CORRESPONDENCE

Delayed Large Local Reactions to mRNA Vaccines

TO THE EDITOR: Blumenthal et al. (April 1 issue)[1] report delayed injection-site reactions in 12 patients who had received the mRNA-1273 vaccine against SARS-CoV-2. We observed a case of a delayed local reaction in a 38-year-old woman who had received the first dose of the BNT162b2 vaccine. Pain at the injection site had completely resolved within 2 days after the vaccination. Six days after the injection, erythema of the upper arm (Fig. 1A) with associated numbness of the fingers appeared. These symptoms resolved within 5 days.

Skin-biopsy specimens showed sparse, superficial, deep lymphohistiocytic infiltrates with CD3+ (including CD8+ and CD4+) T cells and some eosinophils (Fig. 1B through 1E). An immediate reading (at 30 minutes) and late readings (on days 2, 4, and 7) of skin tests (patch, prick, and intradermal tests) with BNT162b2 vaccine were negative (Fig. 1F and 1G). This patient did not have a recurrence of the delayed local reaction after she received the second dose of the BNT162b2 vaccine.

The pathophysiological mechanism underlying cases of "red arms" or "Covid arms" remains unclear. Histologic evaluation confirmed a delayed-type, T-cell–mediated reaction. However, delayed allergic hypersensitivity appears to be improbable, given the low reported incidence of reactions after reexposure to the vaccine with the second dose[1] and the negative results of skin tests. Clinicians should be aware that these low-grade delayed local reactions have been observed with the BNT162b2 vaccine as well as with the mRNA-1273 vaccine.

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1. Blumenthal KG, Freeman EE, Saff RR, et al. Delayed large local reactions to mRNA-1273 vaccine against SARS-CoV-2. N Engl J Med 2021;384:1273-7.

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THE AUTHORS REPLY: Baeck et al. describe a delayed local reaction after vaccination with BNT162b2. This case shows that these reactions can occur with any vaccine,[1] including BNT162b2. However, our experiences with an employee cohort in our health system,[2] a Covid-19 vaccine allergy case registry at Massachusetts General Hospital (MGH) (https://allergyresearch.massgeneral.org), and an international Covid-19 dermatology registry (www.aad.org/covidregistry) suggest that delayed large local reactions are more common with the mRNA-1273 vaccine than with the BNT162b2 vaccine. Of 146 such reactions entered into the MGH allergy case registry in early 2021 (from February 10 through March 13), a total of 139 occurred in persons who had received the mRNA-1273 vaccine and 7 in persons who had received the BNT162b2 vaccine. In the dermatology registry, of 218 delayed large local reactions that occurred in persons who had received messenger RNA vaccines, 206 occurred in persons who had received the mRNA-1273 vaccine and 12 in persons who had received the BNT162b2 vaccine.[3]

Although we agree that the mechanism of these reactions remains unclear, the timing and clinical and pathological appearance of the reactions are consistent with delayed-type hypersensitivity. We do not know the implications of negative results on skin testing or patch testing with these vaccines. However, as these vaccines become more widely available, we hope that these and other diagnostic tests may elucidate the cause of these reactions.

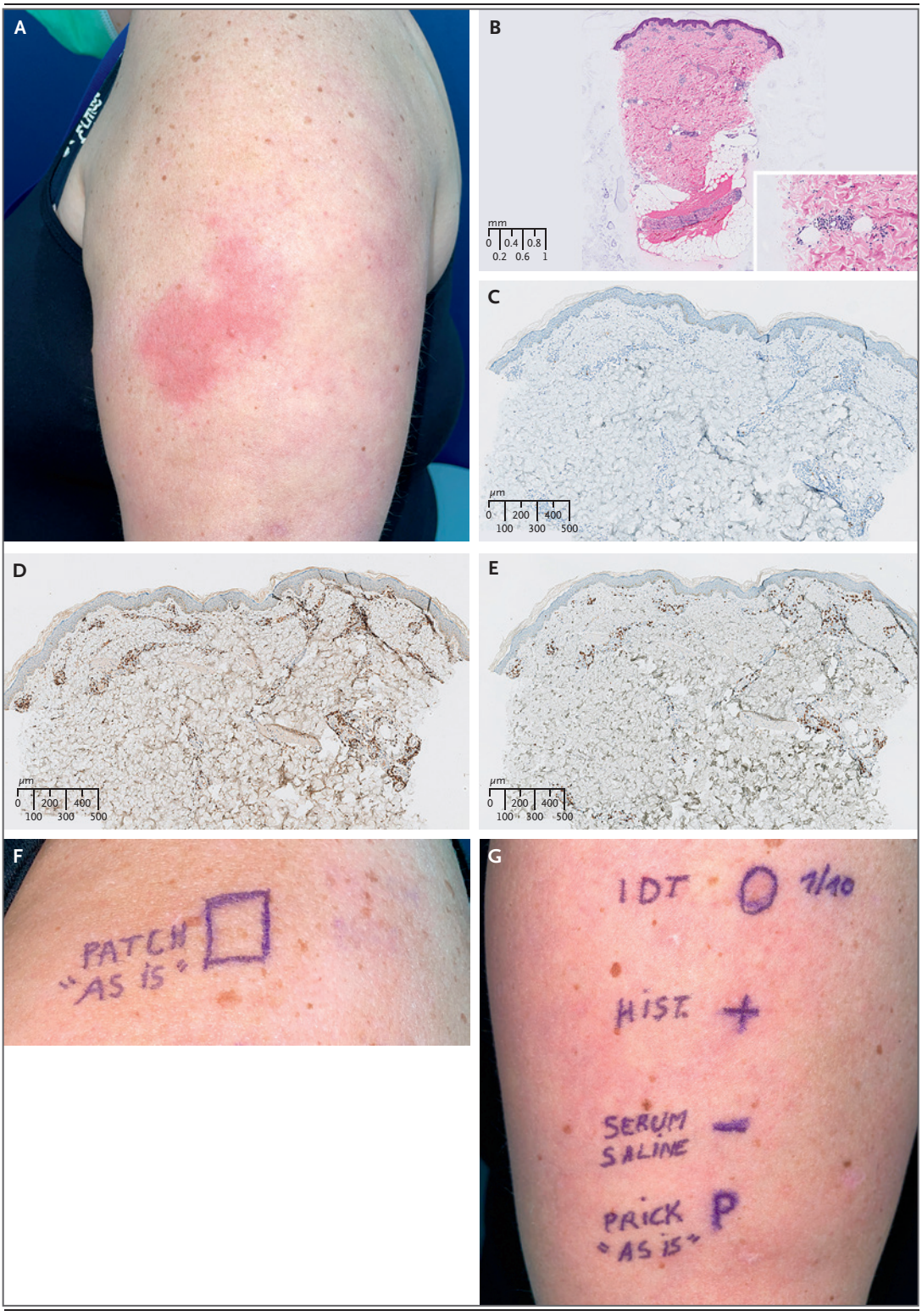

Figure 1 (facing page). Delayed Cutaneous Reaction to BNT162b2 Vaccine in a 38-Year-Old Woman.

The clinical findings of a delayed local reaction with redness and induration on day 6 after receipt of the first dose of the messenger RNA BNT162b2 vaccine (Panel A) are shown. Histopathological analysis of skin-biopsy specimens (hematoxylin and eosin) showed sparse, superficial, and deep lymphohistiocytic infiltrates with some eosinophils (the inset shows the same findings at higher magnification) (Panel B). Immunohistochemical analysis showed very rare CD20+ B cells (Panel C) as well as many CD3+ (Panel D) and CD8+ (Panel E) T cells. The results of skin patch testing on day 4 (Panel F) and the results of skin-prick testing on day 4 with BNT162b2 vaccine tested "as is" (undiluted) and an intradermal test with BNT162b2 vaccine diluted (in a 1:10 ratio) in serum saline solution (Panel G) are shown. IDT denotes intradermal test, and Hist. histamine.

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Since publication of their letter, the authors report no further potential conflict of interest.

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1. Kelso JM, Greenhawt MJ, Li JT, et al. Adverse reactions to vaccines practice parameter 2012 update. J Allergy Clin Immunol 2012;130:25-43.
2. Blumenthal KG, Robinson LB, Camargo CA Jr, et al. Acute allergic reactions to mRNA COVID-19 vaccines. JAMA 2021 March 8 (Epub ahead of print).
3. McMahon DE, Amerson E, Rosenbach M, et al. Cutaneous reactions reported after Moderna and Pfizer COVID-19 vaccination: a registry-based study of 414 cases. J Am Acad Dermatol 2021 April 7 (Epub ahead of print).

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