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DERMATOLOGIC THERAPY WILEY

LETTER

Vitiligo worsened following the second dose of mRNA SARS-CoV-2 vaccine

Dear Editor,

We have read with great interest the recent article on your Journal entitled "Worsening of the vitiligo following the second dose of the BNT162B2 mRNA COVID-19 vaccine" by Okan and Vural.[1]

A 66-year-old male came into our Dermatology Unit for a sudden worsening of a preexisting vitiligo, 2 weeks after the administration of the second dose of the Pfizer-BioNTech vaccine BNT162b2 (Comirnaty®).

The patient was referred to our outpatient clinic 10 years ago for the onset of achromic well-demarcated round macules involving perioral and periocular regions, axillae, genital and sacral region.

The patient had not comorbidities and no familial history of vitiligo or autoimmune diseases.

The skin lesions were clinically consistent with vitiligo and examination under Wood lamp confirmed the diagnosis. The patient was therefore screened for other autoimmune conditions.

Complete blood cell count was within normal ranges while antithyroglobulin and anti-thyroperoxidase antibodies levels were high and, after an endocrinological consultation, a diagnosis of Hashimoto's thyroiditis was made.

In the last 8 years, several topical and physical treatments (topical calcineurin inhibitor for the face, topical medium potency corticosteroid for the body and several courses of ultraviolet B narrowband radiation phototherapy) were prescribed with temporary clinical improvement.

In November 2019, vitiligo worsened with the appearance of new patches at the back of the feet, hands and trunk. Pulse therapy with prednisone at the dosage of 15 mg on two consecutive days per week was prescribed. Within 6 months, an improvement of vitiligo was observed and the treatment was stopped.

In October 2021, 2 weeks after the administration of the second dose of mRNA SARS-CoV-2 vaccine, new multiple and extended vitiligo lesions appeared, involving extremities, extensive areas of upper and lower limbs, face, perioral, and periocular region. Trunk, axillae, and genital area showed large confluent vitiligo lesions. The extent of hypopigmentation was estimated at about 70% of the total patient's body surface area (Figure 1).

A systemic therapy with prednisone at the dosage of 25mg/day for 2 weeks then gradually reduced up to 7 mg/day was prescribed.

Topical treatments with tacrolimus 0.01% for the vitiligo lesions of the face and mometasone furoate 0.1% cream for the lesions of the body were also prescribed.

Although the causal role of vaccination in the worsening of vitiligo cannot be certainly established, the temporal association between vaccination and the clinical worsening of the disease makes it probable in our case.

In the literature, some cases of de novo vitiligo after SARS-CoV-2 vaccination have been described,[2–6] but only one case of worsening of a pre-existing vitiligo following SARS-CoV-2 vaccination was reported.[1]

Interestingly, Piccolo et al. recently reported a case of lichen planus which appeared on skin patches of vitiligo following SARS-CoV-2 vaccination. In this case, the causal relationship between the vaccine and the onset of inflammatory lesions seemed particularly strong, given the bimodal timing of the event (in fact, the manifestation appeared for the first time after the administration of the first dose and shortly relapsed after the second dose).[7]

The pathophysiology underlying the relationship between SARS-CoV-2 vaccination and vitiligo remains unclear, but several

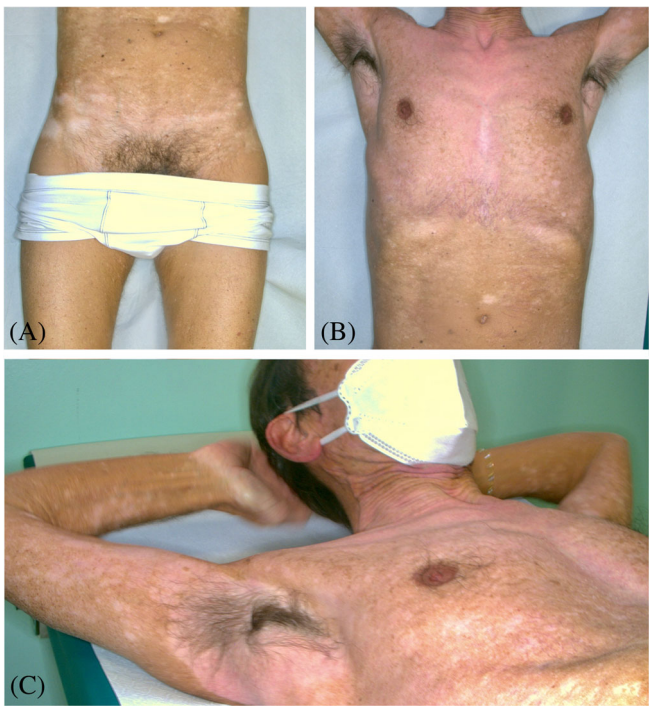

FIGURE 1 Worsening of vitiligo following the second dose of mRNA SARS-CoV-2 vaccination. Clinical examination showed extended vitiligo lesions involving extremities, upper limbs, axillae, trunk, and genital area with large confluent lesions. The extent of hypopigmentation was estimated at about 70% of the patient's body surface area

hypotheses have been made. Vaccines are known as potential trigger factors for the development of several autoimmune diseases in patients with a genetic susceptibility.[8]

About vitiligo, Abdullah et al. hypothesized that the link between SARS-CoV-2 vaccination and vitiligo may be the type 1 interferon (IFN-1) produced by dendritic plasmacytoid cells (pDC).[9]

The activation of pDCs, in fact, induces a high production of IFN-1. The activation of such cells can be induced by viral nucleic acid sequences through toll-like receptors (TLRs) 7 and 9.

SARS-CoV-2 vaccines have been shown to be effective inducers of IFN-1 (via stimulation of pDCs).[10] In the pathogenesis of vitiligo, both IFN-1 and pDCs were demonstrated to play a significant role.

The activation of pDCs and the release of IFN-1 seem to be a key event in early vitiligo progression.[11]

Furthermore, it is known that vitiligo-like lesions can be induced by site application of imiquimod (a TLR-7 agonist) or by treatment with recombinant IFN-alfa.[11]

More and more evidence are emerging regarding a potential association between vitiligo and SARS-CoV-2 vaccination. In our opinion, the risk of skin reactions and skin diseases following SARS-CoV-2 vaccination is far outweighed by the protection conferred by the vaccine against hospitalization and risk of death resulting from SARS-CoV-2 infection. However, further evidence and studies are needed in order to explore the possible link between mRNA SARS-CoV-2 vaccination and the onset of vitiligo and other autoimmune conditions, also considering that this is the first time that a vaccination has been carried out on such a large scale.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Study conception and design: Francesca Caroppo, Maria Ludovica Deotto, Jacopo Tartaglia, Anna Belloni Fortina; Data collection: Francesca Caroppo, Maria Ludovica Deotto, Jacopo Tartaglia, Anna Belloni Fortina; Draft manuscript preparation: Francesca Caroppo, Maria Ludovica Deotto, Jacopo Tartaglia, Anna Belloni Fortina. All authors reviewed the results and approved the final version of the manuscript.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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