A case report of greater saphenous vein thrombosis in a patient with coronavirus (COVID-19) infection

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Case report

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Abstract

In December 2019, the World Health Organization (WHO) announced a series of pneumonia cases caused by an unknown origin, discovered in Wuhan, China. A dangerous virus called SARS-Cov-2 (severe acute respiratory syndrome coronavirus 2) caused a disease named acute respiratory syndrome, which was later popularly called coronavirus infection (COVID-19). Patients with acute COVID-19 are at high risk for thrombosis in various blood vessels due to over-coagulation, blood stasis, and endothelial damage. To date, very little research has been done on the number and side effects of thromboembolic disorders in patients with COVID-19. In this study, we report a case with COVID-19, who was hospitalized in one of the hospitals in Sanandaj, Iran. There were symptoms of fever, chills, muscle aches, cough, and tachycardia. Laboratory tests such as CRP, ESR, Ferritin CLIA, LDH and D-Dimer were observed in this patient at a high level. Doppler ultrasound of this patient revealed an abnormal finding, thrombosis in the right greater saphenous vein. This suggests that COVID-19 may lead to other side effects through damage to blood vessels.

Introduction

Coronavirus has been widespread around the world since the early 2020. The disease is highly contagious and, in severe cases, can lead to acute respiratory syndrome or organ failure[1, 2]. In January 2020, the World Health Organization (WHO) announced the outbreak of the disease as a "public health emergency of International concern" (PHEIC)[3]. So far, the acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused by Coronavirus 2019 (COVID-19) has led to an unprecedented global health crisis with the deaths of more than 600,000 people worldwide. It is estimated that in some countries the mortality rate is around 15%[4]. Studies have shown that venous insuiciency and its complications are one of the most common issues in medical science [5–7].

Premature detection and early treatment of deep vein thrombosis (DVT) due to complications such as pain, swelling, and pulmonary embolism are still significant medical issues[8, 9]. Additionally, several studies have shown that superficial vein thrombosis (SVT) is a common venous disease that appears to be medically benign and can cause serious complications in the body[10, 11].

The prevalence of SVT is estimated to be about 3 to 11 percent among members of a community, while the incidence of thrombosis in the greater saphenous vein (GSV) is disproportionately about 60 to 80 percent of the time[12, 13]. Clinically, GSV thrombosis has been shown to be affected by factors such as heat, edema, and palpable subcutaneous cords in the affected limb[14]. Various studies have shown that factors such as advanced age, smoking, obesity, neoplasm, pregnancy, birth control pills, hormone therapy, autoimmune diseases, and recent surgeries increase the incidence of SVT such as pulmonary embolism (PE) and DVT[15]. In addition, the prevalence of SVT is reported to be two to three times higher than in PE and DVT[16]. SVTs in the proximal greater saphenous vein are the focus of our research in this study. The proximity of the greater saphenous vein to the saphenofemoral junction (SFJ) makes SVT a
serious concern due to the possibility of displacement of blood clots and their entry into the deep venous system[17].

Patients with SARS-CoV-2 are at risk for venous and arterial thrombosis due to excessive coagulation status, blood stasis in blood vessels, and damage to vascular endothelial cells[18]. As the clinical signs of venous and arterial thrombosis are ambiguous, it is very important to use imaging techniques such as Doppler ultrasound and computed tomography (CT) angiography to prevent catastrophic complications such as pulmonary embolism and mortality[19].

A number of studies have also reported that severe cases of COVID-19 are associated with high concentrations of cytokines, including IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1A, and TNFα[20, 21]. In this study, a 40-year-old man with coronavirus who was hospitalized with a right greater saphenous vein thrombosis at Tohid Hospital in Sanandaj, Iran is reported. The risk classification of DVT and SVT is of fundamental importance for predicting the side effects of coronavirus.

**Case Presentation**

A 40-year-old man with one-week symptoms of cough, fever, fatigue, muscle aches, diarrhea, palpitations, and shortness of breath but no chest pain was admitted to Tohid Hospital, Sanandaj, Iran. CT scans (Fig. 1) and the real-time reverse transcriptase-polymerase chain reaction (RT-PCR) method had both confirmed the infection with coronavirus. The patient with a diagnosis of very mild COVID-19 was transferred to one of the hospital coronavirus wards. He had no history of underlying diseases such as diabetes, heart disease, hypertension, or cancer. At the hospital's emergency department, the physical examinations showed that the patient had an irregular heart rate of 145 beats/min, blood pressure of 82/75 mm Hg, temperature of 38.4 °C, respiratory rate of 26 breaths/min, and oxygen saturation of 89%. After the patient’s admission to the hospital, a coronavirus test was again performed using a kit to confirm the previous diagnosis, which fully indicated the presence of the disease. Paraclinical and laboratory results showed that routine blood tests, renal function, and electrolytes were completely normal. The influenza A and B antigen tests were negative. However, the other laboratory findings were completely abnormal, which are briefly listed in Table 1. Therefore, all antiviral, anticoagulant, and supportive treatments were started for the patient.
Table 1
The results of laboratory findings

| Test Name                  | Unit    | Reference Range   | results | Flag |
|----------------------------|---------|-------------------|---------|------|
| 1 BUN                      | mg/dl   | 6–20              | 32      | Hi   |
| 2 CPK                      | IU/L    | male: 0-171       | 55      |      |
| 3 LDH                      | U/L     | 235–470           | 510     | Hi   |
| 4 Na(ser)                  | mEq/L   | 138–145           | 134     | LOW  |
| 5 K(ser)                   | mEq/L   | 3.6–5.9           | 3.8     |      |
| 6 Cr                       | mg/dl   | male: 0.8–1.3 mg/dl | 0.7  | LOW  |
| 7 CRP                      | mg/l    | 0–6               | 30      | Hi   |
| 8 ESR                      | mm      | 5–12              | 18      | Hi   |
| 9 Ferritin CLIA            | ng/mL   | 50–434            | 511     | Hi   |
| 10 D-Dimer (CLIA-Siemens)  | ng/mL   | < 885             | > 7500  | Hi   |

Three days after hospitalization, Doppler ultrasound was performed on the lower limb due to numbness and tingling (paresthesia) of the right leg, in addition to swelling, redness, pain, and sensitivity to touch. Examination of the main veins of both lower limbs showed no evidence of occlusion in the external iliac, common femoral, popliteal, anterior and posterior tibialis, and peroneal. The veins were not compressed and there was flow in them. However, more detailed examination revealed that thrombosis was evident at the beginning of the greater saphenous vein of the right leg from distal to proximal (Fig. 2). The patient was discharged after 12 days of hospitalization with complete recovery of COVID-19 and continuous treatment for the venous thrombosis in the greater saphenous vein of the right leg.

Discussion

Symptoms such as fever, dry cough, shortness of breath, and muscle pain are commonly reported in patients with COVID-19[22]. There was no distinct COVID-19 symptom in this patient, and he had normal SVT symptoms such as swelling and pain sensitivity. While he had no risk factors for SVT, paraclinical tests and CT scans of the chest showed COVID-19, which was also confirmed by a laboratory kit.

Studies have shown that the most important and stable hemostatic disorders associated with COVID-19 include mild thrombocytopenia[23] and an increase in D-dimer amount[24]. Numerous studies have shown that thrombotic abnormalities, along with abnormalities in the function of various organs in patients with COVID-19[25] lead to higher mortality, but there are few reports of SVT and its side effects in patients with COVID-19. In a 2020 study on a patient with COVID-19, CT images of angiography showed signs of acute cerebral infarction and DVT in both lower limbs[26].
According to the Chinese National Health Commission, patients with severe COVID-19 are defined based on one of the following symptoms\[20\]: (a) acute respiratory syndrome, in which patient is able to breathe through mechanical ventilation, (b) shock, and (c) dysfunction of organs or other systems of the body. In addition, studies have shown that patients with COVID-19 are prone to DVT. Pathophysiologically, patients with COVID-19 have been shown to be candidates for venous thrombosis, usually due to diarrhea, hypotension, recurrent long-term infections, and dehydration\[20\]. Therefore, in patients with coronavirus, assessing the risk of DVT and SVT are essential to reduce complications and mortality risk. Studies have shown that patients prone to DVT usually have one of the following criteria: age over 75, respiratory and heart failure, history of previous thrombosis, acute onset of chronic pulmonary obstruction, acute cerebral infarction, malignant tumor, limb varicose veins, obesity, chronic kidney disease, inflammatory bowel disease, and more than 3 days of bed rest\[27\].

In our study, the patient was at first suspected of having thromboembolism because of similar lesions on his leg, but after a CT scan of his chest, he was diagnosed with COVID-19 and there was no evidence of pulmonary thromboembolism. The physicians at the hospital also suspected SVT and DVT due to numbness, swelling, and pain in the right leg, which were examined by Doppler ultrasound of all blood vessels, including the common iliac, small saphenous, and greater saphenous. As many studies have reported respiratory distress along with other clinical evidence of venous thrombosis, the pulmonary embolism should be suspected\[28, 29\].

A recent study of patients with coronavirus found that the rate of thrombotic disorders in these patients was 31%. Medical imaging has also shown that 27% of thrombosis is due to venous thromboembolism and 3.7% to arterial thrombosis. 81% related to pulmonary embolism, which is the most common complication of thrombosis. The study also found that coronavirus disease may be associated with myocardial damage, renal dysfunction, and myocardial infarction due to hospitalization and coagulation disorders\[30\]. The possible reasons for venous thrombosis may include the fact that the COVID-19 attacks the human body via the 2-angiotensin converting enzyme, which is found in various blood vessels and organs of the body\[31\]. Ultimately, coronaviruses cause cytokine waterfalls, including IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1A, and TNF\(\alpha\) in the body, which can increase the risk of complications such as blood clots. This cytokine storm can be related to the severity of the disease and its negative consequences\[21, 32\]. Blood clots formed in deep vein thrombosis may have a variety of causes, including vascular damage, surgery, special medications, and limited mobility\[33\] but the exact cause of COVID-19-induced deep vein thrombosis is still a mystery\[34\].

In summary, in this case report, we present one patient with mild COVID-19 who was hospitalized with a thrombosis in his right greater saphenous vein at one of the hospitals in Sanandaj, Iran. The risk classification of deep vein thrombosis and superficial vein thrombosis are of fundamental importance for predicting the side effects of coronavirus.

**Conclusion**
The main mechanism and process of DVT and SVT formation due to COVID-19 is unknown, despite deficiency of platelets in the blood and has not been examined but is determined as coronavirus signs. Although a COVID-19 case presented with DVT and SVT is a rare case, but in middle-aged patients with sudden start of clinical manifestations, we need to distinguish DVT and SVT from other significant and treatable signs for COVID-19. As for the rapid diagnosis, effective treatment is essential to control the spread of COVID-19.

Declarations

Ethical Approval and Consent to participate: This research has been confirmed by the Research Center of Kurdistan University of Medical Sciences and Ethics Committee with the file number IR.MUK.REC.1399.087.

Consent for publication: Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article which was approved by the Research Center of Kurdistan University of Medical Sciences.

Availability of data and materials: I have presented the data of the patient in the manuscript as a Table. I have submitted the figures separately as figures.

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Authors' contributions: MBHS supervised the study and wrote the manuscript; PF collected the clinical data; MA and FF analyzed the data and images; and NHS reviewed the manuscript.

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**Figures**
Figure 1

axial without contrast-enhanced chest computed tomography (CT) image showing a coronavirus disease (COVID-19) infection
Figure 2

Doppler ultrasound images of the lower right limb showing a superficial vein thrombosis (SVT). Anterior accessory saphenous vein (AASV), great saphenous vein (GSV), common femoral vein (CFV), and common femoral artery (CFA) in the Doppler ultrasound images of the lower right limb.