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A Case of Phlegmasia Cerulea Dolens in a Patient With COVID-19, Effectively Ttreated With Fasciotomy and Mechanical Thrombectomy

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Abstract: Coronavirus disease 2019 (COVID-19) has been widely reported to be associated with increased risk of Venous Thromboembolism, both deep vein thrombosis (DVT) and pulmonary embolism. A rare and extreme manifestation of DVT is Phlegmasia cerulea dolens, characterized by poor tissue perfusion due to marked limb swelling which can progress to limb and life-threatening venous gangrene. We report the case of a 53-year-old man with severe SARS-CoV2 pneumonia who developed acute iliofemoral DVT leading to acute limb ischemia due to Phlegmasia cerulea dolens. The patient underwent successful emergent fasciotomy and mechanical thrombectomy with removal of extensive thrombus burden and restoration of normal venous circulation. Our case highlights the importance of clinical vigilance and early implementation of therapeutic interventions to avoid adverse outcomes in patients who develop SARS-CoV2 induced Venous Thromboembolism complications.

CASE REPORT

A 53-year-old male with medical history of hypertension, remote smoking, and diabetes mellitus, presented to the emergency department with fever, weakness, and dry cough for several days. The patient had no personal or familial history of VTE. Laboratory tests showed elevation of several inflammatory markers, such as CRP, ESR, procalcitonin and ferritin, while d-dimer level was mildly elevated of 385 ng/mL (Table I). CT scan of the chest showed bilateral patchy ground-glass opacities suggestive of COVID-19 pneumonia, which was confirmed by rapid nasopharyngeal PCR test. Due to signs of hypoxic respiratory failure with additional diabetic ketoacidosis the patient was admitted to the intensive care unit. A central venous catheter was inserted in the right common femoral vein due to hemodynamic instability for vasopressor support and prophylactic low molecular weight heparin at 40 mg twice daily was started.

Over the first 3 hospital days, the patients d-dimer level steadily increased from 385 ng/mL to a peak of 13,709 ng/mL. The patient then complained of severe right leg pain. On physical examination, the right leg was edematous, cyanotic, and cold with tense and exquisitely tender thigh and calf compartments. Pedal pulses were not palpable, capillary refill was sluggish, sensation to light touch was decreased and passive range of motion of the entire leg elicited severe pain. Bedside right leg duplex ultrasonography showed occlusive thrombus in the right external iliac vein extending to the common femoral, superficial femoral,

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Table I. Blood results.

	Day of admission	Hospital day 4 when patient developed PCD
White blood cell count (4.8-10.8) K/uL	8.55	11
Procalcitonin (<0.1) ng/mL	3.3	11.9
C-reactive protein (0-0.5) mg/dL	35	37
Ferritin (30-400 ng/mL)	783	675
ESR (0-20 mm/hr)	83	138
D-dimer (<230 D-DU ng/Ml)	385	13,709
HbA1c (4.8-5.6)	9.6	
Serum glucose (70-99 mg/dL)	600	110
Creatinine (0.5-1.2 mg/dL)	1.32	1.8
Blood urea nitrogen (5-20 mg/dL)	45	27
Lactic acid (0.5-2 mmol/L)	2.9	2.4
Asparate aminotransferase (0-40 IU/L)	29	18
Alanine aminotransferase (0-40 IU/L)	28	21
Lactate dehydrogenase (94-250 IU/L)	565	860
Hemoglobin (14-18 g/dL)	12	10.3
Platelets (150-350 K/uL)	188	195
International normalized ratio (0.8-1.2)	0.9	0.9
Activated partial thromboplastic time (21-37)	22.5	26

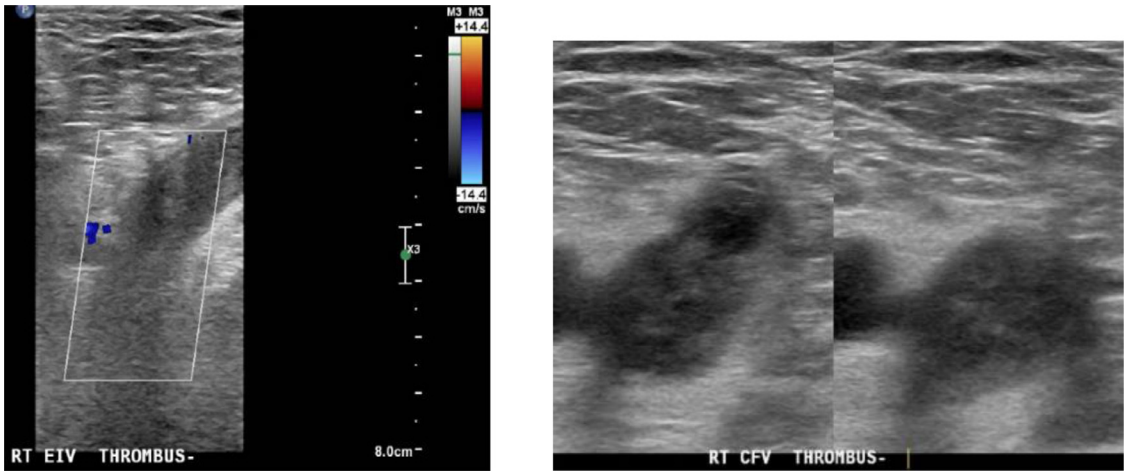

Fig. 1. (A, B) Venous Duplex with extensive thrombus in the right external iliac and common femoral vein.

popliteal and calf veins (Fig. 1A, B). Arterial duplex scan showed patent common femoral, superficial femoral, popliteal, anterior, and posterior tibial arteries with triphasic waveforms and no evidence of stenosis (Fig. 2).

The patient was started on systemic therapeutic anticoagulation with heparin and as the clinical picture along with the duplex ultrasound findings were compatible with the diagnosis of acute limb ischemia due to PCD, the decision was made to proceed emergently to the operative room. We began with fasciotomy of the anterolateral thigh and 4 calf compartments followed by mechanical venous thrombectomy. Ultrasound guidance was utilized for percutaneous distal venous access of the posterior tibial vein while proximal venous access was obtained through cut-down of the common femoral vein after removing the central venous catheter that was in place. A venotomy was performed at the common femoral vein and the glide wire which was previously placed through the distal tibial vein was brought out through the venotomy in order to perform a flossing technique with the use of a 4 × 20 mm and 6 × 20 mm balloon (Medtronic, Minneapolis, Minnesota). An Esmarch bandage (McKesson, Irving, Texas) was used to wrap the leg to compress the clot via the femoral venotomy incision and a contiguous clot spanning the length of the venous system from the tibial vein to the common

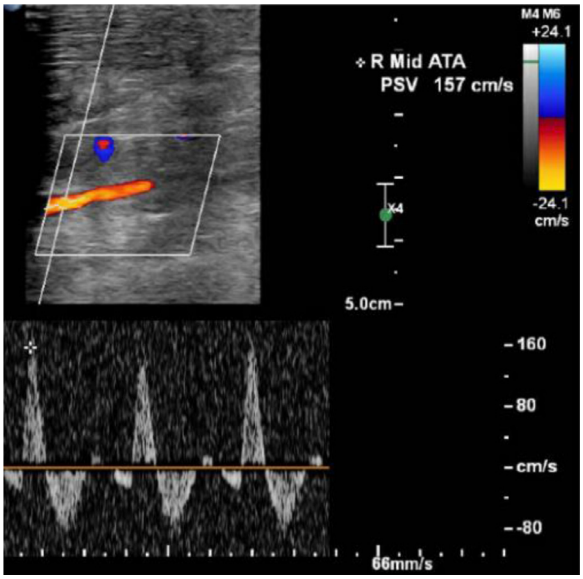

Fig. 2. Arterial Duplex showing patent anterior tibial artery with triphasic waveform.

femoral vein was successfully removed (Fig. 3). Subsequently, fogarty balloon embolectomy of the common and external iliac vein was performed using a No. 8 forgarty (Edwards Lifesciences, Irvine, California) to restore venous outflow. Finally, the venotomy was closed and the leg was wrapped. Postoperatively, there was resolution of leg discoloration and restoration of pedal pulses. Patient's sensory and motor impairment were completely recovered over time. He was placed on a therapeutic anticoagulation with heparin that was eventually transitioned to low molecular weight heparin (LMWH) and the right calf and thigh fasciotomies were closed on postoperative day 3 and 14 respectively, as the swelling improved. Hypercoagulability workup including homocysteine levels, factor V-Leiden, anticardiolipin IgG and IgM Ab, protein C, protein S and Anti-thrombin III deficiency were negative. Patient's hospital course was prolonged secondary to the COIVD-19 virus, but was eventually discharged day 70 on 2.5 mg BID Apixaban (Eliquis, Bristol-Myers Squibb, New York, New York) as the preference for long-term anticoagulation.

DISCUSSION

The novel SARSCoV2 virus has led to a true health pandemic with more than 135 million people infected and nearly 3 million deaths.[1] Although respiratory symptoms are the predominant feature of the disease course, critically ill COVID-19 patients have high incidence (25-47%) of Venous Thromboembolic (VTE) complications even with the use of thromboprophylaxis.[2,3] Several studies have shown that the use of anticoagulation is associated with lower mortality, especially in those critically ill, but there is still no consensus regarding the optimal level of anticoagulation.[4,5,6] The survival benefit of anticoagulation supports the initial speculation that the COVID-19 induced coagulopathy is secondary to a robust inflammatory response, leading to endothelial dysfunction, and a heightened coagulopathic cascade.[7] Our patient had a huge elevation in D-dimer levels on hospital day 3 and developed extensive iliofemoral DVT although he was receiving thromboprophylaxis with LMWH.

Symptom's from DVT can present on a scale of asymptomatic with minor limb swelling, to more life threating complications such as pulmonary embolism, or local limb complications such as phlegmasia cerulean dolens (PCD).[8,9] The pathophysiology behind PCD includes an extensive iliofemoral DVT causing severe venous outflow obstruction, leg edema, impaired arterial flow due to compartment syndrome causing tissue ischemia and ultimately venous gangrene.[10] The diagnosis is usually based on clinical exam along with ultrasonographic findings of extensive thrombus in the superficial and deep venous system, absence of venous flow with reduced flow velocities and increased resistance and pulsatility indices in the arterial waveform due to venous outflow obstruction.[11] Our patient had clinical signs of venous gangrene (stage III PCD),[12] acute limb ischemia (immediately threatened-stage IIb) and compartment syndrome while the venous ultrasound showed extensive ilio-femoral DVT.

While initial management of DVT includes leg elevation and initiation of aggressive systemic anticoagulation, surgical interventions are reserved for patients with acute limb ischemia due to PCD.[12,13] Surgical options span from open thrombectomy.[14,15] to percutaneous techniques including catheter-directed thrombolysis,[16] with or without mechanical thrombectomy[17,18] and percutaneous transluminal angioplasty with or without stenting.[19] All have been acceptable options in the treatment of PCD, as no one has proven to be superior regarding vein patency, and valve function preservation in order to minimize the debilitating sequalae of post-thrombotic syndrome.[12,20] The advantages of percutaneous interventions include avoiding morbidity associated with open incision and the ability to restore patency to the microvascular bed. However, it carries higher risk of bleeding[20] with prolonged infusion of the

Fig. 3. Large blood clots extracted with mechanical thrombectomy from the COVID-19 patient.

thrombolytic agent up to 48hrs.[16] On the other hand, in patients with acute limb ischemia, open surgical thrombectomy is a faster way to restore the venous circulation.[13] In the case described above the patient's presentation of PCD was far advanced as he had already developed compartment syndrome, leading to acute limb ischemia and was at risk of losing his extremity. In this clinical situation surgical thrombectomy with leg fasciotomies was the best option with the intention of restoring the normal venous flow, relieving the venous congestion, and decreasing the compartment pressure.

CONCLUSION

Venous thromboembolism should be considered a prevalent and expected event that can develop in the clinical course of critically ill COVID-19 patients. Extensive proximal DVT can lead to PCD which is a real emergency as it carries a significant risk of morbidity and mortality. Here we describe a patient with COVID-19 admitted for acute hypoxic respiratory failure who subsequently developed an iliofemoral DVT leading to acute limb ischemia due to PCD. He underwent successful emergent fasciotomy and mechanical thrombectomy, emphasizing the importance of early recognition and implementation of the appropriate treatment to avoid life-threatening complications.

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