Exacerbation of Hailey-Hailey Disease Following SARS-CoV-2 Vaccination

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Accepted Aug 25, 2021; Epub ahead of print Aug 26, 2021

Two SARS-CoV-2 mRNA vaccines (Moderna, Cambridge, Massachusetts, US and Pfizer/BioNTech, Philadelphia, Pennsylvania, US) were approved by the US Food and Drug Administration (FDA) in December 2020, based on phase 3 trials that provided information on their efficacy and safety (1, 2). Both vaccines were also approved by the Israeli Ministry of Health, and, following this approval, a large-scale vaccination programme was initiated in Israel with the Pfizer/BioNTech BNT162b2 mRNA Covid-19 vaccine. Several adverse effects were reported previously with this vaccine, including injection site reactions and mild systemic symptoms. However, information on cutaneous adverse effects, and specifically side-effects in specialized populations with chronic skin conditions, is sparse.

CASE REPORTS

We report here an exacerbation of symptoms and signs in 5 out of 11 patients with Hailey-Hailey disease (HHD), who are being followed in our outpatient clinic. All 5 patients are females, between the ages of 42 and 88 years, with both clinically and histologically proven HHD. One of them had also undergone genetic workup that supported the diagnosis of HHD. The patients had good long-lasting control of their HHD before they received the Pfizer/BioNTech vaccine in 2 separate doses 3 weeks apart. The patients experienced exacerbation shortly after receiving the first (2/5 patients) and/or second (4/5 patients) dose of vaccination (Table I).

The exacerbation of HHD was characterized by the appearance of new lesions in locations where the disease was previously active (mainly the axillary, submammary and inguinal folds, as well as the genital area), accompanied by tenderness and a tingling sensation. The lesions had the typical features of HHD, manifesting as erythematous oozing erosive plaques with overlying crusts and fissures (Fig. 1). In several patients, the cutaneous findings were accompanied by mild systemic complaints (Table I). Notably, only 1 of the 5 patients developed fever after vaccination, which was low grade, and familiar to the patient as an early sign of an upcoming attack.

It is of note that this exacerbation of HHD was not seen in the remaining 6 patients from our outpatient clinic (3 females and 3 males).

Table I. Response of patients with Hailey-Hailey disease (HHD) to SARS-CoV-2 mRNA vaccine (Pfizer/BioNTech)

| Patient | Age, years | Background diseases | Skin condition prior to vaccination | Treatment for HHD prior to vaccination | Response to 1st vaccination | Response to 2nd vaccination |
|---------|------------|---------------------|------------------------------------|--------------------------------------|-----------------------------|-----------------------------|
| 1       | F 88       | Ischaemic heart disease, hypertension, hyperlipidaemia, hypothyroidism | Few mild skin lesions | Low-dose naltrexone, topical steroids, topical antibiotics, antihistamines | None | Multiple small erosive plaques, crusts and fissures on the submammary and lower abdominal folds, groins, and thighs 4 days after vaccination |
| 2a      | F 50       | None | No skin lesions | Low-dose naltrexone | None | Single oozing erosive plaque on the medial aspect of the left breast, 37.4°C body temperature, weakness and shivering 2 days after vaccination |
| 3       | F 52       | Chronic urticaria, s/p thyroidectomy d/t papillary carcinoma, s/p morbid obesity resolving after gastric bypass, osteoporosis | No skin lesions | Low-dose naltrexone | None | Single oozing erosive plaque on the left axilla 12 days after vaccination |
| 4b      | F 42       | Chronic urticaria, atopic dermatitis | No skin lesions | Topical zinc oxide | Diffuse tingling and tender erythema of the vulva within 1 day of vaccination | Few tender erosions in the vulva, eczematous plaques at both sides of the neck, weakness, shivering and cervical lymphadenopathy within 1 day of vaccination |
| 5b      | F 78       | Bullous pemphigoid, asthma, diabetes mellitus type 2, ischaemic heart disease | No skin lesions | Low-dose prednisone | Few tender erosions on the vulva 3 days after vaccination | None |

*aCarrier for heterozygous mutation c.832G>C in ATP2C1. bDaughter and mother. s/p: status-post; d/t: due to.

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Society for Publication of Acta Dermato-Venereologica

doi: 10.2340/00015555-3907

Acta Derm Venereol 2021; 101: adv00554
DISCUSSION

Exacerbation of HHD may be triggered by sweating, skin infections, pregnancy, menstruation and physical trauma (3), as well as by irritant or allergic agents and medications (e.g. non-steroidal anti-inflammatory drugs) (4). To the best of our knowledge, vaccinations have not previously been reported to trigger exacerbation of HHD. However, mRNA vaccines have not been used previously in large human populations, and their mechanism of action carries a risk of local and systemic inflammatory responses (5). Such inflammatory responses may also lead to exacerbation in predisposed patients, such as those with HHD.

Following the initiation of large-scale vaccination programmes, it is important to report the possible effects, and, specifically, the cutaneous side-effects of this new class of vaccines. It is especially important to report on such consequences in specialized populations that might not have been included in the initial clinical trials.

We could not explain why the affected patients were all female. Indeed, our cohort comprised mainly female patients, but, at the same time, the current findings are in agreement with new data from a recent registry-based study, in which 85% of cutaneous reactions after Pfizer COVID-19 vaccination were reported in female patients (6). This sex-related difference in the probability of developing exacerbation of HHD requires further study.

The authors have no conflicts of interest to declare

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