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Delayed localized hypersensitivity reactions to COVID-19 mRNA vaccines: a 6-month retrospective study

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Dear Editor,

Delayed local injection site reactions were reported in the clinical trials of the two novel mRNA COVID-19 vaccines (Pfizer/BioNTech and Moderna).[1,2] With the increase in vaccination rates, awareness of associated adverse events (AEs) is needed. We report on a study of delayed localized hypersensitivity reactions to mRNA SARS-CoV-2 vaccines with histopathological confirmation.

The study was approved by the institutional ethics committee of Aristotle University (Thessaloniki, Greece). Informed consent for biopsy and for publication of case details and photographs was obtained from participants.

This was a retrospective study conducted at the First Dermatology Department of Aristotle University between 1 January and 20 June 2021. Patients' demographics, vaccine information (manufacturer and first or second dose administration), medical history, allergies, COVID-19 infection, prior history of vaccine reactions, time of onset and duration of injection-site reaction (ISR) were recorded. Photographs were obtained for six patients during the study course and histopathological examination was performed for two patients. Patients who experienced a cutaneous reaction to the first vaccine dose were followed up until 1 month after the second dose.

Overall, 84 patients referred to the emergency department reporting ISRs after their first and/or second vaccine dose. All 84 patients were white with a mean age of 57 years (range 27–86 years), and the majority (n = 82; 97.6%) were women. Hypertension (n = 25; 29.8%), dyslipidaemia (n = 12; 14.3%) and diabetes mellitus (n = 8; 9.5%) were the most common comorbidities reported. Most participants (n = 80; 95.2%) did not have any history of cutaneous disease; the four who did had eczema (n = 3; 3.6%) and urticaria (n = 1; 1.2%).

All patients had received the Moderna vaccine and none had received the Pfizer/BioNTech vaccine. Most patients (n = 57; 68%) had not been previously infected with SARS-CoV-2 and the majority (n = 76; 90.5%) reported no relevant cutaneous reaction to any other vaccine type. Local ISRs preceded delayed large ISRs in 51 of the 84 patients (60.7%).

Delayed large ISRs occurred in 82 of the 84 patients after their first dose, occurring in 79 of the 84 patients (94%) approximately 9 days after the first dose (range 7–13 days). The plaques were mainly oedematous or indurated and homogeneous or annular, and subsided after a mean of 3 days (range 2–6 days) after starting treatment with topical corticosteroids and oral antihistaminic or anti-inflammatory medication (Fig. 1a).

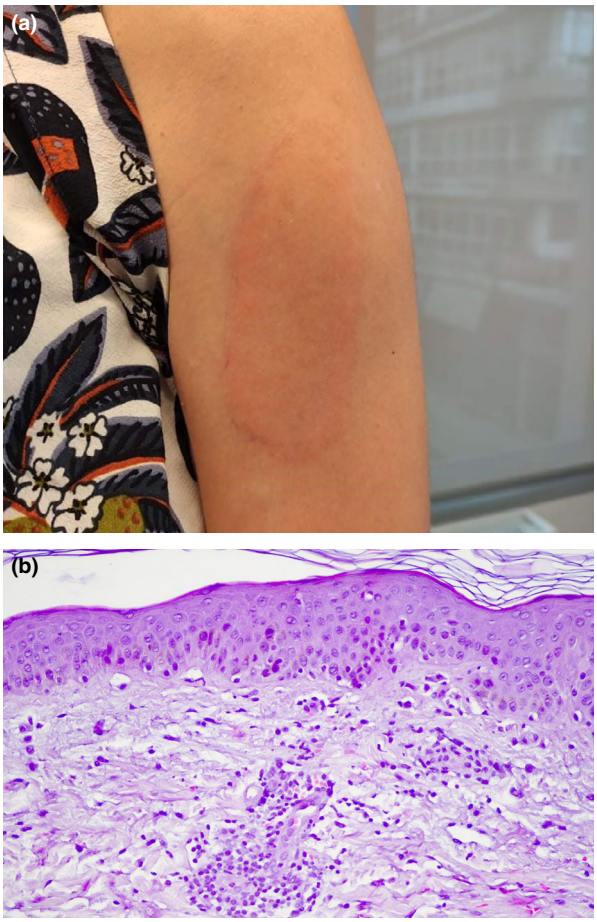

Figure 1 (a) Indurated erythematous patch at the injection site, 10 days after the first dose of the Moderna vaccine; (b) mild to moderate perivascular infiltrate predominantly of lymphocytes, mild dermal focal oedema with red cell extravasation and rare interstitial eosinophils (haematoxylin and eosin, original magnification × 100).

In addition, 37 of the 84 patients (44%) presented delayed large ISRs after their second vaccine dose; 2 of these reported having had no reaction to the first dose. ISRs after the second dose occurred sooner in the 35 patients (41.7%) who had experienced a relevant reaction to the first dose, with a mean onset of 2 days (range 1–6 days) after vaccine administration and with a similar clinical presentation. Of these, 7 (20%) experienced a more pronounced reaction with the second dose.

Histological findings were consistent with delayed localized hypersensitivity reaction, demonstrating mild to moderate perivascular lymphocytic infiltrate, mild dermal focal oedema with red cell extravasation and rare interstitial eosinophils (Fig. 1b).

Limited data on delayed hypersensitivity reactions have been published, primarily after administration of the Moderna vaccine.[3–5] In our study, although the number of Pfizer vaccines allocated to our region was seven times that of the number of Moderna vaccines, relevant reactions presented only in individuals who received the Moderna vaccination. Therefore, it is possible that delayed localized reactions may have been underestimated in the Moderna clinical trial, as they were actively monitored for only 7 days after vaccination.

In conclusion, ISRs can occur after administration of mRNA vaccines, and may be delayed. However, AEs to mRNA vaccines are minor and self-limiting, and should not discourage vaccination.

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Simplifying assessment of dimensions of oral lesions using a syringe and 'impression planimetry' with printer paper

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Dermatoses with oral involvement such as lichen planus and vesiculobullous diseases are commonly encountered, cause considerable morbidity and require effective treatment. Quantifying therapeutic response and comparing relative efficacies of various topical agents requires reproducible measurement of lesion dimensions. Additionally, the dose of intraoral rituximab for oral pemphigus is ideally calculated based on lesional area.[1]

Techniques described to calculate area of oral lesions include serial digital photography, intraoral digital cameras, use of periodontal probes and variable oral devices.[2,3] However, these have several disadvantages. During repeated digital photography, maintaining a constant distance and stretch of the mucosa hinders reproducibility, while periodontal probes, intraoral digital cameras and variable oral devices are not commonly used by dermatologists, may be cumbersome to construct and use, and require scrupulous sterilization before each use, especially during the COVID-19 pandemic. We describe two simple techniques that circumvent these challenges.

These techniques were performed in patients with oral lichen planus, bullous pemphigoid or pemphigus vulgaris under direct illumination after ensuring proper visualization of the lesion. For further standardization and reproducibility, mouth opening is kept at maximum by measuring the distance between the upper and lower incisor teeth in each patient and keeping it constant during serial measurements.

In the first technique, a disposable presterilized tuberculin syringe was cut at the zero mark, discarding the needle adapter. The lesions were dabbed dry with sterile gauze, with lidocaine first sprayed onto any painful lesions. The anterior margin of each lesion was marked with crystal violet (CV) dye (Fig. 1a–c). To measure a lesion, the tuberculin syringe was placed across the lesion without further mucosal stretching, with the zero mark on the posterior margin of the lesion and the barrel of the syringe lying across the dye-stained anterior margin (Fig. 1d–f). The distance from the zero mark to the mark lying on the commencement of the stain gave the largest anteroposterior dimension, which was also checked with a ruler, using the crystal violet mark that transferred onto the syringe (Fig. 1d–f insets).

The second technique we term 'impression planimetry'. The lesion margins were painted with CV dye (Fig. 2a–c).

