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Visual Case Discussion

COVID-19 and limb ischemia

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1. Discussion

A 47-year-old woman with a history of type 2 diabetes and obesity presented to a community emergency department (ED) with bilateral foot and leg pain over the past 2 weeks, worsening over the last 3 days. The pain was provoked by standing and walking. The patient also reported gravity-dependent purple discoloration of the toes and feet. Both pain and discoloration were noted to be worse on the right limb. She reported COVID-19 pulmonary occurring 6 months prior to presentation, and she was known to have received two doses of MODERNA SARS-COV-2 vaccine 11 months prior to presentation.

On examination, the patient appeared uncomfortable and was awake and alert with a Glasgow Coma Scale score of 15. Vital signs were blood pressure 112/62 mmHg, heart rate 88 beats per minute and rhythm regular, respiratory rate 20 breaths per minute, and oxygen saturation 97% on room air. There were no signs of trauma. Extremity examination revealed dependent pedal rubor with purple discoloration, right greater than left. Rubor resolved completely with extremity elevation. The feet were warm, and dorsalis pedis and posterior tibial pulses were palpable and confirmed using Doppler ultrasonography.

On laboratory evaluation, complete blood count demonstrated a hemoglobin level of 6.9 g/dl, mean corpuscular volume of 57 fl, white blood cell count of 16.9 × 10^9/L, and neutrophil level of 11.44 × 10^9/L, and platelet count of 488 × 10^9/L. Hemoglobin A1c was 10.5%, and standard serum chemistry and renal function studies were within normal range.

Electrocardiogram showed sinus tachycardia with a heart rate of 102 beats per minute. Bilateral 3 view foot X-rays were obtained revealing a small plantar calcaneal spur on the right foot, which was otherwise radiographically normal. The left foot film was normal.

The patient’s anemia was attributed to a history of iron deficiency, and the most recent value obtained 6 months prior was 9.7 g/dl. Acute hemorrhage or hemolysis were felt unlikely. Given that she was stable and asymptomatic, in addition to limited transfusion capabilities at the presenting facility, her care providers did not feel emergent blood transfusion was indicated.

The initial presentation occurred at a critical access ED without resources for formal ultrasonography. Her care team pursued an emergency medicine telemedicine consultation through an affiliated tertiary care center. Collaboratively, the teams were concerned for small vessel peripheral vasculopathy. An acute arterial occlusive process was felt unlikely given the progressive nature of her symptoms, warm extremities, and intact distal pulses. The presentation was felt inconsistent with deep venous thrombosis (DVT). The patient was deemed stable for discharge, and arrangements were made for close primary care follow-up. She was instructed to return for acute changes or progression of symptoms.

The day after initial presentation, the patient returned to the same critical access ED with worsening right foot pain. An abdominal and pelvic computed tomography (CT) angiogram with bilateral lower limb runoff was obtained. This demonstrated mild diffuse atherosclerotic changes including an apparent minimal focal intimal plaque in the infrarenal aorta with patent bilateral lower extremity arterial vasculature. The patient was transferred to the affiliated tertiary care facility ED. Examination demonstrated exquisite tenderness to palpation of her feet, right greater than left, with discoloration of the right distal foot and toes with scattered petechiae, purpura and dependent rubor. The clinical picture was felt concerning for microvascular occlusion from an embolic source. (Fig. 1). The dorsalis pedis and posterior tibial pulses were palpable bilaterally. Bilateral arterial and venous lower extremity ultrason studies demonstrated intact arterial circulation; however, an occlusive DVT in the right soleal vein was identified. Anticoagulation

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with unfractionated heparin was initiated, and the patient was admitted to the hospital for further evaluation and treatment.

During her hospitalization, vascular medicine was consulted, who agreed with the concern for hypoperfusion of the distal right foot stemming from an embolic event in the microcirculation. COVID-19 PCR returned positive, and a diagnosis of blue toe syndrome was considered likely. Transthoracic echocardiogram was obtained and revealed no definitive evidence of endocarditis and blood cultures remained negative. During the hospitalization, she was bridged from heparin to oral anticoagulation with warfarin. The patient was discharged on hospital day five with a plan for continued outpatient care.

Three days after discharge, and nine days from initial presentation, the patient returned for evaluation of worsening pain in the right foot. Examination revealed progression of ischemic changes in the right foot with necrosis of the toes and forefoot. Right lower limb arterial ultrasound demonstrated occlusion of the anterior and posterior tibial arteries at the level of the ankle with distal reconstitution via tiny collateral vessels in the foot. The patient was readmitted to the hospital internal medicine service and was evaluated by vascular medicine, vascular surgery, and orthopedic surgery. No options for revascularization were identified due to the distal level of arterial occlusion and the extant extensive right foot necrosis. The patient underwent right transtibial below-knee amputation performed by orthopedic surgery.

2. Visual case discussion

SARS-CoV-2, the novel virus that caused the global COVID-19 pandemic, has been associated with myriad symptoms. “COVID Toes” refers to a painful discoloration of the toes and fingers associated with COVID-19 infection. The clinical appearance is similar to that of Chilblains lesions, which are a vascular complication in response to cold, wet weather. In contrast, the inflammatory response and resultant hypercoagulopathy associated with COVID-19 lead to a higher risk of vascular complications, including venous and arterial thrombosis. These vascular sequelae must be considered in patients with recent, known, or suspected COVID-19 infection.

Peripheral vascular disease represents a spectrum, at its extremes, may be life and limb-threatening. This may progress rapidly from mild to severe symptoms with little warning. Vascular insufficiency is often an early sign of peripheral vascular disease and may manifest with dependent rubor (a dependent, purplish discoloration of feet and legs) and/or claudication (muscle pain with use due to decreased blood flow). Both are important findings of vascular insufficiency and may portend serious complications such as acute limb ischemia.

Acute limb ischemia generally occurs in the setting of acute arterial occlusion, which may result from thrombosis, arterial embolization, or injury. Arterial thrombi are platelet-mediated and often occur in the setting of an existing atherosclerotic plaque, though thrombi may also occur in the setting of arterial dissection or aneurysm. A thrombus may embolize, traveling downstream to lodge in a smaller artery, thus obstructing distal flow and resulting in tissue ischemia. Critical limb ischemia may lead to tissue necrosis and progress to loss of limb. Classically, limb ischemia is identified by the “six P’s”: pain, pulselessness, pallor, paresthesia, paralysis, and poikilothermia; however, these signs
and symptoms are inadequately sensitive to exclude limb ischemia. Acute limb ischemia is treated initially with anticoagulant therapy and, in some cases, thrombolysis, endovascular, or surgical procedures such as thrombectomy or stent placement to achieve arterial revascularization.

Venous thrombosis involves the development of a thrombus in the venous circulation, which may obstruct or impede blood flow and venous drainage from an affected extremity. These include superficial venous thrombosis, DVT, and pulmonary embolism (PE), should the venous thrombus embolize. Rarely, limb ischemia results from massive venous thromboembolic disease (phlegmasia cerulea dolens), which occurs when venous return is occluded to the point at which limb edema compromises arterial circulation. Virchow’s triad describes the constellation of circumstances, including endothelial injury, venous stasis, and a hypercoagulable state contribute to the formation of venous thrombosis. Prompt diagnosis of PE and DVT is required to prevent disease progression and life-threatening complications. DVT and PE are treated with anticoagulant medications, including heparin, warfarin, or direct oral anticoagulant medications.

Questions and answers with a brief rationale true & false and / or multiple-choice questions

**Question 1**
Phlegmasia Cerulea Dolens

A) An emergent vascular complication of DVT that results in a large, discolored limb.
B) An emergent complication of distal arterial embolism.
C) The change in color of the limb in a peripheral arterial disease
D) The area of tissue death after ischemic injury

Correct answer is A; phlegmasia cerulea dolens is an emergent vascular complication of DVT resulting in a large, discolored limb. It is caused by an outflow obstruction of the venous system and often requires surgical or endovascular intervention.

**Question 2**
Requires “bridging” with heparin or Lovenox while it reaches therapeutic levels.

A) Eliquis
B) Xarelto
C) Warfarin
D) All anticoagulants require bridging

Correct answer is C; warfarin takes time to elevate the INR and become effective as a blood thinner; therefore, heparin or Lovenox must be used until the INR reaches therapeutic levels. Both Xarelto and eliquis are effective shortly after administration and do not require bridging.

Declaration of Competing Interest

None.

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