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Pruritic annular erythematous eruption after receiving the COVID-19 vaccine

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Question 1: What is the most likely diagnosis?

- A. Erythema Multiforme
- B. Pityriasis Rosea
- C. Urticaria Multiforme
- D. Guttate Psoriasis
- E. Cutaneous Lupus Erythematosus

Correct answer: C. Urticaria multiforme (immediate-type hypersensitivity reaction) to COVID-19 vaccine. The key finding in this case was onset of rash suggestive of acute urticaria within 4 hours of receiving the COVID-19 vaccine. Urticaria multiforme is a morphological subtype of acute urticaria characterized by blanchable edematous annular or polycyclic erythematous plaques, often with a dusky center.

Case

A woman in her 20s presented with multiple pruritic, pink/red edematous annular blanching plaques with dusky-appearing centers on her face, neck, chest, back, and shoulders. Two weeks prior, 2 pruritic pink-red papules appeared on her face within 4 hours of her first dose of Pfizer-BioNTech COVID-19 vaccine. Within 24 hours, additional lesions appeared, and a 5-day taper of oral prednisone was prescribed. By day 5, all lesions resolved but recurred 24 hours later with increased number and diameter, and central clearing (Fig 1). Antihistamines, hydroxyzine and cetirizine, were prescribed, and lesions resolved within 24 to 48 hours. She had no new medications, anaphylaxis-type symptoms, known allergies, angioedema, or history of autoimmune disease or vaccine reaction. Laboratory test results included normal complete blood count, normal complete metabolic panel, and negative anti-nuclear antibody, anti-dsDNA, SS-A, SS-B, Sm, and Sm/

RNP antibodies. A punch biopsy demonstrated superficial and deep lymphocytic infiltrate with occasional eosinophils.

Discussion

Cutaneous reactions are a common side effect of mRNA COVID vaccines, with >4% of patients who received the 2-dose mRNA COVID vaccine reporting a cutaneous reaction.¹ After local hypersensitivity reactions, urticarial rashes are the second most common cutaneous reaction to mRNA COVID vaccines, occurring in 0.34 to 0.46% of patients after first vaccine dose, and 0.49 to 0.66% of patients previously urticaria-free after second vaccine dose.¹ Key features in establishing a diagnosis of urticaria are the transient nature of lesions and resolution with antihistamines.

As in our patient's case, the majority of cutaneous reactions to mRNA vaccines occur in women with no dermatologic history or vaccine reaction history.² Our patient's case differs from typical post-vaccine urticarial rashes in 2 key aspects: the rash occurred within 4 hours of the first dose and her presentation was consistent with urticaria multiforme. Urticaria multiforme is a morphological subtype of acute urticaria characterized by blanchable edematous annular or polycyclic erythematous plaques, often with a dusky center. To our knowledge, in prior case series on post-COVID vaccination rashes, the morphology of urticarial rashes is not explicitly stated. In a case series of 414 patients with cutaneous adverse events after vaccination with either the Moderna or Pfizer COVID-19 vaccines, a minority of urticarial eruptions occurred within 24 hours after administration (3/37 of cases).² Of the urticarial eruptions occurring within 24 hours, all 3 occurred after the second dose.

Critically, while anaphylaxis is a contraindication to repeat vaccination with the same vaccine type, urticaria without anaphylaxis is not an absolute contraindication to additional vaccine doses.³ Management of patients with urticaria without anaphylaxis after vaccination may include referral to an allergist-immunologist prior to vaccination with the same vaccine type.

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Informed, written consent was received from all patients and confirmed to the journal pre-publication, stating that the patients gave consent for their photos and case history to be published.

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What is known about this subject in regard to women and their families?

- Women are more likely to experience adverse reactions to the COVID-19 vaccine, including both immediate and delayed cutaneous reactions.
- Vaccine hesitancy is affected by concerns about safety and misconceptions regarding vaccine effectiveness and side effects.
- Immediate hypersensitivity reactions including urticaria to mRNA COVID-19 vaccines may not be a contraindication to subsequent vaccination with the same vaccine; evaluation by an allergist-immunologist may be considered



Fig. 1. Physical examination findings at presentation. (A) Left side of face. (B) Upper and lower back.

Pretreatment with fexofenadine 180 to 360 mg or cetirizine 10 to 20 mg 1 to 2 hours prior to subsequent COVID-19 vaccination can be considered for patients with vaccine-associated urticaria.³

Notably, in patients who experienced an urticarial rash after their first vaccine dose, 2.02 to 5.03% developed an urticarial rash after their second dose,¹ but the frequency with which patients may develop chronic urticaria after COVID-19 vaccination is unknown. In our patient's case, after allergist-immunologist evaluation, she was tapered off antihistamines without recurrence. She then received her second Pfizer-BioNTech COVID-19 vaccination with antihistamine premedication of cetirizine 30 mg and famotidine 20 mg administered 30 minutes prior to vaccination, followed by 30 minutes monitoring post-injection without recurrence.

Women are more likely to experience COVID-19 cutaneous vaccine-related side effects. Hence, we emphasize the importance of timely diagnosis, appropriate management, and clear communication and reassurance regarding the side effects of COVID-19 vaccines in women in order to support COVID-19 vaccination efforts and pandemic control.

Question 2: What is the next best step in management?

- Prescribe systemic steroids and proceed with second dose of the same vaccine type.
- Prescribe hydroxychloroquine and refer to rheumatology before second dose of the same vaccine type.
- Prescribe topical steroids and proceed with second dose of the same vaccine type.
- Continue antihistamines and refer to allergy-immunology before second dose of the same vaccine type.

Correct answer: D. Continue antihistamines and refer to allergy-immunology before second dose of the same vaccine type. Topical steroids (C) and hydroxychloroquine (B) may be used to treat cutaneous lupus, some forms of which may also

present as annular pink plaques, but these are not beneficial in urticaria. Systemic steroids (A) may result in rebound urticaria, and patients with immediate allergic reactions to the COVID-19 vaccine should see allergy-immunology prior to second vaccine dose.

Author contributions

D.E.C.: writing - original draft preparation
 J.G.: writing - revisions, reviewing and editing
 A.E.Z.: conceptualization, writing - reviewing and editing, resources
 A.J.L.: conceptualization, supervision, writing - reviewing and editing, resources

Conflicts of interest

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Study approval

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