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Digital Ischemia in COVID-19 Patients: Case Report

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As coronavirus 2019 (COVID-19) continues to cause an immense burden on the global health care systems, it is crucial to understand the breadth of this disease process. Recent reports identified hypercoagulability in a subset of critically ill patients and extremity ischemia in an even smaller cohort. Because abnormal coagulation parameters and extremity ischemia have been shown to correlate with poor disease prognosis, understanding how to treat these patients is crucial. To better describe the identification and management of this phenomenon, we present 2 cases of critically ill patients with COVID-19 who developed fingertip ischemia while in the intensive care unit. (*J Hand Surg Am. 2020;45(6):518–522. Copyright © 2020 by the American Society for Surgery of the Hand. All rights reserved.*)

Key words COVID-19, critical care, digital ischemia, hand, hypercoagulability.

CORONAVIRUS 2019 (COVID-19), the disease caused by the 2019 novel coronavirus, has placed an unprecedented strain on global health care systems. Although the disease is known predominantly for its respiratory manifestations, a subset of critically ill patients demonstrates clinically notable hypercoagulability.^{1–3} This phenomenon has been noted by multiple intensive care unit (ICU) physicians and was further described at the Tongji Hospital in Wuhan, China.^{1,2} Thrombotic events range from acute pulmonary embolism in patients with COVID-19 pneumonia to extremity ischemia, and the precise incidence of thrombotic events has yet to be determined.^{3–6} As our understanding of this disease grows, it is crucial to investigate this trend further because hypercoagulability may worsen disease prognosis in critically ill COVID-19 patients.^{3,7}

Few studies to date have focused exclusively on patients with signs of hypercoagulability. An early analysis from

Wuhan, China described 7 cases of extremity ischemia in critically ill patients with COVID pneumonia.¹ All 7 of these patients, who did not meet criteria for shock and were not undergoing active therapy with vasopressors, demonstrated varying degrees of acral ischemia; the most common manifestations of such ischemia included plantar plaques and acrophytic bruises.¹ Notably, the authors identified a relationship between disease aggravation and the presence of ischemia.¹ Five of the 7 patients died of disease complications. Ultimately, the authors concluded that extremity ischemia portends a poor prognosis in critically ill COVID-19 patients.¹

A recent correspondence published in the *New England Journal of Medicine*² proposed anti-phospholipid antibodies as the source of the coagulopathies in COVID-19 patients. The authors described the cases of 3 ICU patients, all of whom developed extremity ischemia and cerebral infarcts in the setting of a positive serologic test for phospholipid antibodies.² We present the cases of 2 similar ICU patients with confirmed COVID-19, who developed fingertip ischemia during admission, which further suggests that extremity ischemia correlates with poor prognosis in this patient population.

CASE REPORT

We obtained institutional review board approval for deidentified presentation of patient data and images.

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Received for publication April 27, 2020; accepted in revised form April 27, 2020.

No benefits in any form have been received or will be received related directly or indirectly to the subject of this article.

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0363-5023/20/4506-0008\$36.00/0
<https://doi.org/10.1016/j.jhsa.2020.04.024>

Patient A

A 70-year-old woman with no known medical history presented to the emergency department (ED) with a 1-week history of fevers, chills, worsening shortness of breath, headache, and malaise. Several days earlier, she had tested negative for COVID-19 at an outside hospital but presented to our facility because of worsening symptoms. Upon arrival to the ED, her vital signs included a temperature of 36.7° C, pulse of 101 beats/min, respiratory rate of 26 breaths/min, and oxygen saturation of 88% on room air. While in the emergency department, she required oxygen at 6 L/min via a nasal cannula. The initial chest x-ray demonstrated perihilar opacification. She tested polymerase chain reaction positive for COVID-19 and was subsequently admitted to the ICU for management of acute hypoxemic respiratory failure owing to acute respiratory distress syndrome and COVID-19. The patient was intubated shortly thereafter owing to an increasing oxygen requirement. Of note, testing showed antibodies to hepatitis C, indicating likely chronic asymptomatic disease.

Approximately 12 days after presentation to the ED, the patient developed gradually worsening duskiness of the right second, third, and fourth fingertips while in the ICU. Notably, the patient had had 3 arterial line placements on the left side (1 radial and 2 brachial) but none on the right side. The hand service was consulted and the physical examination showed a mottled, dusky appearance to the distal phalanges and nail beds of the index, middle, and ring fingers. The fingers were also noted to be cool to palpation, and Doppler signals were absent at the superficial palmar arch as well as the radial and ulnar divisions of the digital arteries to the index, middle, and ring fingers. The remainder of the vascular examination of the right upper extremity was normal on the Doppler studies. Laboratory values recorded before this encounter included hemoglobin of 7.3 g/dL, C-reactive protein of 25 mg/L, prothrombin time/international normalized ratio of 18.2/1.5, and a partial prothrombin time of 80.9. D-dimer, a measure of fibrin degradation and thus coagulopathy, was 6.89 µg/mL (reference level, 0.4 µg/mL). The D-dimer had been elevated to greater than 20 µg/mL several days prior. The patient's fibrinogen (486 mg/dL) was also elevated 3 days before consultation.

Based on this presentation, the hand service recommended continuation of the patient's 25,000-unit heparin drip at 11 U/kg per hour (previously prescribed empirically because of an elevated D-dimer and then continued for a right femoral deep vein

thrombosis [DVT]) in addition to duplex studies and thermal warming of the affected limb. Application of topical nitroglycerin to the affected area was also recommended.⁸ Results of the arterial duplex ultrasound demonstrated patent brachial, radial, and ulnar arteries without evidence of hemodynamically consequential stenosis, although distal occlusion could not be ruled out.

Throughout the hospital course, the digital ischemia remained stable. Other notable events include septic shock, severe acute respiratory distress syndrome, acute kidney injury, and obstructive shock resulting from mechanical ventilation and intermittent vasopressor use. Other medical therapies included tocilizumab, lopinavir–ritonavir/ribavirin, cefepime, vancomycin, hydroxychloroquine, azithromycin, cefdinir, ceftriaxone, oral vancomycin, and metronidazole. Owing to the patient's worsening clinical status, the decision was made to pursue comfort care; the patient ultimately died.

Patient B

A 43-year-old man with a medical history of obesity, hypertension, and hyperlipidemia presented to the ED with shortness of breath, cough, and chest pain that had been progressively worsening over the past week. The patient also reported fatigue, diarrhea, and decreased urine output. Vital signs upon arrival were notable for a blood pressure of 86/60 mm Hg, a respiratory rate of 20 breaths/min, and an oxygen saturation of 91% on room air; respiratory status deteriorated while he was in the ED and he required oxygen 5 L/min via a nasal cannula. Chest x-ray showed a patchy right perihilar infiltrate concerning for infection. Within the next 24 hours, he tested positive for COVID-19 and demonstrated a worsening respiratory status requiring transfer to the ICU with intubation upon arrival.

While in the ICU, the patient experienced several complications, most notably a retroperitoneal hematoma occurring in the setting of anticoagulation for a right popliteal DVT requiring transfusion and vasopressor support. D-dimer was elevated throughout this period, ranging from 0.86 to 8.22 µg/mL. The patient was extubated 12 days after ICU admission.

Shortly after extubation, the patient reported right hand pain. The hand service was consulted, with physical examination showing ischemic changes with pulp necrosis of the thumb and index fingers and duskiness of the middle finger and little fingertips with sluggish but present capillary refill. Arterial duplex ultrasound demonstrated 100% occlusion of



FIGURE 1: Photograph of the volar hand showing subacute digital ischemia.



FIGURE 2: Photograph of the dorsoradial hand showing subacute digital ischemia.

the distal radial artery at the site of a prior arterial line.

Digital ischemia, likely of subacute duration, was diagnosed (Figs. 1, 2). The hand surgery service recommended forearm and hand warming in addition to topical nitroglycerin application.⁸ Given the recent hemorrhage, anticoagulation was relatively contraindicated; however, given stable hemoglobin measurements, volar pulp discoloration, and a concern for embolic phenomena, low-dose heparin was recommended and was initiated 1 day after the consult recommendation.

The patient's digital ischemia improved throughout the hospital stay with the heparin infusion; dosing was eventually increased to a high dose as hemoglobin stabilized for a longer time. The patient was eventually transitioned to apixaban 5 mg twice daily. Arterial inflow improved and the discoloration lessened with eventual eschar formation on the thumb and index fingers and recovery of flow to the middle and little fingertips.

Other notable in-hospital events included acute kidney failure requiring continuous venovenous hemodialysis as well as hemorrhagic shock. A head

computed tomography scan, taken after sedation had been weaned, demonstrated age-indeterminate cerebral infarcts. Other medical therapies included tocilizumab, lopinavir–ritonavir/ribavirin, cefepime, vancomycin, hydroxychloroquine, azithromycin, tobramycin, ceftriaxone, piperacillin–tazobactam, fluconazole, oral vancomycin, and metronidazole. Ultimately, the patient was discharged to an acute care rehabilitation facility after sufficient clinical recovery.

DISCUSSION

The existing literature strongly supports a link between severe COVID-19 and coagulopathy.^{1–3} These 2 cases contribute to an evolving understanding of underlying hypercoagulability in patients with COVID-19 and identify extremity ischemia as a possible manifestation of this condition. Although previous reports also identified COVID-19 patients with limb ischemia, there are limited data on the clinical course and treatment.^{1,2}

The patients featured in this report demonstrated noteworthy similarities with those already described in the literature. In 2 studies from Wuhan, China, all patients with extremity ischemia demonstrated elevated D-dimer^{1,2}; both patients described here also had D-dimer elevations, with peaks of greater than 20 and 8.22 $\mu\text{g/mL}$ respectively. In addition, 6 of the 7 patients in the study by Zhang et al^{1,2} were treated with anticoagulation; 2 patients survived to the end point in that study, one of whom demonstrated improvement of plantar ischemia. The other patient, who had lower-extremity ischemia, progressed to

TABLE 1. Comparative Characteristics of 2 COVID-19 Patients

Patient Characteristics	Patient A	Patient B
Age, y	70	43
Sex	Female	Male
Medical history	Hepatitis C	Obesity, hypertension, hyperlipidemia
Presenting symptoms	Fevers, chills, shortness of breath, headache, malaise	Shortness of breath, cough, chest pain, fatigue, diarrhea, decreased urine output
Reasons for ICU admission	Respiratory failure	Respiratory failure
Vasopressor use	Yes	Yes
Arterial lines	Left brachial; left radial × 2	Left radial, right radial
Thrombotic manifestation(s)	Ischemia of index, middle, and ring fingers on right hand; right femoral DVT	Right distal radial artery occlusion; right popliteal DVT, ischemia of thumb and index, middle, and little fingers
Anticoagulation	Yes	Yes
Days from ICU admission to upper-extremity thrombotic event	12	14
Days from thrombotic event to death	5	

gangrene.¹ Similarly, both patients in the current report were eventually treated with anticoagulation; patient B demonstrated improvement in skin changes, whereas patient A had persistent upper-extremity ischemia until death (Table 1). Notably, however, patient A only had 5 days between ischemia and death, whereas patient B demonstrated tissue improvement over 2 weeks. Therefore, we recommend the rapid institution of an appropriate anticoagulation regimen for the treatment of this phenomenon, with consideration for prophylactic anticoagulation given the observed incidence of DVTs in these patients and others.⁹ Another possible explanation for the ischemic phenomenon is vasopressor use; however, it is unlikely that vasopressors would cause unilateral ischemia. Another possibility is embolic phenomena. Thrombosis resulting from radial arterial line placement could explain some of patient B's clinical picture, but the small finger ischemia does not fit with this hypothesis.

Zhang and colleagues² recently suggested antiphospholipid antibodies as a contributor to, or perhaps cause of, thrombotic events such as those described in this report. Although we were unable to test these patients for such antibodies, we acknowledge this hypothesis as a potential explanation for these ischemic events.

The relationship between coagulopathy and poor disease prognosis in COVID-19 patients merits discussion. Several studies have demonstrated that

patients with abnormal coagulation markers and those with acral ischemia are at an increased risk for a poor prognosis.^{1,7,9,10} For instance, Guan and colleagues⁷ showed that patients with elevated D-dimer were more likely to have severe disease requiring ICU admission and mechanical ventilation, or to die. In addition, Tang et al¹⁰ noted that patients with COVID-19 pneumonia who had significantly higher D-dimers and fibrinogen degradation products as well as longer prothrombin times at admission were more likely to die than were those without these abnormal parameters. Interestingly, although both patients in the current report demonstrated elevated D-dimer levels, patient A's first D-dimer after admission was only 0.60 µg/mL whereas that of patient B, who survived, was higher at 0.92 µg/mL.

Based on the clinical course of these 2 COVID-19 patients, we hypothesize that coagulopathies, especially those of the hand, are a marker of severe illness and merit close monitoring and early hand service consultation for appropriate intervention. It is critical to monitor for thromboembolic events in the extremities of critically ill patients to avoid permanent damage and/or limb loss.

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