

Acute limb ischemia and aortic mural thrombosis as primary manifestations of severe acute respiratory syndrome coronavirus 2

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ABSTRACT

A variable clinical presentation is emerging as a hallmark of the novel SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2). In addition to hypoxic respiratory failure, multiorgan dysfunction, and septic shock, significant thromboembolic complications posited to result from diffuse coagulopathy have been associated with this viral infection. We report on a unique primary manifestation of SARS-CoV-2 infection presenting as acute limb ischemia and aortic mural thrombosis without clinical evidence of pulmonary disease. Despite our best attempts at limb salvage with therapeutic anticoagulation, emergent aortoiliac and distal embolectomy, the patient developed bilateral dry gangrene and ultimately required lower extremity amputations. (*J Vasc Surg Cases Innov Tech* 2021;7:605-9.)

Keywords: Aortic mural thrombus; COVID-19; Limb ischemia

An unpredictable clinical presentation is emerging as a hallmark of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In addition to high-grade fever, hypoxic respiratory failure and cough, associated extrapulmonary manifestations have occurred, including gastrointestinal distress, renal injury, dermatologic changes, and neuropsychiatric symptoms.^{1,2} Furthermore, significant thromboembolic complications have been documented with SARS-CoV-2 as a consequence of a proinflammatory milieu, hypercoagulable state, and endothelial dysfunction associated with systemic infection.³⁻⁵ We report a case of aortic mural thrombosis (AMT), acute limb ischemia (ALI), and progressive tissue necrosis as the primary clinical manifestations of SARS-CoV-2 infection.

CASE REPORT

A 67-year-old man had presented to the emergency department with a 3-day history of worsening calf pain, bilateral foot numbness, and purple skin discoloration of his left foot. One week before admission, the patient had tested positive for SARS-CoV-2 after experiencing intermittent fevers (maximum temperature, 103°F) and diarrhea for 2 weeks. He had not exhibited any respiratory symptoms and had maintained a

robust exercise regimen, including walking ≤ 5 miles daily before the onset of leg pain.

His pertinent medical history included insulin-dependent diabetes mellitus, hyperlipidemia, and hypertension. He lacked any family history of coagulopathy or venous thromboembolism and was a lifelong nonsmoker. The initial examination revealed cool lower extremities, profound tenderness along the anterior compartment of the left leg, mottling along the lateral and plantar aspects of the left foot, and preserved sensory and motor function bilaterally (Fig 1). The bedside Doppler ultrasound examination revealed faintly audible pedal signals. The initial laboratory findings included a white blood cell count of 13,400/L, hemoglobin of 12.4 g/dL, platelet count 213,000/ μ L, international normalized ratio of 1.1, activated partial thromboplastin time of 27.9 seconds, and creatinine kinase of 3508 U/L. A chest radiograph demonstrated pulmonary nodules, the largest of which was 4 mm, without evidence of infiltrates. In the absence of respiratory symptoms, computed tomography (CT) of the chest was not performed. Similarly, initial D-dimer, fibrinogen, and ferritin levels were not obtained, because, clinically, the index of suspicion for ALI and threatened limb loss was strong.

Run-off CT angiography revealed complete occlusion of the bilateral internal iliac, profunda femoris, and popliteal arteries and extensive intraluminal filling defects located in the infrarenal aorta, extending into the aortic bifurcation and bilateral common iliac arteries, causing near occlusion of these vessels (Fig 2). Given the lack of any visualized collateral pathways, a diagnosis of acute thrombosis was favored, and a standard-dose heparin infusion was started with an activated partial thromboplastin time goal range of 60 to 110 seconds. The patient underwent emergent bilateral aortoiliac, profunda femoris, femoral, and popliteal artery embolectomies and left anterior compartment fasciotomy. He experienced immediate visible improvement in the distal mottling postoperatively, and the Doppler ultrasound examination revealed triphasic common femoral and profunda signals bilaterally but absent pedal pulses.

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Fig 1. Photographs showing left foot mottling on the day of admission.



Fig 2. Computed tomography (CT) angiogram demonstrating extensive infrarenal stenosis.

Postoperatively he continued therapeutic anticoagulation, transitioning from heparin to enoxaparin 1 mg/kg twice daily. The D-dimer level measured 2 weeks after embolectomy was 2109 ng/mL, and the fibrinogen level was 726 mg/dL. His oxygen requirements remained at baseline throughout his hospitalization. Over time, he developed proximal progression of tissue necrosis and dry gangrene of both limbs (Fig 3). A coagulopathy

evaluation did not reveal any underlying predisposition to thromboembolism, including lupus anticoagulant, anticardiolipin antibodies, β 2-glycoprotein-1 antibodies, paroxysmal nocturnal hemoglobinuria fluorescein-labeled proaerolysin, and *JAK2 V617F*. Repeat CT angiography demonstrated a minimal atherosclerotic disease burden in the infrarenal aorta with near full resolution of his mural thrombus (Fig 4). Given the degree of devitalized tissue, he underwent proximal transmetatarsal amputation of the right foot and a below-the-knee amputation of the left lower extremity (Fig 5). He continued therapeutic anticoagulation >6 months after presentation. The patient provided written informed consent for the report of his case.

DISCUSSION

Although high-grade fevers, cough, and dyspnea remain the hallmark symptoms of SARS-CoV-2, our case highlights the occurrence of ALI and a conspicuous absence of respiratory symptoms in a patient with recently diagnosed coronavirus disease 2019 (COVID-19) infection.

Emerging case reports have described arterial thrombotic events among patients with SARS-CoV-2, including AMT and/or ALI with variable treatment approaches and clinical consequences.⁶⁻¹¹ The patient outcomes have ranged from thrombus resolution to repeat embolization, catastrophic reperfusion injury, and multiorgan failure despite aggressive surgical and medical interventions. A recent case study of AMT and rapidly evolving bilateral ALI resulted in transtibial amputation after multiple revascularization attempts.⁹ For ALI without associated AMT, a



Fig 3. Photographs of the patients' feet 6 weeks after lower extremity symptom onset.

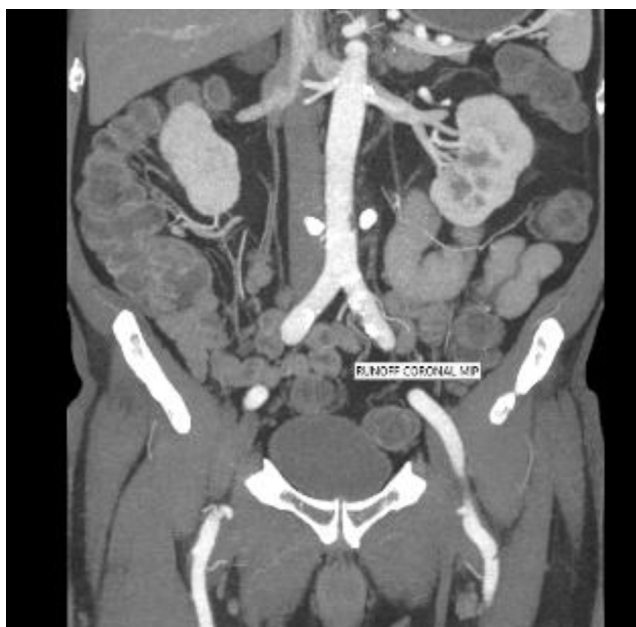


Fig 4. Repeat computed tomography (CT) imaging at ~3 months after onset.

single-center study reported successful revascularization in 12 of 17 patients (70.6%), with 1 patient requiring amputation.¹² To the best of our knowledge, no definitive regimen beyond revascularization and therapeutic anticoagulation has been proved to attenuate the thrombotic burden seen with SARS-CoV-2.

As our findings have demonstrated, despite the best efforts with aggressive surgical intervention and anticoagulation, the significant coagulopathy and thrombotic burden in patients with SARS-CoV-2 can lead to eventual limb loss. Although the outcome was undoubtedly influenced by our patient's delayed presentation and baseline comorbidities, the systemic inflammatory and hypercoagulable

state associated with SARS-CoV-2 was a likely catalyst for the significant morbidity. SARS-CoV-2-associated inflammation and abnormal coagulation has been well-documented, with elevated fibrinogen and D-dimer levels and cases of disseminated intravascular coagulation seen with systemic infection.⁵ Elevated D-dimer levels, in particular, have been associated with increased mortality and the likelihood of developing future hematologic and thrombotic complications.^{3,5} In other cases of ALI and AMT, clinical evidence has been found of diffuse hypercoagulability with pulmonary embolism,^{7,10,11} cerebrovascular accident,^{7,11} and renal infarction^{8,13} documented. Although coagulation testing was not completed on admission, the persistently elevated D-dimer and fibrinogen levels postoperatively could suggest a similarly significant coagulopathy present during the course of our patient's illness, compounding the D-dimer elevation associated with limb ischemia and surgery.

Although our patient had experienced severe morbidity secondary to limb ischemia, even minor respiratory complications of SARS-CoV-2 were conspicuously absent during his clinical course. This is in contrast to other case reports, in which the patients had respiratory symptoms before presentation or imaging findings consistent with respiratory disease, in conjunction with thromboembolic events.^{6-11,13-26}

Across recent European reports, only two patients had presented with ALI as a primary complaint in the absence of respiratory symptoms. In both cases, thoracic imaging demonstrated ground glass opacification and multifocal pulmonary lesions consistent with SARS-CoV-2 infection.^{9,20} Although our patient had had mild bilateral nodularities on the chest radiograph, these had remained stable throughout his admission, and his respiratory status never deteriorated beyond his baseline.

Although the absence of pulmonary symptoms in severe COVID-19 infection is not without precedent, the relative



Fig 5. Left below-the-knee amputation and right transmetatarsal amputation.

frequency of arterial thromboembolic events occurring in isolation remains unclear. In an observational cohort study of 20 patients with ALI, all had presented with viral pneumonia evident on CT.¹² Similarly, in a case series of seven patients with ALI or AMT, all had had associated respiratory symptoms or CT findings consistent with respiratory disease.²⁷ Baram et al²⁸ similarly found pulmonary parenchymal ground glass opacities in 22 patients with large vessel thrombosis, including in 1 patient without respiratory complaints. Finally, a retrospective study of 12,630 patients with COVID-19 identified 49 patients with arterial thromboembolism, including 35 with lower extremity ischemia.²⁹ In the cohort of 49 patients, 22 (45%) had presented with signs of arterial ischemia before the diagnosis of SARS-CoV-2. However, the incidence of coexisting respiratory symptoms in this group was not documented.

As the SARS-CoV-2 pandemic continues to grip society, clinicians should remain vigilant for atypical presentations, including patients who lack respiratory involvement, and be mindful of the rare, but potentially catastrophic, sequelae of AMT and ALI encountered with COVID-19.

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