

LETTER

Eruptive halo nevi: A new COVID-19 vaccine-related cutaneous adverse event or a paraneoplastic phenomenon?

Dear Editor,

Halo nevi, also known as Sutton nevi, are characterized by the development of a rim of depigmentation around a nevus. These nevi usually occur in healthy children or young adults as single lesions and are considered benign entities, whereas in adults, the sudden appearance of numerous nevi in a short period, must be viewed with suspicion and investigated.¹ Indeed, the eruption of multiple Sutton nevi in adults has been reported in the literature associated with neoplasms, immunotherapy, and Turner syndrome.^{2,3} In this study, we describe a patient who presented to our facility complaining of the sudden appearance of multiple Halo nevi on the trunk within a few months. We discussed a possible paraneoplastic etiology or possible association with the anti-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination.

A 35-year-old man presented to our dermatology department complaining of a sudden eruption of Halo nevi on his trunk that occurred within a few months. Thirty-five Halo nevi were detected, ranged from 0.3 to 0.9 cm, and were predominantly located on the trunk (Figure 1). The patient did not take any medication in conjunction with the appearance of the eruption. He confirmed good health and reported no personal and familial history of neoplasms or

autoimmune diseases. After investigating further, the patient reported that 4 weeks before the lesions appeared, he had received the second dose of the AstraZeneca coronavirus disease 2019 (Covid-19) vaccine (ChAdOx1-S) 4 weeks after the first dose. He had no history of the previous SARS-CoV-2 infection.

Lorentzen has recently correlated the sudden appearance of multiple Halo nevi to the presence or development of malignancies, such as melanoma, papillary thyroid carcinoma, and atypical carcinoid tumor in a short time.² To arrive at these conclusions, a series of investigations, including a careful clinical evaluation, blood tests, and radiological investigations (including PET scanning) were performed. Another important study is by Epstein et al. in which five patients with melanoma, removed in all cases, presented shortly after the appearance of multiple Halo nevi.⁴ The development of halo nevi in association with melanomas likely represent a patient's immunological reaction to the neoplasia.⁵

We therefore performed a careful clinical examination in this patient, searching for a cutaneous melanoma; while considering skin, eyes, mucous membranes, mouth, perianal skin, and penis. Computed tomography (CT) of the chest, ophthalmic evaluation, and ultrasonography of the abdomen and thyroid gland were performed. All

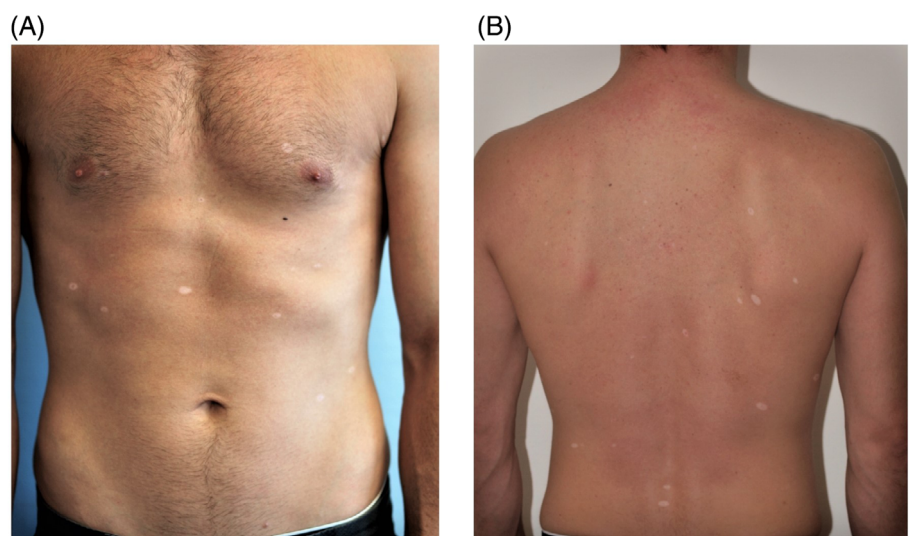


FIGURE 1 Thirty-five-year-old man with sudden onset within a few months of numerous Halo nevi throughout the skin

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TABLE 1 Cases of vitiligo associated to COVID-19 vaccines reported in the literature (up to May 2022)

	Vaccine name	Vaccine platform	Triggering dose	Time between inoculation and clinical manifestation	Clinical manifestations	Age	Sex	Notes
Ciccarese et al. ⁶	Pfizer/BioNTech	mRNA	1st	Several days	Oval and liner-shaped macules on trunk, neck and back	33	F	No new macules after second dose
Kaminetsky et al. ⁷	Moderna	mRNA	1st	1 week	Faint macules on the neck	61	F	New and more widespread macules after second dose
Aktas et al. ⁸	Pfizer/BioNTech	mRNA	1st	1 week	Macular plaques on the face	58	M	
KoçYıldırım ⁹	SinovacBiotech	Inactivated	2nd	2 weeks	Macules and patches on right cheek and forehead	49	M	
Uğurer et al. ¹⁰	Pfizer/BioNTech	mRNA	1st	1 week	White patches on bilateral axilla and forearm flexor surface	47	M	Slow down after second dose
López Riquelme et al. ¹¹	AstraZeneca	Viralvector	1st	3 days	White patches on face and arms	60	F	
Bukhari ¹²	Pfizer/BioNTech	mRNA	1st	2 weeks	White patches on trunk and arms	13	F	Stable after the second dose

investigations resulted negative; therefore, we hypothesized a possible correlation with the recent Covid-19 vaccination. In fact, the patient had received the second dose of the AstraZeneca vaccine just a few weeks before the depigmented spots appeared. After reviewing the literature (Table 1), we found that some cases of vitiligo related to SARS-CoV-2 vaccination had been reported,⁶⁻¹² while no cases of eruptive halo nevi after COVID-19 vaccination had been described so far. Vitiligo and halo nevi are closely connected to each other and share an immune-mediated etiopathogenesis. In particular, given that vaccination against Covid-19 promotes the production of type 1 interferons (IFN-I) by stimulating the recruitment of plasmacytoid dendritic cells,¹³ it has been proposed that vaccine-induced IFN-I production may serve as a trigger to vitiligo in genetically predisposed individuals.¹⁴ Remarkably, the onset of multiple halo nevi has been reported in a 22-year-old female with multiple sclerosis treated with IFN β -1a a few weeks after therapy was started.¹⁵

To the best of our knowledge, this case is the first report of an eruption of multiple halo nevi in correlation with the SARS-CoV-2 vaccine, which may be a simple coincidence; however, the temporal correlation and the increasing number of SARS-CoV-2 vaccine-related autoimmunity cases reported in the literature suggest that the vaccine may have played a role in triggering this sudden eruption.¹⁶ Given the widespread use of the vaccine, whether or not these hypotheses are confirmed by more numerous series await further investigations, particularly in younger populations. In any case, the patient will be monitored with a 6-month clinical follow-up after considering the hypothesis of a paraneoplastic event.

AUTHOR CONTRIBUTIONS

Full access to all data in the study and takes responsibility or data integrity and accuracy in the data analysis, study concept and design:

Vincenzo De Giorgi. **Acquisition of data:** Jacopo Colombo, Federico Venturi, Flavia Silvestri, Biancamaria Zuccaro, and Luciana Trane. **Analysis and interpretation of data:** Vincenzo De Giorgi, Andrea Gemignani, and Lorenzo Salvati. **Drafting of the manuscript:** Vincenzo De Giorgi, Andrea Gemignani, and Jacopo Colombo. **Critical revision of the manuscript for important intellectual content:** Vincenzo De Giorgi, Lorenzo Salvati, and Jacopo Colombo. **Study supervision:** Vincenzo De Giorgi.

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CONFLICT OF INTEREST

The authors have no relevant financial interest in this article.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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