

LETTER

Sudden onset of vitiligo after COVID-19 vaccine

Dear Editor,

Cutaneous and extracutaneous autoimmune diseases (ADs) have rarely been reported in association with COVID-19 vaccine.^{1,2} We described herein a case of sudden onset of vitiligo occurring after the first dose of COVID-19 vaccine. To date, only two cases of vitiligo in COVID-19-vaccinated patients have been described.³

A 33-year-old female presented us with a 45-days history of milky-white well-demarcated, oval and linear-shaped macules on her trunk, neck and back (Figure 1A,B) which had appeared 1 week after receiving her first dose of Pfizer-BioNTech COVID-19 vaccine. The second dose of vaccine was injected 1 months later without the appearance of new macules.

The patient's medical history was unremarkable, and she did not take any drug. She had family history of vitiligo (father) but she had never suffered from it before. The white macules were clinically consistent with vitiligo and examination under wood lamp (Figure 1C) confirmed the diagnosis revealing the characteristic white fluorescence. Since vitiligo is an autoimmune disease, the patient was screened for other autoimmune conditions: complete blood cell count, antibodies against thyroid peroxidase, thyroglobulin, transglutaminase and the thyroid stimulating hormone were within normal ranges; anti-nuclear antibodies were positive (1:160) with nucleolar pattern. Systemic treatment with antioxidants (α -Lipoic Acid, vitamin B1, vitamin C, and vitamin E) and heliotherapy with high sun protection factor cream were prescribed. To date, the patient is still in follow-up. We obtained informed consent from the patient to publish her case (images, case history and laboratory data).

Overall, vaccinations are associated with a low incidence of severe adverse events. Cutaneous reactions after COVID-19 vaccines mainly consisted of delayed inflammatory reactions in the injection site, urticaria, chilblain-like lesions and pityriasis rosea-like eruptions.⁴ Several cutaneous and extra-cutaneous ADs have rarely been reported.^{1,2,5}

The precise triggering mechanisms are still unknown, but several studies suggest that a vaccine component can induce ADs in subjects with genetic susceptibility.¹

To our knowledge this is only the third case of vitiligo associated with COVID-19 vaccination; the first occurred 1 week after the first dose of Pfizer-BioNTech COVID-19 vaccine in a man without family history for vitiligo suffering from ulcerative colitis³; the second case concerned a woman without personal/familial history of vitiligo and other ADs which noted, several days after her first dose of Moderna (mRNA-1273) COVID-19 vaccine, some faint hypopigmented macules on her anterior neck; the macules progressed in size, number and degree of hypopigmentation after the booster dose.⁶ The possible pathogenic mechanisms involving the vaccine as the cause of vitiligo are molecular mimicry and bystander activation. Molecular mimicry occurs when a genetically predisposed individual is infected/vaccinated by an agent carrying antigens that are immunologically similar to host antigens favoring an activation of cross-reactive T or B cells. Subsequently, the tolerance to self-antigens breaks down and the pathogen-specific immune response is directed towards the host tissues. Bystander activation can occur in an antigen-dependent or independent manner. Viral/bacterial agents may induce the release of sequestered self-antigens or modify self-antigens from host tissues



FIGURE 1 (A) White macules with oval and linear shapes on the neck and trunk; (B) White round and oval macules on the upper part of the back; (C) Examination under wood lamp revealed the white fluorescence consistent with vitiligo

that, in turn, activate antigen-presenting cells generating clonal expansion of self-reactive T and B cells. Furthermore, viral/bacterial antigens and vaccine component/adjuvant can induce a strong innate immune response, which causes nonspecific activation of autoreactive CD8⁺/CD4⁺ T and B cells, leading to onset of ADs. Innate immune mediators (cytokines/chemokines) secreted by macrophages, natural killer and dendritic cells exacerbates inflammation and maintain disease activity.⁷ Through these mechanisms, the vaccine could have stimulated the immune system to produce antibodies against SARS-CoV-2 spike protein and incidentally against melanocytes.

Since vitiligo is a common pigmentary disorder afflicting 0.5%–2% of the world population⁸ and COVID vaccination nowadays is a common practice, the possibility that the onset of vitiligo after vaccination is just a coincidence should also be considered. However, the temporal relationship between the vaccine and development of the disease and the instances of autoimmune phenomena manifesting after COVID-19 vaccination,^{1,2,5,6} suggest that the vaccine could play a role in triggering vitiligo.

Further and extensive case studies are needed to demonstrate a causal relationship between COVID-19 vaccination and vitiligo.

Meantime, clinicians should be aware of the possible autoimmune cutaneous reactions to vaccinations, especially when dealing with patients suffering from or genetically susceptible to ADs.

However, the possibility of mild and self-limiting cutaneous adverse events should not discourage all eligible candidates to continue to receive COVID-19 vaccination; indeed, such adverse events represent a small risk in relation to the possible fatal outcome of COVID-19 infection.

CONFLICT OF INTEREST

The authors declares there is no potential conflict of interest.

AUTHOR CONTRIBUTION

Giulia Ciccarese conceived of the presented idea; Giulia Ciccarese wrote the manuscript with support from Samuele Boldrin and Francesco Drago; Matilde Pattaro and Aurora Parodi provided critical feedback; all authors discussed the results and contributed to the final manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

1. Kreuter A, Licciardi-Fernandez MJ, Burmann SN, Burkert B, Oellig F, Michalowicz AL. Induction and exacerbation of subacute cutaneous lupus erythematosus following messenger-RNA or adenoviral-vector based SARS-CoV-2 vaccination. *Clin Exp Dermatol*. 2021. doi:10.1111/ced.14858
2. Ghielmetti M, Schaufelberger HD, Mieli-Vergani G, et al. Acute autoimmune-like hepatitis with atypical anti-mitochondrial antibody after mRNA COVID-19 vaccination: A novel clinical entity? *J Autoimmun*. 2021;123:102706. doi:10.1016/j.jaut.2021.102706
3. Aktas H, Ertugrul G. Vitiligo in a COVID-19-vaccinated patient with ulcerative colitis: coincidence? *Clin Exp Dermatol*. 2021. doi:10.1111/ced.14842
4. McMahon DE, Amerson E, Rosenbach M, et al. Cutaneous reactions reported after Moderna and Pfizer COVID-19 vaccination: A registry-based study of 414 cases. *J Am Acad Dermatol*. 2021;85:46-55. doi:10.1016/j.jaad.2021.03.092
5. Vadalà M, Poddighe D, Laurino C, Palmieri B. Vaccination and autoimmune diseases: is prevention of adverse health effects on the horizon? *EPMA J*. 2017;8:295-311. doi:10.1007/s13167-017-0101-y
6. Kaminetsky J, Rudikoff D. New-onset vitiligo following mRNA-1273 (Moderna) COVID-19 vaccination. *Clin Case Rep*. 2021;9:e04865. doi:10.1002/ccr3.4865
7. Murali-Krishna K, Altman JD, Suresh M, et al. Counting antigen-specific CD8 T cells: a reevaluation of bystander activation during viral infection. *Immunity*. 1998;8:177-187.
8. Bertolani M, Rodighiero E, de Felici Del Giudice MB, et al. Vitiligo: What's old, what's new. *Dermatol Report*. 2021;13:9142. doi:10.4081/dr.2021.9142