Microthrombi in skin biopsy of a patient with COVID-19

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INTRODUCTION

Cutaneous manifestations are interesting presentations of COVID-19 infection, but only a few cases have described the histological findings of skin biopsy in these patients. We present the case of a COVID-19 positive patient with morbilliform rash whose skin biopsy showed the presence of fibrin microthrombi within the small vessels as the main distinctive histologic feature.

CASE REPORT

A 59-year-old Hispanic male with a history of hypertension and alcohol use disorder presented to the emergency department with complaints of cough and progressive shortness of breath. On examination, the patient was noted to be hypoxic to 86% on room air, but otherwise the initial physical examination was unremarkable. The patient was a nonsmoker and non-drug user and consumed alcohol daily. He was unemployed and lived in a shelter. He was allergic to penicillin, which caused him hives. He was not taking any prescribed over-the-counter medications or supplements. His initial laboratory tests showed normal complete white blood cell count of 6.1 K/uL; normal liver and kidney function tests; D-dimer, 212 ng/mL; lactate dehydrogenase, 323 U/L; ferritin, 340 ng/mL; and C-reactive protein, 6.9 mg/L. A computed axial tomography scan of the chest without contrast showed bilateral ground-glass opacities, potentially indicative of COVID-19 infection. After the initial physical examination and laboratory and imaging findings, the patient was admitted to the medical ward for suspected COVID-19 pneumonia. Two nasopharyngeal swabs for polymerase chain reaction for SARS-CoV-2 were performed and reported negative. A serologic test for anti-SARS-CoV-2 antibodies was reported positive. He was treated with 500 mg of oral levofloxacin and 400 mg intravenous tocilizumab for COVID-19 pneumonia. Other medications received during the hospitalization were atorvastatin, famotidine, multivitamins, folic acid, and thiamine. During the hospital stay, his oxygen requirements increased and he was started on high flow, but he did not require mechanical ventilation or intensive care unit admission. On day 3 of hospitalization, a new rash was noted on physical examination. The rash initially appeared in the lower extremities and spread quickly to the trunk and neck, sparing the face, palms, and soles. On examination, a generalized non-blanching morbilliform eruption involving the trunk and extremities was noted, with some of the papules being urticarial (Figs 1 and 2). The patient had bilateral conjunctival injection. There was no other mucosal involvement. Repeat laboratory testing on the day the rash appeared showed total white blood cell count of 9.9 K/uL; elevated D-dimer, 13,646 ng/mL; lactate dehydrogenase, 233 U/L; ferritin, 430 ng/mL; C-reactive protein, 5 mg/L, and normal liver and kidney function tests. Initially, a drug eruption was suspected, and he was treated with antihistamines and steroids, with no improvement. Due to elevated D-dimer and hypoxia, pulmonary embolism was suspected and computed tomography angiography was performed, which showed no emboli. On day 7 of hospitalization, the rash did not improve, so a punch skin biopsy was performed. The biopsy was taken from the rash in

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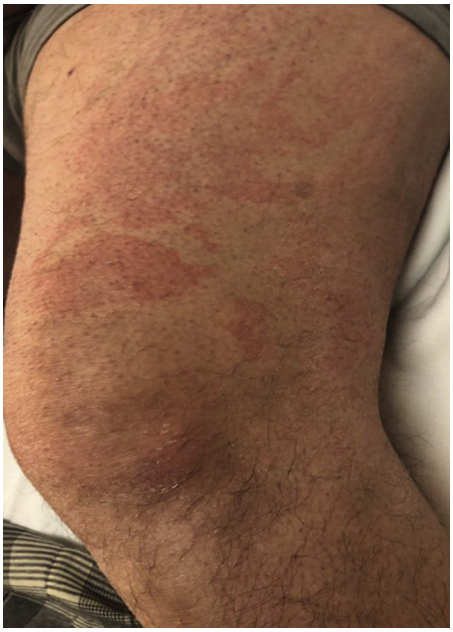

Fig 1. Morbilliform rash involving the left thigh and knee.

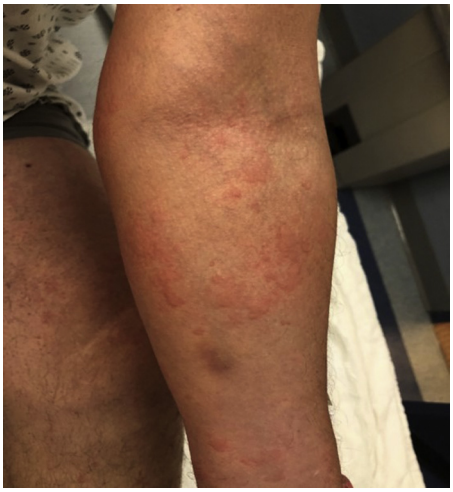

Fig 2. Morbilliform rash involving the left forearm.

the interscapular area. The rash was not blanching and non-urticarial. No repeat laboratory tests were done on the day of biopsy. The hematoxylin-eosin–stained tissue specimens showed post-inflammatory pigmentary alteration, a dermis with distended small vessels, and capillaries filled with fibrin microthrombi (Fig 3).

Due to elevated D-dimer and the risk of thromboembolic events related to COVID 19 infection, apixaban was started. The patient had no other clinical sequela of hypercoagulability. He was hospitalized for a total of 11 days and was discharged after his respiratory status and oxygen requirement improved. Approximately 2 months after discharge, he had another emergency department visit for shortness of breath, and no rash was noted on examination.

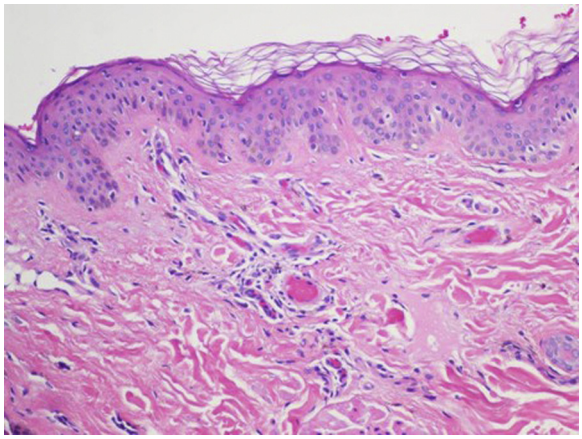

Fig 3. Skin biopsy on high magnification showing microthrombi in the small vessels. (Hematoxylin-eosin stain; original magnification: ×200.)

DISCUSSION

Cutaneous manifestations are an interesting presentation of COVID-19 infection. Several cases of skin involvement like erythematous rashes, urticarial lesions, vesicles resembling chicken pox,[1] petechial eruptions mimicking dengue,[2] livedico reticularis,[3] acral ischemic lesions resembling chilblains,[4] acral perniosis,[5] and erythema multiforme[6] have been reported with COVID-19 infection.

According to the review article by Sachdeva et al, which included 79 COVID-19 patients with skin lesions, the most common cutaneous manifestation of COVID-19 was maculopapular exanthem (morbilliform), presenting in 36.1% of the patients.[7] Other findings included papulovesicular rash (34.7%), urticaria (9.7%), painful acral red purple papules (15.3%), livedo reticularis lesions (2.8%), and petechiae (1.4%). Majority of the lesions were localized on the trunk (66.7%), while 19.4% of the patients had lesions involving the hands and feet. With regard to the timing of the skin lesion, 12.5% of the patients presented with a cutaneous lesion at diagnosis or with the onset of other COVID-19 symptoms. The remaining 69.4% started having lesions after the onset of respiratory symptoms or after the diagnosis of COVID-19, with a majority of them developing cutaneous lesions within 7 days of the onset of COVID-19 symptoms or the diagnosis of COVID-19.

Majority of the studies reported no correlation between COVID-19 severity and skin lesions.[7] The mechanisms of skin lesions found in COVID-19 patients are not well known, and few cases of skin biopsy have been described. In our case, the skin biopsy of the lesion showed microthrombi in the cutaneous microvasculature. The hypercoagulable state and thrombotic microangiopathy related to COVID-19 infection has been reported in many studies.[8-13] Manalo et al suggested that livedo reticularis-resembling manifestation can be due to a low-grade disseminated intravascular coagulation or a low-grade thrombophilic state related to COVID-19 infection.[3] Magro et al reported pauci-inflammatory thrombogenic vasculopathy involving the cutaneous microvasculature. Their evidence suggests that the microvascular injury is thought to be mediated by the activation of the complement pathways and associated procoagulant state.[14]

Reporting uncommon presentations of COVID-19 such as skin lesions can help clinicians stay aware of atypical scenarios and guide their diagnostic approach.

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