Dear Editor,

Acro-ischemic lesions associated with extremely elevated D-Dimer in a child during the COVID-19 pandemic

Acral lesions represent 65% of cutaneous manifestations of COVID-19. Most lesions resemble chilblains affecting hands and feet with asymmetric distribution. Acro-ischemic lesions have also been reported in mild or asymptomatic forms of COVID-19.

The most typical finding in coagulation tests on patients with COVID-19 is an increased D-dimer concentration. Inflammation of endothelial cells could lead to the massive release of plasminogen activators, which could explain the high concentrations of D-dimer and fibrin degradation products in patients with COVID-19.

A 10-year-old boy presented with a dry cough and a fever for 12 days and had acral lesions similar to acro-ischaemia on the toes of both feet during April 2020 in Spain, which coincides with spring and a warm climate (Fig. 1). The patient had no relevant medical history and had not taken any drugs. Blood tests, which included biochemical, haemogram, coagulation, hepatic, and renal profiles, immunoglobulins and an urinalysis, did not show any alterations apart from an elevation in D-dimer (4231 µg/L) and IgE immunoglobulin (1570 U.L/mL). An autoimmunity study was performed that included antinuclear antibodies, complement, autoantibodies against extractable nuclear antigens, anti-dsDNA, anti-histone anti-PM/Scl-100, anti-centromere protein-A/B, anti-ku, anti-ribosomal, anti-thyroid peroxidase antibodies, anti-thyroglobulin antibodies, cold agglutinins, circulating immunocomplexes, rheumatoid factor and a profile of myositis antibodies, which were all negative. Acute-phase reactants, such as C-reactive protein (0.037 mg/dL), erythrocyte sedimentation rate in the first hour (8 mm and serum ferritin levels (39 ng/mL) did not show elevations. Serologies for parvovirus B19, Epstein-Barr virus, cytomegalovirus, Mycoplasma pneumoniae, herpes simplex virus, hepatitis B and C, and RT-PCR for enterovirus were all negative. A nasopharyngeal swab for RT-PCR and a SARS-CoV-2 IgM/IgG rapid antibody test were performed with negative results. After 10 days, new serologies were carried out adding serologies for SARS-CoV-2 (IgA + IgM and IgG antibodies), which were negative.

Conflict of interest: The authors declare that they have no conflict of interest.

Funding statement: The authors received no financial support for the research, authorship and/or publication of this article.

Figure 2  (a) Inflammatory infiltrate involving mid dermis, with scarring (HE, x4). (b) Mixed inflammatory infiltrate which includes lymphocytes, eosinophils, neutrophils and histiocytic giant cells. (HE, x20).

doi: 10.1111/ajd.15424

© 2020 The Australasian College of Dermatologists
A skin biopsy showed both superficial and deep perivascular lymphocytic infiltrates with vacuolar degeneration in the basal epidermal layer. The blood vessels showed swollen endothelium, oedema, fibrin and extravasation of red blood cells in the papillary dermis (Fig. 2). There was complete resolution of the lesions and normalisation of the D-dimer levels after 4 weeks.

Reports of acral lesions in children and young adults coinciding with the COVID-19 pandemic have become more frequent. Despite this, most studies have not been able to show evidence of active or past SARS-CoV-2 infection in diagnostic tests, including serologies, presenting positive diagnostic tests in only 7% of cases.1

The clinical and histopathological findings of the reported case are similar to those of other studies.1,2 However, extremely high levels of D-dimer have not been reported in children or young adults with these lesions. This is probably due to a lack of analytical and coagulation studies carried out when patients present with only mild or asymptomatic forms of COVID-19. In our case, the endothelial damage present in the histopathological findings may explain the elevation of D-dimer levels, as occurs in seriously ill patients with COVID-19.

Significant elevations in D-dimer levels coinciding with acro-ischaemic lesions and the subsequent normalisation along with the exclusion of other cases of D-dimer elevation suggest that the skin lesions are related to COVID-19. These findings reinforce the hypothesis that SARS-CoV-2 infection may cause the lesions, which can be explained by various hypotheses. One of them is that acro-ischaemic lesions are evidence of endothelial damage induced by SARS-CoV-2,2 which in turn produces a hypercoagulable state that raises D-dimer levels. Another explanation would be that the thromboembolic phenomena that usually occur in COVID-19 patients contributed to endothelial damage and subsequent appearance of acro-ischaemic lesions. However, it could also be explained as a combination of the previous aetio-pathogenic hypotheses.

We propose, supported by other studies, that this type of skin lesion be added to the testing criteria for COVID-19 and the consideration for performing PCR tests and serologies.1

Figure 1 (a) Erythematous–purpuric lesions can be seen on the toes with the presence of superficial crusts. (b) Purpuric lesions on the pads of the toes.

Figure 2 (a) Skin biopsy shows superficial and deep perivascular lymphoid infiltrate. (HE, x2). (b) Basal vacuolar changes are present. (HE, x10). (c) The endothelium is enlarged, and fibrin is present focally. (HE, x20).

© 2020 The Australasian College of Dermatologists
ACKNOWLEDGEMENTS
We gratefully acknowledge the multidisciplinary team that contributed to the patient's medical care.

Miguel Fernando García-Gil1 | Juan Monte Serrano1 | Mar García Garcia1 | José Alfonso Pascual-del-Riquelme2 | Mariano Ara-Martín1

1Department of, Dermatology, 2Pathology and 3Microbiology, Lozano Blesa University Clinical Hospital, Zaragoza, Spain

REFERENCES
1. Freeman EE, McMahon DE, Lipoff JB et al. Pernio-like skin lesions associated with COVID-19: a case series of 318 patients from 8 countries. J. Am. Acad. Dermatol. 2020; 83: 486–92.
2. Colmenero I, Santonja C, Alonso-Riaño M et al. SARS-CoV-2 endothelial infection causes COVID-19 chilblains: histopathological, immunohistochemical and ultrastructural study of 7 paediatric cases [published online ahead of print, 2020 Jun 20]. Br. J. Dermatol. 2020. https://doi.org/10.1111/bjd.19327.
3. Zhang Y, Cao W, Xiao M et al. Clinical and coagulation characteristics of 7 patients with critical COVID-2019 pneumonia and acro-ischemia. Zhonghua Xue Ye Xue Za Zhi. 2020; 41: E006.
4. Mazzotta F, Trocoli T. Acute acro-ischemia in the child at the time of COVID-19. [Online ahead of print, 2020]. Eur. J. Pediat. Dermatol. 2020
5. Levi M, Thachil J, Iba T et al. Coagulation abnormalities and thrombosis in patients with COVID-19. Lancet Haematol. 2020; 7(6): e438–e40.

doi: 10.1111/ajd.15450

Case Letter

Dear Editor,

Cutaneous Strongyloides infestation: A rare harbinger of disseminated strongyloidiasis

A 79-year-old Thai man was brought in by ambulance to the emergency department with tachypnoea, fevers and confusion. His family reported 20 kgs of unintentional weight loss. He was being investigated for an anterior mediastinal mass presumed to be lymphoma. Past medical history included diabetes mellitus and hypertension. He was intubated and admitted to intensive care for the treatment of sepsis from a presumed respiratory source requiring ventilation, vasopressors and broad-spectrum antimicrobials. Dermatology was consulted on the fourth day of admission to review a new reticulate, purpuric non-blanching eruption on his right abdomen that rapidly (within hours) extended to involve the entire abdominal surface and groin (Fig. 1). The provisional diagnosis was an infective vasculitis.

Skin biopsies demonstrated linear filariform Strongyloides stercoralis larvae (Fig. 2) scattered within the dermis. There was no vasculitis or eosinophilic infiltrate. Bloods showed peripheral eosinophilia of 0.7 x 10^9/L (normal, <0.5 x 10^9/L) and hypogammaglobulinaemia. Faecal specimens did not demonstrate any organisms; however, bronchoalveolar lavage confirmed the presence of S. stercoralis larvae. Ivermectin (200 µg/kg daily) was given initially via nasogastric tube; additional albendazole was considered but was not given due to further deterioration. Comfort care measures were implemented, as he succumbed to disseminated strongyloidiasis.

Strongyloides stercoralis is a parasitic nematode endemic in South-East Asia, South America and Africa that has a complex life cycle enabling asexual reproduction. Filariform S. stercoralis larvae reside in infested soil and transcutaneously inoculate human hosts to eventually reside in the small intestine. Most cases of strongyloidiasis in the immunocompetent are asymptomatic, or may manifest with urticaria or larva currens. However, in disseminated strongyloidiasis the overwhelming nematode burden causes rampant autoinfection in the immunocompromised host, resulting in widespread S. stercoralis larvae infestation.

Our case highlights a rare presentation of disseminated strongyloidiasis presenting with thumbprint purpura. Risk factors for strongyloidiasis include male gender and Thai origin, which has a prevalence of strongyloidiasis of between 11 and 28%. Disseminated strongyloidiasis, as in

Figure 1  (a, b) Diffuse reticulate purpura and petechiae on the abdominal surface.

Funding statement: None.
Conflict of interest: None.