

Deep vein thrombosis with pulmonary thromboembolism in a case of severe COVID-19 pneumonia

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SUMMARY

A 53-year-old man with diabetes came to the emergency department with fever and dry cough for 5 days, swelling of the left leg for 2 days, shortness of breath and chest pain for 1 hour. He had raised temperature, tachycardia, tachypnoea, reduced oxygen saturation and swollen tender left leg on examination. The frontal chest radiograph showed bilateral ground-glass opacities; he tested positive for COVID-19 with elevated D-dimer. The colour Doppler examination of the left leg revealed acute deep vein thrombosis (DVT) of the common femoral and the popliteal veins. The chest CT showed bilateral diffuse ground-glass opacities predominantly involving peripheral zones and the lower lobes. The CTPA revealed left pulmonary thromboembolism (PTE), treated with low-molecular-weight heparin. COVID-19 predominantly affects the respiratory system. DVT and PTE are common in COVID-19 but lethal. They should be diagnosed early by clinical and radiological examinations and treated promptly with anticoagulants.

BACKGROUND

The coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), was declared a pandemic by the WHO on March 11, 2020.^{1,2} Although it primarily affects the respiratory system, there are abundant reports on thrombotic complications. In patients with COVID-19, diagnosis of deep vein thrombosis (DVT) and pulmonary embolism may be challenging because of overlapping of symptoms.³ We report a case of COVID-19 associated with pulmonary embolism and DVT in a 53-year-old man.

CASE PRESENTATION

A 53-year-old man who was a known case of type 2 diabetes mellitus, presented to the emergency department with a history of fever and dry cough for 5 days, swelling of the left leg for 2 days, and shortness of breath and chest pain for 1 hour. On examination, his pulse rate was 138 beats/min, with blood pressure of 138/70 mm Hg, respiratory rate of 30 breaths/min, and oxygen saturation was 64% on room air with a temperature of 98.6°F. His left leg was swollen, and tenderness was present over the calf region (figure 1). A difference of 5 cm was observed between the left and right calf diameters. On auscultation, bilateral basal crepitation was found. The abdominal, neurological and cardiovascular systems were within normal limits.

INVESTIGATIONS

Laboratory tests showed haemoglobin of 1.41 g/L, total leucocyte count of 10×10^9 cells/L (with neutrophils of 81% and lymphocyte of 13%), total platelet count of 234×10^9 cells/L, random blood sugar level of 481 mg/dL, elevated D-dimer of 35.2 µg/L, lactate dehydrogenase of 724 U/L, with normal liver and kidney functions test. The nasal swab for COVID-19 real-time PCR test was positive. A Chest X-ray revealed GGOs on bilateral lung fields attributed to COVID-19 disease (figure 2).

Colour Doppler study of the left lower limb showed distended, non-compressible common femoral, superficial femoral and popliteal veins, which did not show colour filling or spectral waveform. No flow was seen even in the augmentation test by distal compression. These grey-scale and colour Doppler features were suggestive of acute deep venous thrombosis. CT pulmonary angiography (CTPA) was done to rule out pulmonary thromboembolism (PTE) as the patient has DVT with sudden-onset breathlessness, raised D-dimer and positive PCR test for COVID-19, which itself is now thought to incite inflammation and thrombosis. The CTPA showed a non-enhancing hypodense filling defect in the left main pulmonary artery extending into left lingular and superior basal segmental arteries suggestive of acute PTE (figure 3A,B). The CT sections of the lower limb in the venous phase also revealed the DVT as a hypodense filling defect in the expanded common femoral, superficial femoral and popliteal veins (figure 4A,B). Diffuse GGO and interlobular septal thickening were noted, predominantly involving peripheral zones of bilateral lungs, more so in the



Figure 1 Left lower limb of a COVID-19-positive patient with deep vein thrombosis appears swollen and inflamed.



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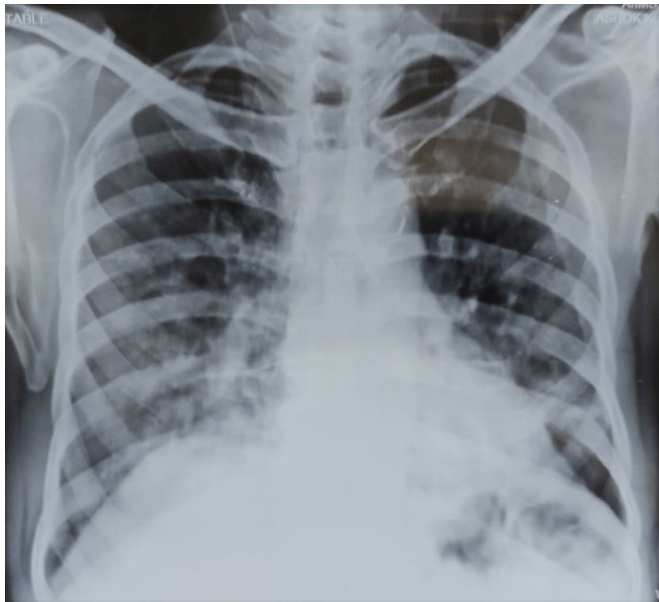


Figure 2 Frontal chest radiograph of a COVID-19-positive patient showing bilateral peripheral ground-glass opacities predominantly affecting the lower lobes.

lower lobes consistent with COVID-19 Reporting and Data System (CORADS) 6 (figure 5). The scoring on CT was 12/25, almost affecting 48% of the lung parenchyma.

TREATMENT

The patient was started on high flow oxygen at 12L/min through a face mask. Oxygen saturation was maintained at 95%, and the respiratory rate decreased to 22 breaths/min. The patient started on injection of low-molecular-weight heparin 60 mg subcutaneous two times per day for DVT with pulmonary embolism. The patient started on injection of methylprednisolone 50 mg intravenous daily, injection of remdesvir 200 mg intravenous on the first day followed by 100 mg intravenous infusion for the next 4 days, injection of doxycycline 100 mg two times per day, ivermectin tablet 18 mg daily on an empty stomach for 3 days, along with zinc and vitamin C. Gradually, oxygen requirement decreased, and swelling of the leg decreased. The patient was discharged in good condition after 2 weeks of admission to this hospital with warfarin 5 mg/day.

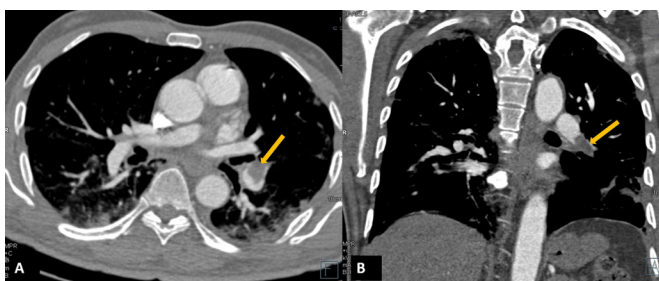


Figure 3 Axial (A) and coronal (B) pulmonary angiography images of a COVID-19-positive patient who developed deep vein thrombosis in the lower limb and presented with sudden onset breathlessness showing a hypodense filling defect (arrows) in the left inferior pulmonary artery suggestive of acute pulmonary thromboembolism.

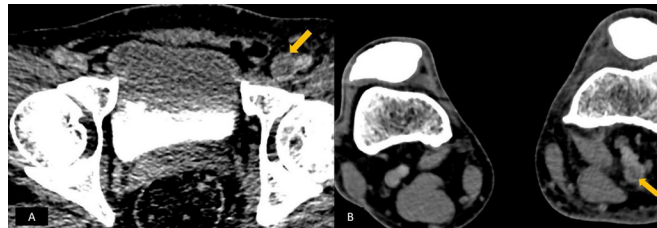


Figure 4 Axial CT images of the venous phase of the lower limbs of a COVID-19-positive patient showing hypodense filling defect in the common femoral (A) and the popliteal (B) veins of the left lower limb indicating deep vein thrombosis. These veins appear distended.

OUTCOME AND FOLLOW-UP

The limb pain had subsided with reduced swelling at follow-up after 1 month. The patient complained of mild swelling on prolonged standing and was advised to use compression stockings and limb elevation. Follow-up colour Doppler imaging showed recanalisation of the thrombosed vessels with wall thickening.

DISCUSSION

Coronaviruses are a group of enveloped RNA viruses responsible for upper respiratory tract diseases, out of which SARS-CoV-2 is known to cause severe and fatal disease in humans.^{1,4} Patients affected by COVID-19 mostly present with fever, dry cough, malaise and shortness of breath.⁵ Patients with COVID-19 have a very high risk of developing DVT.^{3,5} The common symptoms and signs of DVT are swelling, redness and tenderness of the lower limbs. In our patient, all the typical symptoms and signs of COVID-19 and DVT are present.

DVT and PTE in patients with COVID-19 occur mainly due to increased inflammatory response due to the release of proinflammatory cytokines combined with hypoxia, immobilisation and disseminated vascular coagulation.⁵ Hypoxia acts as a prothrombotic condition by increasing blood viscosity and

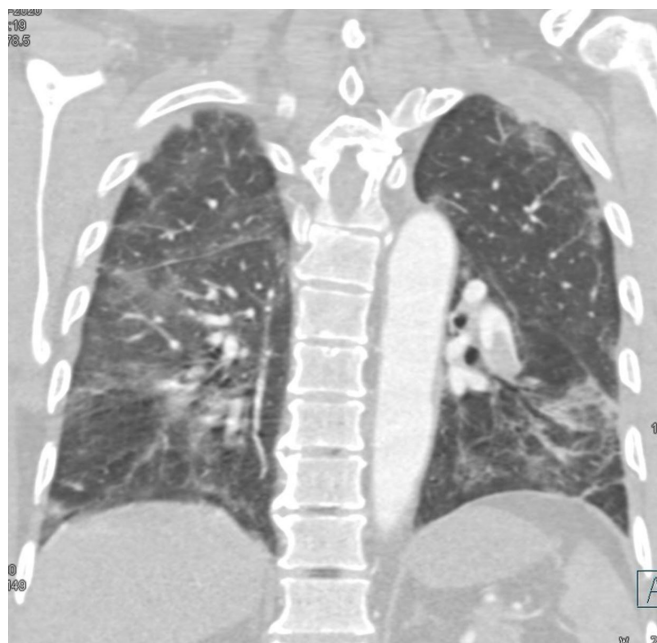


Figure 5 Coronal lung window image of a COVID-19-positive patient showing patchy areas of peripherally distributed ground-glass opacities in bilateral lungs, more so in the lower lobes consistent with COVID-19 Reporting and Data System (CORADS) 6.

triggering a transcription factor-mediated thrombotic pathway.⁶ This can also be due to the disruption of vascular endothelium caused by the viral infection itself.⁷ The other risk factors for DVT development are severely ill patients in the intensive care unit, mechanical ventilation, infection, cancer, obesity, comorbidities, male sex and old age.⁸ Elevation of D-dimer levels and fibrin degradation products seen in patients with COVID-19 are due to the breakdown of fibrin clots.^{3,9}

In the case of COVID-19 pneumonia, which is a prothrombotic condition, the presence of a swollen, painful limb should raise the suspicion of DVT. A progressive increase in breathlessness with falling oxygen saturation, especially with associated DVT and raised D-dimer level, should raise the suspicion of PTE.⁴ Duplex ultrasound of the venous system of the affected limb confirms the diagnosis of DVT. CTPA can clearly demonstrate the pulmonary arterial thrombus even in the subsegmental arteries.⁵

The use of prophylactic anticoagulation in hospitalised patients with COVID-19 decreases venous thromboembolism (VTE) and also decreases mortality.³ A retrospective study by Lodigiani *et al*⁴ reported a 21% incidence of VTE within 24 hours of admission, whereas Klok *et al*⁵ reported a 31% VTE even after thromboprophylaxis. A study by Middeldorp *et al*³ reported that incidence of VTE among hospitalised patients with COVID-19 undergoing thromboprophylaxis was 16%, 33% and 42% at days 7, 14 and 21, respectively. However, ambulation should be the mainstay of thromboprophylaxis in patients who do not require admission.¹⁰ Unfractionated heparin and low-molecular-weight heparin can be used both prophylactically and therapeutically.^{11,12}

Patients with COVID-19 with documented VTE require a minimum of 3 months of anticoagulation.¹³

Learning points

- ▶ An increased inflammatory response occurs in COVID-19, leading to venous thrombosis.
- ▶ 2. The risk factors for deep vein thrombosis (DVT) in patients with COVID-19 are hypoxia, severely ill patients in the intensive care unit, mechanical ventilation, infection, cancer, obesity, comorbidities, male sex and old age.
- ▶ In patients with COVID-19, diagnosis of DVT and pulmonary embolism may be challenging because of overlapping of symptoms.
- ▶ DVT with pulmonary thromboembolism is a well-documented but critical association of COVID-19 and can be detected early by proper clinical examination using duplex ultrasound of extremity venous system and CT pulmonary angiogram.
- ▶ Low-molecular-weight heparin can be used both prophylactically and therapeutically for DVT.

SARS-CoV-2 is known to cause a more severe form of pneumonia in human beings causing severe morbidity and mortality. COVID-19 association with DVT and pulmonary embolism is common yet very critical and lethal and should be detected early by proper clinical examination, using colour Doppler venous ultrasound and CT pulmonary angiogram. The use of anticoagulants judiciously will prevent further complications.

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