Received: 24 April 2022 | Accepted: 16 August 2022

DOI: 10.1111/jdv.18556

LETTER TO THE EDITOR

COVID-19 induced pityriasis rubra pilaris: A superantigenic disease?

Dear Editor,

A wide range of cutaneous manifestations has been described in association with Coronavirus disease 2019 (COVID-19), such as confluent erythematous/maculopapular/morbilliform rash, chilblain-like acral pattern, livedo reticularis/racemosa-like pattern, urticarial rash, papulovesicular exanthem and purpuric vasculitic pattern.[1] Few reports highlight the linkage between SARS-CoV-2 infection and some rare inflammatory dermatoses, such as pityriasis rubra pilaris (PRP).[2,3]

Herein, we report the case of a 28-year-old woman, otherwise healthy and without a remarkable family history, presented to our Dermatology Unit for a 1-month history of cutaneous eruption, appearing 6 days after a mild, paucisymptomatic, COVID-19 infection. The rash started as a palmoplantar scarlatiniform erythema accompanied by a large lamellar, Kawasaki-like, scaling, certified by a previous dermatological visit. At the moment of our examination, the patient presented a yellowish palmoplantar hyperkeratosis and multiple, erythematous-keratotic follicular papules, 2–3 mm of diameter, spreaded at wrists, antecubital fossa and limbs. An erythema with slight orange hue was widely appreciable between the papules, with 'islands of sparing' of unaffected skin (Figure 1a–d). A 4 mm punch biopsy was taken for histopathological examination on an erythematous lesion on the knee. Histopathology revealed orthokeratosis with focal parakeratosis, epidermal acanthosis and papillomatosis with no evidence of frank psoriasiform hyperplasia. In the upper dermis, a perivascular lymphocytic infiltrate, with absence of neutrophils, migrating at the dermo-epidermal junction was observed. Keratotic plugging was not detected (Figure 2a,b). Based on clinical and histological features, a diagnosis of PRP was made.

PRP is a chronic immune-mediated skin disorder, characterized by yellow palmoplantar keratoderma and diffuse hyperkeratotic papules. A background red–orange erythema and isles of healthy skin are other typical clinical features. Most cases are sporadic, but familial cases have been also reported.[2] Pathogenesis of PRP is not yet fully understood; the interleukin (IL)-23/IL-17 axis seems to play an important role, since an increased level of these inflammatory cytokines has been found in PRP lesional skin.[4] Gain-of-function pathogenic variants of *CARD*14 (Caspase Recruitment Domain Family Member 14) have been found in PRP familial cases; the constitutive activation of inflammasome, whose CARD14 gene product is a major component, leads to a hypersecretion of CCL20 chemokine, a potent activator of the T-helper (Th) 17 pathway.[5]

An environmental trigger may induce PRP onset in genetically predisposed individuals. Acute post-infectious PRP has been proposed by Larregue et al.[6] as a new subtype of the disease, typical of children, defined by a scarlatiniform erythema which evolves in the classical juvenile PRP, appearing some weeks later an infectious episode, in patients with no family history of the disease. Post-infectious PRP presents an acute clinical course with good outcomes and no tendency towards recurrence. Two other cases of post COVID-19 PRP have been reported in literature until now (in a 7-year-old child[2] and in a 32-month-old boy[3]). Our case, to date, is the first to report a post COVID-19 PRP in an adult (28-year-old woman).

The prodromic scarlatiniform presentation seems to be a specific feature of post-infectious PRP, including COVID-19, as outlined in the above-mentioned reports and our case.[2,3]

Ferrándiz-Pulido et al.[7] defined post-infectious PRP as a superantigen-mediated dermatosis, according to the clinical similarity of the prodromic scarlatiniform phase with other skin disorders mediated by superantigen, such as staphylococcal scalded skin syndrome, scarlet fever and Kawasaki disease.

The superantigenic nature of SARS-Cov2 is still under debate, but it has been proved that the virus contains at least one unique superantigen-like motif.[8] Moreover, COVID-19 can clinically mimic a superantigenic disease, such as the Kawasaki disease in Multisystem Inflammatory Syndrome (MIS) in children (MIS-C).[9] Concerning PRP, we hypothesized that a genetic background could drive the superantigenic action into the Th17 pathway, thus triggering the disease. A new concept of post-Covid PRP as a superantigenic disease should be considered, but further efforts to better clarify the superantigenic nature of the SARS-CoV-2 virus are needed.

AUTHORS' CONTRIBUTIONS

IFA, MR: concept and design, article drafting. AP, DR, FB, CM, MR: acquisition of data. CM: article drafting. AVM, CM, MR: revision. All the authors revised the manuscript and approved its final version.

Chiara Moltrasio and Maurizio Romagnuolo equally contributed.

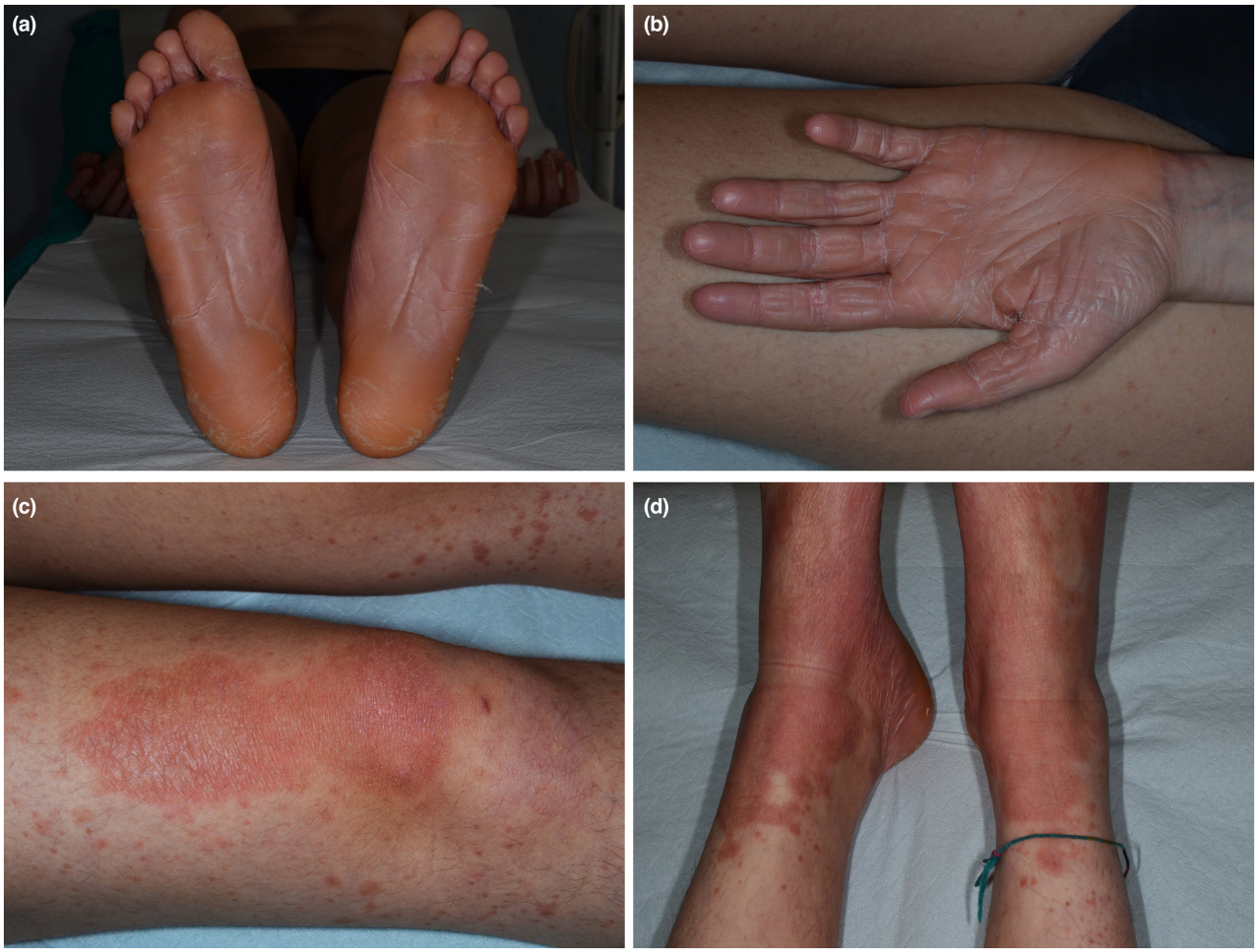

FIGURE 1 Clinical images showing (a) erythematous-to-orange plantar keratoderma; (b) dry, scaly lesions with an orange–red discoloration on the left palm; (c) an erythematous, irregular, plaque on the left knee with some erythematous and follicular papules on the lower extremities; (d) erythematous macules with an orange hue on the dorsa of the feet with the characteristic 'islands of sparing' of unaffected skin

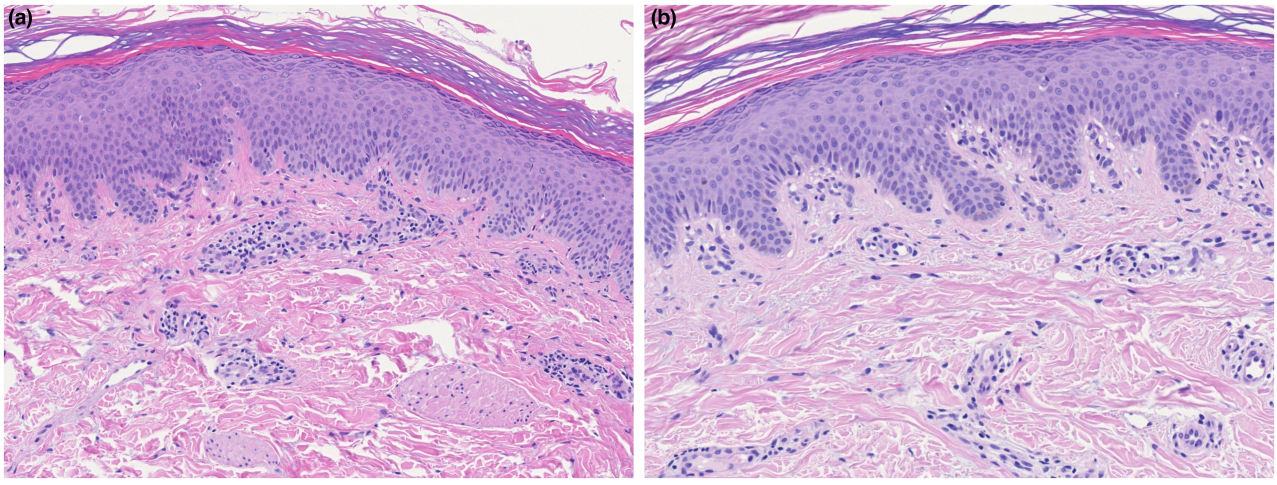

FIGURE 2 Histopathological examination showing (a) thickened horn layer with areas of parakeratosis, slight acanthosis and papillomatosis of the epidermis and a perivascular lymphocytic infiltrate (H&E, ×20); (b) a detail of epidermal changes showing an area of orthokeratosis, moderate acanthosis and papillomatosis with an admixed lymphocytic infiltrate disposed alongside the dermo-epidermal junction in a lichenoid pattern

FUNDING INFORMATION
This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

CONFLICT OF INTEREST
The authors have no conflict of interest to declare.

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

ETHICAL APPROVAL
The study was conducted in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national), with the Helsinki Declaration of 1975, as revised in 2000, and with the Taipei Declaration.

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

Italo Francesco Aromolo[1,2]
Armando Pisapia[1,2]
Davide Riva[1,2]
Francesco Barberi[1,2]
Angelo Valerio Marzano[1,2]
Chiara Moltrasio[2,3]
Maurizio Romagnuolo[1,2]

[1]*Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Milan, Italy*
[2]*Dermatology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[3]*Department of Medical Surgical and Health Sciences, University of Trieste, Trieste, Italy*

Correspondence
Maurizio Romagnuolo, Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Via Pace 9, 20122, Milan, Italy.
Email: maurizioromagnuolo@hotmail.it, maurizio.romagnuolo@unimi.it

ORCID
Italo Francesco Aromolo https://orcid.org/0000-0003-0996-6963
Angelo Valerio Marzano https://orcid.org/0000-0002-8160-4169
Maurizio Romagnuolo https://orcid.org/0000-0002-7015-8319

REFERENCES
1. Genovese G, Moltrasio C, Berti E, Marzano AV. Skin manifestations associated with COVID-19: current knowledge and future perspectives. Dermatology. 2021;237:1–12.
2. Kadylak D, Barańska-Rybak W. Acute postinfectious pityriasis rubra pilaris as a cutaneous manifestation in COVID-19: a case report and its dermoscopic features. J Eur Acad Dermatol Venereol. 2021;35(10):e622–4.
3. Aguilar-Gamboa FR, Cubas-Alarcon D, Villegas-Chiroque M, Failoc-Rojas VE. Pityriasis rubra pilaris post-infection due COVID-19: case report. Colomb Med. 2021;52(1):e7014577.
4. Feldmeyer L, Mylonas A, Demaria O, Mennella A, Yawalkar N, Laffitte E, et al. Interleukin 23-helper T cell 17 axis as a treatment target for pityriasis rubra pilaris. JAMA Dermatol. 2017;153(4):304–8.
5. Wang M, Zhang S, Zheng G, Huang J, Songyang Z, Zhao X, et al. Gain-of-function mutation of Card14 leads to spontaneous psoriasis-like skin inflammation through enhanced keratinocyte response to IL-17A. Immunity. 2018;49(1):66–79.e5.
6. Larregue M, Champion R, Bressieux JM, Laidet B, Lorette G. Acute pityriasis rubra pilaris in childhood. Four cases. Ann Dermatol Venereol. 1983;110:221–8.
7. Ferrándiz-Pulido C, Bartralot R, Bassas P, Bodet D, Repiso T, Aparicio G, et al. Pitiriasis rubra pilaris aguda postinfecciosa: una dermatosis mediada por superantígenos [Acute postinfectious pityriasis rubra pilaris: a superantigen-mediated dermatosis]. Actas Dermosifiliogr. 2009;100(8):706–9.
8. Cheng MH, Zhang S, Porritt RA, Noval Rivas M, Paschold L, Willscher E, et al. Superantigenic character of an insert unique to SARS-CoV-2 spike supported by skewed TCR repertoire in patients with hyperinflammation. Proc Natl Acad Sci USA. 2020;117(41):25254–62.
9. Kouo T, Chaisawangwong W. SARS-CoV-2 as a superantigen in multisystem inflammatory syndrome in children. J Clin Invest. 2021;131(10):e149327.