

MASTER CASE PRESENTATION

Unilateral deep vein thrombosis with gangrene involving the ascending aorta with sepsis and pulmonary thromboembolism—a pertinent cutaneous marker of severity of COVID-19

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Abstract

While myriad skin manifestations have been reported with COVID, they are insignificant as compared to the number of cases and do not indicate specificity as the studies that report them have either been based on telephonic consultation or have not been compared with case-control analysis from a normal skin OPD or IPD referral population. The most feared complication of COVID-19 is the combination of coagulopathy and thromboembolism, which is consequent to thrombo-inflammation and a heightened prothrombotic state. It is exaggerated in severe COVID associated with sepsis and skin manifestations that correlate with severity are more useful to clinicians. We had a case of COVID-positive 65-year-old man with features of thromboembolism followed by general symptoms of cough and fever. D-dimer test was positive, and the Ultrasound Doppler showed thrombosis in the right lower limb arteries and deep vein thrombosis in right lower limb veins.

KEYWORDS

arterial thrombosis, color doppler, COVID-19, deep vein thrombosis, pulmonary thromboembolism

1 | CASE REPORT

A 65-year-old man with no known comorbidities or history of any prothrombotic disease presented with complaints of weakness and pain in right lower limb for 10 days, followed by cough and fever (102°Fahrenheit) for 5 days. On assessment, the patient had altered sensorium but was hemodynamically stable. Saturation was 70% on room air and increased to 95% with high flow nasal cannula at FiO₂ (fraction of inspired oxygen) ~40% with a flow of 70 liters/minute. On chest examination, there were bilateral decreased breath sounds.

Local examination showed diffuse dark discoloration of the right lower limb 5–6 cm below the sacroiliac joint with a livedoid pattern bordering the lesion, with no line of demarcation present between affected and the normal skin. Skin showed wet gangrenous changes in the right lower limb with the presence of edema over it. (Figure 1A) Distal pulsations of right lower limb arteries (femoral, popliteal, anterior tibial and posterior tibial and deep peroneal) were absent. COVID-19 test was positive (via RT-PCR-Reverse Transcriptase-Polymerase chain reaction). Chest X-ray shows bilateral peripheral infiltrates. (Figure 1B). INR was 1.9. Antibiotics and steroids were started for the treatment of sepsis and COVID along with aggressive management of thrombosis

FIGURE 1 (A) Local examination—diffuse dark discoloration of the right lower limb with a livedoid pattern bordering the lesion, with no line of demarcation present between affected and the normal skin. Skin changes—wet gangrenous changes in the right lower limb with presence of edema over it. (B) Chest X-ray shows bilateral peripheral infiltrates. (C) Venous and Arterial Doppler—complete occluding echogenic content suggestive of subacute thrombosis in the common femoral vein (CMV) and common femoral artery (CFA). Antibiotics and steroids were started for the treatment of sepsis and COVID along with the management of thrombosis (Table 1)

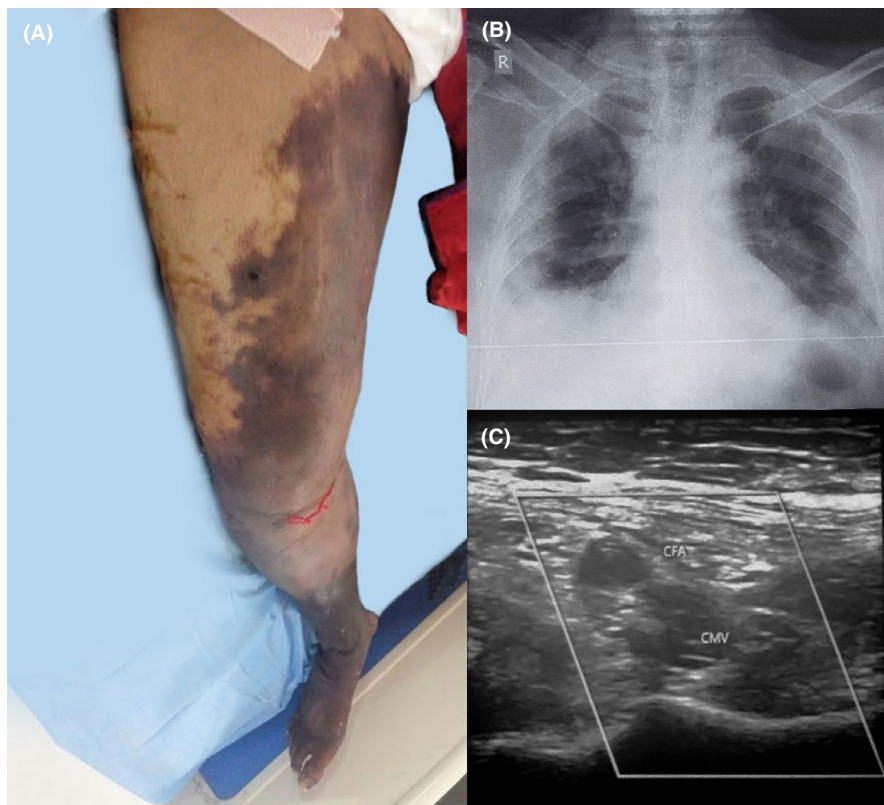


TABLE 1 Management of thrombosis

Doppler Study of right lower limb

Venous Doppler—deep vein thrombosis in right common femoral vein and right superficial femoral vein.

Arterial Doppler—complete occluding echogenic content suggestive of subacute thrombosis in the arteries—common iliac, external iliac, common femoral, superficial femoral, popliteal, anterior tibial, and posterior tibial with no color flow distal to all the arteries (Figure 1C).

There was atherosclerotic wall thickening of the above arteries.

Treatment

Anti-thrombotic agents

Tablet Aspirin 150 mg OD
Tablet Cilastazole 50 mg BD
Inj. Pentoxifylline 400 mg TDS
Inj. Low-Molecular Weight Heparin 60 mg HS

but the patient died of pulmonary embolism 5 days after the admission (Table 1).

2 | DISCUSSION

While many cutaneous manifestations have been seen in COVID, it is difficult to ascribe them to the infection consistently unless a case control study and histological and virological proof can be ascertained in the rash. The skin findings are highly varied and may not relate to the severity of the condition.¹ COVID-19 may result in multi-organ dysfunction, characterized by a release of cytokine storm leading to fever, thrombocytopenia, and increase in inflammatory markers with occasional fatal consequences.²

Activation of the defense system of the host leads to immunothrombosis and thrombo-inflammation. Significant inflammatory changes due to cytokine storm are seen in COVID-19 patients based on increased interleukin 6, C-reactive protein, and fibrinogen. This leads to elevated D-dimer values and thromboembolism, which has been postulated to be a consequence of adhesion of SARS-CoV-2 to the ACE-2 thus, resulting in endothelialopathy and microvascular prothrombosis.¹

Even though it has been surmised that microvascular injury and thrombosis associated with COVID-19 can cause skin manifestations, unilateral thrombosis has never been reported. It is a challenge to diagnose thromboembolic events in COVID-19 patients since it can be masked by the features of COVID-19 itself. An increase in D-dimer, fibrinogen, and fibrinogen degraded products in the

COVID-positive patients shows the presence of a hypercoagulable state in COVID-19 patients.³

Our patient presented with features of thrombosis as suspected by gangrenous edematous changes, loss of distal pulsations, increased D-dimer levels to more than 10 000 ng/dL (normal <500 ng/dL) and later proved by the color Doppler of right lower limb. The symptoms of pain and weakness in the right lower limb preceded the respiratory manifestations.

Of the varied manifestations, the major forms are maculopapular eruptions, urticarial lesions, acral areas of erythema with vesicles or pustules (pseudo chilblain), other vesicular eruptions, and livedo or necrosis. In children, acral, chilblain-like lesions, papulovesicular eruptions, or Kawasaki disease-like pediatric inflammatory multisystem syndrome were seen. Most of these manifestations were seen with the infection though in some it preceded the onset of COVID-19 symptoms.⁴ While some unusual manifestations have been recently reported like exfoliative shock syndrome, COVID-19-induced rash and mucositis (CIRM), and calciphylaxis with thrombotic vasculopathy, notably viral mRNA was not detected using RNA ISH for SARS-CoV-2, suggesting that cutaneous manifestations associated with COVID-19 are secondary to dysregulation of the immune and coagulation pathways rather than direct viral skin toxicity.⁵

Our case had visibly manifest clinical thrombosis and was diagnosed as a case of sepsis with thromboembolism with fatal pulmonary embolism, and thus, such a clinical morphology can portend a fatal prognosis. While we report an atypical and hitherto unreported unilateral thrombosis with gangrene, we feel that such clinical manifestations that can predict severity and are suggestive of aggressive clinical intervention will have more clinical utility in practice than other skin findings, which may be inconsequential for the clinical course of the disease.

3 | CONSENT FROM PATIENT FOR PUBLICATION

Yes.

ETHICAL APPROVAL

This case was a single case managed in the ICU according to prevailing recommendations and thus did not require approval of an ethics committee.

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