Correspondence

Urticarial vasculitis in a COVID-19 recovered patient

Dear Editor,

Coronavirus disease 2019 (COVID-19) typically presents with fever and respiratory symptoms, but the clinical spectrum appears to be wide.[1] Skin is rarely involved in the course of COVID-19, but its involvement may be underreported.[2] Herein, we report a case of COVID-19 who developed urticarial vasculitis after recovery.

On March 24, 2020, a 64-year-old woman presented to the emergency room with fever, dry cough, dyspnea, nausea, and anorexia. The past medical history was significant for diabetes mellitus and hypertension. She was screened for COVID-19 with a low-dose chest CT scan that showed patchy parenchymal ground-glass opacities with peripheral distribution typical for COVID-19 infection. Her lab tests showed a normal WBC count without lymphopenia and elevated levels of both lactate dehydrogenase (LDH: 554 U/L) and C-reactive protein (CRP: 61 mg/l; Positive > 10). Nasopharyngeal swab reverse transcription polymerase chain reaction (RT-PCR) was positive for SARS-CoV-2.

She was treated with hydroxychloroquine (200 mg BD) and azithromycin 250 mg/day for 5 days with advice to keep home quarantine, which led to a gradual improvement of the symptoms.

On April 22, 2020, she presented again with weakness, malaise, anorexia recurring for the previous 1 week, and new-onset generalized skin lesions. Skin lesions had appeared abruptly 48 hours before the presentation.

Cutaneous examination revealed prominent periorbital edema with annular purpuric patches. Annular and polycyclic urticarial lesions were noted on the trunk. Acral nonpitting edema and annular polycyclic wheals with a noticeable purpuric component were found on the upper and lower limbs (Figure 1). Mucosal findings were insignificant, and there was no lymphadenopathy, organomegaly, or arthritis.

The PCR nasal swab was negative, but serology for COVID-19 came back positive for both IgM and IgG (levels: 8.91 and 16.61, respectively). The follow-up chest CT scan showed nonspecific ground-glass infiltration of the lung bases.

The histopathological examination demonstrated dermal edema and evidence of leukocytoclastic vasculitis consistent with urticarial vasculitis (Figure 2).

The patient was treated with an antihistamine that resulted in clearance of skin lesions over a week with annular postinflammatory hyperpigmentation.

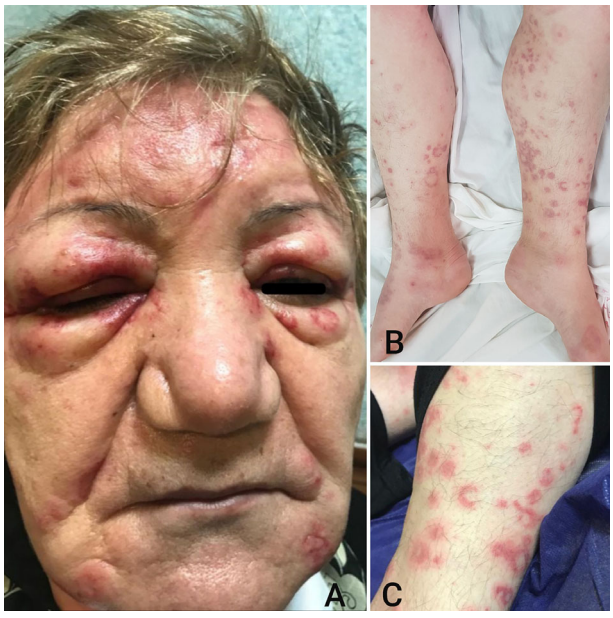

Figure 1 Facial and periorbital edema with multiple purpuric lesions (a). Annular purpuric urticarial lesions on the extremities with some targetoid lesions (b,c)

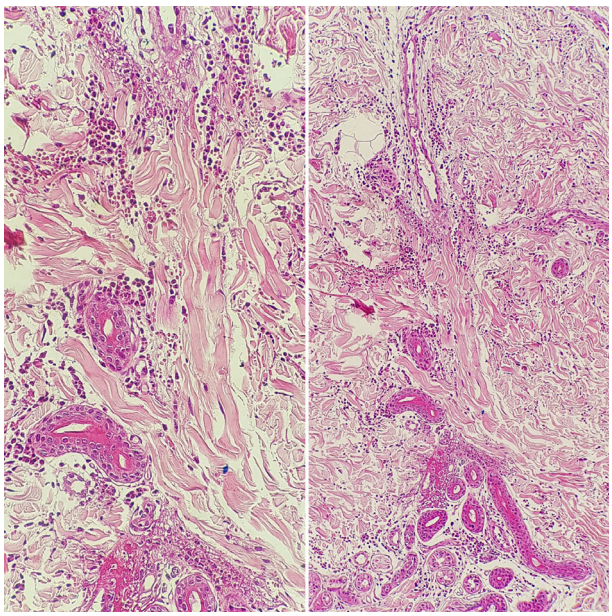

Figure 2 Dermal edema, red blood cell extravasation, and vascular damage in the background of mixed neutrophil & eosinophil infiltrate and small vessel vasculitis are evident (H&E staining. Right ×100, and left ×400 magnification)

On arrival serum creatinine was 1.6 mg/dl (range 0.6–1.2). The patient developed a rise in the creatinine level up to 4.2 mg/dl during the admission period that responded to the fluid replacement therapy compatible with the diagnosis of prerenal azotemia. All other kidney function tests and urine analysis were insignificant except for a mild proteinuria.

Urticarial vasculitis (UV) is an entity characterized by persistent urticarial lesions resolving with residual purpura or hyperpigmentation and histopathologic features of leukocytoclastic vasculitis.[3] Although UV is most commonly idiopathic, it can also occur in the context of autoimmune disorders, infections, medications, or as a paraneoplastic syndrome. Several viral etiologies have been labeled as plausible causes.[3] To our knowledge, this case is the first reported case of urticarial vasculitis in the setting of COVID-19.

Several vascular lesions including violaceous macules, livedo reticularis, purpura, chilblain, and acro-ischemia have been reported in association with COVID-19.[4] These manifestations may present on the onset of disease or afterward.[4] Henry et al. reported a case of disseminated urticaria that presented 48 hours before the onset of COVID-19 symptoms, but no vasculitis was observed.[5]

It is difficult to identify the exact etiology of UV development in our patient. Hydroxychloroquine and azithromycin are not among the frequent drug-related causes of UV, making them the less probable cause. On the other hand, UV is mediated by immune complex deposition and complement system activation, so the time needed for antibody formation may be the reason for the delayed manifestation of UV in our case. Complement pathways activation with subsequent membrane attack complex (MAC)-mediated microvascular endothelial cell injury may lead to a significant degree of interstitial and perivascular neutrophilia with prominent leukocytoclasia as a result of the neutrophil chemoattractant properties of complement.[6] Activation of the complement pathways in the pathogenesis of viral infections such as hepatitis C virus (HCV) and cryoglobulinemic vasculitis has also been reported.[7]

Although a transient rise in the serum creatinine level and a mild proteinuria were detected during laboratory evaluations, these changes could be attributed to the prerenal azotemia and the history of diabetes, respectively.

The patient's symptom recurrence, development of UV, detection of IgM on the serum, and some nonspecific ground-glass infiltrations in the chest CT scan following a month raises some concerns about infection persistence and infectivity despite international guideline recommendation of a quarantine period of just 15 days.

This case report highlights the variety of skin manifestations in the context of SARS-CoV-2. On the other hand, UV can be associated with several viral infections such as COVID-19. Therefore, dermatologists need to be vigilant and consider COVID-19 in any susceptible patient during the current pandemic.

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The patient in this manuscript gave written informed consent for the publication of her case details.

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REFERENCES

1 Zhou F, Yu T, Du R, *et al.* Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The Lancet* 2020; **395**: 1054–1062.
2 Suchonwanit P, Leerunyakul K, Kositkuljorn C. Cutaneous manifestations in COVID-19: lessons learned from current evidence. *J Am Acad Dermatol.* 2020; **83**: e57–e60.
3 Davis MD, Brewer JD. Urticarial vasculitis and hypocomplementemic urticarial vasculitis syndrome. *Immunol Allergy Clin North Am* 2004; **24**: 183–213.
4 Bouaziz JD, Duong T, Jachiet M, *et al.* Vascular skin symptoms in COVID-19: a french observational study. *J Eur Acad Dermatol Venereol.* [published online ahead of print,] 2020 Apr 27. https://doi.org/10.1111/jdv.16544
5 Henry D, Ackerman M, Sancelme E, Finon A, Esteve E. Urticarial eruption in COVID-19 infection. *J Eur Acad Dermatol Venereol.* 2020; **34**: e244–e245.
6 Magro C, Mulvey JJ, Berlin D, *et al.* Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: a report of five cases. *Transl Res* 2020; **220**: 1–13.
7 El-Shamy A, Branch AD, Schiano TD, Gorevic PD. The complement system and C1q in chronic hepatitis C virus infection and mixed cryoglobulinemia. *Front Immunol* 2018; **9**: 1001.