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Extensive Arterial Thrombus Following Discharge after a Covid-19 Infection

Murat Bastopcu, Bitlis, Turkey

The novel coronavirus pandemic is associated with coagulopathy and an increased risk of thromboembolic events. A case of an extensive arterial thrombus in the left leg of a patient that occurred after discharge from Covid-19 pneumonia is described. Some patients may be under continued risk of thromboembolism after discharge and the value of extended thromboprophylaxis should be investigated.

INTRODUCTION

The novel coronavirus pandemic is associated with coagulopathy and an increased risk of thromboembolic events.^{1,2} Most reports of thromboembolism are venous; however, severe arterial thrombi are reported and can worsen the prognosis of Covid-19 patients. Below described is a case of an extensive arterial thrombus in the left leg of a patient that occurred after discharge from Covid-19 pneumonia.

CASE

A 55-year-old male presented to the emergency department with malaise and shortness of breath. Patient history was remarkable only for diabetes mellitus on insulin treatment. He was evaluated for a Covid-19 infection. His lung computed tomography (CT) showed ground-glass opacities on both lungs (Fig. 1), and the reverse-transcriptase polymerase chain reaction (RT-PCR) test was positive for Covid-19. The patient was admitted to the infectious diseases ward and started on chloroquine,

favipiravir, meropenem, levofloxacin, intravenous methylprednisolone, and prophylactic anticoagulation, with a single dose daily enoxaparin. Initially, the patient was supported with oxygen via a face mask. The patient's oxygenation improved after 6 days, and he no longer required supplemental oxygen. The patient was discharged in one week, at which time, the second RT-PCR test returned negative for Covid-19. The patient discontinued his medications, including prophylactic low-molecular-weight heparin, and was advised home isolation.

Four days after discharge from the hospital, the patient presented to the emergency department with gradual onset pain and numbness on the left leg that started one day prior. On examination, the left lower extremity was cold, the distal foot appeared ischemic, and mottling of the skin was evident below the knee (Fig. 2). Sensory loss below the knee and paralysis of the calf muscles were observed. All pulses in the left leg were absent. The patient corresponded to Rutherford Stage IIb for acute limb ischemia. Doppler ultrasound revealed acute thrombus in the main, superficial, and deep femoral arteries, anterior tibial, posterior tibial, and peroneal arteries. He was started on a heparin drip, and a CT scan was performed to assess the large vessels, which showed thrombus also in the left external iliac artery (Fig. 3). No thrombus was evident in the patient's thoracic or abdominal aorta. No evidence of peripheral arterial disease was observed in the thrombosed or contralateral leg arteries, nor wall thickening associated with vessel wall inflammation could be seen in CT.

D-dimer could not be measured as laboratory resources were limited in our remote hospital, and D-

Author Contributions: Murat Bastopcu was involved in conception, drafting, data collection for, and review of this manuscript.

Department of Cardiovascular Surgery, Tatvan State Hospital, Bitlis, Turkey.

Correspondence to: Murat Bastopcu, Tatvan State Hospital, 13200 Karşıyaka Mah. Hastane Cad. No:1 Tatvan, Bitlis, Turkey; E-mail: muratbastop@gmail.com

Ann Vasc Surg 2021; 72: 205–208

<https://doi.org/10.1016/j.avsg.2020.11.008>

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Manuscript received: September 8, 2020; *manuscript accepted:* November 19, 2020; *published online:* 13 January 2021



Fig. 1. Thoracic CT showing bilateral ground-glass opacities associated with Covid-19 pneumonia.

dimer tests were reserved for critical patients. His C-reactive protein level was 251 mg/L, neutrophil-to-lymphocyte ratio was 29.29, prothrombin time was 11.5 s. His electrocardiograms in the period of admission for pneumonia and emergency admission for acute limb ischemia showed normal sinus rhythm. His echocardiographic study did not show any valvular pathology, endocarditis, or a patent foramen ovale.

Urgent thrombectomy was performed to the external iliac artery; main, deep, and superficial femoral arteries; and below-the-knee arteries with Fogarty catheters. Abundant thrombus was removed proximally and distally, restoring arterial flow. Heparin was continued after the operation. Discoloration, numbness, and pain receded in the calf and foot. The patient is followed up with paralysis of the foot, without a need for amputation.

DISCUSSION

Coagulopathy associated with the novel coronavirus has been observed in the early months of the pandemic, and the addition of anticoagulation to the treatment of Covid-19 patients has been game-changing.¹ Nevertheless, coagulopathy remains an essential problem in these patients. Markers of inflammation increase with the severity of disease, associated with worsened prognosis and thromboembolic complications. The proinflammatory cytokines that increase over the course of infection activate the coagulation cascade by multiple mechanisms, including increased expression of tissue



Fig. 2. Ischemia of the left leg with ischemic discoloration in the foot and mottling of the skin below the knee.

factor and endothelial activation.^{2,3} Critical patients are more prone to thromboembolic complications, while patients treated in the general wards are also under risk. Lodigiani et al.⁴ reported a rate of 27.6% for thrombotic events in intensive care unit (ICU) patients, and a rate of 6.6% for general ward patients. Disease severity is associated with increased inflammation, but not all patients adhere to the same chronological progression or symptomatology, and some patients present with thromboembolism as their first symptom.^{5,6}

The acute phase of the Covid-19 infection is associated with a cytokine storm and its resulting coagulopathy. Complications that arise later than the acute phase may result from a different mechanism. After the initial innate immune response with cytokines and monocyte activation, the transition to the adaptive immune response is an important step in the prolonged excessive inflammatory state. About a week after the onset of the Covid-19 infection, antibody-mediated response by the B-cells and sustained activation of T-cells by viral antigens may exacerbate tissue damage.⁷ The dysregulated

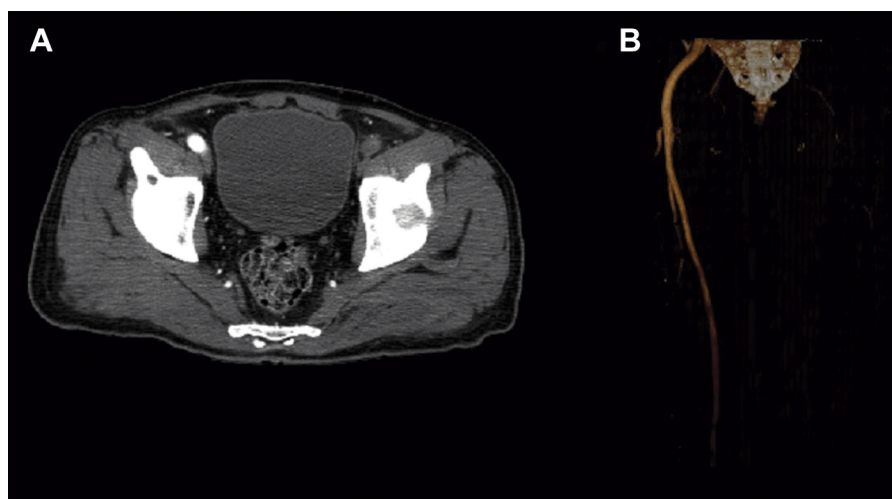


Fig. 3. (A) Contrast-enhanced CT showing thrombus in the external iliac artery. (B) Three-dimensional reconstruction showing thrombus extending from the external

iliac artery to the peripheral arteries. CT scan was not continued to the foot as thrombus in below-the-knee arteries was evident in Doppler ultrasonography.

adaptive immune response by B- and T-cells may persist even after viral clearance.⁸ Differences in immune responses in Covid-19 patients are still being elucidated and can explain the varying emergence of complications.

Normally, acute arterial thrombosis arises in the setting of arterial atherosclerosis or cardiac diseases. With the novel coronavirus, patients can suffer from thrombosis in the absence of traditional risk factors for acute thromboembolism.⁹ Arterial thromboembolism associated with Covid-19 infection can arise in the extremities, mesenteric arteries, or cerebral arteries, and thrombi can be present in multiple locations.⁶ There are reports of low-risk patients whose courses are complicated by arterial thrombosis.^{10,11}

Thrombosis in Covid-19 can also be more extensive with higher associated limb loss and death.¹² In the retrospective cohort of Etkin et al.,⁶ the rate of limb loss was 18% in patients hospitalized with Covid-19 who developed arterial thromboembolism. With the increased risk of limb loss and thrombus burden in this patient group, it may be advisable to continue anticoagulation after discharge, weighing the risks of hemorrhage and the benefits of continued prophylaxis for high-risk patients.¹³ Patients with advanced age and other comorbidities may be under greater risk of post-discharge thrombosis. A retrospective study by Patell et al.¹⁴ found a 2.5% incidence of venous and arterial thrombosis in post-discharge Covid-19 patients, with similar rates of hemorrhagic

events, emphasizing the need for new evidence to guide extended thromboprophylaxis. Beccara et al. reported a 52-year-old patient without any risk factors who developed superior mesenteric arterial thrombosis 4 days after discharge from Covid-19 pneumonia. A case reported by Singh et al.¹¹ describes a 69-year-old female Covid-19 patient who presented with aortic thrombus and multiple emboli one week after discharge. These cases demonstrate a thrombotic milieu that likely continues after the regression of symptoms. Although severe Covid-19 patients are certainly under greater risk of venous and arterial thrombosis, identifying patients with milder courses of infection and high thrombosis risk is a challenge.

CONCLUSION

Covid-19-associated coagulopathy can cause thrombosis in the arterial circulation with poor outcomes. The risk of thromboembolic events continues after discharge from hospital. Patients recovering from the novel coronavirus infection should be followed up for thromboembolic complications, and the value of continued prophylactic anticoagulants should be investigated.

CONFLICT OF INTEREST

No conflict of interest to declare.

FUNDING

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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