Case Report
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The Path to Amputation in Patients with Myositis And Foot Drop Caused by Popliteal Aartery Thrombosis Following COVID-19 Infection

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Abstract

Introduction: The COVID-19 pandemic has been affecting the whole world since 2019. The new type of corona virus has a wide range of symptoms, including hypercoagulability. It may be due to a prothrombotic state induced by the disease itself. We report a case of amputation after arterial thrombosis due to Covid-19 infection.

Case Report: A 68-year-old male patient admitted to a pandemic hospital with cough, fever and weakness was diagnosed with COVID-19, and he was hospitalized for treatment. On the 7th day after being discharged, the patient who had pain, redness, and foot drop that developed in his right leg was diagnosed with ischemic myositis and foot drop due to popliteal artery thrombosis. Because the clinical condition of the patient undergoing a percutaneous transluminal angioplasty (PTA) was not improved and a necrotic demarcation line appeared, the right leg of the patient was amputated above the knee. This case shows that cases of venous thromboembolism as well as arterial thrombosis in COVID-19 patients can lead to negative consequences leading to amputation.

Conclusions: In order to prevent this condition, it will be effective to continue therapeutic anticoagulation for at least 2 more weeks after discharge to avoid arterial and venous thrombosis.

Key words: *COVID-19, thrombosis, myositis, foot drop, popliteal arter.*

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Introduction

COVID 19 was first isolated in humans in the 1960s but was not thought to cause death in humans (1). However, this belief has changed as a result of the pandemic that began in December 2019 after the World Health Organization identified COVID-19 as a new viral pneumonia (1). The coronavirus disease, first detected in Wuhan, Hubei Province, China, and called COVID-19, has spread rapidly throughout the world through respiration (1). In March 2020, the World Health Organization declared a pandemic, reporting that there were more than 118,000 COVID-19 patients in 114 countries and that the disease was spreading worldwide (2).

Since the beginning of the coronavirus disease 2019 (COVID-19) pandemic, the association between coagulation abnormalities, including disseminated intravascular coagulation and hypercoagulable state, and COVID-19 has been increasingly reported. Corona virus infection activates the inflammation and multiple systemic coagulation response. Increased proinflammatory cytokines trigger coagulation and consumptive coagulopathy.

Here, we aimed to present an amputation case that developed as a result of arterial coagulopathy after covid 19 infection.

Case Report

A 68-year-old male patient, who was admitted to the pandemic hospital one month ago with cough, fever and weakness complaints, was diagnosed with COVID-19. The patient was hospitalized and received 9 days of Favicovir treatment and low-molecular-weight heparin treatment. The patient developed redness and pain in the right leg and foot droop 1 week after discharge. The patient who presented to the emergency service and was thought to have cellulitis, began to be given Amoxicillin-clavulanic acid 1000 mg two times a day, Diosmin 500 mg two times a day, Dexketoprofen 25 mg two times a day and Enoxaparin 0.6 mL 2 subcutaneous (sc) treatment, and the patient was referred to the dermatology outpatient clinic. The patient presented to the dermatology outpatient clinic, the dermatology service considered eosinophilic fasciitis during the preliminary diagnosis and requested a biopsy and a contrast-enhanced MRI of the right tibia. The MRI findings revealed more pronounced edematous signals in the skin/subcutaneous tissues of the distal anterolateral region of the right crus, increased diffused edematous signals in the tibialis anterior and flexor digitorum longus muscles, and contrast fixations with faint borders (myositis?). The possibility of eosinophilic fasciitis was ruled out. The patient's condition was consulted to us due to myositis and drop foot. The patient's history had coronary artery disease (CAD) and 25 years of diabetes mellitus (DM). He had no sensory-motor complaint suggesting polyneuropathy (PNP) before the complaint.

Physical examination of the patient revealed erythema, pain with palpation and sensitivity in the right pretibial region. On the front face of the tibia, vesiculobullous and hemorrhagic lesions with linear placement were discovered. The right extensor hallucis longus and dorsiflexion muscle strength was 0 out of 5. There was a foot drop on the right foot. The patient was asked to undergo hemogram sedimentation and C-reactive protein (CRP) tests, and, to determine the cause of his foot drop, an electromyography (EMG) test. The laboratory results were as follows: white blood count (WBC) = 11, CRP = 57, and erythrocyte sedimentation rate (ESR) = 59. The EMG test revealed a chronic

polyneuropathy of mixed type, and a partial lesion in the tibial nerve and a near-complete lesion in the peroneal nerve, which led to subacute axon damage to the leg segment of the peroneal and tibial nerves. The patient's polyneuropathy of mixed type was linked to the existing DM disease, and the subacute axonal damage to the peroneal and tibial nerves was thought to occur secondary to myositis-related edema and inflammation. The patient was referred to cardiovascular surgery (CVS) and infectious diseases services in terms of possible vascular pathologies. The infectious diseases service began administering Cipro 500 mg two times a day and Ceftriaxone treatment to the patient. In CT angiography (CTA), critical leg ischemia was detected in the right popliteal artery, and peripheral artery revascularization was achieved by administering a percutaneous transluminal angioplasty (PTA) to the popliteal artery. The condition of the patient was consulted to the dermatology and neurology services during his hospitalization. In his neurological evaluation, the onset of the complaints with pain and algidity after COVID-19 suggests that the clinical picture may be associated with malnutrition in the foreground. The presence of pain, secondly, can suggest an atypical diabetic amyotrophy. However, rather than edema, a pronounced atrophy is expected in the post-pain period. First of all, it was recommended that the condition of the patient who had a d-dimer level above 1000 be consulted to the CVS service in terms of recommendations on advanced vascular imaging and low-molecular-weight heparin treatment. Second, it was suggested that the patient begin receiving pregabalin 75 mg two times a day for pain, that the dose be increased if necessary, that the patient receive B12 support therapy, and that his EMG be checked within the first month. In the dermatology evaluation, the erythematous area in the leg was considered to be related to ischemia. It was recommended that a gauze patch soaked in physiological saline solution be applied twice a day to the area where ischemic necrosis had begun. Following that, it was recommended to treat the affected area by wiping the wetness with a dry gauze patch and impregnating a single layer gauze patch with a mixture of Fucidin cream + Vaseline and leaving the patch on the area. The CVS service reassessed the patient. There were no signs of occlusion or thrombus on the arterial and venous Doppler ultrasound scans. Pentoxifylline 600 mg was started as a once-a-day treatment. A referral to rheumatology was suggested to the patient whose complaints did not improve during the follow-up period. Despite the fact that no obvious primary vasculitis findings were detected on the skin during the rheumatological consultation, tests for polyarteritis nodosa (PAN) vasculitis or myositis were requested based on the patient's current clinical condition. Histopathological diagnosis was suggested with the existing comorbidities. Creatine kinase (CK) values were normal in terms of myositis. Accordingly, it was recommended to regulate glycemia, evaluate the area for biopsy including deep dermis if skin findings persist despite local treatment, and consult to the neurology service in terms of EMG and muscle biopsy indications according to the myopathy protocol of the patient whose CK values were normal in terms of myositis. The result of the rheumatoid factor (RF) test administered to the patient was 18 IU/mL, that is, positive. Other rheumatological tests (ANA, PR3 ANCA antimyeloperoxidase, MPA ANCA) were negative. The patient's clinical condition and acute phase values gradually deteriorated. At this point, orthopedics was consulted, and amputation was recommended for the patient when a demarcation line formed. The patient's leg was amputated above the knee as acute phase reactants continued to be high and a demarcation line formed during the follow-up.

Discussion

Although the cause of hemostatic system irregularity in COVID-19 infection is not fully known, the severe inflammatory response generated by the virus is thought to disrupt the coagulation cascade (3). Cytokine storms have been shown to stimulate coagulation cascade and pave the way for microvascular thrombus formation through monocyte macrophage cells and vascular endothelial cells (4). Increases in IL-6, one of the proinflammatory cytokines, have been linked to higher fibrinogen levels. This supports the relationship between inflammation and procoagulant factors (5).

Venous thromboembolism has been shown to be an important cause of morbidity and mortality in both hospitalized patients and the intensive care unit patients among COVID-19 patients (6–8). Incidence of venous thromboembolism (VTE) in patients with COVID-19 is between 0–8% in services and 16–35% in intensive care units (9). This rate was reported as 58% in postmortem autopsies performed on patients who died due to COVID-19 (9). On the other hand, there are also case reports of arterial thrombosis detected in coronary arteries (6,10) and brain (6,11), and in mesenteric (12-14) and aortoiliac (6,12) arteries. Singh et al. (15) identified patients with tibial artery, visceral aorta, popliteal artery, and iliac artery occlusions following COVID-19 infection, as well as a case of hemiplegia due to left middle cerebral artery occlusion during hospitalization due to COVID-19. Levolger et al. (16) identified 4 cases of arterial thrombosis with occlusion in the common iliac arteries, subclavian arteries, internal carotid artery, and proximal superior mesenteric artery. Goldman et al. (17) conducted a study to determine the presence and magnitude of the relationship between lower extremity arterial thrombosis and COVID-19 after discovering an increase in positive lower extremity CT angiography (CTA) examinations in patients with leg ischemia during the peak of the COVID-19 pandemic. They retrospectively examined the radiological records of patients who were admitted to the emergency department of their hospital with complaints of leg pain and discoloration and underwent CT angiography in January–April 2019 and during the same period of a year earlier. They compared 16 COVID-positive patients and 32 COVID-negative patients. In CTAs of all patients with COVID-19 infection, arterial thrombosis was found in the lower extremity, compared to 69% in COVID-negative individuals. When the subsequent surveys of these patients were examined, amputation was necessary in 4 of the 16 COVID-positive patients who were diagnosed with clots, while only 1 of the 22 COVID-negative patients who were diagnosed with clots underwent amputation. While 6 of the COVID-positive patients died, 1 patient died in the COVID-negative group. In conclusion, the lower extremity arterial thrombosis associated with COVID-19 has been reported to be characterized by greater thrombus burden and increased amputation and mortality rates. Popliteal artery thrombosis developed after COVID-19 infection in our patient, too, and the patient's leg was amputated above the knee after there was no response to the conservative treatment.

Irregularity in clotting parameters and high d-dimer levels were found to be associated with poor prognosis in COVID-19 patients (18,19). LMWH and unfractionated heparin (UFH) are recommended by the World Health Organization to prevent the risk of venous thromboembolism in these patients (20). While the authors recommend VTE prophylaxis for hospitalized patients, many argue that this scope should be extended and continued at home for another 7–14 days after discharge (21-23). On the other hand, its role in

preventing arterial thromboembolism is unknown. Our patient used LMWH during the hospitalization period but did not use it after discharge. This resulted in thrombosis in the right popliteal artery. When PTA and medical therapy failed to improve the patient's condition, his leg was amputated above the knee.

Conclusion

In patients who have COVID-19 infection, it is important for early diagnosis that those presenting with extremity pain and discoloration complaints may have arterial thrombosis. Continued anticoagulation treatment for another 7–14 days, not only while in the hospital but also after discharge, will be effective in preventing arterial and venous thrombosis in COVID-19 patients.

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References

1. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVİD-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA 2020;323(13):1239.
2. World Health Organization. WHO director-general's opening remarks at the media briefing on COVİD-19—11 March 2020 [Internet]. Geneva: World Health Organization; 2020 [cited at 2020]. Available from: https://www.who.int/dg/ speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-COVID-19-11-march-2020.
3. Marietta M, Coluccio V, Luppi M. COVİD‑19, coagulopathy and venous thromboembolism: more questions than answers. Internal and Emergency Medicine https://doi.org/10.1007/s11739-020-02432-x.
4. Grover SP, Mackman N. Tissue factor: an essential mediator of hemostasis and trigger of thrombosis. Arterioscler Thromb Vasc Biol 2018;38:709–725.
5. Ranucci M, Ballotta A, Di Dedda U, Bayshnikova E, Dei Poli M, Resta M at al. The procoagulant pattern of patients with COVİD-19 acute respiratory distress syndrome J Thromb Haemost 2020;18(7):1747-1751.
6. Lodigiani C, Iapichino G, Carenzo L, et al. Venous and arteriyel thromboembolic complications in COVİD-19 patients admitted to an academic hospital in Milan, Italy. Thromb Res. 2020;191:9-14.
7. Middeldorp S, Coppens M, van Haaps TF, Foppen M, Vlaar AP, Müller MCA et al. Incidence of venous thromboembolism in hospitalized patients with COVİD-19. J Thromb Haemost 2020;18(8):1995-2002.
8. Llitjos JF, Leclerc M, Chochois C, Monsallier JM, Ramakers M, Auvray M et al. High incidence of venous thromboembolic events in anticoagulated severe COVİD-19 patients. J Thromb Haemost. 2020;18(7):1743-1746.
9. Wichmann D, Sperhake JP, Lütgehetmann M, Steurer S, Edler C, Heinemann A et al. Autopsy findings and venous thromboembolism in patients with COVİD-19: a prospective cohort study. Ann Intern Med. 2020 Aug 18;173(4):268-277.

10. Dominguez-Erquicia P, Dobarro D, Raposeiras-Roubín S, Bastos-Fernandez G, Iñiguez-Romo A. Multivessel coronary thrombosis in a patient with COVİD-19 pneumonia (published online ahead of print, 2020 May 6). Eur Heart J. 2020 ;7;41(22):2132.
11. Hess DC, Eldahshan W, Rutkowski E. COVİD-19-Related Stroke. Transl Stroke Res. 2020;1-4.
12. Vulliamy P, Jacob S, Davenport RA. Acute aorto-iliac and mesenteric arteriyel thromboses as presenting features of COVİD-19. Br J Haematol. 2020;189(6):1053-1054.
13. De Barry O, Mekki A, Diffre C, Seror M, Hajjam ME, Carlier RY. Arteriyel and venous abdominal thrombosis in a 79-year-old woman with COVİD-19 pneumonia (published online ahead of print, 2020 Apr 29). Radiol Case Rep. 2020; 29;15(7):1054-1057.
14. A Beccara L, Pacioni C, Ponton S, Francavilla S, Cuzzoli A. Arteriyel Mesenteric Thrombosis as a Complication of SARS-CoV-2 Infection. Eur J Case Rep Intern Med. 2020;30;7(5):001690.
13. Singh G, Attique H, Gadela N, Mapara K, Manickaratnam S et al. COVİD-19 Related Arteriyel Coagulopathy. Cureus 2020;12(7): 9490.
15. Levolger S, Bokkers RPH, Wille J, Kropman RHJ, Vries JPM. Arteriyel thrombotic complications in COVİD-19 patients J Vasc Surg Cases Innov Tech2020;6(3):454-459..
16. Goldman JA , YE K, Scheinfeld MH. Lower-extremity Arteriyel Thrombosis Associated with COVİD-19 Is Characterized by Greater Thrombus Burden and Increased Rate of Amputation and Death. Radiology 2020;297(2):263-269.
17. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. 2020;18:844–847.
18. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med. 2020;180(7):934-943.
19. WHO Interim guidance (2020) Clinical management of severe acute respiratory infection (SARI) when COVİD-19 disease is suspected. Published 13 March 2020. https ://apps.who.int/iris/ handl e/10665 /33144 6. Accessed May 5 2020.
20. Marietta M, Ageno W, Artoni A, De Candia E, Gresele P, Marchetti M, Marcucci R, Tripodi A. COVİD-19 and haemostasis: a position paper from Italian Society on Thrombosis and Haemostasis (SISET). Blood Transfus. 2020 May;18(3):167-169.
21. Zhai Z, Li C, Chen Y, Gerotziafas G, Zhang Z, Wan J et al. Prevention treatment of VTE associated with COVİD-19 Infection Consensus Statement Group. Prevention and treatment of venous thromboembolism associated with coronavirus disease 2019 infection: a consensus statement before guidelines. Thromb Haemost. 2020 Jun;120(6):937-948.
22. American Society of Hematology COVİD-19 Resources. COVİD19 and VTE/Anticoagulation: frequently asked questions. https :// www.hemat ology .org/COVİD -19/COVİD -19-and-vte-anticoagulation. Accessed 06 May 2020.

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