The appearance of purpuric and/or CLL lesions after administration of different SARS-Cov-2 vaccines seems to suggest however that these lesions could be also considered as a particular form of exanthema induced by the activation of the immune system against the viral spike protein irrespectively of its natural o synthetic origin in predisposed individuals.

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Conflicts of interest

The authors have no financial obligations or conflict of interest to declare.

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Data availability statement

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

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Association between vaccination and immunobullous disorders: a brief, updated systematic review with focus on COVID-19

Editor,

Autoimmune bullous diseases (AIBDs), including the heterogeneous groups pemphigus and pemphigoid, are rare and potentially life-threatening chronic inflammatory blistering disorders characterized by autoantibodies against desmosomal adhesion proteins and structural proteins of the dermal–epidermal junction, respectively.[1,2]

We have previously provided an overview of different vaccines against bacterial and viral infections possibly associated with the development of AIBDs, but information specifically pertaining to COVID-19 vaccines was lacking at the time of publication.[3] Given the accumulating evidence of a possible association between COVID-19 vaccines and AIBDs since then, a rapid, updated systematic review focusing on this potential link was performed.

The systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Literature from the inception of the database until 09 February 2022 was explored using PubMed. Keywords were 'pemphigus' or 'pemphigoid' or 'bullous' or 'blistering' combined with 'COVID-19 vaccination' or 'COVID-19 vaccine' or 'SARS-CoV-2 vaccination' or 'SARS-CoV-2 vaccine'. Additional author searches, including screening of bibliographies, were done to find further relevant publications. Inclusion criteria were peer-reviewed, English language articles about AIBD cases in association with COVID-19 vaccination. Pure reviews and basic research studies as well as articles not meeting the inclusion criteria were excluded. Collected data were checked by a second author, and any disagreement or data inconsistency were resolved by discussion.

At the end of our selection process with critical screening of titles, abstracts and full text, we included 30 papers (Fig. 1). These comprised 27 case reports/series (n = 272 vaccine recipients; 218 [80.1%] unspecified AIBDs, 41 [15.1%] bullous pemphigoid, 10 [3.7%] pemphigus vulgaris, 2 [0.7%] linear IgA disease and 1 [0.4%] pemphigus foliaceus), one prospective observational case–control study (n = 8 vaccine recipients; 8 [100%] unspecified pemphigus subtype), one registry-based

study (n = 12 vaccine recipients; 12 [100%] bullous pemphigoid) and one cross-sectional study (n = 640 vaccine recipients; 640 [100%] unspecified AIBDs).[4] Among the 932 immunized individuals, patients either presented clinically with *de novo* AIBDs (n = 53; 5.7%) or had a flare/worsening of pre-existing AIBDs (n = 91; 9.7%) after vaccination, whereas vaccination did not negatively influence the clinical course in 788 (84.5%) patients. The COVID-19 vaccines used were mRNA vaccines (Pfizer-BioNTech or Moderna; n = 756, 81.1%), adenoviral vector vaccines (AstraZeneca or Johnson & Johnson; n = 144, 15.5%), and inactivated vaccines (Sinovac/CoronaVac or Sinopharm; n = 17, 1.8%), whereas information about the vaccine type was not available in 18 (1.9%) patients. The reported time between receiving the first or second dose of the vaccine and manifestation of AIBDs ranged between 1 day and 6 weeks, with some patients experiencing aggravation of their AIBD symptoms after the second dose. The clinical courses of post-vaccinal AIBDs were mostly well controlled with conventional immunosuppressive therapy.

These results complement our previous systematic review by showing that, in addition to the standard vaccines against different microbes,[3] newly developed vaccines against COVID-19 may also possibly induce or trigger AIBDs, albeit in a relatively small fraction of vaccinated subjects. Whether this represents a *bona fide* causal relationship or is pure coincidence, however, is unknown, taking into account that the information is mainly derived from single case reports/series with a low level of evidence and a cross-sectional study biased by subjective patient self-reports.[4] In addition, the lack of cross-reactivity between circulating anti-SARS-CoV-2 antibodies and pemphigus or pemphigoid autoantigens argues against immunization-driven autoimmunity from a mechanistic perspective,[5] although alternative immunocellular modalities potentially promoting autoimmune processes by COVID-19 vaccines cannot be excluded.

In conclusion, while causality between COVID-19 vaccination and AIBDs remains unproven and should not affect present vaccination recommendations for this group of patients,[6] raised awareness and timely recognition of rare post-SARS-CoV-2-vaccinal cases would be important for their optimal management.

Conflicts of interest

None.

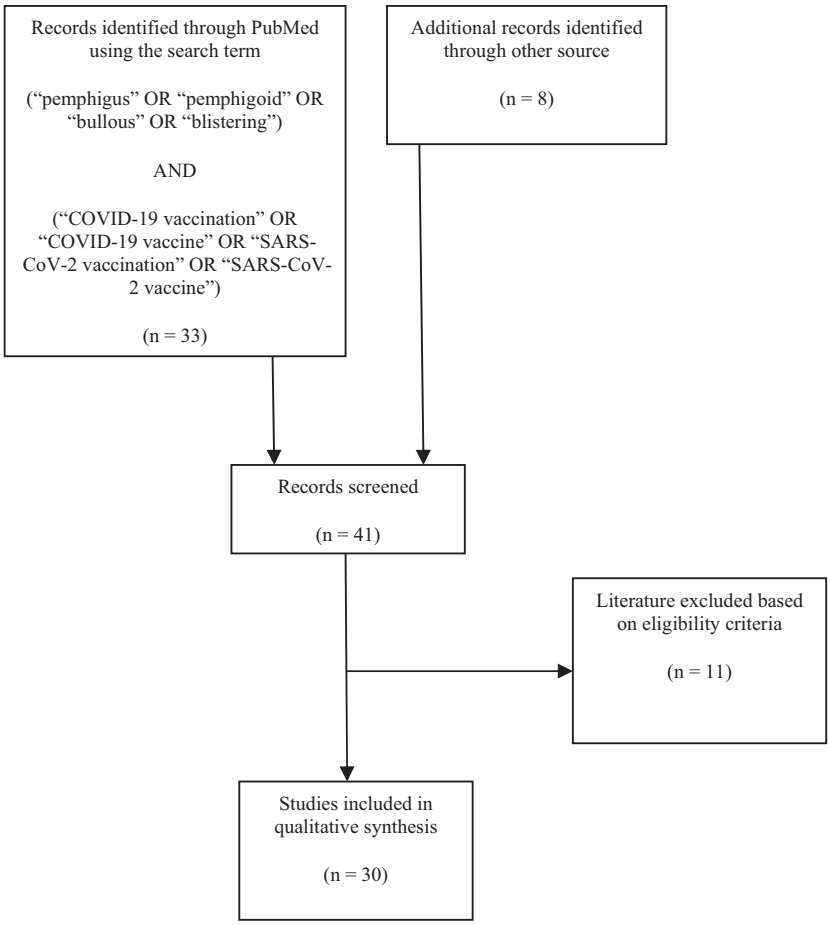

Figure 1 Flowchart of the article selection process.

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Data available on request from the authors.

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Successful treatment of generalized granuloma annulare with baricitinib

Editor

Granuloma annulare (GA), a granulomatous inflammatory cutaneous disorder with predilection for women is always prevalent during the fifth decade of life. Patient is categorized as localized or generalized, depending on lesion distribution. Generalized GA, being characterized by at least 10 widespread annular plaques, prevails 15% of all cases.[1] Localized GA is often self-limited and responds well to topical or intralesional corticosteroids, while generalized GA remained challenging to treat and always recur after discontinuing systemic corticosteroids or immunosuppressors.[2] Here, we reported a patient with recalcitrant generalized GA, whose lesions subsided almost with the treatment of JAK1/2 inhibitor baricitinib.

A 67-year-old man presented progressed plaques on upper limbs and trunk for half a year. He denied the medical history of diabetes, hyperlipidaemia or any immune diseases. Dermatological physical examination revealed generalized erythematous circinate papules and plaques on the bilateral shoulder, upper limbs and back, with coalescence in the extensor lateral forearms. The BSA of the lesions was approximately 8%. The biopsy from the plaques on the forearm revealed granulomatous inflammation with histiocytes, lymphocytes and multinucleated giant cells throughout the dermis, in accordance with granuloma annulare (Fig. 1). The diagnosis of generalized GA was

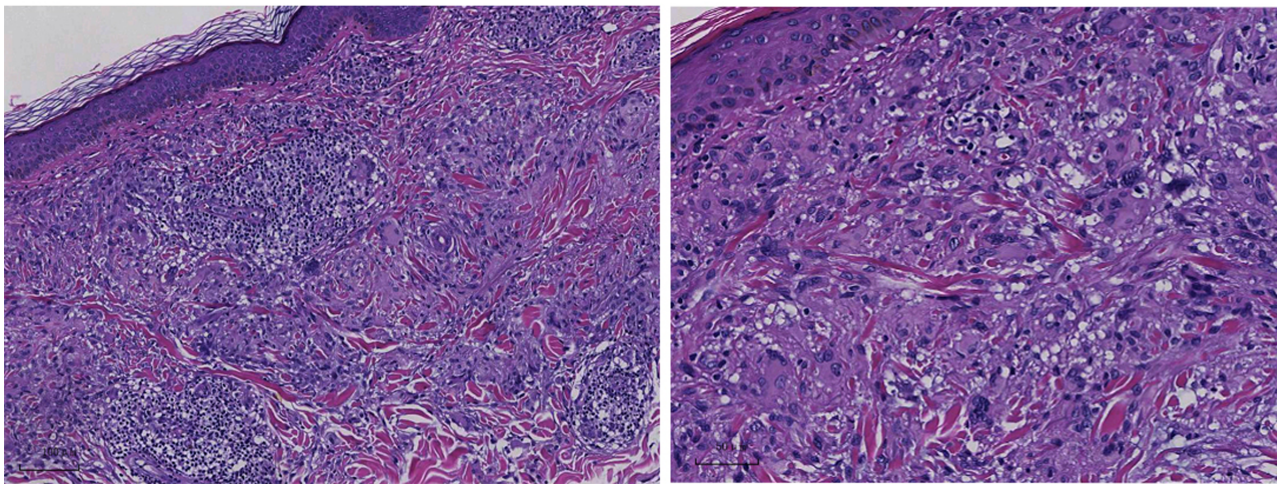

Figure 1 Skin section biopsy showing the foci of chronic interstitial reticular dermis inflammation (H&E, ×10) (a) and the necrosis of collagen fibres, along with palisading lymphohistocytic infiltration, granulomatous inflammation with histiocytes, lymphocytes and multinucleated giant cells throughout the dermis. (H&E, ×40) (b).