

changes in COVID and post-COVID patients in order to obtain a panoramic image of COVID-19's systemic manifestations. Nails can function as an alarm sign for physicians regarding systemic diseases, including COVID-19.

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None.

Conflicts of Interest

None declared.

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Recurrence of previous chilblain lesions during the second wave of COVID-19: can we still doubt the correlation with SARS-CoV-2?

To the editor,

Between March and April 2020, after the onset of the first wave of the COVID-19 pandemic, a cluster of acral chilblain-like lesions (ACBLL) was observed in young subjects.^{1,2} Despite efforts to substantiate the correlation of ACBLL with SARS-CoV-2 infection, only a minority of cases have tested positive on reverse transcriptase-polymerase chain reaction (RT-PCR) or serology. Only 3 of the 33 patients with ACBLL seen at our

hospital in this period had evidence of recent SARS-CoV-2 infection on these tests. In all cases, skin lesions developed 1–4 weeks after the COVID-19 pandemic peak in the local population and resolved spontaneously within 4–12 weeks after their onset.

Following the start of the second pandemic peak, in the fall of 2020, we observed 7 new cases of ACBLL with clinical and laboratory features similar to those of the cases seen in the first wave. Again, only one of the seven patients tested positive on RT-PCR or serology for SARS-CoV-2. The temporal relationship between this second cluster and the pandemic outbreak was similar to that observed previously.

Importantly, besides the 7 new cases, 6 of the 33 patients seen during the first wave returned to our observation because of the recurrence of ACBLL, which developed 1–4 weeks after the second COVID-19 peak; the clinical features were comparable to those of the previous episode. Three of the six had systemic and/or respiratory symptoms before the relapse of ACBLL. Three reported recent contact with a confirmed case of COVID-19. All patients tested negative for SARS-CoV-2 on RT-PCR. Only one patient, who was already positive for IgG at the first evaluation, had positive IgM and IgG for SARS-CoV-2 (Maglumi, 2019-nCoV IgM and IgG CLIA assays; Snibe diagnostics) at the time of relapse.

Skin biopsy, performed in 5 of the 6 patients with reactivated lesions, showed a non-specific histological picture consistent with published reports of COVID-19-associated ACBLL^{3,4} (Fig. 1). Constant features were as follows: cuffed perivascular lymphocytic infiltrate with oedema and variable fibrinoid changes – consistent with lymphocytic vasculitis – in the dermis, often extending into the subcutaneous tissue. A lymphocytic infiltrate around sweat glands was also present in all cases. On immunohistochemistry, the inflammatory infiltrate was mostly composed of CD3+ T lymphocytes (with a normal CD4/CD8 ratio), together with scattered CD20+ B lymphocytes and occasional CD68+ histiocytes. Inconstant features were as follows: dermal oedema, vacuolar interface changes and accumulation of dermal mucin among the collagen fibres of the dermis.

Of note, 6/6 reactivations occurred at the identical anatomical site involved in the first episode, and the pattern, shape and morphology were the same as those of the previously observed lesions (Fig. 2).

Recent dermatoscopic observations and histopathological data of microvascular damage^{5,6} argue in favour of our hypothesis that SARS-CoV-2-induced vascular damage could have persisted subclinically after the disappearance of skin lesions, as a consequence of smouldering T-cell-mediated immune response. Further contact with SARS-CoV-2 might have again triggered a local inflammatory response, which, in turn, might have led to the recurrence of full-blown ACBLL.

Our observation of the reactivation of ACBLL during the second COVID-19 wave in patients who had comparable lesions in

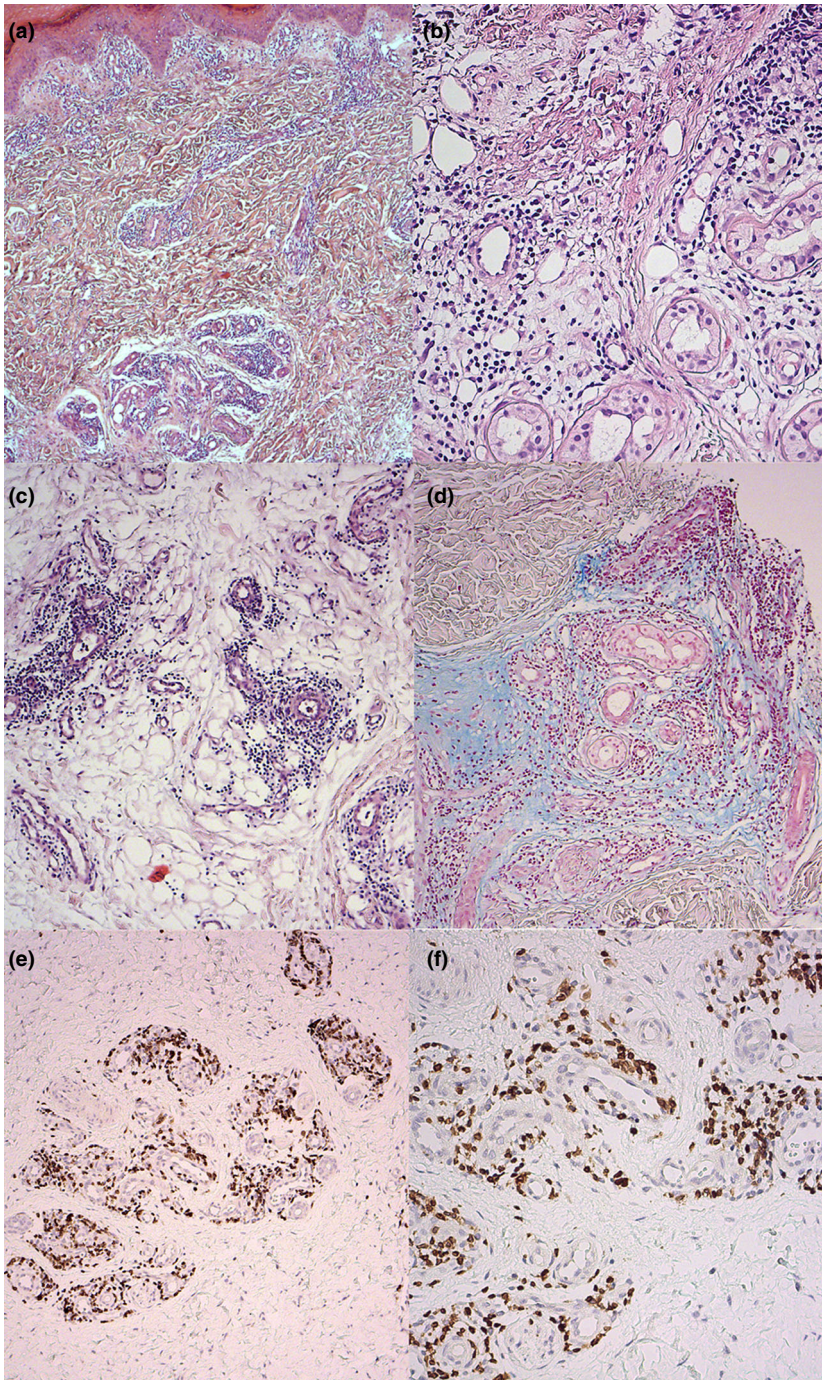


Figure 1 Biopsies of relapsed chilblain-like lesions: (a) H&E. Magnification 5 \times . Presence of perivascular and peri-eccrine lymphocytic infiltrate. (b) H&E. Magnification 20 \times . In the mid-dermis, presence of perivascular and peri-eccrine lymphocytic infiltrate. (c) H&E. Magnification 10 \times . In the hypodermis: lymphocytic perivascular and mural infiltrate. (d) Alcian blue (pH 2.5) stain, magnification 10 \times . The histochemical stain reveals the presence of mucin in the reticular dermis, around vessels and sweat glands. (e-f) Immunohistochemical reaction against T-cell marker CD3: The perivascular infiltrate consists mostly of T lymphocytes; the picture is consistent with lymphocytic vasculitis; (e: magnification 10 \times ; f: magnification 20 \times).

the same anatomic areas in the previous pandemic wave, together with the occurrence of new cases after the disappearance of the phenomenon in the summer season, strongly suggests that this disorder is closely related to SARS-CoV-2 infection. The reason why the diagnostic tests for the virus are

often negative is unclear, but may depend on the intensity of the viral load, the characteristics of the virus or particular genetic or environmental factors. Further studies are needed to elucidate the pathogenetic mechanisms underlying this peculiar clinical manifestation of SARS-CoV-2 infection.



Figure 2 Clinical features of onset and reactivation of chilblain lesions in two patients: (a–b) Patient 1, 13-year-old girl: (a) first manifestation of chilblains in March 2020 spontaneously regressed at the end of April 2020. (b) reactivation of chilblains at the same anatomical site in December 2020. (c–d) Patient 2, 15-year-old boy: (c) in a foot with a pre-existing subungual haematoma, first manifestation of chilblains in March 2020 spontaneously regressed in June 2020. (d) reactivation of chilblain-like lesions at the same anatomical site in December 2020.

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Conflict of interests

The authors have no conflict of interest to declare.

Ethical approval

All procedures performed in studies involving human participants were in accordance with ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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COVID-19-triggered sarcoidal granulomas mimicking scar sarcoidosis

Editor

Diverse cutaneous manifestations of coronavirus disease-2019 (COVID-19) have been reported including morbilliform, pernio-like, urticarial, vesicular and papulosquamous eruptions.¹ In