

Psoriasiform Dermatitis Associated With the Moderna COVID-19 Messenger RNA Vaccine

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PRACTICE POINTS

- The differential diagnosis for a new-onset psoriasiform rash in an elderly patient should include a vaccine-related rash.
- A rash following vaccination that necessitates systemic corticosteroid therapy can decrease vaccine efficacy.

To the Editor:

The Moderna COVID-19 messenger RNA (mRNA) vaccine was authorized for use on December 18, 2020, with the second dose beginning on January 15, 2021.¹⁻³ Some individuals who received the Moderna vaccine experienced an intense rash known as “COVID arm,” a harmless but bothersome adverse effect that typically appears within a week and is a localized and transient immunogenic response.⁴ COVID arm differs from most vaccine adverse effects. The rash emerges not immediately but 5 to 9 days after the initial dose—on average, 1 week later. Apart from being itchy, the rash does not appear to be harmful and is not a reason to hesitate getting vaccinated.

Dermatologists and allergists have been studying this adverse effect, which has been formally termed *delayed cutaneous hypersensitivity*. Of potential clinical consequence is that the efficacy of the mRNA COVID-19 vaccine may be harmed if postvaccination dermal reactions necessitate systemic corticosteroid therapy. Because this vaccine stimulates an immune response as viral RNA integrates in cells secondary to production of the spike protein of the virus, the skin may be affected secondarily and manifestations

of any underlying disease may be aggravated.⁵ We report a patient who developed a psoriasiform dermatitis after the first dose of the Moderna vaccine.

A 65-year-old woman presented to her primary care physician because of the severity of psoriasiform dermatitis that developed 5 days after she received the first dose of the Moderna COVID-19 mRNA vaccine. The patient had a medical history of Sjögren syndrome. Her medication history was negative, and her family history was negative for autoimmune disease. Physical examination by primary care revealed an erythematous scaly rash with plaques and papules on the neck and back (Figure 1). The patient presented again to primary care 2 days later with swollen, painful, discolored digits (Figure 2) and a stiff, sore neck.

Laboratory results were positive for anti-Sjögren syndrome-related antigens A and B. A complete blood cell count; comprehensive metabolic panel; erythrocyte sedimentation rate; and assays of rheumatoid factor, C-reactive protein, and anti-cyclic citrullinated peptide were within reference range. A biopsy of a lesion on the back showed psoriasiform dermatitis with confluent parakeratosis and scattered necrotic keratinocytes. There was superficial perivascular inflammation with rare eosinophils (Figure 3).

The patient was treated with a course of systemic corticosteroids. The rash resolved in 1 week. She did not receive the second dose due to the rash.

Two mRNA COVID-19 vaccines—Pfizer BioNTech and Moderna—have been granted emergency use authorization by the US Food and Drug Administration.⁶ The safety profile of the mRNA-1273 vaccine for the median 2-month follow-up showed no safety concerns.³ Minor

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FIGURE 1. A, Scattered 2- to 5-mm, pink-erythematous, scaly plaques were present on the posterior trunk (back). B, Scattered scaly papules with mild macular erythema were present on the left upper chest and clavicular region, with pink to deep red-erythematous papules coalescing linearly on the neck and left shoulder 2 days after vaccination.

localized adverse effects (eg, pain, redness, swelling) have been observed more frequently with the vaccines than with placebo. Systemic symptoms, such as fever, fatigue, headache, and muscle and joint pain, also were seen somewhat more often with the vaccines than with placebo; most such effects occurred 24 to 48 hours after vaccination.^{3,6,7} The frequency of unsolicited adverse events and serious adverse events reported during the 28-day period after vaccination generally was similar among participants in the vaccine and placebo groups.³

There are 2 types of reactions to COVID-19 vaccination: immediate and delayed. Immediate reactions usually are due to anaphylaxis, requiring prompt recognition and treatment with epinephrine to stop rapid progression of life-threatening symptoms. Delayed reactions include localized reactions, such as urticaria and benign exanthema; serum sickness and serum sickness-like reactions; fever; and rare skin, organ, and neurologic sequelae.^{1,6-8}

Cutaneous manifestations, present in 16% to 50% of patients with Sjögren syndrome, are considered one of the most common extraglandular presentations of the syndrome. They are classified as nonvascular (eg, xerosis, angular cheilitis, eyelid dermatitis, annular erythema) and vascular (eg, Raynaud phenomenon, vasculitis).⁹⁻¹¹ Our patient did not have any of those findings. She had not taken any medications before the rash appeared, thereby ruling out a drug reaction.

The differential for our patient included post-urinary tract infection immune-reactive arthritis and rash, which is not typical with *Escherichia coli* infection but is described with infection with *Chlamydia* species and *Salmonella* species. Moreover, post-urinary tract infection immune-reactive arthritis and rash appear mostly on the palms and soles. Systemic lupus erythematosus-like rashes have a



FIGURE 2. Pink hands with edematous phalanges 2 days after vaccination.

different histology and appear on sun-exposed areas; our patient's rash was found mainly on unexposed areas.¹²

Because our patient received the Moderna vaccine 5 days before the rash appeared and later developed swelling of the digits with morning stiffness, a delayed serum sickness-like reaction secondary to COVID-19 vaccination was possible.^{3,6}

COVID-19 mRNA vaccines developed by Pfizer-BioNTech and Moderna incorporate a lipid-based nanoparticle carrier system that prevents rapid enzymatic degradation of mRNA and facilitates in vivo delivery of mRNA. This lipid-based nanoparticle carrier system is further stabilized by a polyethylene glycol 2000 lipid conjugate that provides a hydrophilic layer, thus prolonging

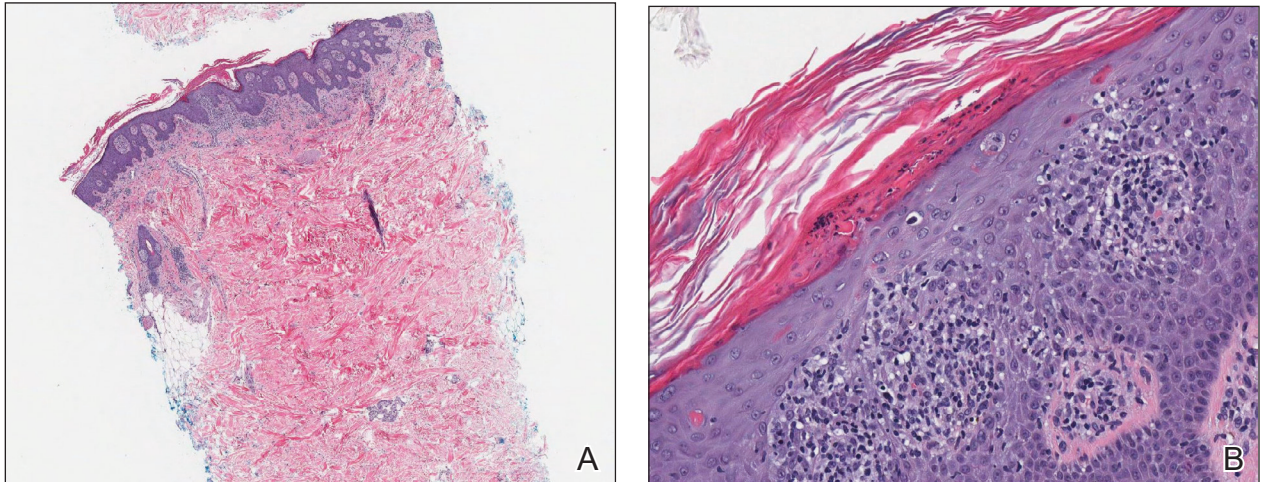


FIGURE 3. A, Histopathology of one of the lesions on the back showed mainly epidermal and superficial dermal involvement (H&E, original magnification $\times 40$). B, Psoriasiform dermatitis with confluent parakeratosis and scattered necrotic keratinocytes also were noted (H&E, original magnification $\times 400$).

half-life. The presence of lipid polyethylene glycol 2000 in mRNA vaccines has led to concern that this component could be implicated in anaphylaxis.⁶

COVID-19 antigens can give rise to varying clinical manifestations that are directly related to viral tissue damage or are indirectly induced by the antiviral immune response.^{13,14} Hyperactivation of the immune system to eradicate COVID-19 may trigger autoimmunity; several immune-mediated disorders have been described in individuals infected with SARS-CoV-2. Dermal manifestations include cutaneous rash and vasculitis.¹³⁻¹⁶ Crucial immunologic steps occur during SARS-CoV-2 infection that may link autoimmunity to COVID-19.^{13,14} In preliminary published data on the efficacy of the Moderna vaccine on 45 trial enrollees, 3 did not receive the second dose of vaccination, including 1 who developed urticaria on both legs 5 days after the first dose.¹

Introduction of viral RNA can induce autoimmunity that can be explained by various phenomena, including epitope spreading, molecular mimicry, cryptic antigen, and bystander activation. Remarkably, more than one-third of immunogenic proteins in SARS-CoV-2 have potentially problematic homology to proteins that are key to the human adaptive immune system.⁵

Moreover, SARS-CoV-2 seems to induce organ injury through alternative mechanisms beyond direct viral infection, including immunologic injury. In some situations, hyperactivation of the immune response to SARS-CoV-2 RNA can result in autoimmune disease. COVID-19 has been associated with immune-mediated systemic or organ-selective manifestations, some of which fulfill the diagnostic or classification criteria of specific autoimmune diseases. It is unclear whether those medical disorders are the result of transitory postinfectious epiphenomena.⁵

A few studies have shown that patients with rheumatic disease have an incidence and prevalence of

COVID-19 that is similar to the general population. A similar pattern has been detected in COVID-19 morbidity and mortality rates, even among patients with an autoimmune disease, such as rheumatoid arthritis and Sjögren syndrome.^{5,17} Furthermore, exacerbation of preexisting rheumatic symptoms may be due to hyperactivation of antiviral pathways in a person with an autoimmune disease.¹⁷⁻¹⁹ The findings in our patient suggested a direct role for the vaccine in skin manifestations, rather than for reactivation or development of new systemic autoimmune processes, such as systemic lupus erythematosus.

Exacerbation of psoriasis following COVID-19 vaccination has been described²⁰; however, the case patient did not have a history of psoriasis. The mechanism(s) of such exacerbation remain unclear; COVID-19 vaccine-induced helper T cells (T_H17) may play a role.²¹ Other skin manifestations encountered following COVID-19 vaccination include lichen planus, leukocytoclastic vasculitic rash, erythema multiforme-like rash, and pityriasis rosea-like rash.²²⁻²⁵ The immune mechanisms of these manifestations remain unclear.

The clinical presentation of delayed vaccination reactions can be attributed to the timing of symptoms and, in this case, the immune-mediated background of a psoriasiform reaction. Although adverse reactions to the SARS-CoV-2 mRNA vaccine are rare, more individuals should be studied after vaccination to confirm and better understand this phenomenon.

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