

Generalized Fixed Drug Eruption Following Pfizer-BioNtech COVID-19 Vaccination

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Abstract

Fixed drug eruption is a cutaneous drug reaction which recurs at the same site when the individual is exposed to the causative drug, characterized by single or multiple round sharply demarcated erythematous-to-violaceous patches. Here, we report a patient with generalized non-bullous fixed drug eruption following mRNA-based Pfizer-BioNtech COVID-19 vaccine.

Title page

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INTRODUCTION

Fixed drug eruption (FDE) is a cutaneous drug reaction which recurs at the same site when the individual is exposed to the causative drug. The eruption is characterized by single or multiple round sharply demarcated erythematous-to-violaceous patches and rarely with generalized bullae resembling Stevens-Johnson syndrome or toxic epidermal necrolysis. The erythematous-to-violaceous hue usually improves over several days, resulting in a characteristic round hyperpigmented patch [1]. Although the culprit agent is usually a medication, such as a sulfa antibiotic or a nonsteroidal anti-inflammatory drug (NSAID), FDE has also been reported following vaccinations such as the influenza, yellow fever, and human papilloma virus vaccines [1-3].

To date, only five cases of FDE following COVID-19 vaccination have been reported, 3 following mRNA and 2 after adenoviral vector-based vaccines (**Table 1**) [4-8]. Here, we report a patient with generalized non-bullous fixed drug eruption following vaccination with the mRNA-based Pfizer-BioNTech COVID-19 vaccine.

CASE PRESENTATION

A 50-year-old female presented to the dermatology clinic for her initial visit, with a concern of multiple dark spots on her skin. The patient reported that approximately 1 year prior to presentation, she noticed an erythematous tender patch on her left upper back 2 days following her second dose of the Pfizer-BioNTech COVID-19 mRNA vaccine. Of note, both doses of the vaccine had been administered in her right arm. Over the next several days, the lesion gradually lost its erythematous hue and became a nontender round hyperpigmented patch. Approximately 1 month later, she noticed similar tender erythematous plaques gradually developing on her trunk and upper extremities. These lesions similarly progressed to non-tender hyperpigmented patches over the next several days. She continued to develop new lesions over the course of 9 months. No bullous lesions were reported.

Her past medical history was notable for breast cancer treated with left mastectomy and chemoradiation 3 years prior to presentation. Additionally, she started taking amlodipine for hypertension 1 week prior to presentation. She denied taking any other medications both at the time of presentation and for the past year, including over the counter medications such as acetaminophen or NSAIDs. She reported a history of pruritus after taking a sulfa antibiotic many years prior to presentation, but she did not remember the name of that medication. She denied any history of vaccine allergies. Her family history was noncontributory.

On examination, multiple round hyperpigmented patches ranging from 2 to 8 cm in size were seen on the left upper back (**Figure 1a**), right forearm, right and left anterior chest wall (**Figure 1b**), left abdomen, and left axilla. The remainder of the cutaneous and mucosal exam was unremarkable. A punch biopsy was obtained from the round hyperpigmented patch on the left upper back. Histopathological examination was notable for post-inflammatory pigmentary alteration with rare eosinophils consistent with a resolving FDE (**Figures 2a + 2b**). The patient was reassured and advised to weigh the potential benefits and harms prior to receiving any booster doses of the COVID-19 vaccine.

DISCUSSION :

COVID-19 vaccination has been associated with an array of cutaneous adverse effects, ranging from a localized pruritic erythematous eruption to a case of Stevens-Johnson syndrome. FDE following Covid-19 vaccination has only been reported in a handful of cases [9]. The pathogenesis of FDE following Covid-19 vaccination has yet to be determined. One potential mechanism is an immune response to the polyethylene glycol (PEG) excipient of the mRNA vaccine [8]. Similarly, a reaction to ChAdOx1 nCoV-19 virotopes in

adenoviral vectored vaccines [4] has been proposed as a possible mechanism. Notably, polysorbate 80, the vaccine excipient, does not seem to be the culprit allergen [4, 7].

FDE following COVID 19 vaccination appears to have a very low incidence rate, and its outcome is generally favorable. However, our case illustrates the potential for prolonged cosmetic sequelae following FDE secondary to the Pfizer-BioNTech Covid-19 vaccination. As such, a clear conversation about the risk of FDE should be included in the informed consent discussion when weighing the risks and benefits of Covid-19 vaccination and booster doses.

Table1. Patient characteristics of the reported cases of fixed drug eruption following COVID-19 vaccination

Nationality	Thailand ⁴
Gender	Male
Age	74
Time when lesions started to appear	25 hours after the 1 st dose
COVID-19 vaccine type	Adenoviral-vectored
Associated symptoms	None reported
Past medical history	End stage renal disease, Atrial fibrillation, Ischemic stroke
Medication history	None reported
Skin Exam	Multiple, well-defined, round to oval, erythematous to violaceous plaques with
Location	Trunk and both extremities
Labs	Unremarkable
Pathology	Subepidermal separation with superficial and deep perivascular inflammatory c
Final diagnosis	Generalized bullous fixed drug eruption
Treatment	Topical 0.25% desoximetasone cream
Outcome	Lesions gradually resolved within 2 weeks with subsequent post-inflammatory h

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Figures

Figure 1a & 1b. Fixed drug eruption: Sharply demarcated round hyperpigmented patches on the left upper back and left anterior chest wall

Figure 2a. Fixed drug eruption: Dense aggregate of melanophages in the superficial dermis

Figure 2b. Fixed drug eruption: Sparse perivascular infiltrate with eosinophils





