Cutaneous hypersensitivity reaction with acute hepatitis following COVID-19 vaccine

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INTRODUCTION

Here, we present a report of a generalized cutaneous hypersensitivity reaction with liver dysfunction following the COVID-19 vaccine.

CASE REPORT

A 61-year-old woman with a remote history of breast cancer in remission presented with a worsening cutaneous eruption that began 5 days after receiving her second dose of the Pfizer COVID-19 vaccine. On the day following her vaccination, she experienced subjective fever, fatigue, generalized myalgia, nausea, and headache that lasted for 4 days. On day 5 following vaccination, she noticed a pruritic cutaneous eruption on her abdomen, which generalized over the next 5 days. Diffuse erythematous morbilliform papules and plaques were noted over the neck, trunk, and proximal aspects of the extremities. In addition, there were faintly targetoid erythematous-to-violaceous plaques over the distal aspects of the extremities extending onto the palms and soles (Fig 1, *A* and *B*). There was no lymphadenopathy or mucosal involvement; however, the patient was jaundiced. The patient was admitted to a

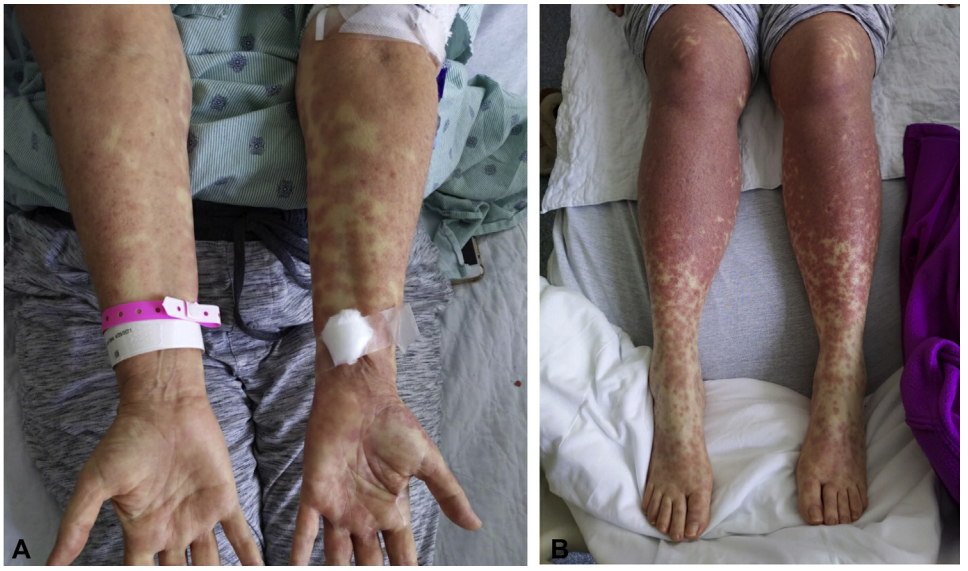

Fig 1. Clinical images on transfer. **A**, Coalescing faintly targetoid erythematous-to-violaceous plaques were observed on the upper extremities. **B**, Similar morphology was observed on the lower extremities.

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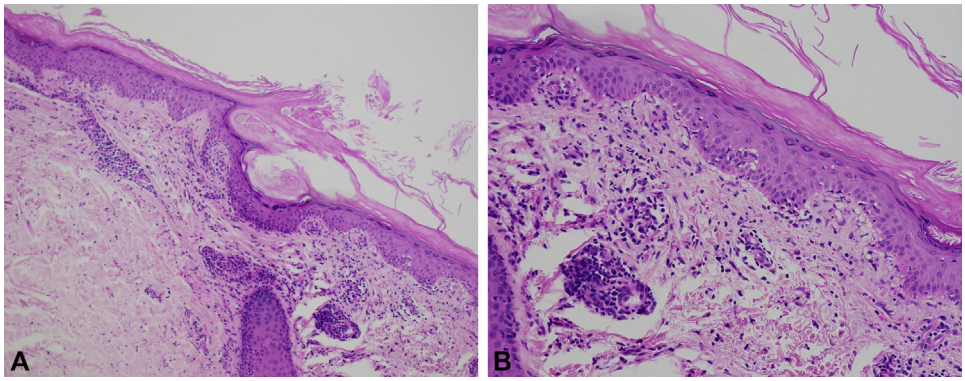

Fig 2. Histologic images of leg biopsy. **A** and **B**, Interface dermatitis and a perivascular and perifollicular lymphohistiocytic infiltrate without eosinophils. (**A** and **B**, Hematoxylin-eosin stain; original magnifications: **A**, ×100; **B**, ×200.)

local hospital, and she was subsequently transferred to our institution for inpatient dermatologic care.

Laboratory results on admission were notable for a normal complete blood cell count without eosinophilia, normal creatinine level, elevated alanine aminotransferase level of 1201 U/L (peak value, 1852 U/L), elevated aspartate aminotransferase level of 425 U/L (peak value, 642 U/L), and elevated total bilirubin level of 7.9 mg/dL (peak value, 12.5 mg/dL). Herpes simplex virus, human herpesvirus 6, and *Mycoplasma pneumoniae* polymerase chain reaction serologies were negative.

A skin biopsy demonstrated interface dermatitis and a perivascular and perifollicular lymphohistiocytic infiltrate without eosinophils (Fig 2, *A* and *B*). Extensive workup for the cause of acute hepatitis, including viral hepatitis panel, cytomegalovirus, Epstein-Barr virus, ceruloplasmin, iron, HIV, α_1-antitrypsin, ultrasound of the upper portion of the right quadrant, and magnetic resonance imaging of the abdomen, was unremarkable. The patient's acute hepatitis was ultimately attributed to a vaccine-induced hypersensitivity reaction with end-organ dysfunction. The patient denied having taken any medications or supplementation, apart from 1 dose of meloxicam 1 week prior to the rash onset for back pain and acetaminophen/ibuprofen 1 day prior to the rash onset for headache and myalgia following vaccination. A reaction to these medications could not be ruled out, however this was deemed much less likely as the patient had taken these medications intermittently in the past. Clinicopathologic correlation and the European Registry of Severe Cutaneous Adverse Reactions score of 3 supported a cutaneous hypersensitivity reaction with liver dysfunction likely triggered by the COVID-19 vaccine.

The patient was treated with intravenous methylprednisolone and topical corticosteroids. She was transitioned to oral prednisone with improvement in her cutaneous eruption and liver function tests. It was recommended that the patient should proceed cautiously with future booster doses of the Pfizer COVID-19 vaccine.

DISCUSSION

To our knowledge, this is the first report of a generalized cutaneous hypersensitivity reaction with liver dysfunction following the administration of the COVID-19 vaccine. The most commonly reported cutaneous reactions following the Moderna and Pfizer COVID-19 vaccines are delayed large local reactions, local injection site reactions, urticarial eruptions, and morbilliform eruptions.[1]

We favor a vaccine precipitant given the strong temporal relationship among vaccination, symptom onset, and the absence of an alternative trigger.[2] The mechanism of vaccine-induced cutaneous hypersensitivity is believed to arise from vaccine antigens that are expressed on the surface of keratinocytes, which elicit a $CD8^+$ T cell lymphocyte immune response against epidermal cells. There is generally a 3- to 5-day latency period before keratinocyte damage is observed.[3]

Of interest, an erythema multiforme–like eruption has been described in response to various vaccines, including influenza, diphtheria-tetanus-pertussis, human papillomavirus, and smallpox.[4] A systematic review found that cases of Stevens-Johnson syndrome/toxic epidermal necrolysis following vaccination commonly resemble erythema multiforme initially.[3] Our patient similarly demonstrated initial targetoid morphology suggesting that an early erythema multiforme–like eruption should prompt consideration of a vaccine trigger.

Vaccine-induced cutaneous hypersensitivity is rare, and the majority of reported cutaneous reactions to the COVID-19 vaccine have been minor and self-limited.[1] It is the author's viewpoint that

vaccination in the general population should not be discouraged. If booster COVID-19 vaccinations are to be considered in the future, patients who have demonstrated previous cutaneous hypersensitivity with internal organ involvement should proceed cautiously.

Conflicts of interest

None disclosed.

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