for all covariates, patients with depression were at a 76% increased risk of psoriasis compared with the general population (HR 1·76, 95% CI 1·68–1·85; P < 0·001; Table 1). Antidepressants produced a confounding effect, which decreased the HR > 10% when removed from the model. Patients with depression who used antidepressants had a lower absolute risk of developing psoriasis (1·38%) compared with nonusers (2·10%, P < 0·001). Similar findings were observed in the general population, with antidepressant users having a lower absolute risk of psoriasis (1·15%) than nonusers (1·26%, P < 0·001). Sensitivity analyses revealed that imposing a minimum of 6 months between diagnosis of depression and psoriasis decreased the effect size of the risk of psoriasis (HR 1·57, 95% CI 1·49–1·65, P < 0·001), which was further reduced by imposing a 12-month restriction (HR 1·39, 95% CI 1·32–1·47; P < 0·001). The median time from depression to psoriasis diagnosis was 3·7 (interquartile range 5·7) years.

Our analysis supports that depression is a significant risk factor for developing psoriasis. This risk may be mitigated by antidepressant use and even patients in the general population without depression who used antidepressants seemed to have a slightly lower risk of psoriasis. The exact mechanisms by which antidepressants produce this effect remain unknown. While accounting for potential reverse causality or diagnostic delays in our sensitivity analyses, the relationship between depression and psoriasis decreased but remained significant over time. It is plausible that the risk of psoriasis is highest when depression severity is at its worst (leading patients to seek medical attention) and over time, treated depression confers less risk of immune-mediated changes to the body. Future research should aim to account for depression severity and remission to assess dose–response relationships.

One potential limitation of this study is misclassification of depression or psoriasis. We presume this likely occurred at random, thus not preferentially within one of the subgroups. Additionally, although the study hypothesis was based on apparent inflammatory associations, it was not possible to assess cytokines, systemic inflammation levels or disease extent/severity. These limitations are offset by the length of follow-up and large sample size.

In conclusion, this is the first study to identify a temporal relationship of depression predisposing to psoriasis, and further strengthens the importance of identifying the relationship between systemic inflammation with mental health. Healthcare providers should be aware of the influence that mental health can have on the development of dermatological disease including psoriasis.

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I.A. Vallerand,[1,2] R.T. Lewinson,[2] L.M. Parsons,[2] M.W. Lowerison,[1] S.B. Patten[1,3] and C. Barnabe[1,4]

[1]*Department of Community Health Sciences,* [2]*Division of Dermatology,* *Department of* [3]*Psychiatry and* [4]*Division of Rheumatology, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada*

Email: ivall@ucalgary.ca

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COVID-19 chilblain-like lesion: immunohistochemical demonstration of SARS-CoV-2 spike protein in blood vessel endothelium and sweat gland epithelium in a polymerase chain reaction-negative patient

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Dear Editor, A 35-year-old woman with no significant previous medical history presented at the emergency department of Fundación Jiménez Díaz Hospital (Madrid, Spain) on 14 April

2020 with acral purpuric lesions of 3 weeks' duration. These had started as oedematous, erythematous areas and had appeared coincidentally with fever and coughing, which lasted only 2 days. There was no history of diarrhoea, ageusia, hyposmia or dyspnoea. The patient stated that the skin of her feet acquired a bluish discoloration when she was standing for some time. On examination, arterial pedal pulses were not palpable, and violaceous areas were seen on the dorsa of several toes on both feet (Figure 1a). An ultrasound study ruled out vascular thrombosis. A nasopharyngeal swab reverse-transcriptase polymerase chain reaction study for SARS-CoV-2 RNA and an immunochromatographic assay kit for serum IgG and IgM antibodies performed the same day were negative.

A skin biopsy obtained while the patients was in the emergency department showed mild perivascular and periadnexal lymphocytic inflammation and focal thrombosis of a small vessel (Figure 1b). There was mild erythrocyte extravasation and occasional evidence of endothelial damage, but no overt vasculitis was identified. Employing a commercially available antibody (SARS-CoV/SARS-CoV-2 spike 1A9; GeneTex, Inc., Irvine, CA, USA), optimized in our laboratory, viral spike protein was distinctly detected by conventional immunohistochemistry as fine-to-coarse, bright red granular deposits in the cytoplasm of cutaneous dermal vessels and eccrine cells (both secretory and excretory) (Figure 1c, d). Appropriate negative and positive controls were performed: adult tonsil, a chilblain specimen from early 2019, biopsies from non-COVID-19-related inflammatory dermatoses and substitution of the antibody with saline serum as negative controls, and a post mortem lung specimen from a patient with COVID-19 as a positive control (Figure 1d, inset).

Perivascular deposits of C5b9, C3 and C1q were seen on direct immunofluorescence study of formalin-fixed, paraffin-embedded tissue. Treatment with low-molecular-weight heparin and low-dose aspirin was started; the lesions subsequently healed, and at the time of latest follow-up (7 June) the patient had recovered completely and pedal pulses were palpable. A second serological study (2 months after the start of the disease), this time by enzyme-linked immunosorbent assay, was negative for IgG and IgM against SARS-CoV-2.

The ongoing COVID-19 pandemic due to SARS-CoV-2, initially regarded as a primarily pulmonary disorder, has evolved into a multisystemic disease reflecting the tropism of the virus and the inflammatory and thrombotic immunological response. Cutaneous manifestations of COVID-19 have gained the attention of dermatologists worldwide, and six patterns of involvement have been recognized: urticarial rash, morbilliform–maculopapular, papulovesicular, chilblain-like, livedo reticularis/livedo racemosa like and purpuric–vasculitic.[1] Chilblain-like acral lesions are being increasingly reported as possibly related to COVID-19, but a causal relationship is hard to establish, as in many cases (like in ours) no serological or microbiological evidence of SARS-CoV-2 infection is detected. This might be due to a swift response from the innate immune system, or to an antibody response different from that of patients without this cutaneous presentation. Nevertheless, systemic or cutaneous endothelial damage might initiate local or systemic thrombotic phenomena, so that involvement of the endothelium is likely to be of pathogenic significance.

Other than in respiratory and alveolar epithelial cells or in alveolar macrophages, the virus has so far been identified by electron microscopy and/or immunohistochemistry in lung

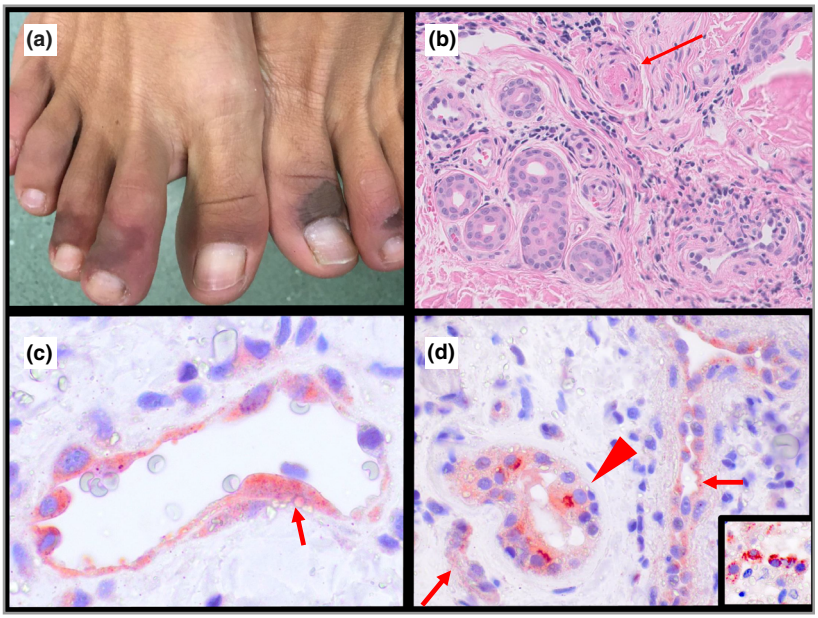

Figure 1 (a) Clinical photograph of chilblain-like lesions. (b) Perivascular and periadnexal lymphocytic inflammation, with focal evidence of thrombosis in a small vessel (arrow) (haematoxylin and eosin, original magnification × 200). (c, d) Immunohistochemical study of SARS-CoV-2 spike protein showing granular staining in endothelial cells (arrows) and sweat gland cells (d, arrowhead). Inset in (d): positive control (cells in lung tissue from an autopsy of a patient with COVID-19). Original magnification (c) × 400, (d) × 200, (d, inset) × 400.

alveolar capillaries,[2] endothelial cells of kidney glomeruli,[3] brain blood vessels,[4] colonic mucosa[5] and skin.[6] Our immunohistochemical study represents a straightforward means of linking SARS-CoV-2 infection and endothelium.

The presence of the virus in eccrine glands suggests sweat as a source of contagion, but this should be interpreted with caution. Given the similarities of SARS-CoV and SARS-CoV-2, it is worth mentioning that in a 2004 study of four autopsied patients with SARS, Ding *et al.*[7] found SARS-CoV nucleoprotein and RNA by immunohistochemistry and *in situ* hybridization, respectively, in a wide array of tissues, including sweat glands, intestine and kidney. They speculated accordingly the possibility of virus transmission through faeces, urine and sweat. A number of viruses, like hepatitis C virus, are known to replicate in sweat glands and keratinocytes; this could be investigated in sweat obtained by pilocarpine stimulation.[8]

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C. Santonja ,[1] F. Heras,[2] L. Núñez[2] and L. Requena [2]

[1]*Department of Pathology; and* [2]*Department of Dermatology, Fundación Jiménez Díaz, Madrid, Spain*

Email: csantonja@fjd.es

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Global Hidradenitis Suppurativa COVID-19 Registry: a registry to inform data-driven management practices

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Dear Editor, The management of hidradenitis suppurativa (HS), a chronic inflammatory skin disease, deserves special consideration in the context of the Coronavirus 2019 (COVID-19) pandemic. A new Global Hidradenitis Suppurativa COVID-19 Registry has been developed to capture data on the risks, clinical course and outcomes of COVID-19 in patients with HS. Caused by the virus SARS-CoV-2, COVID-19 is an easily transmissible disease, which, in its most severe form, is characterized by respiratory failure and multiple organ dysfunction triggered by a cytokine storm response. It predominates in older adults and those with significant comorbidities.[1]

Although HS is not considered a specific risk factor for COVID-19 illness, individuals with HS are potentially at increased risk for severe COVID-19 and poor outcomes, for several reasons. Firstly, although HS typically affects younger individuals, it is associated with diabetes and obesity, comorbidities that may predispose to more severe COVID-19 infections.[2] Secondly, immunomodulating biologic agents such as tumour necrosis factor inhibitors, which are associated with increased risk of infection, comprise the mainstay of therapy for moderate-to-severe HS and may put patients at increased risk of severe COVID-19 illness.[3] Thirdly, HS disproportionately affects people of racial and ethnic minorities, and patients with HS experience significant barriers to healthcare access even under usual circumstances.[4] These data, in conjunction with limited healthcare resources during the COVID-19 pandemic and recent data demonstrating racial and ethnic disparities in COVID-19 transmission, management and outcomes, suggest that disparities in care may disproportionately affect individuals with HS.[5–7]

Given the time required to develop effective COVID-19 vaccination and treatment strategies, HS management in the context of COVID-19 will need to be grappled with for the foreseeable future. As evidence is lacking to guide management recommendations, there is an urgent need for observational data to understand better the risks, clinical course and outcomes of COVID-19 in patients with HS. The Global Hidradenitis Suppurativa COVID-19 Registry was launched by an international team of investigators and patient partners from the USA, Canada, UK, Australia, Italy and Denmark in collaboration with the US, Canadian and Asia-Pacific hidradenitis suppurativa foundations, Hope for HS and Hidradenitis Suppurativa Warriors. This international paediatric and adult registry aims to identify predictors of COVID-19 outcomes in order to improve the care of patients with HS. Wide participation and case reporting by healthcare providers and patients with HS with suspected or confirmed