

Case Report

Phlegmasia Cerulea Dolens as the Initial Sign of COVID-19 Infection

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Abstract

A 56-year-old woman with asthma, diabetes, hypertension, hyperlipidemia, and obesity presented with acute ischemic venous thrombosis (phlegmasia cerulea dolens) of the left calf and popliteal veins due to asymptomatic COVID-19 infection. We believe that this is the first case report of this distinct clinical presentation and should alert clinicians that the hypercoagulability associated with COVID-19 infection may occur in the absence of respiratory symptoms.

Introduction

There have been numerous recent reports of hypercoagulability associated with symptomatic, severe COVID-19 respiratory infection. We present an atypical case of limb-threatening, focal phlegmasia cerulea dolens of the lower extremity in a patient with asymptomatic COVID-19 infection.

Case Report

A 56-year-old woman presented to the emergency department with complaints of left lower extremity pain and swelling for four days. Her comorbidities included diabetes mellitus, hypertension, hyperlipidemia, and obesity. Of note, she did not have cough, fever, chest pain, shortness of breath, loss of smell or other respiratory symptoms. She denied recent trauma, surgery, immobility, hospitalizations, prior venous thromboembolism, hypercoagulable disorder, or prior use of anticoagulation therapy. Her past surgical history was notable for total abdominal hysterectomy with bilateral salpingo-oophorectomy for endometrial cancer. Her endometrial cancer had been in remission since 2013. She was not using hormone replacement therapy.

On examination, she was awake and alert and complained exclusively of pain in the left foot and calf. Her vital signs were normal

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with the exception of a heart rate of 110 beats per minute. Her chest was clear to auscultation. She had moderate left leg swelling up to the knee with significant calf tenderness and cyanotic discoloration of the toes. She had a palpable left femoral and popliteal pulse, but absent pedal pulses. Both venous and arterial Doppler signals were absent at the ankle. She had reduced movement and sensation of the left foot up to the lower calf. Her right lower extremity was normal. Labs were notable for creatinine of 2.18 mg/dl (normal <1.2 mg/dl) and creatinine kinase of 12,151 u/L (normal <192 u/L).

Venous duplex ultrasound of the left lower extremity showed Deep Venous Thrombosis (DVT) in the left popliteal vein extending into the calf veins. In addition, there was an incidental finding of "significantly decreased or absent arterial blood flow" in the popliteal, posterior tibial, and dorsalis pedis arteries.

A CT scan of the abdomen was obtained to rule out the possibility of recurrent pelvic malignancy. No evidence of pelvic pathology was identified but surprisingly the images of the lower chest showed bilateral "ground glass" opacities consistent with COVID-19 lung infection. Nasopharyngeal PCR confirmed that she had acute COVID-19 infection. On further questioning, she denied any of the common symptoms associated with COVID-19 infection including loss of smell or taste, cough, headache, nausea, or vomiting. She did acknowledge that her son had recently been diagnosed with COVID-19.

Based on the clinical and ultrasound findings of simultaneous venous and arterial thrombosis, she was diagnosed with isolated Phlegmasia Cerulea Dolens (PCD) confined to the arteries and veins below the left knee. The forefoot was not salvageable (Rutherford 3) and therefore she was treated with hydration, limb elevation and systemic anticoagulation with heparin. Her creatinine elevation and myoglobinuria resolved. However, the already advanced limb ischemia did not improve and became demarcated in the mid-foot necessitating below knee amputation. She continued to test positive for COVID-19, but she never developed any signs or symptoms of COVID-19 respiratory infection.

Discussion

Phlegmasia Cerulea Dolens is a severe form of so-called "ischemic venous thrombosis" that leads to a reduction in arterial inflow due to elimination of virtually all venous outflow. The literal translation is "Painful Blue Inflammation". PCD occurs most commonly in patients with hypercoagulability secondary to metastatic cancer [1]. The distribution of thrombosis invariably involves the proximal ilio-femoral vessels which was absent in the current case. PCD is associated with a high risk of amputation (up to 50%) and mortality (40%) [2,3]. Treatment usually includes a combination of aggressive elevation, systemic anticoagulation, pharmaco-mechanical thrombolysis and, occasionally, open femoral thrombectomy [2,4,5].

This patient's case was distinctly unusual because of the limited distribution of thrombosis in the veins and arteries below the knee and the absence of any obvious inciting factors. It should be emphasized that DVT limited to the popliteal and calf veins usually

asymptomatic or only mildly symptomatic and, virtually never progresses to limb loss. The predominant reason that calf vein DVT is treated with anticoagulation is to prevent proximal propagation of thrombus to femoral and iliac veins.

PCD is considered a vascular emergency requiring immediate initiation of parenteral anticoagulation and vascular surgery consultation to prevent further ischemia and potential limb loss [3]. Initial therapy with intravenous heparin, bed rest with steep leg elevation, and fluid resuscitation is recommended for all cases. Currently, there are multiple additional treatment options that can be selected either alone or in combination such as systemic thrombolysis, catheter-directed thrombolysis, or surgical thrombectomy [5,6]. All of these additional treatments are associated with substantial risks, especially bleeding. Given the advanced nature of the ischemia injury at the time of presentation, these adjunctive invasive treatments were not employed in this patient.

Currently, there is emerging literature relevant to the recognition and treatment of COVID-19 associated peripheral thrombosis. The term “COVID leg” is frequently used by specialists to describe the finding of peripheral thrombosis in patients with COVID-19. Most patients with “COVID leg” have severe respiratory infection and are frequently in the ICU. There is no consensus regarding optimal therapy [7]. Zhai, et al. in the *International Journal of Thrombosis and Hemostasis* recommended therapeutic heparin or low molecular weight heparin in patients with suspected or confirmed venous thromboembolism without mention of surgical intervention [8]. Conversely, Bikdeli, et al. discussed possible revascularization options in severe cases or those with refractory symptoms [9]. There have reports both online and in print suggesting that conventional surgical treatments may be ineffective in the management of COVID-19 associated peripheral venous and arterial thrombosis [10].

This case is significant for several reasons. First, while hypercoagulability is a newly recognized complication of COVID 19 infection, most case reports of limb-threatening ischemia have occurred in critically ill patients in the ICU setting. This patient’s presentation was distinctly unusual in that her symptoms were confined to her left leg and she never experienced any respiratory symptoms throughout her hospital course. COVID-19 infection was not suspected until her CT scan showed the typical peripheral ground glass opacities. We have added acute limb ischemia to the COVID-19 screening questionnaire in our Emergency Department. Second, PCD occurs almost exclusively in patients with extensive proximal DVT in the ilio-femoral veins. The presentation of acute combined arterial and venous thrombosis confined to the distal extremity vessels leading to amputation is extremely uncommon in our experience and further emphasizes the protean manifestations of COVID-19 infection. Finally, there is no consensus regarding the optimal treatment of patients who have COVID-19 and critical limb ischemia. Anecdotal reports have suggested that routine treatments including heparin and surgical thrombectomy are less effective in COVID-19 related thrombosis than in other non-COVID patients.

Summary

This patient presented with limb-threatening ischemic venous thrombosis due COVID-19 infection in the absence of respiratory symptoms or signs. We are unaware of prior reports of localized phlegmasia cerulea dolens confined to the veins and arteries of the lower leg that resulted in amputation. Front line clinicians should be aware that acute limb ischemia may be the presenting symptom of COVID-19 infection.

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