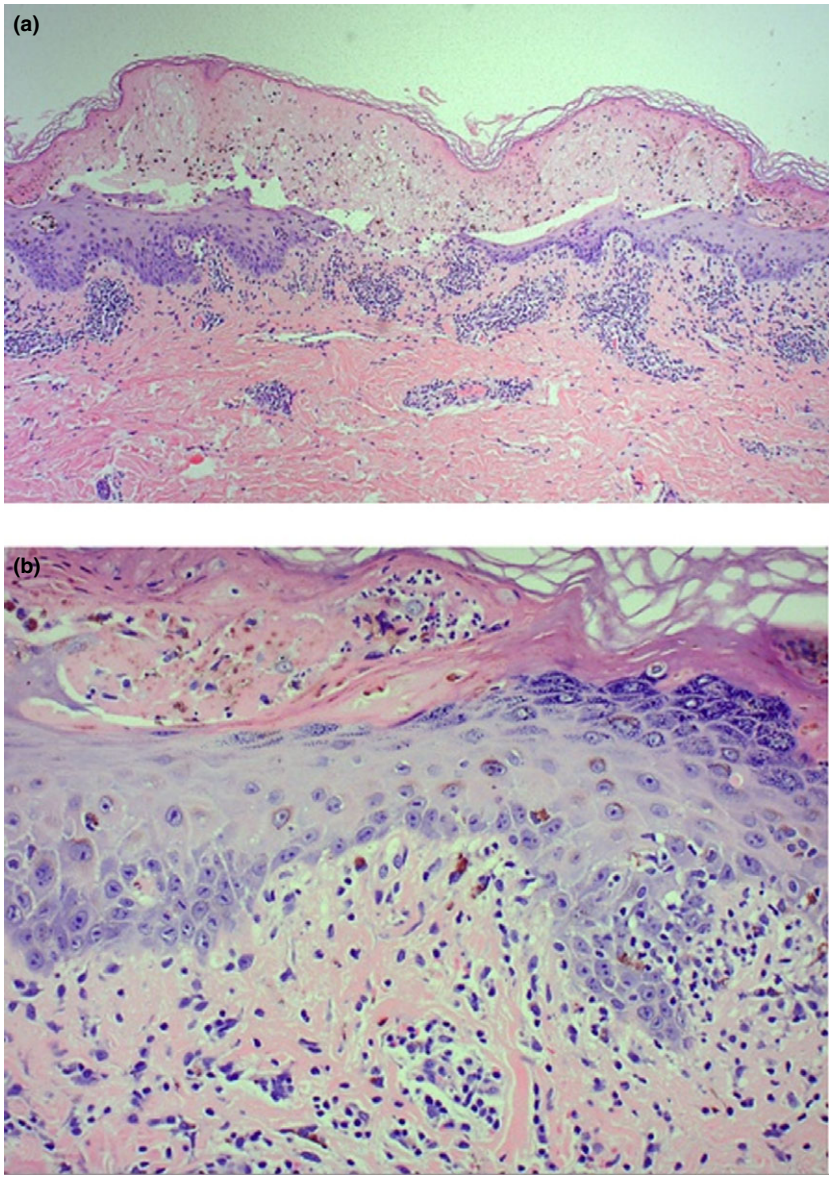

Figure 2 (a) Histology showed a patchy perivascular and interstitial lymphocytic infiltrate in the upper dermis, with focal epidermal erosion and overlying fibrin and crust. (H&E x 100) (b) Lymphocytic infiltration of the basal layer of the epidermis is appreciated, associated with vacuolar interface damage of basal keratinocytes, occasional apoptotic keratinocytes in all levels of the epidermis and pigment incontinence; confirming a lichenoid inflammatory reaction (H&E x 200).

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Early atypical injection-site reactions to COVID-19 vaccine: a case series

Dear Editor,

Currently available COVID-19 vaccines have shown a good safety profile. However, adverse effects such as local reactions have been frequently observed. Based on existing evidence, after administering the BNT162b2 (Pfizer) or AZD1222 (AstraZeneca) vaccines, more than 80% of participants developed injection site pain, while erythema and swelling were present in about 10%.[1,2]

We report a series of adverse reactions consisting of early local reactions with atypical morphological appearance coinciding

with vaccination against COVID-19. From 2 January 2021 to 31 March 2021, a total of 16217 (9382 female and 6835 male, median age 33, 53 years) and 1377 (693 female and 683 male, median age 47.3 years) subjects including health workers, medical students and university staff, were vaccinated with Pfizer and AstraZeneca vaccine, respectively, at the Vaccination Center of the University Hospital "G. Martino" of Messina, Italy. During the same period, 28 patients with early atypical injection-site skin reactions presented to our Unit of Dermatology after receiving Covid-19 vaccines, at the above-mentioned vaccination centre. In particular, 12 injection-site skin reactions were described after the Pfizer vaccine (0.1%) and 16 after the AstraZeneca vaccine (1.2%). The onset of these lesions occurred between 4 and 12 h after the first dose of both vaccines. These reactions had a variable appearance (Figure 1). In most cases (n = 15, 53.6%), a pink or red-purple or red-brown patch with a smooth surface and well-defined edge was observed. In eight patients, there was a red-brown plaque with vesicular lesions on the surface, in two cases flowing into a single bulla or, in the others, occurring only on the lesion edge. Lastly, five patients presented an erythematous, oedematous plaque. No other cutaneous lesions were reported in the rest of the body. The majority of patients reported burning, itching and pain on palpation (n = 23; 82.1%). Some patients had concurrent systemic symptoms: headache (n = 4; 14.3%), fever (n = 14; 50%) and myalgia (n = 3; 10.7%). Only 5 subjects (17.9%) had a history of other skin diseases and allergies, particularly drug allergic reactions. After the onset of these symptoms, patients were followed up by their primary care doctor and were invited by the vaccination centre for a consultation at the Unit of Dermatology. All the patients received a therapy consisting of topical glucocorticoids and antihistamines. The symptoms resolved in about one week after onset, while the lesions gradually became hyperchromic patches or crusted lesions (Figure 2) and, in the end, entirely disappeared in <2 weeks.

Recent published literature about Covid-19 vaccines described delayed significant local reactions: in the majority of cases, adverse events occurred within 7–8 days after the first dose of Pfizer or Moderna COVID-19 vaccines.[3,4] Patients presented variable manifestations, including annular or erythematous-oedematous or targetoid plaques. These reactions were probably the result of delayed-type or T-cell-mediated hypersensitivity. Other authors also described delayed and early site injection skin reactions after Pfizer and Moderna vaccines.[5,6] A delayed-type hypersensitivity reaction, which is a T-cell-mediated reaction depending on both CD4+ and/or CD8+, cannot be excluded as a possible reason for our reported reaction. Symptoms of delayed hypersensitivity can indeed onset within 6 h and can include localized skin ones, not only disseminated rashes with systemic symptoms.[7] However, this mechanism cannot be the only explanation for our injection-site early reactions. These lesions could be ascribed as irritative or allergic contact dermatitis to the excipient of the vaccine (e.g. polyethylene glycol)[8] or alcohol skin cleansing solution.[9] Local thermographic changes or local immune-inflammatory cells could also be involved in the development.[10] Nevertheless, further studies regarding allergy skin tests (e.g. prick and patch tests) are needed to better understand the underlying mechanisms of these early injection-site

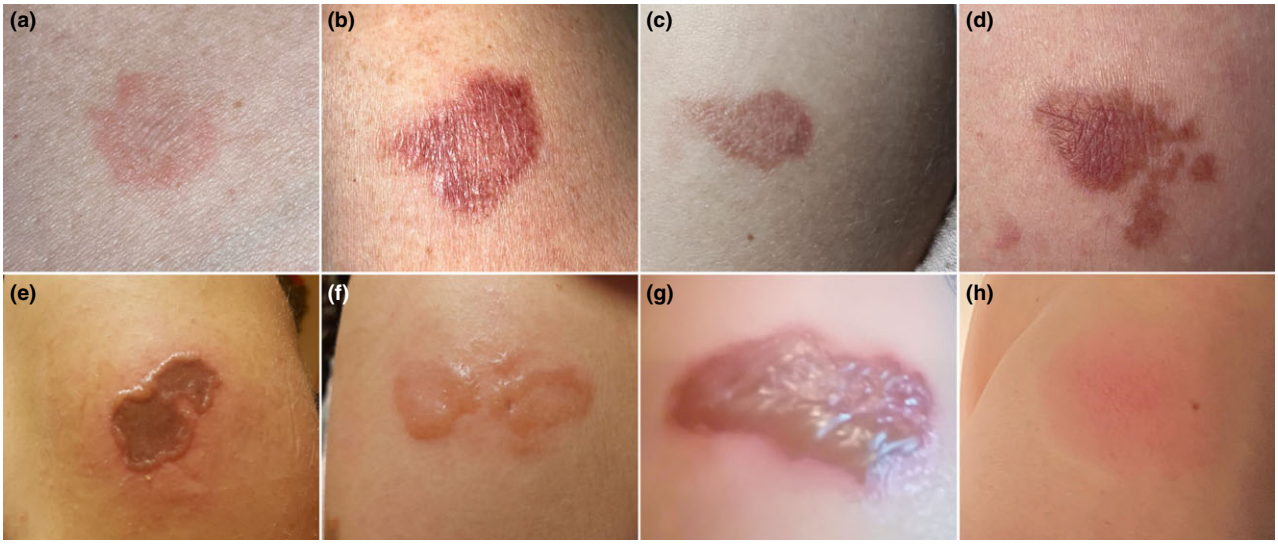

Figure 1 Spectrum of morphologic characteristic of early injection-site reactions: pink (a) or red-purple (b) or red-brown (c–d) patch with a smooth surface and well-defined edge; red-brown plaque with vesicular lesions on the lesion edge (e) or on the surface (f); a single bulla (g); erythematous, oedematous plaque (h).

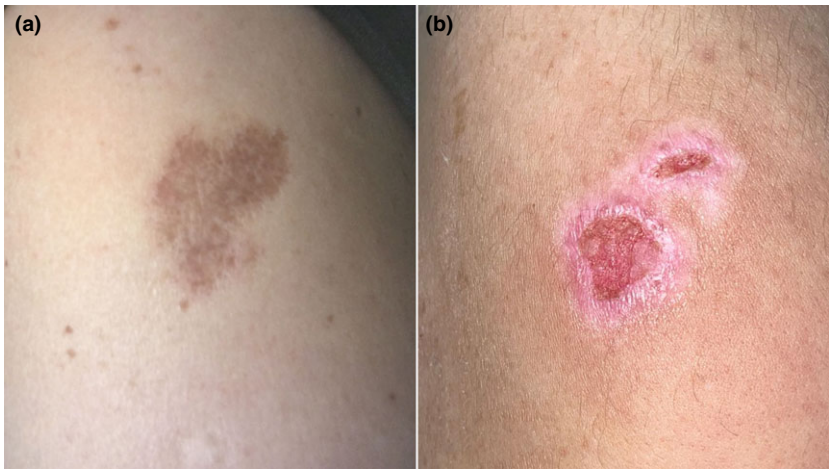

Figure 2 Clinical aspect of the lesions after about 1 week of onset: (a) hyperchromic patch or crusted lesion (b).

reactions. In conclusion, although some patients reported local adverse reactions after the first dose of their COVID-19 vaccine, it is essential to encourage all patients to complete vaccination because these reactions are not a contraindication.

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The patients have given written informed consent to the publication of their case details and photos.

Conflict of interest

The authors have no relevant conflict of interest.

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Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Eosinophilic cellulitis after BNT162b2 mRNA Covid-19 vaccine

Dear Editor,

We observed a case of eosinophilic cellulitis or Wells syndrome after the BNT162b2 vaccine.

A 71-year-old woman with a history of treated high blood pressure and atrial fibrillation presented with a painful eruption