

Female genital mucosal lesions associated with COVID-19 vaccination: A brief review of the literature

Dear Editor,

The current pandemic has propelled an exceptional partnership between governments and the scientific community to identify innovative and effective solutions to tackle the burden of the novel coronavirus SARS-CoV-2. Since 2020, numerous vaccines have been rolled out¹: DNA vaccines, mRNA vaccines, nonreplicating viral vector vaccines, inactivated vaccines, live attenuated vaccines, subunit vaccines and trained immunity-based vaccines are now available in many countries.

Despite the effectiveness and good safety profiles of COVID-19 vaccines, researchers from different parts of the world have reported the onset of cutaneous adverse reactions following their inoculation.² Local injection site reactions, pityriasis rosea-like eruptions, pernio-like reactions, morbilliform rashes, herpes zoster, urticaria, eczematous dermatitis and autoimmune bullous reactions are examples of the skin manifestations which have been described in the medical literature after the vaccination.² Moreover, flare events were observed in people with chronic dermatological conditions like hidradenitis suppurativa, psoriasis, atopic dermatitis and acne.^{2,3}

We reviewed the PubMed (MEDLINE) database to identify the articles that have described the appearance of female genital mucosal lesions following the administration COVID-19 vaccines.

We identified seven studies which reported the appearance of female mucosal findings after the inoculation of COVID-19 vaccines (Table 1).

According to the data that were retrieved from our literature search, 15 patients (mean age = 18.9 ± 5.3 years) developed reactive nonsexually related genital ulcers after the administration of mRNA vaccines (60%) and the AstraZeneca (Vaxzevria) ChAdOx1 nCoV-19 vaccine (40%). Genital mucosa complications were reported the most after the second dose of the BNT162b2 mRNA vaccine (47%; mean latency time = 2.7 days). On the other hand, for what concerns the AstraZeneca vaccine (mean latency time = 2 days), in five cases the dose after which the genital lesions appeared was not reported.⁴

The only vaccine types which have been described to be associated with genital mucosa lesions in women are part of the mRNA and vector vaccine families. We may speculate that this could be traced back to the tendency of physicians

to not publish about mild cases. Moreover, this could be explained by the reluctance of patients to seek medical advice when intimate areas of the body are affected by what might be perceived as unaesthetic lesions or the manifestation of sexually transmitted infections.

The vulvar ulcers described resolved in most instances with or without the aid of symptomatic treatment.

Nonsexually transmitted genital ulcers have been reported in association to COVID-19 and cytomegalovirus in the medical literature.⁵ The mechanism behind nonsexually related vulvar ulcers associated with COVID-19 vaccines is yet to be determined, however, Salusti-Simpson et al.⁶ endeavoured to hypothesize that such lesions may be the consequence of a type III hypersensitivity mechanism triggered by vaccines which leads to microvascular damage.

Wojcicki et al.⁷ have observed that COVID-19 vaccines may be associated with an exaggerated immune response in people who have a predisposition to oral and/genital ulcers thus causing flare-ups. Of note, the host response involved in the genesis of mucosal ulcers appears to be polarized toward T helper 1 lymphocytes.⁸ However, it appears plausible that an innate immune component may be involved in their pathogenesis as well.⁹

All in all, this short review summarized the evidence describing the genital mucosa lesions detected in association to the inoculation of COVID-19 vaccines. No causal relationship has been confirmed yet, but the close temporal relationship between the two suggests the existence of some type of link which connects genital lesions to SARS-CoV-2 vaccines, especially in people with predisposing risk factors.

FUNDING INFORMATION

None.

CONFLICT OF INTEREST

Dr Tamaro, Dr Kulakowska, Dr Cantisani, Dr Parisella, Dr Scarabello and Dr Adebajo have nothing to declare.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.


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TABLE 1 Female genital mucosa lesions associated with COVID-19 vaccines

Author, year	Country/ region	Age (years)	Vaccine type	Latency after vaccination (days)	Treatment	Genital mucosa finding	Detailed description of genital findings	Comorbidities	Time to resolution
Salusti-Simpson et al., ⁶ 2022	USA	22	BNT162b2 booster vaccine	2	Prednisone, clobetasol ointment, mupirocin ointment	Acute vulvar ulcers	Vulvar edema and extensive ulceration bilaterally, with yellow, grey purulent drainage and pseudomembrane	History of oral aphthous ulcers and 2 previous episodes of acute vulvar ulcers	Improvement in discomfort after 3 weeks
Wojcicki et al., ⁷ 2022	USA	16	Second dose of BNT162b2 vaccine	1	Topical clobetasol, ibuprofen, acetaminophen, oral norethidrone	Vulvar ulcers	Well demarcated ulcerated lesion with adherent yellow and grey fibrinous exudate and a necrotic- appearing border. Desquamation of the surrounding tissue	Soft palate cleft, club foot, syndactyly of her left foot, and congenital hearing impairment in the right ear, history of recurrent oral ulcerations	Improvement in symptoms at 2 weeks follow-up
Hsu et al., ¹⁰ 2022	USA	12	Second dose of BNT162b2 vaccine	2	Topical clobetasol ointment, lidocaine jelly, oral acetaminophen, ibuprofen	Vulvar ulcers	Well-circumscribed, shallow ulcers with yellowish sloughing and purulent exudate, labial edema	None	Complete healing after 2 weeks
	USA	14	Second dose of BNT162b2 vaccine	3	Clobetasol ointment, lidocaine gel, ibuprofen, oral nortriptyline, oral prednisone	Vulvar ulcers	Labial swelling, labial ulcers with overlying grey eschar	History of genital ulceration	Almost complete ulcer resolution after 4 weeks
	USA	29	First and second doses of Moderna SARS- CoV-2 vaccine	1 (after 1st dose) and 2 (after 2nd dose)	Clobetasol ointment	Vulvar ulcers	Erythematous erosions	Recurrent genital ulcers, asthma, recurrent oral aphthous ulcers	Complete resolution (time not reported)
Wijaya et al., ¹¹ 2022	Australia	16	Second dose of the BNT162b2 vaccine	4	Oral prednisolone	Vulvar aphthosis	Multiple well- demarcated vulvar ulcers with yellow- grey exudate	None	No symptoms at 4- week follow-up
	Australia	14	Second dose of the BNT162b2 vaccine	5	Oral prednisolone	Vulvar aphthosis	Vulvar ulcers and edema	Medical history of monthly oral ulcers	Full resolution at 1- week follow-up
	Australia	19	First dose of AstraZeneca (Vaxzevria) ChAdOx1 nCoV-19 vaccine	3	Ibuprofen	Vulvar aphthosis	Mild vulvar aphthosis	None	Full resolution at 1- week follow-up

TABLE 1 (Continued)

Author, year	Country/ region	Age (years)	Vaccine type	Latency after vaccination (days)	Treatment	Genital mucosa finding	Detailed description of genital findings	Comorbidities	Time to resolution
Drucker et al., ¹² 2022	USA	14	Second dose of the BNT162b2 vaccine	2	Topical lidocaine	Vulvar aphthous ulcers	Purple-pink shallow- based ulcerations with sloughing yellow roof at the core and surrounding edema	Type I von Willebrand disease	Ulcer resolution after 10 days
González- Romero et al., ⁴ 2021	Spain	24	AstraZeneca vaccine (dose not specified)	3	Prednisone and analgesics	Acute noninfectious genital ulcer	Ulcers with an erythematous border and a fibrinous, nonsuppurative centre	Vulvar ulcers 9 months earlier	Complete resolution after 3 weeks
	Europe	18	AstraZeneca vaccine (dose not specified)	1	Not reported	Acute noninfectious genital ulcer	Not reported	None	Not reported
	Europe	25	AstraZeneca vaccine (dose not specified)	2	Not reported	Acute noninfectious genital ulcer	Not reported	None	Not reported
	Europe	24	AstraZeneca vaccine (dose not specified)	1	Not reported	Acute noninfectious genital ulcer	Not reported	None	Not reported
	Europe	25	AstraZeneca vaccine (dose not specified)	2	Not reported	Acute noninfectious genital ulcer	Not reported	None	Not reported
Popatia et al., ¹³ 2022	USA	12	Second dose of the BNT162b2 vaccine	2	Lidocaine jelly, triamcinolone ointment, acetaminophen, ibuprofen	Vulvar aphthous ulcer	Ulcers with a red rim and a white-grey necrotic crust	None	Complete resolution after 10 days

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