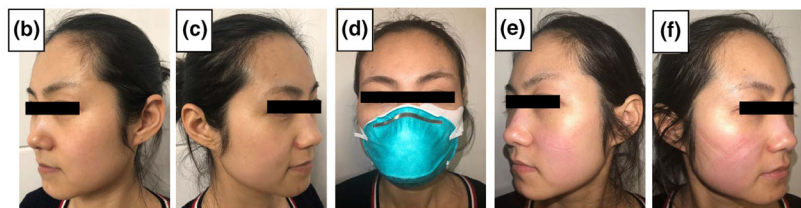




**Figure 2** Mean score plotted with regard to different skin reactions (a) and representative photographs: the left (b) and right (c) sides of the face before the intervention; wearing N95 mask with hydrogel patch applied on the left face (d); the hydrogel side (e) showing less adverse skin reactions in contrast with the control side (f) subsequent to at least 4 h N95 mask compression.



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## Acral purpuric lesions (erythema multiforme type) associated with thrombotic vasculopathy in a child during the COVID-19 pandemic

Editor

Since the beginning of the COVID-19 pandemic, different types of cutaneous manifestations have been reported. In Spain, there were reports in the first weeks of April 2020 of an increase in purpuric acral lesions similar to perniosis on the hands and especially the feet of children and young adults. These patients do not normally present with clinical manifestations linked to COVID-19, and their PCR and serological tests are usually negative for specific IgM and IgG.<sup>1,2</sup>

These acral lesions manifest in two clinical forms and can present in an isolated or concomitant manner. The first type of



**Figure 1** Clinical image. Purpuric lesions and vesicles located on the soles and ankles of the feet.

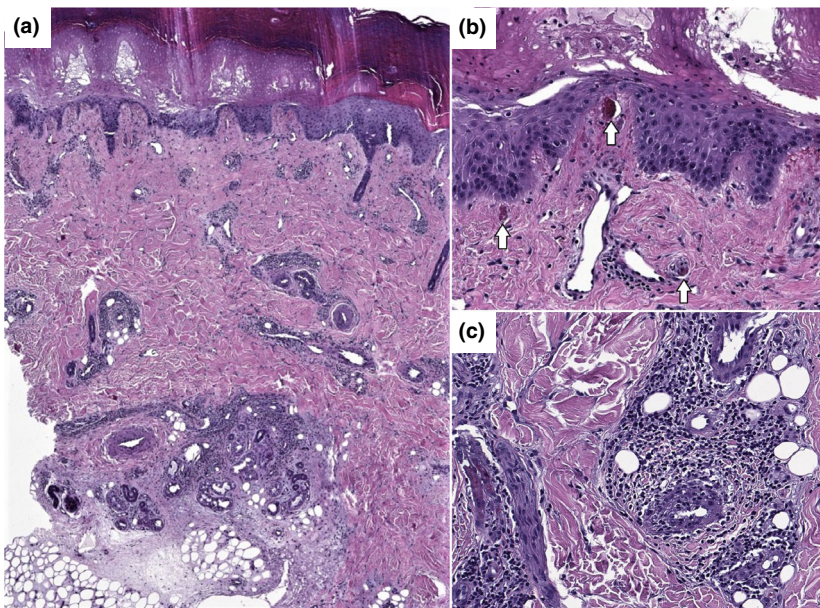
lesions is located on the fingers and toes as a type of erythematous-purpuric pernio, which can evolve into vesicles, blisters and crusts. The second type of lesions is found on the palms of the hand, soles of the feet or on the heels with macular or papular purpura characteristics that are similar to vasculitis or to erythema multiforme, being generally asymptomatic or pruriginous. This clinical and histopathological study reports on the second type of clinical presentation, associated with a thrombotic vasculopathy in the histological study, a finding that has not been reported in asymptomatic patients during the COVID-19 pandemic.<sup>2</sup>

A 12-year-old boy who, during the period of COVID-19 lockdown, presented with a pruriginous, haemorrhagic purpuric eruption and vesicular blisters on the heels of both feet, which had developed over a period of 4 days (Fig. 1) The patient had not taken any new medications and neither he nor his family presented with respiratory symptoms. The tests, which included biochemical, hepatic and renal tests, hemogram, coagulation test and urinalysis, showed no alterations. Nasopharyngeal swabs were taken for a specific PCR for COVID-19 and for an IgM and IgG rapid test, both of which were negative. A nasopharyngeal swab was also taken to carry out tests for influenza and other respiratory viruses, which were also negative. Serological tests were carried out for Epstein–Barr virus, cytomegalovirus, parvovirus B19, *Mycoplasma pneumoniae*, herpes simplex virus, measles, rubella, parotitis, HIV and hepatitis B and C, all of which were negative. PCRs of blood samples and of the cutaneous lesions were also carried out for enterovirus, which were also negative.

The serological tests were repeated 15 days after the symptoms started, and a test for SARS-Cov-2-specific IgM and IgG was also added, all of which were negative.

The histopathological study of a cutaneous biopsy revealed partial epidermal necrosis and perivascular lymphoid infiltrate in superficial and deep dermis. In addition, some capillaries in papillary dermis showed images of microthrombi, with extravasation of red blood cells. Vasculitic changes were present in relation to the lymphoid component but not in the thrombotic one (Fig. 2).

In cases or series of cases of pernio-like acral lesions, the histopathological findings have been unspecific. Dermal oedema, vacuolar alteration of the basal layer, necrotic keratinocytes and



**Figure 2** Histopathological findings (a). At low power view, a perivascular lymphoid infiltrate is present in dermis, both superficial and deep. (H&E, 2 $\times$ ). (b) Epidermal necrosis is identified. Focal images of microthrombi are observed in capillaries of the papillary dermis accompanied by extravasation of red blood cells. (White arrows) (H&E, 10 $\times$ ). (c). Vasculitic changes can be seen, with thickening of the vessel wall and activation of the endothelium with nuclear enlargement. In addition, lymphocytes are observed permeating the vessel wall (H&E, 20 $\times$ ).

mixed infiltrate with a mainly perivascular and perieccrine distribution in the superficial and deep dermis and the hypodermis have been notified.<sup>2-4</sup>

However, our histological findings are reminiscent of the pauci-inflammatory thrombogenic vasculopathy that occurs seriously ill hospitalized COVID-19 patients with COVID-19. This thrombogenic vasculopathy is due to activation of the complement pathways and an associated procoagulant state.<sup>5,6</sup> However, no cases of thrombotic vasculopathy have been reported to date in asymptomatic children or young adults with acral lesions.

In conclusion, the histological findings of purpura-erythema multiforme appearing on soles and heels reveal thrombogenic vasculopathy similar to that found in COVID-19 patients with severe forms of the disease, which suggests that these acral lesions may be related to SARS-CoV-2 or its etiopathogenesis.

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### Conflicts of interest

The authors declare that they have no conflict of interest.

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## Are chilblain-like acral skin lesions really indicative of COVID-19? A prospective study and literature review

To the Editor

Recently, young COVID-19 patients have presented with erythematous and purpuric acral lesions similar to chilblains.<sup>1-3</sup> Despite the scarcity of published cases, this topic has attracted significant mass media attention.<sup>4</sup> Dermatologists have noted that more people than would be expected at this time of year are seeking medical attention for these chilblain-like lesions. Some have suggested that people presenting with this manifestation should be tested and isolated.<sup>2</sup> Determining the accuracy of this association is, therefore, crucial.

To establish the real prevalence of COVID-19 in patients with acral skin lesions, we firstly evaluated all the cases of acral lesions presented in dermatology and paediatrics departments and family doctors' offices in an eastern Spanish region over a 3-week period. Then we prospectively performed a SARS-CoV-2 PCR on nasopharyngeal aspirates taken from all available patients to determine whether their cutaneous manifestations were predictive of a positive result.

To put our findings into context, we reviewed all the articles published before May 2020 concerning COVID-19 patients with cutaneous lesions.

We evaluated 58 patients, whose characteristics are summarized in Table 1. In most cases, lesions were chilblain-like. Fifteen patients had already been tested, and only one had a positive result: an 85-year-old man admitted for severe Covid-19 pneumonia. He had an ulcer on a toe that was finally determined to be vascular in nature.

We performed prospective PCR testing in 24 patients. All test results were negative. In total, then, PCR was negative in 38 patients and positive in a single patient whose lesion was very unlikely to be due to COVID-19.

Our bibliography search returned 97 articles and we found two more through cross-references. Nine of these articles dealt with acral lesions specifically. Their results are summarized in Table 2.