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Pityriasis lichenoides et varioliformis acuta after SARS-CoV-2 infection and relapse after vaccination

Editor

A 21-year-old, otherwise healthy, woman presented in emergency with a 4-week history of a widespread eruption. She had no past history of skin diseases, and her only medication was birth control pills. In early July, she had presented fever for 2 days and cough for 5 days. She was subsequently found a positive nasopharyngeal swab for SARS-CoV-2. She also reported sore throat 1–2 weeks after COVID-19 infection. She had not received COVID-19 vaccination. At the end of July, 2–3 weeks after COVID-19 infection, a rash started on the abdomen and spread widely from scalp to the lower limbs. Upon referral at the end of August, she presented with an itchy and painful eruption of monomorphous dark red papules. The skin lesions represented different stages, ranging from recent active papules to crusts and hypopigmented scars. They were distributed widely on the trunk, abdomen, back with a ‘Christmas tree’ pattern (Fig. 1a), upper arms, tights and legs (Fig. 1b). All mucosae were spared. The patient was in good general health with no systemic symptoms. A skin biopsy of a recent lesion revealed focal

necrosis of the epidermis, parakeratosis, lymphocytic exocytosis and an inflammatory infiltrate of lymphocytes, macrophages and neutrophils as well as extravasation of red blood cells were found in the upper dermis (Fig. 2). The clinical presentation and histological findings were consistent with pityriasis



Figure 1 (a) Extensive eruption on the back, consisting of papules, crusts and hypopigmented scars with a Christmas tree distribution. (b) Dark papules of the tights and legs.

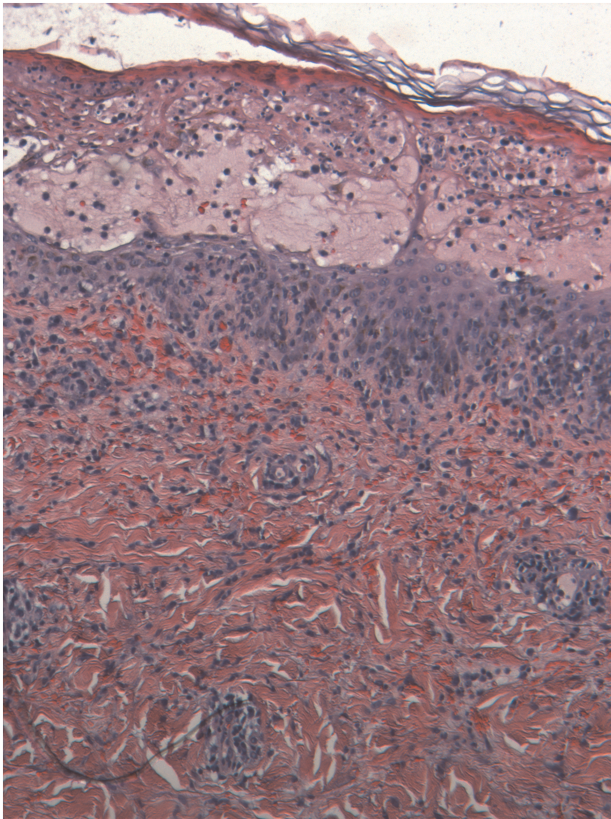


Figure 2 Microscopic examination of skin biopsy shows necrosis of the epidermis, exocytosis of lymphocytes, lymphocytic infiltration of the upper dermis and numerous extravasated red blood cells (H&E, ×20).

lichenoides et varioliformis acuta (PLEVA). Laboratory findings (complete blood count, C-reactive protein) were unremarkable; and serology for any other possible triggering infection (EBV, CMV, toxoplasmosis, parvovirus B19, HIV, hepatitis B and C) was negative. The patient was hospitalized for a week and was given a course of oral prednisolone (40 mg/daily, 0.7 mg/kg/day) with topical betamethasone dipropionate 0.1% ointment. Because of a lack of response after 1 week of treatment, narrowband UVB phototherapy (nbUVB) thrice weekly was initiated. Prednisolone was tapered during the first 2 weeks of phototherapy. Her skin began to improve slowly during nbUVB. At completion (20 sessions, 2 months), the rash had completely subsided leaving only hyperpigmented and hypopigmented macules. The patient was satisfied with the result and received her first COVID-19 vaccination (Pfizer-BionTech) 2 days later. She had no flare-up after the first dose. However, she was given a second dose at her healthcare center 1 month later and a flare-up of PLEVA occurred 10 days after the second vaccination, that is, 6 weeks after completion of phototherapy. The flare was milder but still affected the trunk and limbs and nbUVB was initiated again, with highly potent topical corticosteroid ointment.

Viral infections and vaccinations have been reported as possible triggers of pityriasis lichenoides (PL) in predisposed individuals.¹ The occurrence of PLEVA in our patient could be fortuitous. She reported a sore throat 1–2 weeks after COVID-19 infection and before the onset of PLEVA, but no other relevant viral infection was found as possible trigger. One case of PL chronica has been reported in a 42-year-old woman 10 days after COVID-19 infection,² and Guelimi et al have reported two patients with PL among French patients with unconfirmed COVID-19 infection.³ A series of 10 children with a papulo-purpuric rash with features of PLEVA have been reported among Italian paediatric COVID-19 patients.⁴ Besides, three cases of PLEVA after SARS-CoV-2 vaccination have recently been reported: a 70-year-old man,⁵ a 31-year-old woman⁶ and a 81-year-old man⁷ developed PLEVA, 5, 10 and 9 days, respectively, after the second and first BNT162b2 vaccination (Pfizer-BioNTech). Our case is specific as PLEVA occurred after a confirmed COVID-19 infection and relapsed after the second, short-interval vaccination, confirming thereby a link between SARS-CoV-2 infection and this inflammatory reaction.

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Conflicts of interest

None declared.

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Data availability statement

Data available on request due to privacy/ethical restrictions.

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Reply to ‘The first dose of COVID-19 vaccine may trigger pemphigus and bullous pemphigoid flares: is the second dose therefore contraindicated?’ by Damiani G *et al*.

Editor

We read with interest the article by Damiani *et al.*,¹ who reported three bullous pemphigoid (BP) and two pemphigus vulgaris (PV) patients in complete remission who experienced a disease flare-up after the first dose of COVID-19 vaccination. One of them showed an additional BP worsening following the second dose of BNT162b2 vaccine. The authors raise the question whether the second dose should be contraindicated.

We describe the case of a patient who recently came to our attention because of a PV relapse after BNT162b2 vaccine.

In September 2021, an otherwise healthy 46-year-old man with a one-year history of PV presented with mild blistering lesions developed on the trunk and arms five days after the first dose of

BNT162b2 vaccine. Small erosive lesions on the oral mucosa were observed as well. Detection of anti-desmoglein antibodies 1 and 3 titre (170 and 78 U/mL, respectively) was performed. Histological examination and direct immunofluorescence confirmed our hypothesis of PV relapse (Fig. 1a,b). The patient had been in remission for 10 months after oral prednisone and azathioprine and was on maintenance therapy with 5 mg/day of prednisone when he came to our attention for the relapse.

Based on updated recommendations,^{2,3} the low-dose oral steroid was maintained. Therefore, the patient received the second dose of vaccine 21 days after the initial one: five days later he was admitted to our department because of a sudden worsening of his pre-existing skin lesions. The physical examination revealed several confluent erosions and crusts on the upper part of the body accompanied by few flaccid, thin-walled blisters (Fig. 2a,b). Worsening of the oral lesions was not observed. Blood tests were performed and showed a further elevation of anti-desmoglein antibodies 1 and 3 (221 and 160 U/ml, respectively). Eventually, rituximab (two infusions of 1000 mg each 15 days apart) was given in combination with oral prednisone (50 mg/day), which is still ongoing.

Although a direct pathological link between the vaccine and PV onset cannot be established, the temporal association between the two events should not be overlooked either.

Thus, our work adds on to the already suspected association between mRNA vaccines and relapses in autoimmune bullous disease patients, as shown in other works.^{4,5} The particularity of our case lies in the PV flares observed after both the first and second dose, with a progressive worsening of severity.

To date, no clear explanation of this phenomenon has been provided. However, immunological mechanisms of mRNA vaccines could be partially held accountable for it. The vaccine

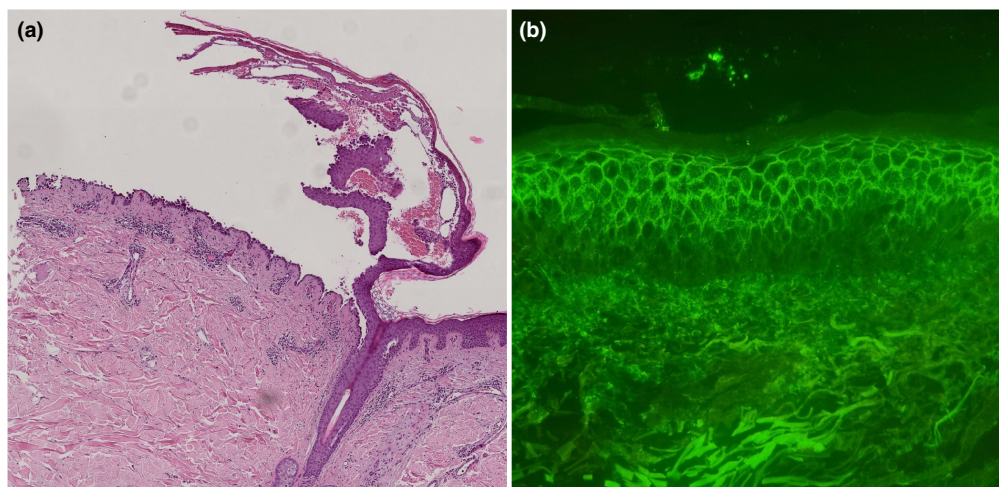


Figure 1 (a) Established suprabasal blister containing a few acantholytic cells (H&E, magnification 10×) (b) Direct immunofluorescence: IgG in the intercellular regions of the epidermis.