LETTERS TO THE EDITOR



Papular skin reaction after the administration of the Ad26Cov2-S vaccine

Dear Editor,

Over the last months, the scientific community has made strenuous efforts to develop new vaccine formulations to tackle the global health issues brought by COVID-19.

The vaccines that fight the clinical manifestations of COVID-19 are numerous: there are mRNA-based vaccines, inactivated formulas, attenuated and viral vector vaccines, protein subunit vaccines, and DNA vaccines.¹

The Ad26Cov2-S vaccine developed by Janssen Pharmaceuticals is an adenovirus-based vector, which expresses the S protein of the novel coronavirus and which is administered through a single dose.¹

A 75-year-old man presented because of a diffuse pruritic rash which had appeared on his back 1 week after the administration of the Ad26Cov2-S vaccine. On physical examination, he presented multiple erythematous papules on the upper part of his back and on his neck (Figure 1). The lesions had been present in the patient's skin for a day. Notably, the patient did not have a fever nor respiratory symptoms. The blood pressure, pulse and respiratory rate were normal.

He had no past medical history of atopy, severe allergic events, or dermatologic diseases.

The patient was prescribed oral antihistamines, topical gentamycin, and corticosteroids, which lead to the resolution of the lesions without scarring after 10 days.

The cutaneous lesions which appeared on the skin of this patient may be presumptively attributed to the administration of the Ad26Cov2-S vaccine; indeed, we may hypothesize that they might have been the expression of a delayed hypersensitivity reaction or of a non-immune-mediated inflammatory event.

It is plausible to say the resolution of the skin manifestations after the application of topical gentamycin may be attributed to the presence of a bacterial superinfection after the patient scratched the lesions.

Recently, type 4 delayed hypersensitivity reactions, which are not vaccine-specific, have been speculated to be one of the mechanisms underlying the occurrence of skin lesions distant from the site of injection.² However, there are reports that granulomatous reactions leading to the appearance of adverse cutaneous manifestations may occur as well.²

Non-immune-mediated anaphylactoid reactions resulting from the direct activation of the complement system have been described in association to the administration of mRNA COVID-19 vaccines.³ Nevertheless, if a similar mechanism were to be true for the Ad26Cov2-S vaccine, it is still unclear which component of the vaccine formulation would be able to trigger it.

According to recent reports, self-limited injection-site cutaneous manifestations are the most common dermatological adverse events following the administration of COVID-19 vaccines.³

Interestingly, the term "COVID Arm" has become popular in numerous studies to describe the late injection site reactions, which are generally deemed to be harmless, following COVID-19 vaccination with mRNA formulas.⁴ Moreover, emerging evidence shows that the ChAdOx1 nCoV-19 vaccine may be linked to cutaneous adverse events such as erythema, pruritus, and nonspecific rashes as well.^{5,6}

A recent article by Song et al.⁷ reported a 83-year-old woman who developed a erythematous annular patches 48 hours after the injection of the Ad26.COV2.S vaccine. The condition was successfully managed with antihistamines and steroids.

Another published case report described an elderly woman who presented to the emergency department with widespread



FIGURE 1 Diffuse erythematous papular lesions which appeared on the upper back of the patient 1 week after the administration of the Ad26Cov2-S vaccine

Papular skin reaction after the administration of the Ad26Cov2-S vaccine.

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"erythematous-to-violaceus" plaques 72 hours after the administration of the Janssen COVID-19 vaccine.⁸

Lospinoso et al.⁹ described a 74-year-old male patient who developed a generalized erythematous rash with plaques and pustules, which spared the groin and face, 3 days after the administration of the Johnson and Johnson's Janssen Ad26.COV2.S vaccine. The skin lesions were associated with swelling of the extremities.

Notably, the close temporal association with the administration of the vaccine reported in our case and by the few reports that have been published in the medical literature suggest that the Ad26. COV2.S vaccine might be connected to the appearance of benign dermatological manifestations like the other COVID-19 vaccines.

All in all, the Ad26.COV2.S vaccine may be linked to the onset of widespread cutaneous reactions a couple of days after its administration, however, such reactions do not appear to be common. Hence, patients should not be deterred to have it administered a priori without having sought the advice of a qualified medical professional.

AUTHOR CONTRIBUTIONS

Antonella Tammaro, Michele Pezza, and Gabriella De Marco performed the literature review, wrote the article, and prepared the manuscript. They created the idea, reviewed the manuscript and photography. Ganiyat Adenike Ralitsa Adebanjo, Francesca Romana Parisella, and Verdiana Zollo took part in literature review, writing, and preparation of the manuscript.

CONFLICT OF INTEREST

None.

CONSENT STATEMENT

The patient in this manuscript has given informed consent to publication of their case details.

ETHICAL APPROVAL

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to. No ethical approval was required as no experimental procedure was performed on the patient.

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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REFERENCES

- Kyriakidis NC, López-Cortés A, González EV, Grimaldos AB, Prado EO. SARS-CoV-2 vaccines strategies: a comprehensive review of phase 3 candidates. *Npj Vaccines*. 2021;6(1):1-17. doi:10.1038/ s41541-021-00292-w
- Niebel D, Novak N, Wilhelmi J, et al. Cutaneous adverse reactions to COVID-19 vaccines: insights from an Immuno-dermatological perspective. Vaccine. 2021;9(9):944. doi:10.3390/vaccines9090944
- Bogdanov G, Bogdanov I, Kazandjieva J, Tsankov N. Cutaneous adverse effects of the available COVID-19 vaccines. *Clin Dermatol.* 2021;27:523-531. doi:10.1016/j.clindermatol.2021.04.001
- Ramos CL, Kelso JM. "COVID arm": very delayed large injection site reactions to mRNA COVID-19 vaccines. J Allergy Clin Immunol Pract. 2021;9(6):2480-2481. doi:10.1016/j.jaip.2021.03.055
- Kim JE, Lee H, Paik SS, Moon JY, Yoon HJ, Kim SH. Delayed cutaneous reaction to ChAdOx1 nCoV-19 vaccine: is it an "AstraZeneca arm"? J Eur Acad Dermatol Venereol JEADV. 2021;24:e711-e714. doi:10.1111/jdv.17476
- Tammaro A, Adebanjo GAR, Magri F, Parisella FR, Chello C, De Marco G. Local skin reaction to the AZD1222 vaccine in a patient who survived COVID-19. J Cosmet Dermatol. 2021;20(7):1965-1966. doi:10.1111/jocd.14205
- Song EJ, Wong AJS. Widespread annular eruption after Ad26. COV2.S COVID-19 vaccine. JAAD Case Rep. 2021;13:30-32. doi:10.1016/j.jdcr.2021.04.032
- Sowell J, Bevans SL, Elston CA. Widespread cutaneous reaction to the Johnson & Johnson Ad26.COV2.S vaccine. JAAD Case Rep. 2021;22:56-57. doi:10.1016/j.jdcr.2021.08.037
- Lospinoso K, Nichols CS, Malachowski SJ, Mochel MC, Nutan F. A case of severe cutaneous adverse reaction following administration of the Janssen Ad26.COV2.S COVID-19 vaccine. JAAD Case Rep. 2021;13:134-137. doi:10.1016/j.jdcr.2021.05.010