Correspondence

Widespread cutaneous small vessel vasculitis secondary to COVID-19 infection

Dear Editor,

Since the beginning of the coronavirus disease (COVID)-19 pandemic, various dermatological manifestations including chilblain-like lesions, livedo reticularis, urticaria, varicella-like, petechial, and maculopapular exanthems have been reported.[1–4] COVID-19-induced cutaneous small vessel vasculitis (CSVV) has also been recently described.[5] CSVV refers to a subgroup of vasculitis localized to the skin. Drugs and infections are chief causes of CSVV.

A 47-year-old otherwise healthy male presented to our emergency department with a 6-day history of skin and oral lesions, low grade fever, malaise, and polyarthralgia. The rash started as small red to violaceous plaques on the legs and extended to the arms and trunk. He simultaneously developed a painful tongue sore and gum bleeding. On the third day, a persistent dry cough developed. He denied a history of recent travel, sick contacts, insect bites, medication use, and family history of autoimmune disorders.

On examination, temperature was 37.5 °C (99.5°F). Chest examination revealed bilateral lower zone fine crepitations. On cutaneous examination, targetoid papules and plaques with central necrosis and peripheral erythema were distributed symmetrically on all extremities, buttocks, and lower trunk (Fig. 1a–c). Palpable purpura and areas of vesiculation were also present. Mucosal examination showed a tender ulcer of size 1 cm on the undersurface of the tongue with moist pale granulation tissue on its floor and gingival and lingual purpura (Fig. 1d,e). Our differential diagnoses included CSVV, erythema multiforme, and viral exanthem.

On admission, investigations revealed a normal complete blood count and renal function. Liver enzymes ALT 55 U/l, AST 66 U/l (0–40 U/l), C-reactive protein 72.1 mg/l (<5 mg/l), serum ferritin 1062.6 ng/ml (30–400 ng/ml), procalcitonin 0.21 ng/ml (<0.05 ng/ml), lactate dehydrogenase 234 U/l (105–222 U/l), and fibrinogen 427 mg/dl (200–400 mg/dl) were elevated. Coagulation profile was normal. Chest x-ray showed bilateral ground glass opacities. Nasopharyngeal sampling for severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) RNA PCR was positive. Vasculitic work-up included negative antineutrophil cytoplasmic, antinuclear, anti-dsDNA, anti-Ro, anti-La, antiphospholipid antibodies, rheumatoid factor, and cryoglobulins with normal serum complement levels. Herpes simplex 1, 2, HIV, hepatitis B and C, Epstein–Barr virus, cytomegalovirus, parvovirus B19, and *Mycoplasma pneumoniae* serologies were negative.

Histopathology of a targetoid leg papule revealed endothelial swelling, neutrophilic vessel wall infiltration, karyorrhectic debris, and fibrin deposition in small and medium-sized dermal vessels with extravasated erythrocytes (Fig. 2a). There were microthrombi occluding lumina of smaller dermal capillaries (Fig. 2b). Based on a positive SARS-CoV-2 RNA PCR, histopathological confirmation of CSVV with microthrombi, and a negative vasculitic work-up, a final diagnosis of CSVV secondary to COVID-19 infection was established. Topical betamethasone valerate 0.12% cream was applied twice daily to skin lesions.

Vascular damage in COVID-19 infection is postulated to occur due to immune response against viral antigen deposition.[5] The current hypothesis involves angiotensin II. The receptor of SARS-CoV-2 virus, angiotensin converting enzyme (ACE) 2, is present on vascular endothelial cells in addition to alveolar pneumocytes.[6] Binding and inhibition of ACE2 by SARS-CoV-2 leads to increased angiotensin II levels and resultant vasoconstriction, endothelial dysfunction, and thrombosis.[6]

Our patient was a previously healthy man who developed widespread targetoid plaques with central necrosis, palpable purpura, and oral lesions as the initial manifestation of COVID-19 infection prior to respiratory symptoms. Viral clearance was complemented by gradual resolution of skin lesions. Although cases of CSVV have been recently reported, our case is unique as the skin biopsy revealed microthrombi in dermal capillaries thus adding evidence to the current premise on COVID-19 pathogenesis.

In summary, we describe a patient with CSVV as the chief manifestation of COVID-19 infection with mild respiratory involvement. Physicians should be aware that in the era of the

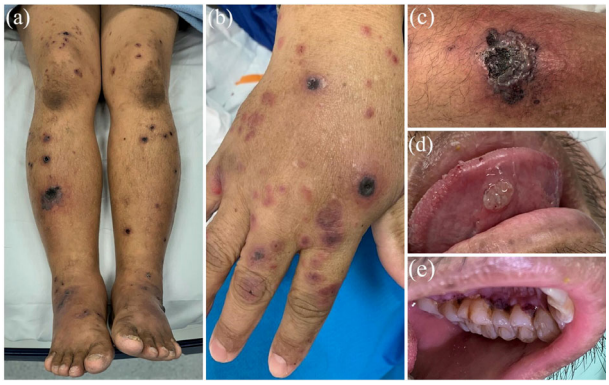

Figure 1 Mucocutaneous findings. Targetoid plaques with central necrosis on the lower extremities (a) and dorsum of the hand (b). Close-up view of purpuric plaque with central black eschar and peripheral vesiculation on the right shin (c). Ventral surface of the tongue showing an ulcer of size 1 cm × 1 cm with pale moist granulation tissue on the base. Note the petechiae on the tip of the tongue (d). Gingival purpurae on the upper dental arch near the teeth (e)

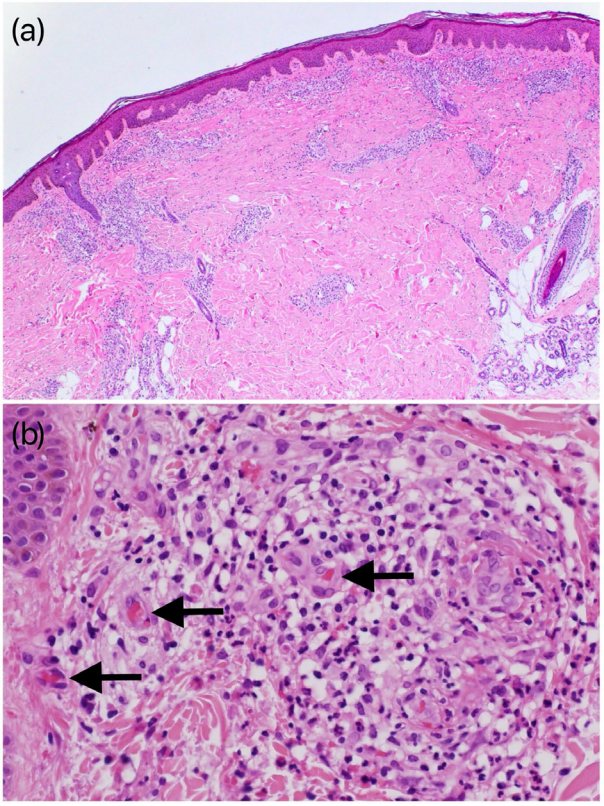

Figure 2 Skin pathology. Histopathology of targetoid leg papule demonstrating upper and mid dermal perivascular infiltrate (a) (hematoxylin–eosin stain; original magnification, ×100) with endothelial cell swelling, neutrophilic infiltration of vessel wall, karyorrhectic debris, fibrin deposition, extravasated erythrocytes and microthrombi (black arrows) occluding the lumina of the smaller capillaries in the dermis (b) (hematoxylin–eosin stain; original magnification, ×400)

COVID-19 pandemic, CSVV may be one of the initial manifestations of the disease.

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