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Erythema multiforme after third COVID-19 vaccination (Pfizer-BioNTech)

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ABSTRACT

We present a case of erythema multiforme (EM) associated with a third (booster) dose of COVID-19 vaccination in a patient who had no cutaneous reactions to previous doses. To our knowledge, this is the first documented case of vaccine-associated EM occurring after a third/booster vaccination. Furthermore, our case emphasizes the need to remain vigilant for vaccine-associated EM in any patient recently vaccinated, regardless of whether previous vaccinations were administered without cutaneous reactions.

KEYWORDS Coronavirus; COVID-19; erythema multiforme; vaccination

Erythema multiforme (EM) may occur in the setting of recent COVID-19 infection or vaccination. Timely recognition and treatment are necessary to exclude other potential causes of EM and prevent worsening of skin and mucous membrane involvement.

CASE DESCRIPTION

A 31-year-old Hispanic woman presented with a 1-day history of asymptomatic, well-circumscribed erythematous maculopapules with faint central clearings on the bilateral palms and forearms *(Figure 1)*. She noted that the rash appeared approximately 8 hours after she received her third COVID-19 BNT162b2 (Pfizer-BioNTech) vaccination the previous day. She denied any history of similar rashes. She had no history of herpes simplex virus infection in the past or concurrent with this rash. Three months earlier, the patient had a moderate COVID-19 infection treated with a casirivimab/imdevimab infusion. She had been previously vaccinated with two doses of BNT162b2 about 10 months beforehand. A diagnosis of EM was made based on clinical features and history. A 6-day oral prednisone taper was prescribed with complete resolution of the rash.

DISCUSSION

Cutaneous eruptions occur in 1% to 2% of patients infected with SARS-CoV-2.[1] EM is one of many types of rashes that may occur, though it is uncommon, comprising a minority of documented cutaneous reactions. In the setting of COVID-19 infection, EM may result from a hypersensitivity reaction mediated by CD8+ T lymphocytes targeting antigens in the skin, leading to apoptosis of keratinocytes and satellite cell necrosis.[2,3] Moreover, the presence of acral involvement suggests type III and/or IV hypersensitivity involving small vessels responsible for endothelial activation and dermal and perivascular lymphoid infiltration, resulting in interface dermatitis and exocytosis of lymphocytes.[2] Histological observations support this theory, showing dermal infiltrates with lymphohistiocytic infiltration surrounding superficial and mid-dermal vessels.[4] Alternatively from infection, EM may be medication or vaccine induced.

EM is a known reaction to various COVID-19 vaccines including BNT162b2 (Pfizer-BioNTech), mRNA-1273 (Moderna), and Corona Vac (Sinovac).[5–9] While the exact incidence is unknown, studies suggest EM accounts for approximately 0.72% to 4.8% of adverse cutaneous reactions

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Figure 1. Multiple erythematous maculopapules with dusky central clearings on the palmar surface of the left hand.

associated with these vaccinations.[7,10,11] Similar to natural COVID-19 antigens, vaccine antigens are thought to trigger EM through inflammatory cascades that result in keratinocyte necrosis, epidermal antigen exposure, and T-cell recruitment.[8] COVID-19 vaccine–associated EM typically erupts within 2 to 3 days after first or second vaccination, although onset may occur up to 6 days after vaccination.[5–9] This report is unique in that it attributes EM to the third vaccine, while prior reports have attributed the outbreak to one of the first two doses in the COVID-19 vaccine series. Our patient received her first two BNT162b2 doses 10 months earlier without issue, suggesting that EM may occur with any dose, even if previous doses were administered without cutaneous reactions.

While most cases of COVID-19 vaccine–associated EM are mild, at least one case has been severe enough to warrant hospitalization.[7,8] As such, clinicians should remain vigilant for EM when presented with a maculopapular rash in the setting of recent COVID-19 vaccination, regardless of whether it is the first or second dose or beyond.

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