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LETTER TO THE EDITOR

Association of interstitial granulomatous dermatitis with messenger Rna–1273 Sars-Cov-2 vaccine

Dear Editor,

Cutaneous reactions to messenger RNA (mRNA)-1273 SARS-CoV-2 vaccine had an important impact on dermatology practice, posing diagnostic and therapeutic challenges. Most reactions consist in injection site adverse events, although reports about generalized exanthemas, urticaria, chilblain-like lesions, autoimmune diseases and severe acute adverse reactions are growing.[1,2]

We report a case of interstitial granulomatous dermatitis developed after the (m-RNA)-1273 vaccine and recurring after booster.

A previously healthy 57-year-old Caucasian woman was referred to our outpatient dermatologic clinic due to multiple itchy dome-shaped skin-coloured or erythematous papules coalescing into plaques, located on the back, lateral part of the thighs and forehead (Figure 1a,b).

In anamnesis, the patient reported the onset of an erythematous lesion at the site of injection 3 days after the first dose of (mRNA)-1273 vaccination. The lesion rapidly progressed to an erythematous plaque associated with homolateral axillary adenopathy. The lesion lasted for 10 days, followed by fever, wrists and knees arthralgias, and the development of dome-shaped papules. She was treated with oral prednisolone 25 mg/day for 20 days, leading to remission of all signs and symptoms. Upon administration of the second dose of vaccine as scheduled, the same clinical picture recurred and skin biopsy was performed. Antineutrophil cytoplasmic antibodies (ANCA), extractable nuclear antigens (ENAs), anticyclic citrullinated peptide (Anti-CCP) antibodies and rheumatoid factor were absent. Erythrocytes sedimentation rate (ESR) and C-reactive protein (CRP) levels were within normal range. Screenings for Borrelia Burgdorferi and Giardia Lambia resulted negative, as was drug intake history.

On histology, the skin biopsy showed mild perivascular lympho-histiocytic infiltrate in the upper dermis and areas of interstitial infiltration of small CD68-positive histiocytes with rare giant cells; the histiocytes were in intimate apposition to collagen; no mucin deposition was observed. At the dermoepidemral junction, focal basal vacuolopathy and rare lymphocytes were found (Figure 2a–d). Vascular damage or necrosis were not observed. All together the findings supported a diagnosis of interstitial granulomatous drug-induced dermatitis (IGDR).

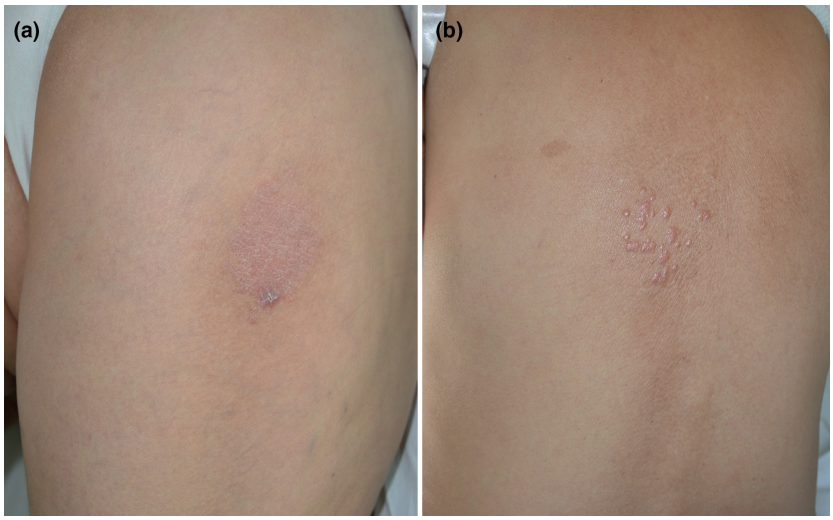

FIGURE 1 Clinical Images of Interstitial granulomatous drug-induced dermatitis-associated with messenger RNA (mRNA)–1273 SARS-CoV-2 Vaccine. (a) Erythematous to violaceous plaque with annular configuration associated with multiple dome-shape papules on the left thigh. (b) Multiple erythematous domee-shape papules and plaques on the upper back.

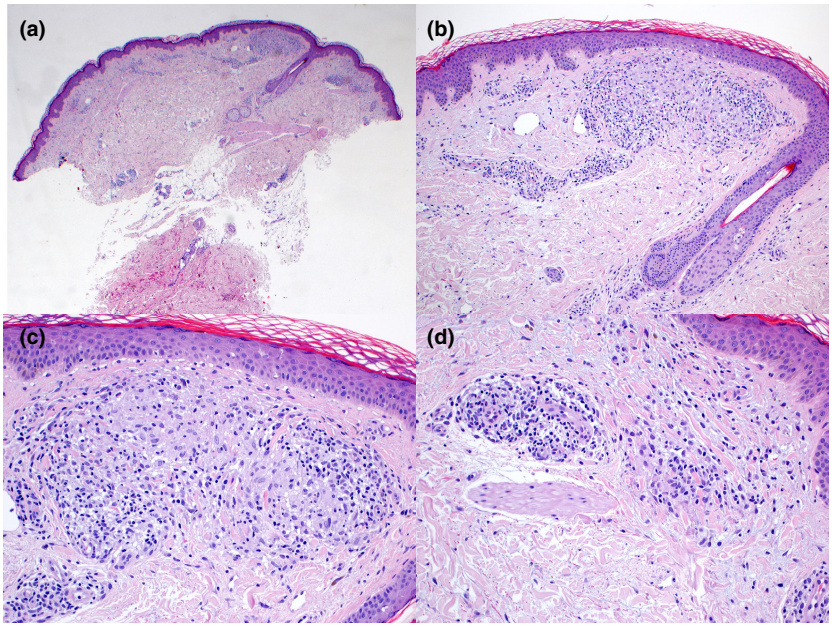

FIGURE 2 Histopathologic Images of Interstitial granulomatous drug-induced dermatitis-associated with messenger RNA (mRNA)–1273 SARS-CoV-2 Vaccine. (a) Punch biopsy showing superficial dermal infiltrate. Original magnification ×2. (b) Lympho-histiocytic infiltrate in the upper dermis and perivascular lymphocytes associated with mild interfacies damage. Original magnification ×10. (c) Particular of histiocites infiltrate in the upper dermis. Original magnification ×20. (d) Particular of interstitial infiltration with histiocytes and rare giant cells. Original magnification ×20.

Interstitial granulomatous drug-induced dermatitis, first described by Magro et al,[3] represents a drug-associated skin disease reported in association with various medications.[4] Histopathologically, it resembles interstitial granulomatous dermatitis but lacking of deep dermis extension and rimming of collagen bundles, while it shows a vacuolar interface reaction.

Time of onset, correlation with vaccine administration with relapse after the second dose, the absence of previous medications intake able to induce IGDR and negative history for any correlated autoimmune or infectious disease, also support the hypothesis of a cutaneous reaction to (m-RNA)-1273 SARS-CoV-2 vaccine. The clinical differential diagnoses that should be considered are cutaneous T-cell lymphoma (CTCL), erythema annulare centrifugum (EAC), granuloma annulare (GA), subacute cutaneous lupus erythematosus (SCLE) and sarcoidosis. Various dermatoses have been reported to be induced by vaccines including granulomatous reactions, either localized or as a generalized eruption. Rare cases of granuloma annularis following antitetanus, Bacillus Calmette-Guérin (BCG) and hepatitis B vaccinations have been reported,[5] there are no data in literature about IGDR.

To the best of our knowledge, this is the first reported case of IGDR following (mRNA)-1273 SARS-CoV-2 vaccination. We hypothesize that IGDR may be related to the host immune response against one or more transcriptional products of the m-RNA-1273 sequence, capable to cause an immune dysregulated environment promoting a reaction against dermal collagen antigens.[6] Development of IGDR after (mRNA)-1273 SARS-CoV-2 vaccination appears to be a rare event, therefore further reports are needed to determine the exact incidence of this entity.

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CONFLICT OF INTEREST

The authors report no conflict 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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