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.
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. 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.

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.

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.

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