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LETTER TO THE EDITOR

Augmented interferon I signaling in a patient with COVID toes

Dear Editor

Dermatological manifestation in Coronavirus Disease 2019 (COVID-19) can occur either as a direct implication of COVID-19 or due to other incidental skin changes during COVID-19 infection. Since the detail of each subtype has not been fully described, careful evaluation will be needed.

A 49-year-old man presented with a 7-days history of violaceous, infiltrated plaques on the distal site of extremities with a 4-day history of acute fever and headache at July 2020. The skin lesion was not accompanied by purpura, ulcer, target lesion, but with pain and burning sensation (Figure 1). The patient had experienced herpes simplex on the lips several times before, however, did not have any other disease/medication/family history. Complete skin and mucosal examination results were otherwise unremarkable. Blood cell counts were normal in white blood cells (7620/μL), and thrombocytes (148,000/μL) with elevated atypical lymphocyte count up to 980/μL and elevated eosinophil count (460/μL), and decreased lymphocyte count to 530/μL. General biochemistry was normal except for high aspartate trans aminase (38 U/L), alanine transaminase (80 U/L), lactic acid dehydrogenase (446 U/L; normal < 221) and C-reactive protein (1.65 mg/dL). Although polymerase chain reaction (PCR) test result for COVID-19 on a nasopharyngeal swab was negative, serum IgM antibody against SARS-CoV-2 was turned positive from day 25 to 45 (by antibody test kit: Artron Laboratories, Burnaby, BC, Canada). Antibody test of other viruses, including cytomegalovirus, Epstein–Barr virus, herpes simplex virus, rubeola virus, rubella virus, human herpes virus-6, or influenza virus showed negative or inactive. Autoantibodies, including antinuclear antibody and antimelanoma differentiation antigen five antibody were negative. Computerized tomography revealed no complications in the lung. Histopathological findings of the skin biopsy taken from the dorsal site of the right foot at day 2 showed spongiosis and enhanced edema in epidermis, with mononuclear cell infiltration to epidermis, dermal vessels, and appendix (Figure 1d). The expression of

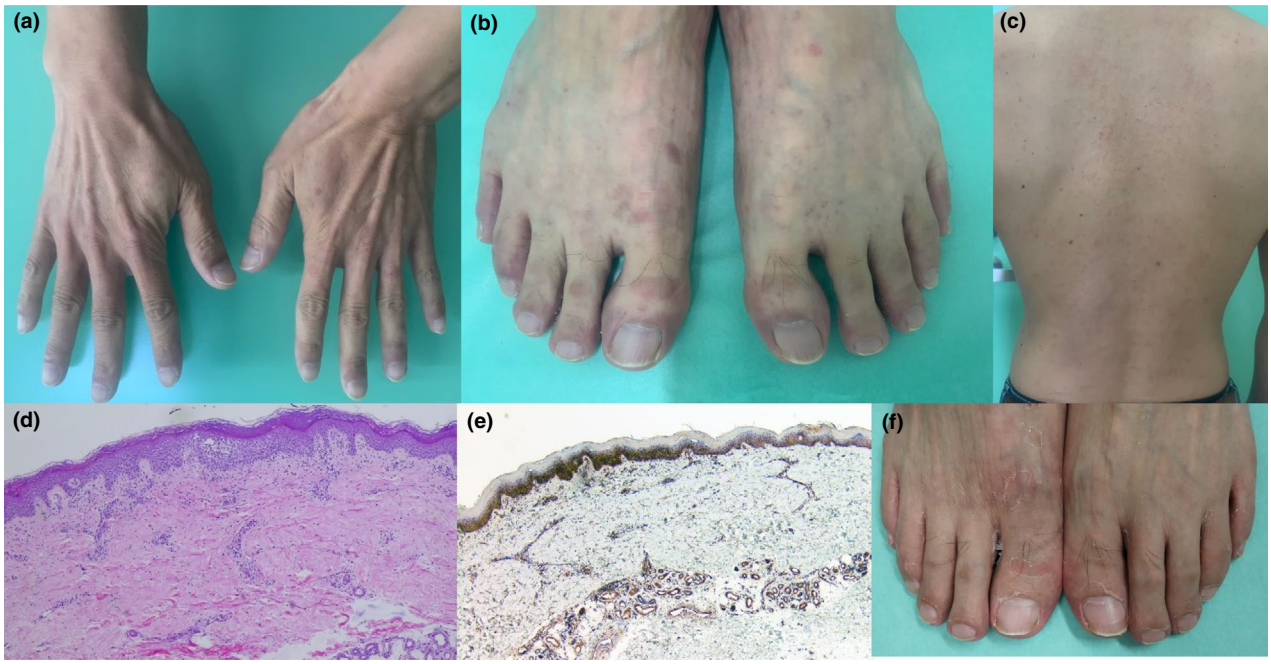

FIGURE 1 Clinical appearance at the first visit. (a) hands, (b) dorsal site of feet, and (c) trunk. Multiple circular purple erythema of 2 to 20 mm in diameter occurred symmetrically on the dorsal hands, feet, and trunk. Individuals were sharply circumscribed, round shaping. The center of the erythema was not concave. The affected area simultaneously showed new and old lesions that may fuse and consist clusters into map-like patterns with later surface scale. The skin lesion did not accompany blisters nor erosions. Pathological findings of the skin biopsy taken from dorsal site of right foot. (d) H&E stain showed spongiosis and enhanced edema in epidermis, with mononuclear cell infiltration to epidermis, dermal vessels, and appendix. (e) The expression of myxovirus resistance protein 1 (MxA, a type 1 interferon-inducible protein) was significantly up-regulated in basal layer of epidermis, dermal vascular lesions, and appendix. (f) Clinical appearance of feet at day 33 [Color figure can be viewed at wileyonlinelibrary.com]

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myxovirus resistance protein 1 (MxA, a type 1 interferon-inducible protein) was significantly up-regulated in epidermis, dermal vascular lesions, and appendix (detected by specific antibody, ss-166412: Santa Cruz, Dallas, TX, USA: Figure 1e).[1,2] The patient was treated by initial 30 mg/day prednisolone (started from day 4, reduced the dose 10 mg/day every week). The symptoms and signs disappeared with pigmentation and membrane-like desquamation after two weeks (Figure 1f).

The relationship between this acral lesion and SARS-CoV-2 is controversial, mainly because there is a minority of patients with COVID toes who are positive (only 13 patients out of 88) for PCR tests.[3] The current patient showed positive IgM antibody against SARS-CoV-2, although SARS-CoV-2 IgG antibody had been negative. This did not indicate that IgM SARS-CoV-2 was false positive, since the system uses the same antigen for both IgM and IgG in the same strip. The patient did not switch the antibody class to IgG.

Monogenic autoinflammatory interferonopathy, Aicardi-Goutières syndrome, appears similar to toe lesions of the current case. The expression of MxA was up-regulated in this case. Therefore, local interferon induced by COVID19 may cause the erythema. Taken together, toe lesions of COVID-19 could be one of the valuable indicators for COVID-19, although further studies are needed.

CONFLICT OF INTEREST

None declared.

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REFERENCES

1. Okiyama N, Yamaguchi Y, Kodera M, Hamaguchi Y, Yokozeki H, Ishiguro N, et al. Distinct histopathologic patterns of finger eruptions in dermatomyositis based on myositis-specific autoantibody profiles. *Jama Dermatol*. 2019;155(9):1080–2.
2. Magro CM, Mulvey JJ, Laurence J, Sanders S, Crowson AN, Grossman M, et al. The differing pathophysiologies that underlie COVID-19-associated perniosis and thrombotic retiform purpura: a case series. *Brit J Dermatol*. 2021;184(1):141–50. https://doi.org/10.1111/bjd.19415
3. Docampo-Simón A, Sánchez-Pujol MJ, Juan-Carpena G, Palazón-Cabanes JC, Vergara-De Caso E, Berbegal L, et al. Are chilblain-like acral skin lesions really indicative of COVID-19? A prospective study and literature review. *J European Acad Dermatology Venereol Jeadv*. 2020;34. https://doi.org/10.1111/jdv.16665