

## Covid-19 and Covid-19 vaccine can slide along sides: a report of two cases of unilateral periflexural exanthema

Dear Editor,

We herein report two cases of unilateral peripheral rash occurring in a paediatric patient and a young adult, respectively, during SARS-CoV-2 infection and after Covid-vaccine administration.

Case 1: a healthy 24-year-old woman presented an unilateral maculopapular eruption arising from her left groin, spreading up the side to involve the trunk and the left armpit, and to a lesser extent, contralateral groin (Fig. 1). The rash was moderately itchy and consisted of discrete 1–4 mm-sized macules and papules with a tendency to coalescence in patchy erythema. Acral sites and mucous membranes were spared. The patient's past history was unremarkable, but she had received the second dose of Comirnaty® in the 48 h preceding the onset of the rash. Notably, the patient had never contracted the Sars-Cov2 infection, and her serological tests and swab test performed shortly before the first dose were negative. No other triggers could be identified, as the patient did neither complain of any systemic symptoms nor had taken any drugs or applied any products in the preceding three weeks. Laboratory screenings for blood count, autoimmunity, renal and hepatic functions were within normal ranges, whereas a mild raise of C-reactive protein was found (5.2 mg/dL). The patient was dismissed with the prescription of topical mometasone 1%, and the rash eventually resolved 3 weeks after. Case 2: a 1-year-old female child, isolated with her family due to a positive nasopharyngeal swab for Sars-Cov2, sought our teleconsultation for a unilateral maculopapular rash that appeared a couple of days before. Cutaneous lesions were asymptomatic and exclusively affected the right side of the body, mostly at the trunk and limbs (Fig. 2). Systemic symptoms were mild and included flu-like symptoms, namely cough and cold. Currently, the rash is still present after 10 days, but is progressively fading with time. Since the advent of the pandemic, multiple skin manifestations have been reported in association with SARS-CoV-2 infection<sup>1</sup> or as immune-mediated events triggered by the administration of Covid-vaccines.<sup>2,3</sup> However, only a few reports of predominant unilateral rash have been linked to Covid-19. These include a case of asymmetrical periflexural rash arising with a marked predominance of the right side in a 42-year-old woman affected by Covid-19,<sup>4</sup> and a purpuric rash involving unilaterally the left inguinal region of a 58-year-old



**Figure 1** Mildly itchy macules and papules spread along the left lateral thoracic wall and, in a less predominant fashion, the contralateral groin.

man, hospitalized for Covid-19, which mainly ran asymptomatic, but caused ground glass pulmonary changes on the CT-scan.<sup>5</sup> Unilaterality was also reported as a distinctive feature in one case of leukocytoclastic vasculitis of the lower limbs, which occurred 4 days after the second dose of COVAXIN® administered to a 31-year-old woman, unaffected by previous medical conditions.<sup>6</sup> Few exanthems are characterized by a distinct one-side predominance, including asymmetric periflexural exanthem of childhood (APEC), unilateral laterothoracic exanthem, and its variant known as unilateral medi thoracic exanthem.<sup>6</sup> The terms often design the same affection, although APEC is extremely rare in adults, being predominant among 1- to 5-year-old



**Figure 2** Covid-positive child with unilateral papular eruption located at his right side of the trunk and proximal lower limbs.

children; also it recognizes a viral aetiology in most cases, and usually peaks in the winter and springtime.<sup>7</sup> The reason for the unilateral predilection is still unexplained, although a post-zygotic mutation that makes one-sided keratinocytes more susceptible to infectious triggers has been postulated.<sup>8</sup> It is possible that in our cases the keratinocytes of one side show, for the same reason, different reactivity to potential triggers. The production of the spike protein is a key element to elicit immune-driven skin reactions, mainly because it shares genetic analogies to human endogenous cross-reactive antigens.<sup>9</sup> As a consequence, both Sars-CoV-2 infection and Covid-vaccine, which are based on spike protein sequences, could trigger similar effects in genetically predisposed individuals. Besides molecular mimicry, other mechanisms may be implied, including T-cell mediate immune reactions, superantigen spreading, generation of

autoreactive lymphocytes and cross-reactive antibodies with consequent release of pro-inflammatory cytokines.<sup>3,10</sup>

### Acknowledgement

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

### Conflict of interest

None declared.

### Data availability

Data sharing is not applicable to this article as no new data were created or analysed in this study.

A. Sechi,<sup>1,2</sup>  A. Bassi,<sup>3,\*</sup>  C. Mazzatenta,<sup>3</sup> M. Cutrone,<sup>4</sup> L. Naldi,<sup>1</sup> G. Argenziano,<sup>5</sup> V. Piccolo<sup>5</sup>

<sup>1</sup>Dermatologic Unit, San Bortolo Hospital, Vicenza, Italy,

<sup>2</sup>IRCCS University Hospital of Bologna S Orsola-Malpighi Polyclinic Dermatology Division - Department of Experimental, Diagnostic and Specialty Medicine (DIMES), Alma Mater Studiorum University of Bologna, Bologna, Italy, <sup>3</sup>UO Dermatologia Lucca- Azienda USL Toscana Nordovest, Lucca, Italy, <sup>4</sup>Pediatrics Unit, San Bortolo Hospital, Vicenza, Italy, <sup>5</sup>Dermatology Unit, University of Campania, Naples, Italy

\*Correspondence: A. Bassi. E-mail: bassiderma@gmail.com

### References

- Piccolo V, Neri I, Filippeschi C *et al*. Chilblain-like lesions during COVID-19 epidemic: a preliminary study on 63 patients. *J Eur Acad Dermatol Venereol* 2020; **34**: e291–e293.
- Sechi A, Pierobon E, Pezzolo E *et al*. Abrupt onset of Sweet syndrome, pityriasis rubra pilaris, pityriasis lichenoides et varioliformis acuta and erythema multiforme: unravelling a possible common trigger, the COVID-19 vaccine. *Clin Exp Dermatol* 2022; **47**: 437–440.
- Piccolo V, Bassi A, Argenziano G *et al*. BNT162b2 mRNA COVID-19 vaccine-induced chilblain-like lesions reinforces the hypothesis of their relationship with SARS-CoV-2. *J Eur Acad Dermatol Venereol* 2021; **35**: e493–e494.
- Glick LR, Fogel AL, Ramachandran S, Barakat LA. Unilateral laterothoracic exanthem in association with coronavirus disease 2019. *JAAD Case Rep* 2020; **6**: 900–901.
- Karaca Z, Yayli S, Çalışkan O. A unilateral purpuric rash in a patient with COVID-19 infection. *Dermatol Ther* 2020; **33**: e13798.
- Kharkar V, Vishwanath T, Mahajan S *et al*. Asymmetrical cutaneous vasculitis following COVID-19 vaccination with unusual eosinophil preponderance. *Clin Exp Dermatol* 2021; **46**: 1596–1597.
- Niedermeier A, Pfützner W, Ruzicka T *et al*. Superimposed lateralized exanthem of childhood: report of a case related to adenovirus infection. *Clin Exp Dermatol* 2014; **39**: 351–353.
- Chuh AA, Chan HH. Unilateral mediothoracic exanthem: a variant of unilateral laterothoracic exanthem. *Cutis* 2006; **77**: 29–32.
- Kanduc D, Shoenfeld Y. Molecular mimicry between sars-cov-2 spike glycoprotein and mammalian proteomes: implications for the vaccine. *Immunol Res* 2020; **68**: 310–313.
- Perricone C, Colafrancesco S, Mazor RD, Soriano A, Agmon-Levin N, Shoenfeld Y. Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) 2013: unveiling the pathogenic, clinical and diagnostic aspects. *J Autoimmun* 2013; **47**: 1–16.

DOI: 10.1111/jdv.18093