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COVID-19 Presented With Deep Vein Thrombosis: An Unusual Presenting

Lotfollah Davoodi, MD[1], Hamed Jafarpour, MD[2], Morteza Taghavi, MD[3], and Alireza Razavi, MD[2]

Abstract

On December 31, 2019, the World Health Organization was informed of a cluster of cases of pneumonia of unknown cause detected in Wuhan City, Hubei Province, China. The pneumonia was caused by a virus called SARS-Cov-2 (severe acute respiratory syndrome coronavirus 2), which was later named coronavirus infectious disease 2019 (COVID-19). The symptoms most commonly reported by patients affected by COVID-19 include fever, dry cough, and shortness of breath. In this report, we present a case of a 57-year-old woman who presented to the clinic's infectious department with swelling, pain, warmth, and redness in the left leg who was treated with therapeutic heparin. There were no typical and distinguished symptoms of COVID-19, and she had no risk factor for deep vein thrombosis. Then chest X-ray revealed bilateral patchy ground-glass opacity, and computed tomography angiography was performed to rule out pulmonary thromboembolism, which showed no evidence of thrombosis. Left lower limb venous color Doppler ultrasound revealed dilatation and thrombosis in the external iliac and left iliac veins up to the level of the bifurcation of the common iliac veins, as well as thrombosis to the superficial and small saphenous veins. Because of ground-glass opacity and lymphopenia, nasal swabs were used for sampling, and SARS-CoV-2 nucleic acid was detected by reverse transcription polymerase chain reaction (RT-PCR). This case aims to arouse the medical staff's awareness of deep vein thrombosis as a clinical symptom of COVID-19 even if the patient has no typical symptoms of COVID-19.

Keywords

COVID-19, deep vein thrombosis, pulmonary thromboembolism, bilateral patchy ground-glass opacity

Introduction

On December 31, 2019, the World Health Organization was informed of a cluster of cases of pneumonia of unknown cause detected in Wuhan City, Hubei Province, China. The pneumonia was caused by a virus called severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2), which was later named coronavirus infectious disease 2019 (COVID-19). Symptoms are similar to the common cold, most notably fever and dyspnea.[1,2] The disease is highly contagious, and the World Health Organization's 51st situational report on March 11, 2020, announced a total of 118 319 people affected and 4292 deaths.[3] It is possible that SARS-CoV-2 enters host cells through the binding of spike glycoprotein to the enzyme 2 angiotensin-converting enzyme (ACE2), sialic acid receptor, transmembrane 2 serine proteinase (TMPRSS2), and extracellular slow cell matrix metalloproteinase (CD147). This condition, which causes endothelial dysfunction, is exacerbated by hypoxia and causes thrombosis by increasing blood viscosity as well as the signaling pathway associated with the hypoxia transcription factor.[4] In this report, we present a patient with COVID-19 who developed deep vein thrombosis (DVT).

Case Presentation

A 57-year-old woman presented to the clinic's infectious department with swelling, pain, warmth, and redness in the left leg on March 17, 2020. Also, she complained of mild dry cough since 3 days ago. She had no history of an underlying disease, drug usage, smoking, and also did not have a history of recent surgery, trauma, and insect bite. Her temperature was 38 °C, and other vital signs were normal. Oxygen saturation was 90%. On physical examination, the dilated superficial vein of the calf was observed and she had

[1]Department of Infectious Diseases, School of Medicine, Antimicrobial Resistance Research Center, Mazandaran University of Medical Sciences, Sari, Iran
[2]Student Research Committee, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran
[3]Department of Cardiology, School of Medicine, Cardiovascular Research Center, Mazandaran University of Medical Sciences, Sari, Iran

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Corresponding Author:
Alireza Razavi, MD, Student Research Committee, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.
Email: razavialireza33@gmail.com

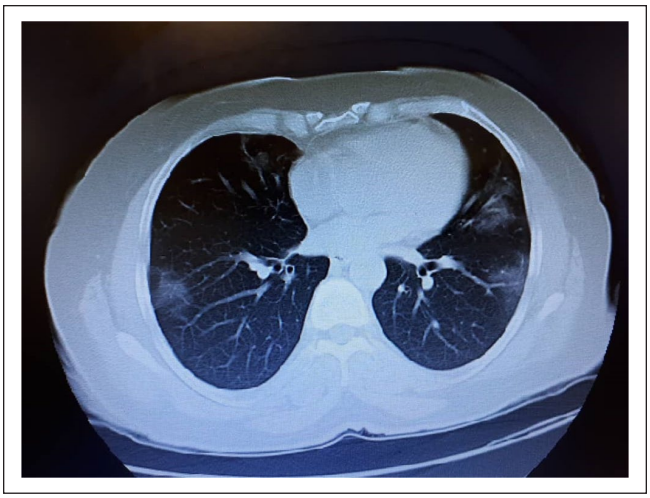

Figure 1. Chest computed tomography showed persistent multifocal ground-glass opacities with or without superimposed reticulation.

tenderness along veins. The difference in diameters of calf compared with the right side was 6 cm. Routine laboratory tests and imaging was requested. Laboratory tests revealed elevated white blood cell count was 2300 $\times$ 10^9/L (with 65.7% neutrophils and 23% lymphocytes), thrombocytopenia (138 $\times$ 10^3/μL), and also elevated C-reactive protein level (47 mg/L, normal: <10 mg/L), lactate dehydrogenase (655 U/L, normal range = 140-280 U/L), D-dimer (1.3 μg/mL, normal range: <0.5 μg/mL), and aspartate aminotransferase (59 U/L, normal range = 10-40 U/L). Initially, chest X-ray revealed bilateral patchy ground-glass opacity (GGO), and computed tomography (CT) angiography was performed to rule out pulmonary thromboembolism, which showed no evidence of thrombosis (Figure 1). Left lower limb venous color Doppler ultrasound revealed dilatation and thrombosis in the external iliac and left iliac veins up to the level of the bifurcation of the common iliac veins, as well as thrombosis to the superficial and small saphenous veins (Figures 2 and 3). There was no evidence of vascular flow. Finally, DVT was definitely diagnosed. Thrombus in inferior vena cava was not observed. Other tests including antinuclear antibody, anti-double-stranded DNA, rheumatoid factor test, anti-cardiolipin antibodies, factor V Leiden, and S, C protein test were normal. Because of GGO and lymphopenia, nasal swabs were used for sampling, and SARS-CoV-2 nucleic acid was detected by RT-PCR (reverse transcription polymerase chain reaction). Considering to DVT and COVID19, heparin at a dose of 80 units/kg intravenous bolus, then continuous infusion of 18 units/kg/h, chloroquine 400 mg single dose, and lopinavir/ritonavir (Kaletra) 400 mg twice daily were started. After a week, RT-PCR of nasal swabs was negative; swelling and tenderness had been disappeared gradually. The patient discharged with the normal condition and starting rivaroxaban (10 mg per os daily).

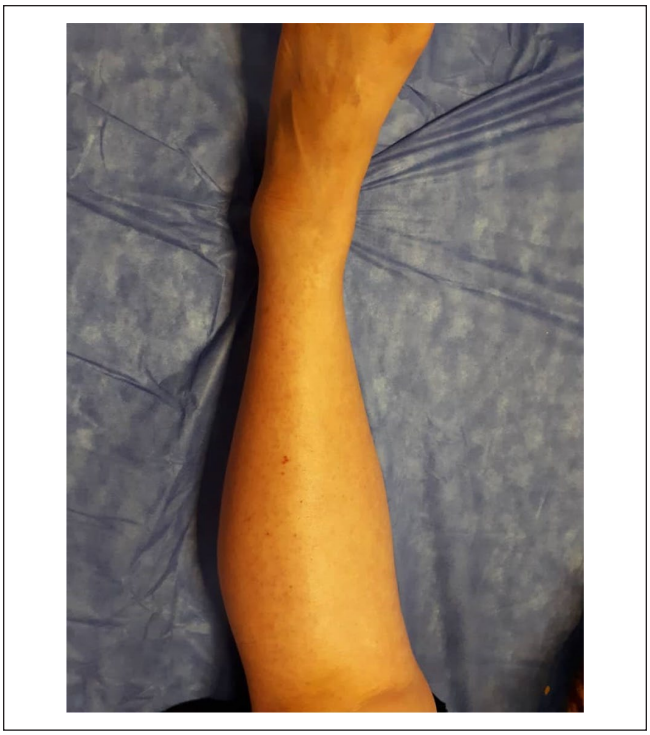

Figure 2. Clinical image of redness, and leg swelling due to deep vein thrombosis.

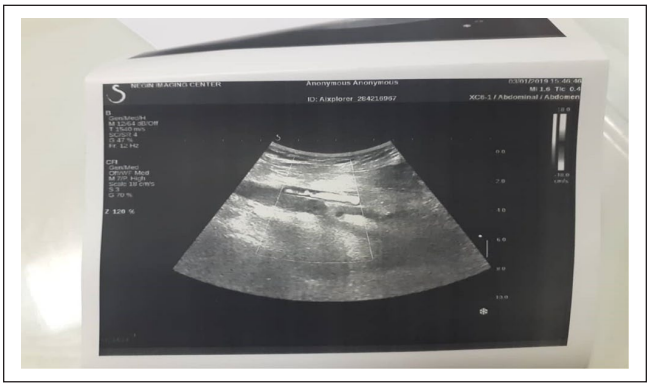

Figure 3. Abdominal color Doppler ultrasound image for deep vein thrombosis detection.

Discussion

The symptoms most commonly reported by patients affected by COVID-19 include fever, dry cough, and shortness of breath.[1] There were no typical and distinguished symptoms of COVID-19 in our patient, and the patient presented with typical symptoms of DVT, such as swelling, redness, and tenderness. While she had no risk factor for DVT, laboratory tests and chest X-ray tests showed COVID-19, which was eventually confirmed by RT-PCR testing. The most stable hemostatic abnormalities with COVID-19 include mild thrombocytopenia[5] and increased D-dimer levels.[6] There have been reports of thrombotic disorders with organ

dysfunction in patients with COVID-19 resulting in higher mortality[7] but there are few reports of DVT in patients with COVID-19. In a study by Zhou et al, a patient with COVID-19 presented with symptoms of acute cerebral infarction. After CT angiography, acute cerebral infarction and DVT in both lower limbs were confirmed.[8] In our case, DVT was suspected due to redness, pain, and tenderness at the leg veins, which was seen by color Doppler ultrasound in external iliac, common iliac, small saphenous, and large saphenous. Seeing this lesion on the leg, our patient was initially suspected of having thromboembolism, which, after a CT scan, revealed a person with COVID-19, with no evidence of pulmonary thromboembolism. However, in some studies, respiratory deterioration with other clinical evidence of venous thrombosis should lead to suspected pulmonary embolism (PE).[9,10] In a study by Fu et al, 2 middle-aged patients with a history of acute ischemic stroke in middle age developed COVID-19 with neurological symptoms of acute ischemic stroke, including paralysis of the tongue, dysarthria, and weakness of the limb muscles. Despite high levels of D-dimer, they showed no signs of DVT,[11] which was different from our study. Eventually, CT of the head and neck showed blockage of cerebral arteries, blockage of small vessels, and an acute ischemic stroke was confirmed.[11] In a study by Klok et al, 128 patients with COVID-19 symptoms were admitted to the intensive care unit. The cumulative incidence of thrombotic disorders was 31%. Using CT pulmonary angiogram or ultrasonography, venous thromboembolism was detected at 27% and arterial thrombotic events at 3.7%. PE was the most common thrombotic complication (81%). DVT was also diagnosed in 3 patients. These disorders occurred after the diagnosis of COVID-19 in patients due to hospitalization,[12] which was different from our patient. Also in some patients with COVID-19, nonspecific myocardial damage, renal dysfunction (leading to troponin accumulation), myocarditis, PE, and myocardial infarction type I and II due to hospitalization and, as a result, coagulation disorders were observed.[7]

The initial assumption is that DVT is a secondary lesion after COVID-19. The possible mechanism may be that coronavirus attacks the human body through the enzyme 2-angiotensin-converting enzyme,[13] which is distributed over blood vessels and various organs. The virus then causes cytokine waterfalls, which can increase blood clotting problems and damage.[4] Finally the blood clots of DVT can be caused by anything that prevents blood from circulating or clotting normally, such as injury to a vein, surgery, certain medications, and limited movement,[5,14] but the exact cause of DVT caused by COVID-19 is still unknown.

Conclusion

The exact mechanism of DVT formation due to COVID-19 is unknown despite thrombocytopenia and has not been investigated but it resolved as COVID-19 symptoms, tenderness, and leg pain improved. Although COVID-19 presented with DVT is a rare condition, in middle-aged people with sudden onset of manifestations, we should recognize DVT from other symptoms as an important and treatable symptom for COVID-19 diagnosis. Rapid diagnostic assays, efficient treatment, and prudent use of CT scan are important to control future COVID-19 spread.

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Author Contributions

AR analyzed the data and was a major contributor in writing the manuscript. MT performed the diagnostic tests. LD collected the clinical data. LD designed the case report and was responsible for communicating the work. All authors read and approved the final manuscript. HJ edited clinical data.

Declaration of Conflicting Interests

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Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series. Consent for publication.

Informed Consent

Informed consent for patient information to be published in this the article was not obtained because our institution does not require informed consent for individual case reports.

ORCID iD

Alireza Razavi https://orcid.org/0000-0002-4386-4672

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