Received: 22 May 2022 | Accepted: 5 August 2022

DOI: 10.1111/jdv.18498

LETTER TO THE EDITOR

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

Dear Editor,

The article by Welsh et al.[1] describing three patients with pityriasis rosea-like eruptions (PR-LE) and positive immunohistochemistry (IHC) for SARS-CoV-2 spike protein in skin biopsies prompted us to make some observations. We really appreciated the effort to search for the SARS-CoV-2 spike protein in cutaneous biopsies. Indeed, to date, IHC studies on this topic are rare.[2–4] The studied patients had negative IgG antibody testing for SARS-CoV-2 spike and nucleocapsid proteins (SARS-CoV-2-SNP), but, despite the presence of systemic symptoms and skin manifestations suggesting coronavirus disease (COVID-19), a nasal/oropharyngeal swab for SARS-CoV-2 RNA[1] has not been performed for confirming the diagnosis. Indeed, it is surprising such a rapid decline of antibodies in the described patients (5 months and 3 weeks) after SARS-CoV-2 infection since they usually persist for several months.[5] Despite serologic tests of antibodies against SARS-CoV-2-SNP having high sensitivity and specificity, different commercial assays can vary in their individual performance characteristics such as antibody decay. Unfortunately, the authors did not specify which serological assay they have used. In the absence of assays detecting SARS-CoV-2 RNA, it is appropriate to use at least two different commercial serological assays to achieve a specificity of at least 97% for the detection of previous SARS-CoV-2 infection.[5,6] Establishing the presence or absence of acute SARS-CoV-2 infection in the Welsh's described patients would be crucial because IHC may produce non-specific staining,[7] and the authors did not evaluate the presence of SARS-CoV-2 RNA in the same tissue sections. The description of the clinical features is incomplete[1]: the authors did not mention the possible presence of the herald patch and the oropharyngeal involvement, the morphology of the lesions, and how long the skin eruptions lasted. Furthermore, histological examinations of the skin biopsies, showing acanthosis, focal parakeratosis, spongiosis, extravasated erythrocytes and perivascular lymphocytic infiltrate in the dermis,[1] are quite typical of PR, instead of PR-LE. Indeed, PR-LE is histologically characterized by an interface dermatitis with scattered single necrotic keratinocytes, dyskeratotic keratinocytes in cluster, diffuse perivascular infiltrate of lymphocytes, histiocytes and eosinophils in the dermis and by enlargement of endothelial cells.[8] Unfortunately, the authors have not investigated potential signs of human herpesvirus (HHV)-6 and HHV-7 reactivation such as detection of HHV 6/7 DNA in plasma and of positive IgM antibodies against HHV-6/7 in serum, that are distinctive features of pityriasis rosea (PR) and that are usually absent in PR-LE.[8,9] We believe that for the patients described by Welsh et al., even if several diagnostic criteria have been neglected, the most likely diagnosis is PR. Indeed, PR is supported by the young age of the patients, the prodromal symptoms, the clinical presentation of the exanthem as shown in Figure 1 (erythematous papulosquamous lesions with marginal collarettes of scales distributed in a 'theatre curtain' pattern on the trunk) and the histopathologic features. Last but not the least, the patients did not take any drugs/vaccines which could have caused hypersensitivity reactions such as PR-LE.[1]

PR-LE is a drug/vaccine-induced skin rash with clinical features that closely resemble genuine PR; however, in PR-LE the skin lesions are more itchy, diffuse and confluent than in typical PR, and the mucous membranes are usually involved; the herald patch is absent, and the patients never experience prodromal symptoms.[8,9] Furthermore, patients with PR-LE may have blood eosinophilia as a marker for adverse cutaneous drug reactions,[8–10] a laboratory data not mentioned by Welsh et al.[1] In conclusion, we suggest to consider the clinical, histopathologic and virologic criteria proposed for distinguishing PR and PR-LE, also applicable in the setting of COVID-19 and COVID-19 vaccination.[8,9] The distinction is of paramount importance since the two eruptions have completely different pathogenesis, duration and therapeutic options.[8,9]

ACKNOWLEDGEMENT

None.

FUNDING INFORMATION

None.

CONFLICT OF INTEREST

None.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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