LETTER TO THE EDITOR

Negative SARS-CoV-2 antibodies in patients with positive immunohistochemistry for spike protein in pityriasis rosea-like eruptions

Dear Editor

Pityriasis rosea-like eruptions (PR-LE) have been recently associated with COVID-19 infection and vaccines. Negative SARS-CoV-2 PCR and serology have been reported in patients with skin manifestations, suggestive of COVID-19 with positive immunohistochemistry (IHQ) for SARS-CoV-2 spike protein in skin biopsies.[1–3] SARS-CoV-2 IHQ studies in biopsies of PR-LE are limited to a case report.[4] Herein, we report on 3 patients with PR-LE with positive IHC for SARS-CoV-2 spike protein and negative serology.

Three patients were evaluated between January and May 2021, and none of them had received COVID-19 vaccines at the time of evaluation or biopsy. IHQ with SARS-CoV/SARS-CoV-2 was performed on all cases [SARS-CoV/SARS-CoV-2 (COVID-19) spike antibody (1A9), dilution 1:100, lot no.43943, GTX632604; GeneTex Inc., Irvine, CA, USA]. The clone employed has shown specific immunoreactivity.[5] We performed positive controls on placental tissue of postpartum women with SARS-CoV-2 infection, and negative controls on normal skin and in 7 skin biopsies with a pityriasis rosea diagnosis from 2019.

The first case is a 22-year-old man with a 7-day history of a papulosquamous rash on his trunk, arms and legs (Fig. 1a), and petechiae in the feet dorsum. He referred fatigue, sore throat and close contact with a person diagnosed with COVID-19. IHC for SARS-CoV/SARS-CoV-2 spike protein was positive on the endothelium. IgG antibody testing for SARS-CoV-2 spike and nucleocapsid protein were both negative 5 months after the initial diagnosis.

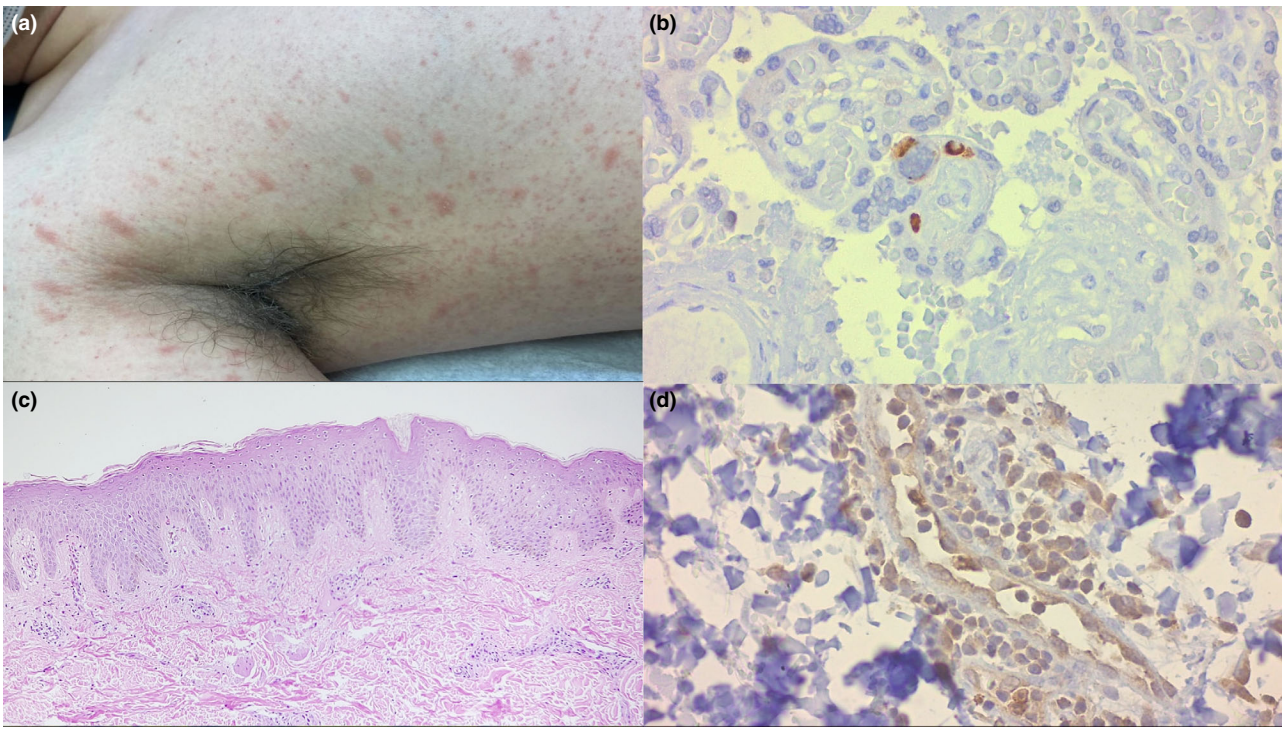

Figure 1 (a) Pityriasis rosea-like eruption in the trunk. (b) Positive control on placenta showing cytotrophoblast cells with nuclear and cytoplasmic SARS-CoV/SARS-CoV-2 spike protein positivity (10×). (c) Skin biopsy with acanthosis, focal parakeratosis, mild spongiosis, extravasated erythrocytes and a perivascular superficial lymphocytic infiltrate (haematoxylin and eosin, 10×). (d) Positive immunohistochemistry for SARS-CoV/SARS-CoV-2 spike protein in the endothelium and perivascular lymphocytes (40×).

The second case is a 26-year-old woman with a 2-week history of a disseminated rash on her trunk and arms. She referred headache and sore throat 2 weeks prior. IHC for SARS-CoV/SARS-CoV-2 spike protein was positive on the endothelium. IgG antibody testing for SARS-CoV-2 spike and nucleocapsid protein were both negative 5 months after the initial diagnosis.

The third case is a 31-year-old woman with a 1-month history of a disseminated rash on her trunk and arms. She referred headache during the last month. IHC for SARS-CoV/SARS-CoV-2 spike protein was positive on the endothelium and perivascular lymphocytes (Fig. 1d). IgG antibody testing for SARS-CoV-2 spike protein was negative 3 weeks after the initial evaluation.

All the biopsy specimens presented acanthosis, focal parakeratosis, mild spongiosis, extravasated erythrocytes and a superficial perivascular lymphocytic infiltrate in the dermis (Fig. 1c). Minimal neutrophils were present in the stratum spinosum similar to another case reported.[6] Due to the clinical features, evolution, histological findings and lack of human herpesvirus 6 (HHV-6) and 7 testing, we diagnosed the patients as having PR-LE.[7] All three patients were treated with topical corticosteroids, and the rash resolved after 1 week without recurrence; the first patient received his first dose and the third patient received two doses of the COVID-19 vaccine without adverse events.

The relationship between pernio and other cutaneous findings in COVID-19 has been challenging and complex. In SARS-CoV-2-associated perniosis, recent hypotheses have postulated that a robust innate and intrinsic immune activity driven by interferon-1 may explain the negative serological and PCR testing as it may drive viral clearance without inducing detectable antibody production.[8,9] If a similar immunological cascade happens in other COVID-19-associated manifestations, it warrants further investigation, but may explain the negative testing in the patients reported herein. More studies with IHC analysis of skin biopsies and lymphocyte assays for SARS-CoV-2-reactive T cells are necessary to clarify the relationship between SARS-CoV-2 and skin manifestations.[9] Limitations of our report include the lack of HHV-6/7 investigation and the possibility of cross-reaction with other antigens or viruses.

In conclusion, IHQ for SARS-CoV-2 may represent an important tool in the diagnosis of COVID-19 PR-LE especially in patients with negative serology or PCR. The prognosis of the dermatosis seems similar to other causes of PR-LE.

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The patients in this manuscript have given written informed consent to the publication of their case details.

Conflicts of interest

None to declare.

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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