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Letter

De novo annular pustular psoriasis following mRNA COVID-19 vaccine

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Dear Editor,

With the COVID-19 mass vaccination, many cutaneous reactions related to vaccines have been described, including flare-up or new-onset of common chronic inflammatory skin diseases like psoriasis¹.

We present here the case of a *de novo* annular pustular psoriasis (APP) following mRNA vaccine.

A 64-years-old woman followed in our dermatologic department for a systemic lupus erythematosus (SLE) complained of a cutaneous eruption onset few days after the first dose of Pfizer-BioNTech BNT162b2 COVID-19 vaccine and worsened after the second dose. Prior to the newly onset eruption, LES cutaneous involvement was well-controlled by treatment with belimumab 200 mg once weekly, prednisone 12.5 mg per day and mycophenolate mofetil 1 g daily. Previous therapies included hydroxychloroquine, withdrawn due to pruritic rash and a single cycle of rituximab. Clinical examination revealed multiple erythematous-violaceous, annular-polycyclic, slightly infiltrated and scaling lesions distributed on her trunk, neck and limbs (Fig.1a-c). Pustules were visible in some lesions (Fig.1d). No fever and/or systemic symptoms were present and laboratory examination excluded systemic inflammation. Two 4 mm punch biopsies were taken for histopathological examination on two lesions located respectively on the right thigh and left arm. Histopathology revealed diffuse epidermal acanthosis with parakeratotic hyperkeratosis accompanied by granulocytes with a band-like lichenoid lymphocytic infiltrate. Focal vacuolization at the dermo-epidermal junction and neutrophil exocytosis associated with

subcorneal spongiform pustules were also observed. In the superficial dermis, a perivascular inflammatory infiltrate, mainly consisting of lymphocytes with scattered neutrophils was present (Fig.2a-d). The clinico-pathological findings were consistent with a diagnosis of APP.

Methotrexate 15 mg per week was introduced with clinical improvement at 1-month follow-up.

APP is a rare variant of generalized pustular psoriasis (GPP) in which the plaques are distributed in a circinate pattern with scaling and pustules on the edges of the lesions, with mild-to-no systemic symptoms². It could be induced by drugs, steroid withdrawal, infections and, rarely, vaccinations³. Recently, cases of GPP related to COVID-19 vaccines have been described⁴⁻⁸. In most of the cases patients experienced a flare-up of a pre-existing GPP or had a previous diagnosis of plaque-type psoriasis evolved in GPP or palmo-plantar pustulosis. The mean time of the eruption ranged from 4 days to 3 weeks after the vaccine. Up to date, only one case of *de novo* GPP has been reported in a 66-years-old woman 3 weeks after receiving the first dose of Oxford-AstraZeneca vaccine, successfully managed with acitretin⁵. The exact pathomechanism of the exacerbations and/or new onset of GPP after vaccination are not yet understood but the role of Type I interferon (IFN-I) signalling in genetically susceptible individuals has been postulated⁹. Vaccines may activate the plasmacytoid and dermal myeloid dendritic cells (pDCs) that promote the expression of Toll-like receptors (TLR) 7-8-9 with consequent release of Interleukin (IL)-6 which, in turn, promotes the development of Th1 and Th17 cells⁴. Enhancement of Th1 and Th17 trigger the release of several inflammatory cytokines, including IFN- γ , that play a crucial role in the epidermal changes commonly seen in psoriasis⁹. INF-I signature has been mainly demonstrated in GPP where *IL36RN* pathogenic variants have been revealed. Additionally, *CARD14* pathogenic variants have been found in some GPP case as well as in a patient with APP¹⁰. Thus, COVID-19 vaccination can induce GPP, in genetically susceptible individuals through an IFN-driven response, and APP based on *CARD14* mutation, a risk locus for psoriasis onset.

Our report, to the best of our knowledge, is the first to describe a new-onset annular pustular psoriasis, confirmed by histopathology, following mRNA vaccine.

In consideration of the mass vaccination dermatologist should be aware of the possibility of severe cutaneous adverse reaction following COVID-19 vaccinations such as GPP for a prompt diagnosis and an effective treatment.

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Figure legends

Figure 1: (a) erythematous to violaceous annular patches on the legs of our patient; (b) a detail of the lesions on the right thigh in different stages of activity; (c) same annular lesions on the right arm showing the active edge; (d) a detail of a lesion on the leg showing macroscopically visible pustules and scales.

Figure 2: Histopathology showing (a) diffuse epidermal acanthosis with parakeratotic hyperkeratosis and a band-like lichenoid lymphocytic infiltrate. Superficial dermis is characterized by perivascular inflammatory infiltrate (hematoxylin & eosin staining). (b) Close-up view revealing epidermal acanthosis with parakeratotic hyperkeratosis and focal vacuolization at the dermo-epidermal junction with subcorneal spongiform pustule formation. Band-like lichenoid lymphocytic infiltrate is also shown (hematoxylin & eosin staining). (c) A detail showing neutrophil exocytosis and a neutrophil rich subcorneal spongiform pustule (hematoxylin & eosin

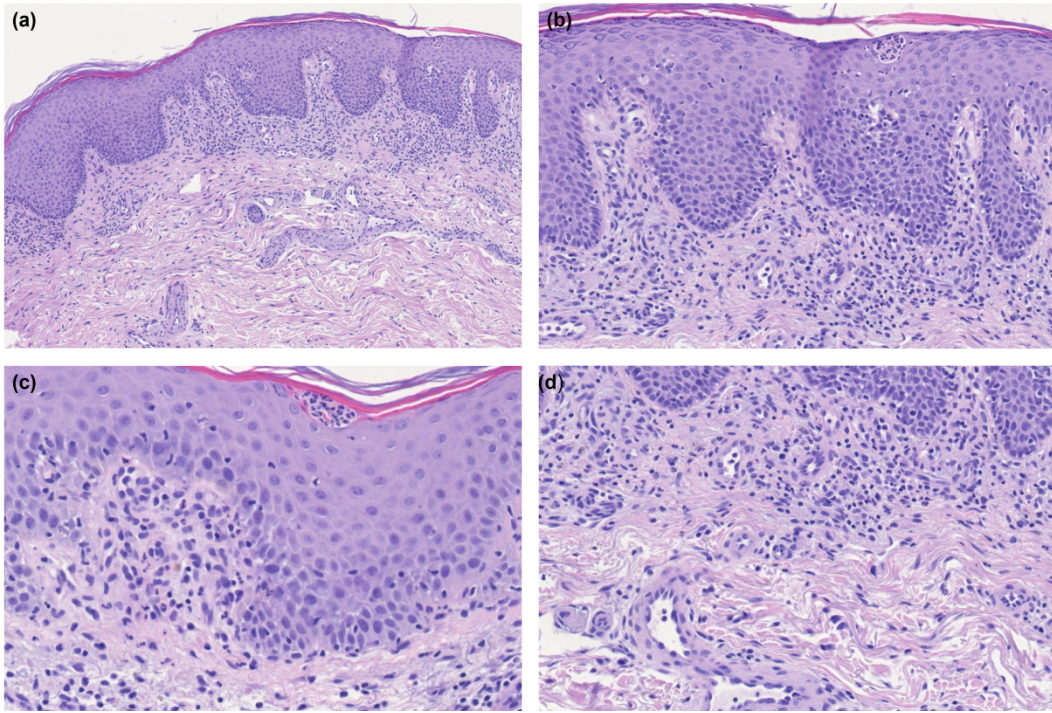
staining). (d) A detail of the dermal perivascular inflammatory infiltrate, mainly consisting of lymphocytes with scattered neutrophils (hematoxylin & eosin staining).

Author contributions: MR: concept and design, article drafting. PP and SM: acquisition of data. CM: article drafting. AVM: revision. All the authors revised the manuscript and approved its final version.

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