



Figure 2 Erythematous indurated plaque 9 days after the first dose of the Moderna vaccine.

reaction supported by the histopathologic findings, as previously reported.⁵ No hypothesis on predisposing factors can be made as all patients were Caucasians, vaccination policy with the mRNA vaccines was age group-targeted and the cases reported are too limited to assess possible comorbidities.

Even though both vaccines are administered intramuscularly, one cannot rule out the possibility that some final solution particles could be inoculated intradermally in the process of needle insertion. In such cases, a delayed hypersensitivity reaction might be more easily initiated. However, assessment of such a hypothesis on a prospective model is difficult to investigate.^{7,8} Differences in the biodistribution and pharmacokinetics of mRNAs, as well as the properties of the different lipid nanoparticles, could also have a role in the pathogenesis of this late-onset reaction; however, pharmacokinetic data of both vaccines in humans are scarce.

We believe that the term ‘COVID vaccine arm’ would be more appropriate than ‘COVID arm’ to describe the phenomenon, and it should not be considered a contraindication to subsequent vaccine doses.⁵

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Two cases of papulo-pustular rosacea-like eruptions following COVID-19 vaccinations

Dear Editor,

Cutaneous reactions after COVID-19 vaccines mainly consisted of delayed inflammatory reactions in the injection site, urticaria, chilblain-like lesions and pityriasis rosea-like eruptions.^{1,2} We describe herein two patients who developed rosacea-like eruptions following COVID-19 vaccination.

In a 60-year-old woman, an itchy skin rash developed 4 days after receiving the first dose of Vaxzevria (AstraZeneca) COVID-19 vaccine. She had no history of dermatological diseases, allergies, recent infections nor contact with COVID-19 patients. She had not taken any drug except anti-hypertensives for 2 years. Examination revealed erythema, telangiectasias and papulo-pustules on the cheeks and nose (Fig. 1a,b). Vaccine-associated papulo-pustular rosacea-like eruption was diagnosed, and sun protection cream was prescribed. Since rosacea can be associated with *Helicobacter pylori* (HP) infection,³ a stool antigen test for



Figure 1 (a) Erythema, telangiectasias and papules on the right cheek and nose; (b) erythema, papules and pustules on the left cheek.



Figure 2 Erythema of the face, papules and pustules (a), sometimes confluent in plaques (b), on the cheeks, forehead, temporal and mandibular regions (b, c).

HP detection was performed and proved negative. The cutaneous eruption healed in 30 days, and the second dose of Vaxzevria COVID-19 vaccine was injected without cutaneous reactions.

A 47-year-old woman presented with an itchy facial skin eruption that had developed 5 days after the second dose of Pfizer-BioNTech COVID-19 vaccine. The patient was previously healthy and denied any drug intake. Examination showed erythema and papulo-pustules on the cheeks, forehead and temporal-mandibular regions (Fig. 2a,b,c). A stool antigen test for HP was negative. A diagnosis of vaccine-associated papulo-pustular rosacea-like eruption was made, and sun protection cream was prescribed. The cutaneous lesions completely healed in 20 days. Given the location of the eruptions, both the patients refused a skin biopsy.

The skin eruptions of our patients resemble the skin toxicity associated with administration of the epidermal growth factor receptor (EGFR) inhibitors, targeted therapies that inhibit the tumour cell proliferation in several solid cancers. This condition, manifesting as erythematous papulo-pustules on the face, as in our patients, and trunk,^{4,5} may be related to the increase of cutaneous chemokines (CCL2, CCL5 and CXCL10) with CD4⁺T cells, monocyte/macrophages and polymorphonucleates chemotaxis and skin infiltration.⁶ Moreover, inhibition of EGFR signalling increases angiogenic factors, as vascular endothelial growth factor (VEGF), that are overexpressed in these skin lesions.^{4,5} Such toxicity, however, can be excluded in our patients since they did not receive any EGFR inhibitors.

To our knowledge, these are the first described cases of COVID-19 vaccine-associated rosacea-like eruptions. The pathogenetic link between COVID-19 vaccination and rosacea-like eruptions is difficult to establish.

Both Vaxzevria and Pfizer-BioNTech vaccines, through different mechanisms, induce the generation of neutralizing antibodies against SARS-CoV-2 spike protein and specific T-cell expansion with cytokine secretion (IFN- γ , IL-2 and IL-10).^{6,7} Such immune response may play a role in the onset of rosacea-like eruptions, especially in patients with predisposing factors.

Indeed, the pathophysiology of rosacea is multifactorial, implicating a dysregulated innate and adaptive immune system and neurogenic dysregulation favouring excessive inflammation and vasodilation. In all types of rosacea, perivascular and pilosebaceous skin infiltrates show marked expression of innate immune cells, with the additional influx of macrophages and mast cells in papules and of neutrophils in pustules.⁸ A recent study showed higher IL-17 levels in the serum of rosacea patients than in healthy controls, suggesting a pathogenetic role of IL-17.⁹ Other mediators involved in rosacea vasodilatation and angiogenesis are as follows: nitric oxide, cathelicidins and VEGF, the main positive regulator of pathological angiogenesis. Elevated tissue VEGF expression has been found in rosacea, and VEGF receptors serum levels were higher in patients with rosacea than in controls.¹⁰

It could be postulated that COVID-19 vaccination, as EGFR inhibitors, might trigger the secretion of cytokines and angiogenic factors causing the rosaceiform eruption. Regrettably, extensive investigations could not be performed in our cases.

Meanwhile, clinicians should be aware of the possible cutaneous reactions to vaccinations and reassure the patient since most of them are transient and mild.

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Conflict of interest

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