An Autopsy Review: “COVID Toes”

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Abstract: “Severe acute respiratory syndrome coronavirus-2” (SARS-CoV-2) infection has variable described dermatologic manifestations. “COVID (coronavirus disease) toes” became a hallmark of the disease in young and largely asymptomatic patients, who may have negative test results for SARS-CoV-2. Pernio (chilblains)-like lesions are seen mostly in infected pediatric patients and are purple painful, frequently bilateral, ill-defined plaques with prominent inflammation on histological examination. In contrast to pernio-like presentation in children, critically ill adult patients with SARS-CoV-2 develop “purple” digits that may be sharply demarcated and may demonstrate asymmetric areas of ischemia. These 2 contrasting entities are sometimes grouped together as “COVID toes” due to some similarities in clinical appearance and presentation. Here, we summarize histopathologic examination from an autopsy, including the cutaneous lesions from the affected and normal contralateral toes and correlate them with systemic findings. In contrast to pernio-like lesions, the skin of the affected necrotic toes contained thrombi in vessels without prominent inflammation, suggestive of an embolic event. This is further supported by the clinical history of and autopsy findings of popliteal artery thrombus and multiple subsegmental pulmonary emboli. Our findings suggest that critically ill patients with SARS-CoV-2 have different pathological processes affecting skin at peripheral sites (ie, fingers, toes, ears, and nose), which may be due to thromboembolic events. The skin is a mirror of the body and skin pathology may shed light into overall pathogenesis of systemic illness and processes.

Key Words: dermatopathology, dermatology, COVID-19, autopsy, COVID toes

INTRODUCTION

The cutaneous manifestations of “severe acute respiratory syndrome coronavirus-2” (SARS-CoV-2) infection have been recently reported and span a broad-spectrum nonspecific demonstrations such as maculopapular exanthem (morbilliform), papulovesicular rash, urticaria, painful acral red purple papules, livedo reticularis, petechiae, and skin eruptions.1,2 One of the mostly pronounced cutaneous finding of SARS-CoV-2 infections is “COVID toes” (coronavirus disease toes) phenomenon, which is commonly referred “SARS-CoV-2–induced pernio/chilblains.”3–4 Even though pernio is one of the common etiologies for these cutaneous findings, it is not the only explanation for “purple” digits in SARS-CoV-2–infected patients. An alternative cause of COVID toes are thrombi in subcutaneous vessels, as in the case described here. In contrast to the pediatric predominant pernio-like lesions, thrombi-associated COVID toes are more commonly seen in adult patients with other coagulation issues.5 Furthermore, pernio-like presentations are associated with inflammation and are ill defined on digits, whereas thromboembolic lesions are not necessarily associated with inflammation and are well demarcated. A shared finding of our case with pernio-like lesion, it is observed in the later course of the disease, when SARS-CoV-2 test was negative.

CASE REPORT

A 63-year-old man with medical history of type-2 diabetes was admitted to the hospital with SARS-CoV-2 pneumonia with a positive SARS-CoV-2 real-time polymerase chain reaction test. He received a course of treatment with azithromycin and Plaquenil and discharged from the hospital. Five days later, he represented with worsening symptoms of respiratory insufficiency and acute respiratory distress syndrome, for which he needed intubation. His hospitalization course was complicated by right lower extremity arterial clot requiring embolectomy of the popliteal artery, multiple subsegmental pulmonary emboli, and multiorgan failure; the patient expired 19 days after admission. Of note, his repeat SARS-CoV-2 RT-PCR was resulted negative 2 days before his death. The postmortem examination revealed the cause of death as respiratory failure in the setting of diffuse alveolar damage, massive pulmonary edema, and necrotizing pneumonia caused by superimposed fungal and bacterial lung infection. Microscopic examination of the heart revealed foci of acute ischemic damage without any significant atherosclerosis in the coronary arteries. There was no systemic evidence of an embolic process.

Cutaneous examination revealed a violaceous discoloration of the right toes on both plantar and dorsal surfaces (Fig. 1). The left foot and hands were unaffected. The patient had no reported skin lesions or history of clotting disorder before SARS-CoV-2 infection. Laboratory workup on the day of death demonstrated d-dimer 1.38 µg/mL (≤0.80 µg/mL), procalcitonin 1.42 ng/mL (≤0.08 ng/mL), and an activated partial thromboplastin time (aPTT) >180 seconds (23.9–34.7 seconds). Biopsies of the skin was obtained from the lesion on the right big toe and the unaffected left big toe (control). Histology demonstrated thrombi in cutaneous, small vessels with fibrin in the right toe with no significant inflammation or vasculitis (Fig. 2).

DISCUSSION

SARS-CoV-2 infection has variable presentations that range from asymptomatic to severe respiratory failure, multiorgan failure, and death. Approximately, 20% of the infected individuals develop severe course with high mortality rate.6 There are different theories about underlying reasons for poor disease progression as compared with the seasonal flu. One of the most commonly accepted mechanisms is hypercoagulable
state with micro- and macrocirculatory thrombosis. This hypercoagulability is thought to emerge from complement-mediated thrombotic microvascular injury of the lungs and skin according to one report by Magro et al.

In this case review, a cutaneous symptom of a patient with recent SARS-CoV-2 pneumonia infection is evaluated. Histological examination demonstrated that these lesions are consistent with clot formation in superficial capillaries. The lesion was observed in the later course of the disease and maintained after the resolution of the infection. Additionally, prior thrombi in the lungs appeared to have resolved because there was no evidence of pulmonary clots on autopsy. This suggests that COVID toes are late findings, indicative of prior hypercoagulable status.

As the novel coronavirus pandemic continues to grow worldwide, COVID toes on SARS-CoV-2 patients are likely the sequelae of the hypercoagulable status in select patients. Although these lesions are associated with inflammation as with pernio-like presentations, inflammatory responses are not necessarily present in thromboembolic lesions. Furthermore, well-demarcated lesions, such as those described here, are more likely related to thrombi formation, and thrombi always should be highly considered in these types of dermatologic findings because they may provide insight into patients’ coagulable status. In this case, given the prior thromboembolic events, absence of inflammation around clots, and well-demarcation of the lesion, the clot is most consistent with thromboembolic process.

REFERENCES