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LETTER

Pemphigus foliaceus triggered after inactivated SARS-CoV-2 vaccine: Coincidence or causal link?

Dear Editor,

Pemphigus is a group of autoimmune blistering disorders associated with autoantibodies against the keratinocyte cell surface. Its exact cause is still unknown, but neoplasms, infections, medications, or vaccines are considered as possible triggering factors. Only one case of pemphigus vulgaris (PV) following vaccination with mRNA vaccine BNT162b2 has been reported.[1] At the time of submission of the present report, this is the first case of Pemphigus foliaceus (PF) type triggered after inactivated SARS-CoV-2 vaccination.

A 44-year-old male presented with 2 months history of an erythematous progressive eruption, which appeared 7 days after the first shot of BBIBP-CorV (Sinopharm). He denied any previous medical history or medication use. Few erythematous and crusted lesions first appeared on his shoulders. These lesions were neglected by the patient, and he received the second dose 21 days later. That is when the lesions spread to the face and the trunk. On his admission in our department, physical examination showed scaling erythema affecting the whole trunk, and several erosion-crusts on the face and limbs, with a positive Nikolsky sign (Figure 1A,B). Mucosal surfaces and nails were not affected. His rash continued to worsen during the first week of hospitalization, leading to an exfoliative erythroderma. Histopathologic examination of skin biopsy revealed acantholysis with superficial intra-epidermal cleavage (Figure 1C). Intercellular IgG deposition in the epidermis with honeycomb pattern was seen in direct

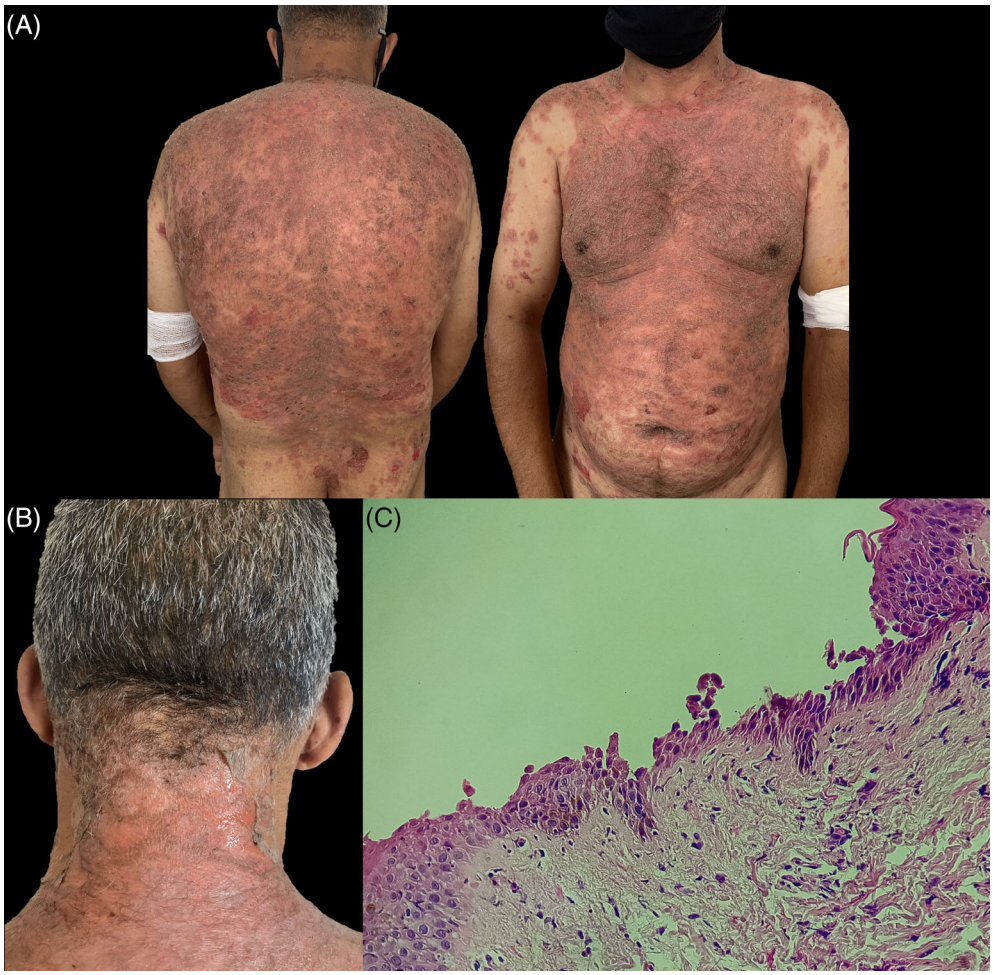

FIGURE 1 (A) Clinical examination on admission showing scales and crusts with erythematous bases and superficial blistering all over the trunk. (B) Large erosions of the neck after extension of the superficial detachment. (C) Histopathology of lesion showing subcorneal loss of adhesion with acantholytic cells

immunofluorescence from perilesional skin. Anti-intercellular cement substance antibodies were positive in indirect immunofluorescence (titer, 1: 160), as well as anti-desmoglein 1 antibodies that was positive in ELISA test (Euroimmun; Qualitative/Semiquantitative detection). Autoantibodies against desmoglein 3 were absent. He was diagnosed with PF and treated with prednisone, 2 mg/kg daily and azathioprine 150 mg/day. The patient is currently still hospitalized and is a candidate for rituximab treatment.

Although no clear etiology has been established, we know that aberrant immune responses contribute to the development of pemphigus. Indeed, any stimulation of the immune system may be considered as a potent threat. Drugs are the most common cause of pemphigus.[2] There is some evidence of pemphigus induction or exacerbation as a consequence of different types of vaccines against hepatitis B, rabies, influenza, anthrax and tetanus.[3–5] Recently, the first case of PV declaring itself after a 5-day delay of the mRNA vaccine BNT162b2, has been reported.[5] Two other patients experienced a flare-up of their known PV, after that they had undergone COVID-19 vaccination during a period of remission.[6]

In this case, although the relation between these two events could be a mere coincidence, such strict time succession is clearly suspicious. There are several proposed mechanisms regarding the link between the vaccine and the onset of pemphigus. Components of the vaccine-induced immunization could themselves act as foreign antigens, leading to cross-reacting antibodies targeting both the foreign antigen and desmoglein-1.[7] The neutralizing antibodies against infectious SARS-CoV-2 are detected in 18%, on day 7 after the first inoculation of BBIBP-CoV vaccine.[8] This could be the scenario for this patient, explaining the development of pemphigus on the seventh day following vaccination. Also, a hyper-immune reaction could result in autoantibody formation against the 160-kd antigen. All this probably took place on a genetic predisposition ground.[2]

At the time of writing, this is the first case of PF triggered after inactivated COVID-19 vaccination. Yet, the benefits of SARS-CoV-2 virus prevention far outweigh the risk of pemphigus, and our case shows that further research is needed to identify individuals at risk of developing autoimmunity following vaccination.

AUTHOR CONTRIBUTIONS

Sofia Alami: Literature search, data acquisition, manuscript preparation, manuscript editing. Leila Benzekri: Definition of intellectual content, data acquisition, manuscript review. Karima Senouci: Data acquisition, manuscript preparation. Mariame Meziane: Concepts, design, definition of intellectual content, manuscript review, guarantor.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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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