic Images.

Computed tomography of the chest demonstrating extensive peripheral patchy ground-glass opacities throughout bilateral lungs.

Figure 3. Postoperative examination.

Palmar view of the hand showing three non-viable digits.

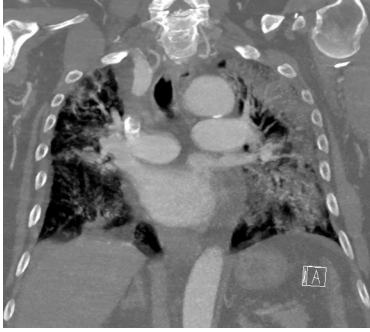
Table 1. Hypercoagulable and embolic work-up.

Various tests performed to identify the cause of this patient's acute limb ischemia.

Ble Test	Result
Lupus anticoagulant panel	Positive
Homocysteine level	Normal
Anticardiolipin antibodies	Negative
Factor 5 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



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