Symmetric drug–related intertriginous and flexural exanthema–like eruption related to coronavirus disease 2019 vaccine

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CASE REPORT

A 53-year-old man presented with an erythematous papular skin eruption. Ten days prior to the appearance of the lesions, he had received the second dose of the coronavirus disease 2019 (COVID-19) vaccine (ChAdOx1 nCoV-19 [AstraZeneca]). He denied taking any medication or supplements within 2 months before and after the second vaccination. He also denied history of any other contact or exposure. After the first injection of the COVID-19 vaccine, no adverse events occurred. Physical examination showed well-demarcated erythematous macular patches distributed symmetrically over the axillary and inguinal areas, with skin desquamation and swelling in the scrotal area and on the glans penis (Figure 1A-C). Systemic signs were absent. The blood test results were normal. Findings of direct

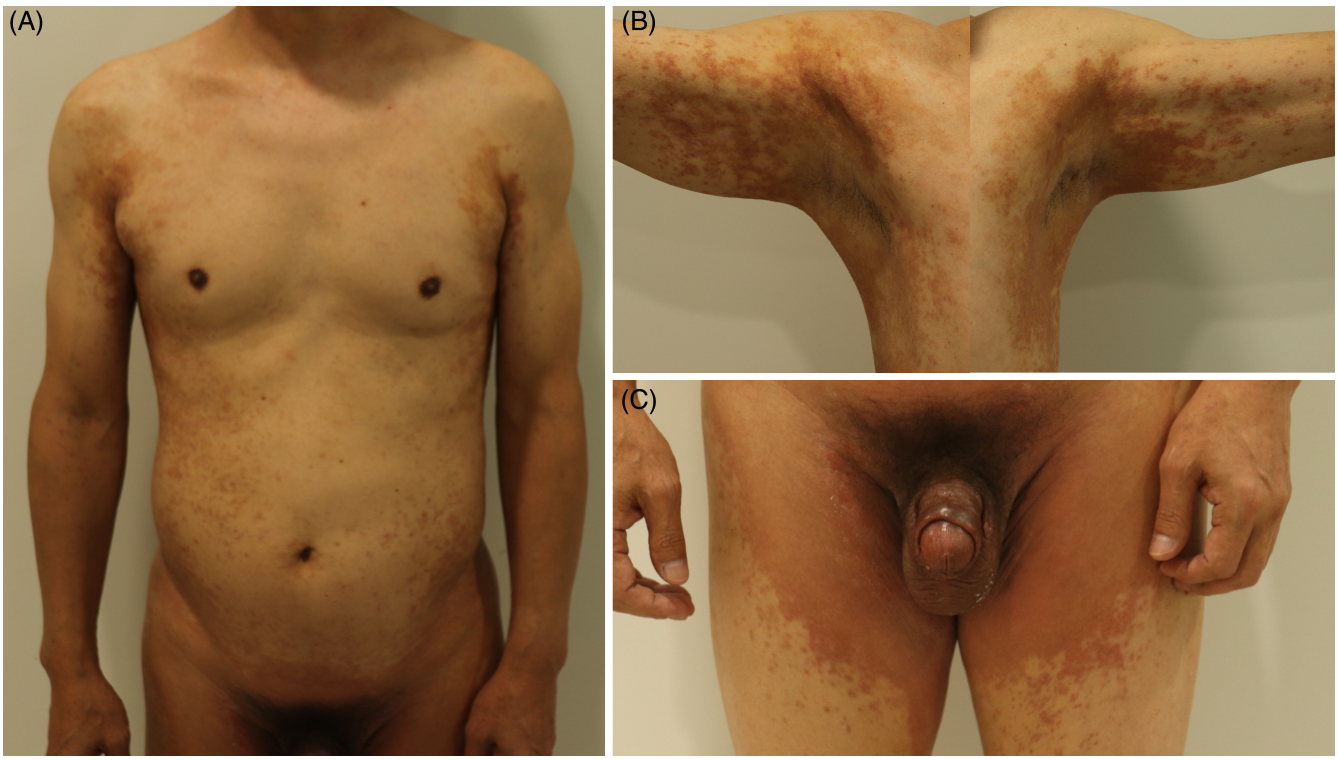

FIGURE 1 (**A**) A 53-year-old man in whom erythematous maculopatches that were distributed symmetrically over the axillary, inguinal, and perigenital areas developed 10 days after COVID-19 vaccination (ChAdOx1 nCoV-19). (**B, C**) Involvement of both axillary areas and the characteristic V-shaped erythema of the inguinal/perigenital area

TABLE 1 Reported cases of COVID-19 vaccine–related symmetric drug-related intertriginous and flexural exanthema

	Orenay et al. (2021)[5]	Lim and Wylie (2021)[2]	Hai et al. (2021)[3]		Bellinato et al. (2021)[4]	This case
Vaccine	CoronoVac	ChAdOx1 nCoV-19	BNT162b2		BNT162b2	ChAdOx1 nCoV-19
Manufacturer	SinoVac biotech corporation	AstraZeneca-oxford	Pfizer-BioNTech		Pfizer-BioNTech	AstraZeneca-oxford
Type	Purified, inactivated antigen	Recombinant, replication-deficient adenoviral vector	Messenger mRNA		Messenger mRNA	Recombinant, replication-deficient adenoviral vector
Sex/age	M/87	M/61	M/23	F/38	M/65	M/53
Onset/injection number	4 days/1st	1 day/2nd	6 weeks/2nd	2 weeks/2nd	2 weeks/ unknown	7 days/2nd
Past medical history	• Hypertension • Coronary artery disease • Chronic obstructive pulmonary disease • Chronic kidney disease	Type II diabetes mellitus (well-controlled)	None	• Depression (paroxetine 30 mg/day for many years)	Unknown	None
Treatment	• Prednisolone (40 mg/day, tapered over 3 weeks) • Antihistamine • Topical corticosteroid	• Prednisolone (30 mg/day tapered over 4 weeks) • Topical corticosteroid/ antifungal agents	• Topical corticosteroid	• Prednisolone (40 mg/day tapered over 9 days) • Topical corticosteroid	Unknown	• Prednisolone (30 mg/day tapered over 2 weeks) • Cyclosporine (200 mg/day for an additional 2 weeks) • Antihistamine • Topical corticosteroid
Prognosis	Improved after 3 weeks	Improved after 1 month	Improved after a month	Gradually improved	Unknown	Improved after 2 weeks

Abbreviations: COVID-19, coronavirus disease 2019; F, female; M, male.

microscopy with 10% potassium hydroxide (KOH) and wound culture were negative. The patient refused to undergo a skin biopsy. Based on these findings and the patient's history, we considered symmetric drug-related intertriginous and flexural exanthema (SDRIFE)–like eruption. Methylprednisolone 30 mg/day was administered for 1 week, and the dose was tapered to 15 mg/day for another week with topical corticosteroid cream. After 2 weeks, his condition resolved.

DISCUSSION

SDRIFE, a type IV hypersensitivity drug-related skin eruption that affects the skin folds, is commonly caused by β-lactam antibiotics, 5-aminosalicylic acid, iodine radiocontrast, and monoclonal antibodies. Häusermann et al. have proposed five diagnostic criteria for SDRIFE.[1]

Cutaneous reactions after COVID-19 vaccines, such as adenoviral (including ChAdOx1 nCoV-19) and messenger RNA (mRNA) vaccines (including BNT162b2; [Pfizer-BioNTech] and mRNA-1273 [Moderna Biotech), have been observed. Reports of COVID-19 vaccination-related SDRIFE are rare.[2-5] To date, five cases induced by an inactivated whole-virus vaccine (CoronaVac [Sinovac Life Sciences]), messenger RNA (mRNA) vaccine (BNT162b2), and adenoviral vaccine (ChAdOx1 nCoV-19) have been published (Table 1). Although it is not possible to discern the immunological mechanism of vaccine-associated SDRIFE, it is considered a type IVc and IVd delayed-type systemic allergic dermatitis. One possible causative agent is polysorbate 80, a well-known suspected antigen of the ChAdOx nCoV-19 (AstraZeneca) and Ad.26.COV2.S (Janssen Biotech) vaccines. Polysorbate 80 has been reported to cause delayed skin manifestations, and delayed local skin reactions near the injection site have been described after adenoviral COVID-19 vaccine administration (ChAdOx1-S [AstraZeneca]).[6,7]

Polyethylene glycol (PEG), a known excipient in mRNA COVID-19 vaccines, is a widely accepted potential culprit that causes allergic reactions, including anaphylaxis and skin manifestations, related to COVID-19 vaccination.[8-10] It is structurally similar to polysorbate 80 and has possible cross-reactivity with polysorbate 80.[11]

The CoronaVac and BNT162b2 vaccines have shared components including sodium chloride and disodium hydrogen phosphates.[3] These components are also included in many other vaccines; however, there are no previous reports of SDRIFE-like skin eruptions associated with these components. Therefore, the possibility of these being the causative agent seems relatively low.

Further investigations are warranted to clarify the correlation between vaccines and skin manifestations, and to determine the culprit of COVID-19 vaccine-induced SDRIFE.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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