Toxic epidermal necrolysis-like linear IgA bullous dermatosis after third Moderna COVID-19 vaccine in the setting of oral terbinafine

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INTRODUCTION

Linear IgA bullous dermatosis (LABD) can be idiopathic or drug-induced. It is an autoimmune blistering disorder characterized by linear deposition of IgA antibodies along the dermoepidermal junction. Drug-induced linear IgA disease (DILAD) occurs more commonly in adults and is more severe than idiopathic LABD, rarely mimicking toxic epidermal necrolysis (TEN) with positive Nikolsky sign and large bullae.[1,2] DILAD typically occurs within 1 to 15 days of the first dose of the inciting medication and resolves within 2 weeks of its discontinuation. Although vancomycin is the most commonly reported drug associated with DILAD, other drugs, such as amiodarone, diclofenac, captopril, naproxen, and phenytoin, have been associated with DILAD.[3] Although the list of inciting medications that have been implicated in DILAD is extensive, there have yet to be any reports of DILAD associated with the use of terbinafine. We report the case of an 86-year-old woman, who developed TEN-like DILAD in the setting of oral terbinafine and recent administration of the third dose of the Moderna COVID-19 vaccine.

Abbreviations used:

DILAD:	drug-induced linear IgA disease
ED:	emergency department
LABD:	linear IgA bullous dermatosis
TEN:	toxic epidermal necrolysis

CASE REPORT

An 86-year-old woman developed a pruritic and painful rash on the upper portion of her left arm 1 day after her third dose of the Moderna COVID-19 vaccine at the vaccine administration site (day 1) (Fig 1). The patient then presented to the emergency department (ED) on day 3, but dermatology was not yet consulted at this time. The patient was discharged from the ED with a 5-day course of prednisone 40 mg daily for a presumed diagnosis of vasculitis secondary to the vaccine. On day 8, she returned to the ED because of worsening of the rash, which had spread to include her neck, trunk, groin, and extremities. Of note, she had started oral terbinafine for tinea pedis of her right foot 12 days prior to the onset of the rash.

At this point (day 8), the patient returned to the ED, and dermatology was consulted. The patient denied any systemic symptoms but reported having a fever of 100.4 °F 2 days previously. The patient's examination was notable for diffuse erythema, bullae, and positive Nikolsky sign (Fig 2).

Two biopsies were taken at the right and left aspects of the abdomen, including a frozen section,

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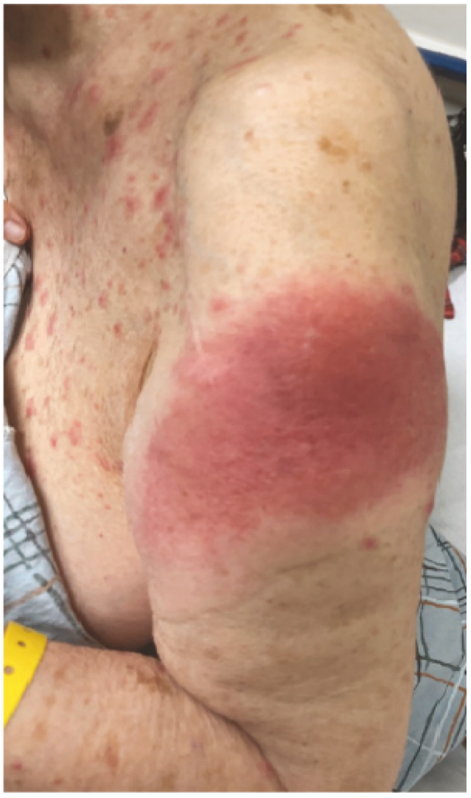

Fig 1. The initial site of the rash on the patient's upper portion of the left arm 14 days after starting terbinafine and 3 days following the third dose of the Moderna COVID-19 vaccine. This photo was taken during the patient's first emergency department visit (day 3; 5 days prior to returning to the same emergency department and dermatology consult).

which was analyzed immediately by surgical pathology, revealing an interface dermatitis consistent with TEN. Terbinafine was emergently stopped, and the patient was transferred to another hospital with a burn unit owing to the working diagnosis of TEN. At that hospital, repeat biopsies were taken from the right lower part of the abdomen. Hematoxylin-eosin staining revealed a neutrophil-rich subepidermal blister, consistent with a TEN-like presentation of LABD, and direct immunofluorescence showed dominance of IgA at the epidermal basement membrane zone, consistent with LABD (Fig 3). During admission in the second hospital, the permanent sections from the initial hospital were interpreted by dermatopathology as also consistent with LABD, but not TEN.

When the patient was transferred to the second hospital, she received 1000 mg of intravenous methylprednisolone, which was tapered to 250 mg over 5 days. She was then transitioned to oral prednisone, starting at 80 mg daily, which was tapered over 10 days. She also received topical triamcinolone 0.1% ointment twice daily to the trunk and clobetasol 0.05% ointment twice daily to the arms and legs. During the course of her oral prednisone taper on day 20, the patient's rash resolved (Fig 4). The patient was closely observed in the hospital throughout her corticosteroid taper.

DISCUSSION

Given the patient's initially localized rash and the temporal relationship with her recent Moderna COVID-19 vaccine booster, which is speculated to

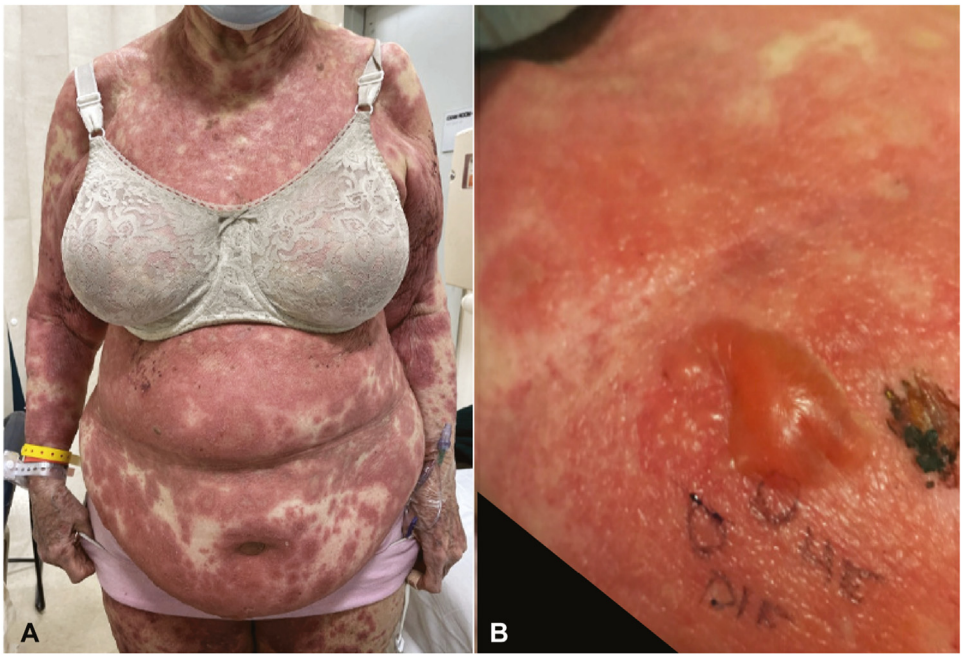

Fig 2. A, Progression of the rash with diffuse distribution at the time of dermatology consult (Day 8), 19 days after starting terbinafine and 8 days following the third dose of the Moderna COVID-19 vaccine. **B,** Biopsy sites on the right lower part of the abdomen.

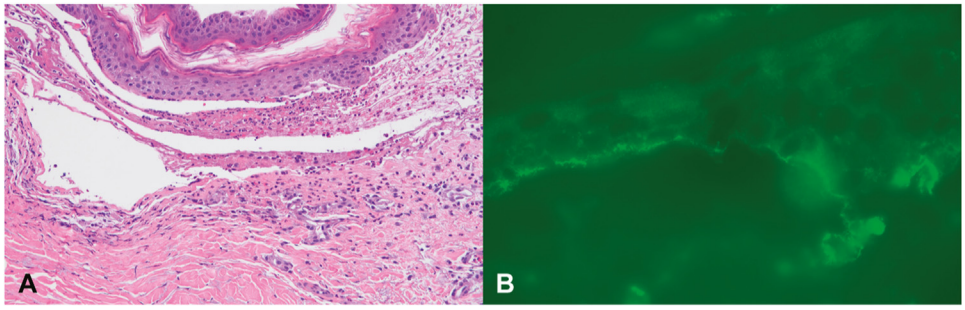

Fig 3. A, Hematoxylin-eosin–stained skin biopsy of the right lower part of the abdomen (magnification ×20) showing a neutrophil-rich subepidermal blister, consistent with toxic epidermal necrolysis-like presentation of linear IgA bullous dermatosis. **B,** Direct immunofluorescence showing linear staining pattern for IgA at the base of the detached epidermis.

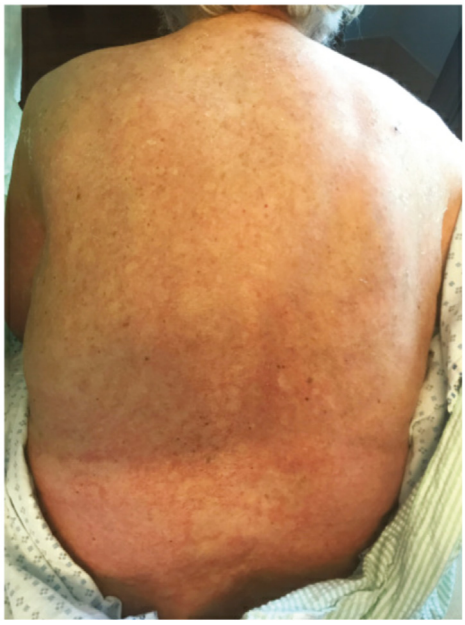

Fig 4. Resolution of the rash 12 days after the initial dermatology consult (day 20; during the course of her oral prednisone taper) on the patient's back.

cause autoimmune manifestations,[4] we posit that her booster unmasked a subclinical hypersensitivity syndrome, resulting in a TEN-like presentation of LABD, possibly secondary to terbinafine. Alternatively, it is possible that the terbinafine administration may have been coincidental and that her presentation was entirely secondary to her COVID-19 vaccination.

To date, there have been only 2 other reported cases of LABD potentially associated with COVID-19 vaccination.[5,6] Coto-Segura et al[5] reported on a 71-year-old man, who developed small vesiculobullae, some in a rosette-like pattern, over the thighs 3 days after receiving a second booster of the Pfizer COVID-19 vaccine. The patient was not taking any concomitant drugs at the time of his Pfizer COVID-19 vaccine booster. Unlike our patient, this patient had a significantly less severe disease course and required less intensive treatment. Hali et al reported the case of a 61-year-old man, who developed tense bullae with erythematous and purpuric bases on his legs as well as target-like lesions on his abdomen and trunk 3 days after receiving his COVID-19 vaccine booster. This patient did not report any new infections or medications in the weeks preceding his booster. Of note, the patient received the Oxford AstraZeneca vector vaccine, which is not an mRNA vaccine.[6]

Various mechanisms exist that could potentially explain our patient's heightened immunogenicity following her COVID-19 vaccination. One possible mechanism lies within the role of certain vaccine adjuvants. These vaccine adjuvants could trigger immunogenicity by stimulating the NLR pyrin domain containing 3 inflammasome. The mRNA present in vaccines is identified by Toll-like receptors and cytosolic inflammasome components, thereby causing inflammation.[7] The NLR pyrin domain containing 3 inflammasome plays a vital role in the innate and adaptive immune response and contributes to several autoimmune diseases.[8] Another potential explanation for the patient's hyperinflammatory condition is the acute increase in type I interferon expression after the vaccination. This activation of type I interferon can induce the adaptive immune response and subsequently influence antibody production.[4] Thus, given the potent immune response generated by the COVID-19 vaccines, aberrations in the host's immune milieu may occur; especially in the setting of beginning a new drug as in our case. Finally, as vaccines are nonspecific activators of the immune response, this may consequently cause molecular mimicry between vaccine antigens and host proteins, thereby inducing *de novo* autoimmune diseases.[9]

Conflicts of interest

None disclosed.

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