

JAMA Clinical Challenge

Urticaria 12 Days After COVID-19 mRNA Booster Vaccination

Anna R. Wolfson, MD; Esther E. Freeman, MD, PhD; Kimberly G. Blumenthal, MD, MSc



Figure. Wheal and flare lesions on patient's forearm (left) and eyelids (right).

A healthy 27-year-old woman received a COVID-19 mRNA booster vaccine (Moderna) on December 7, 2021. She had not experienced adverse effects after the first 2 vaccine doses on January 17 and February 5, 2021. Twelve days after the booster vaccination, she developed pruritic wheals on her face and bilateral, transient eyelid swelling. Over the next week, a pruritic rash spread over her neck, chest, trunk, and arms; each lesion faded without scarring within 24 hours. She did not experience lip, tongue, or neck swelling; shortness of breath; wheezing; chest pain; or palpitations. Application of pressure to her forearm in a circular motion using a pen cap elicited wheal and flare lesions (Figure, left panel). On physical examination, performed 17 days after the onset of rash, her vital signs were normal. She had no tongue, lip, or throat swelling, and her lungs were clear to auscultation bilaterally. Wheal and flare lesions developed on her upper eyelids during the examination and resolved after approximately 30 minutes (Figure, right panel). Light pressure applied to her skin with a tongue depressor elicited wheal and flare lesions within 3 to 5 minutes.

The patient had no history of atopy, urticaria, angioedema, or food or drug allergy and no recent infections. She took no prescription medications and reported no recent use of over-the-counter medications, including nonsteroidal anti-inflammatory drugs. She had no recent travel, exposure to animals, or use of new personal care products.

WHAT WOULD YOU DO NEXT?

- A.** Advise the patient against future COVID-19 mRNA vaccination because of allergy
- B.** Prescribe a preloaded epinephrine autoinjector and refer for allergy testing
- C.** Prescribe a nonsedating antihistamine at a standard dose and increase to high-dose antihistamine if symptoms persist
- D.** Prescribe oral prednisone (60 mg per day for 5 days)

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Diagnosis

Inducible urticaria (symptomatic dermatographism) and acute urticaria

What to Do Next

C. Prescribe a nonsedating antihistamine at a standard dose and increase to high-dose antihistamine if symptoms persist.

The key to the correct diagnosis is recognition of urticaria and dermatographism, an exaggerated wheal and flare response that occurs within minutes of skin being stroked, scratched, or having pressure applied to it.¹ Advising the patient against future COVID-19

mRNA vaccination (choice A) is incorrect because she did not have a vaccine allergy. An immediate allergic reaction occurs within 4 hours of vaccination; vaccine anaphylaxis typically occurs within 30 minutes of vaccination, is rapidly progressive, and includes systemic signs such as hypotension or hypoxemia.^{2,3} A preloaded epinephrine autoinjector (choice B) is not indicated for acute urticaria or angioedema, unless there is a strong suspicion of anaphylaxis.⁴ Systemic glucocorticoids (choice D) are not recommended for most patients with acute urticaria with or without angioedema.^{1,4} Moreover, glucocorticoids may alter the immune response to COVID-19 vaccination.^{4,5}

Discussion

Urticaria is predominantly a mast cell-mediated condition that presents with wheals (hives), defined as superficial skin swelling and erythema that resolves within 30 minutes to 24 hours with or without angioedema, which is swelling in the lower dermis or the subcutaneous or mucous membranes that resolves within 72 hours.¹ Urticaria is often idiopathic but can be triggered by infection with viruses, bacteria, and parasites, medications (such as nonsteroidal anti-inflammatory drugs and narcotics), food (such as tree nuts and shellfish), and insect stings or bites. Approximately 20% of people develop urticaria over their lifetime, with two-thirds experiencing acute urticaria, defined as lasting less than 6 weeks.⁶ Urticaria is considered chronic if it recurs over a duration of 6 weeks or longer.¹

Urticaria can occur spontaneously or may be induced by specific triggers. The most common type of inducible urticaria is dermatographism, meaning “to write on the skin.” Simple urticarial dermatographism, which is a benign condition that affects 1.5% to 5% of healthy individuals and is sometimes associated with atopic dermatitis,⁷ presents as nonpruritic wheals. Symptomatic dermatographism involves dermatographic skin wheals that are pruritic.

Symptomatic dermatographism is initially treated with a non-sedating antihistamine, such as cetirizine or fexofenadine, which can be increased to up to 4 times standard dose if symptoms persist.¹ Patients with persistent symptomatic dermatographism despite high-dose antihistamines may benefit from omalizumab or possibly leukotriene receptor antagonists.¹

While this patient’s symptomatic dermatographism could have occurred spontaneously, it may have been triggered by COVID-19 mRNA booster vaccination. In a survey of health care workers, 1.62% reported hives within 4 weeks of COVID-19 mRNA vaccination.⁸ A prospective study of hospital employees who received a COVID-19 mRNA vaccine found that 0.4% developed urticaria and 0.3% had angioedema within 3 days of their first vaccination. Urticaria recurred in 3.3% and angioedema recurred in 2.6% of these individuals after their second COVID-19 mRNA vaccination.⁹ The Centers for Disease Control and Prevention states that cutaneous reactions occurring more than 4 hours after COVID-19 vaccination are not a contraindication to subsequent vaccination.¹⁰

Patient Outcome

The patient’s urticaria did not resolve with standard-dose fexofenadine (180 mg daily) or with 4 times the standard dose, so montelukast (10 mg nightly) and an additional midday dose of 360 mg fexofenadine was added. Four weeks later, her urticaria resolved but symptomatic dermatographism persisted. Twelve weeks after the onset of urticaria, she was given omalizumab (300 mg subcutaneously), montelukast was stopped, and fexofenadine was decreased to 360 mg twice daily. Two weeks after receiving omalizumab, her dermatographism resolved. Fexofenadine was decreased to 180 mg twice daily. The plan is to continue omalizumab monthly for a total of 3 doses. She was counseled to increase her dose of non-sedating antihistamines starting 3 days prior to another COVID-19 mRNA vaccination.

ARTICLE INFORMATION

Author Affiliations: Harvard Medical School, Boston, Massachusetts (Wolfson, Freeman, Blumenthal); Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Boston (Wolfson, Blumenthal); Department of Dermatology, Massachusetts General Hospital, Boston (Freeman).

Corresponding Author: Kimberly G. Blumenthal, MD, MSc, The Mongan Institute, Massachusetts General Hospital, 100 Cambridge St, 16th Floor, Boston, MA 02114 (e-kblumenthal@mgh.harvard.edu).

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Submissions: We encourage authors to submit papers for consideration as a JAMA Clinical Challenge. Please contact Dr Walter at kristin.walter@jamanetwork.org.

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