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CASE REPORT

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# Presentation of vitiligo in a case of COVID-19 infection concomitant with receiving remdesivir

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**Key Clinical Message**

The occurrence of vitiligo following COVID-19 infection and vaccination is well-documented. The mitochondrial dysfunction of melanocytes in vitiligo and the potential impact of RDV on mitochondria raise concerns about RDV possibly causing vitiligo.

**KEYWORDS**

COVID-19 infection, remdesivir, vaccination, Vitiligo

## 1 | INTRODUCTION

Vitiligo is an autoimmune disease characterized by depigmented patches resulting from the progressive damage of melanocytes that can involve skin or mucous membranes.[1–3] It affects 0.5%–2% of the world population.[1,4] Vitiligo is subclassified by location and distribution of affected skin.[3] Both genetic and environmental triggers are predisposing factors for the development of vitiligo.[5] The etiology of vitiligo is unknown; however, T-cell autoimmunity and chronic cytokine release are thought to play an important role in the pathogenesis of vitiligo. The incidence of vitiligo has risen secondary to COVID-19. The virus itself, vaccination, medication, and mental stress can all be responsible for such an increase.[1]

## 2 | CASE HISTORY/EXAMINATION

A 60-year-old woman presented to our dermatology clinic for the evaluation of asymptomatic white patches that started on her lower limbs 2 months ago, while she was hospitalized for COVID-19. The lesions extended progressively to her face, neck, and trunk.

Her past medical history was positive for diabetes type II and Hashimoto thyroiditis thus she was on metformin and levothyroxine for a long time and were under control. In her family history, she also reported that her sister suffered from hypothyroidism and rheumatoid arthritis.

Regarding COVID-19 vaccination she had received two doses of AstraZeneca vaccine 6 and 4 months before presenting with COVID-19 infection. She presented with COVID-19-related symptoms including fever, fatigue, dyspnea, sore throat, and runny nose. Therefore, a nasopharyngeal swab real-time polymerase chain reaction test was performed for her which was positive. Consequently, she was hospitalized and azithromycin, naproxen, and N-acetyl cysteine were started. Her oxygen saturation ($SpO_2$) was 96% with a respiratory rate of 18/min. In para-clinic she had a low white blood cell count ($WBC = 3 \times 10^3$), lymphocyte percentage of 27%, and mildly elevated

C-reactive protein (CRP: 20). Other factors were within the normal range. Her first chest computed tomography (CT) was normal. However, 2 days later her general health condition declined. The second chest CT showed bilateral multiple ground-glass opacities which was compatible with a decrease in $O_2$ saturation (91%). Considering the mentioned changes; infectious disease service started RDV for 5 days (200 mg IV on the first day and 100 mg for 4 days). Within the second day of RDV administration, a depigmented patch of about 10 × 10 cm appeared on her right shin. A few days later she was discharged from the hospital with relative improvement.

## 3 | METHODS

By the time we visited our patient 2 months after her hospitalization, most of her body surface area was depigmented, while partial pigmentation had remained around the neck, and the face (Figures 1 and 2). She had not sought any treatment for the depigmented patches before coming to our clinic. We diagnosed vitiligo for her based on the clinical findings straightforwardly, and Wood's lamp examination confirmed the diagnosis of vitiligo.

Monobenzyl ether of hydroquinone was prescribed for her with complete explanation of the sun radiation avoidance.

## 4 | CONCLUSION AND RESULTS

The patient refused to take any treatment.

## 5 | DISCUSSION

Vitiligo is an autoimmune skin disease affecting approximately 0.5%–2% of the world population and can be accompanied by other autoimmune diseases.[6,7] It is a multifactorial disorder comprising genetics and environmental factors. The exact pathogenesis of vitiligo is not entirely understood, but immune cells and their chemokines have an important role in the etiology of the disease. Important factors such as CD8+ T cells and secretion of IFN-Y from CD8+ T cells due to oxidative stress are thought to play a central role in the destruction of melanocytes and the development of vitiligo.[5,8,9] External factors such as exposure to environmental toxins, agents such as phenolic and catecholic chemicals, UV radiation, and viral infections such as cytomegalovirus, Epstein–Barr virus, HIV, and many others are suggested as potential etiologic factors for autoimmune diseases including vitiligo, as they can induce oxidative stress.[8,10,11] Accordingly, the incidence of vitiligo has also been reported to increase secondary to COVID-19 infection. Different theories have been suggested for the increased incidence of vitiligo in the COVID-19 pandemic including the virus itself, vaccination, medication, and mental stress.[1]

It is suggested that SARS-CoV2 virus may initiate or activate vitiligo through the direct destruction of melanocytes or stimulating the immune system and shifting it to adaptive type 1 immunity.[12] During the infection, mitochondrial function alters and results in oxidative stress, pro-inflammatory state, cytokine production, and cell death.[13]

Melanocytes in vitiligo show several structural imperfections such as endoplasmic reticulum dilatation and abnormal melanosome structure which, in combination

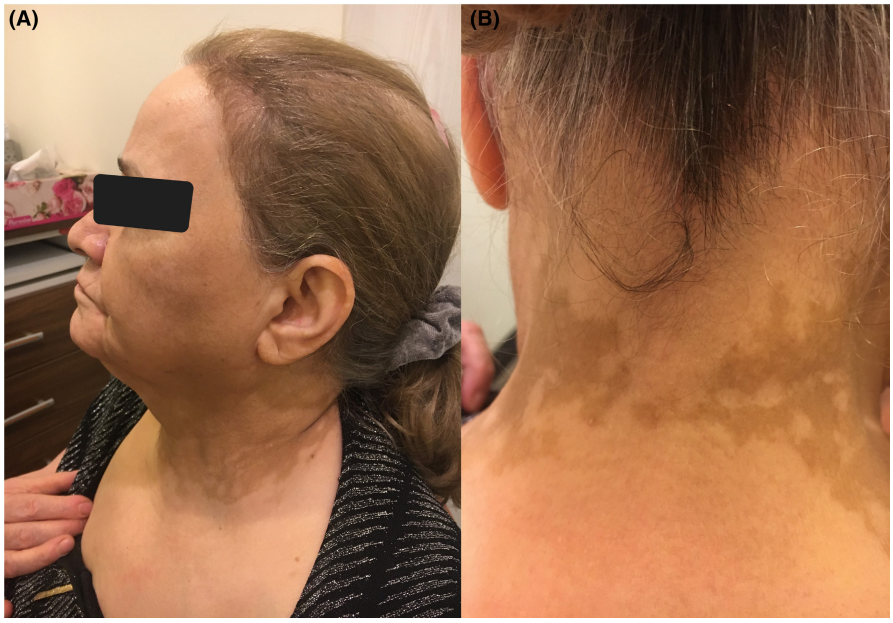


**FIGURE 1** Depigmented patches with partial remaining pigmentation on the face and neck area (A, B).

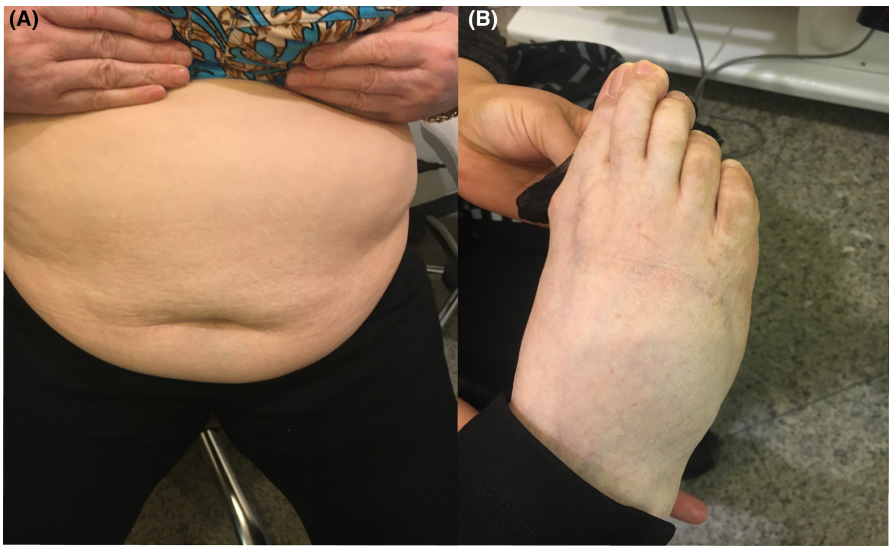


**FIGURE 2** Depigmented patches on trunk (A), and the right foot with partial pigmentation on the toe fingers (B).

with mitochondrial dysfunction, can increase the genuine defective melanocytic defense against oxidative stress.[5]

In addition to the virus itself, the stress caused by the pandemic can also be a trigger for the disease. Lack of habitual social activity and limitation of interpersonal relationships leads to stressful situations which may increase the catecholamines, neuropeptides, and cortisol levels that are known to play a role in the pathogenesis of vitiligo.[9]

Moreover, evidence shows that SARS-CoV-2 vaccine is related to development of autoimmune diseases such as vitiligo.[14,15] In fact, vaccines stimulate the immune system to produce antibodies. Some of these antibodies may be more harmful to the host, as they can provoke autoimmune diseases in genetically susceptible individuals. The most probable pathophysiologic mechanisms suggested for vaccine-induced autoimmunity are Molecular imitation and spectator activation.[1]

Laura Macca et al reviewed 16 cases of vitiligo after COVID-19 infection and COVID-19 vaccination reported in the literature. They realized that the symptoms of vitiligo usually appear within 1 week after vaccine administration.[6] Our patient had received the COVID-19 vaccine 6 and 4 months before the initiation of vitiligo and the depigmented lesions appeared on the second day of receiving RDV during SARS-CoV-2 infection, therefore, it can be said that vaccine is unlikely to have caused the disease. Although it cannot be stated with certainty, it can be concluded that the chance of the SARS-CoV-2 virus itself or the RDV causing the disease are higher. Furthermore, considering the patient's medical history of thyroid disease and the presence of autoimmune diseases in the family, there might be an increased susceptibility to developing vitiligo in this patient.

RDV is a nucleotide prodrug of an adenosine analog that binds to the viral RNA-dependent RNA polymerase and inhibits viral replication by terminating RNA transcription prematurely. It is one of the few antiviral medications that has been accepted for severe cases of SARS-CoV-2 infection.[16] Nucleotide analogs are associated with mitochondrial toxicity. Kwok et al. showed that RDV suppresses mitochondrial respiration, induces mitochondrial fragmentation, and decreases the redox potential resulting in cardiotoxicity.[17] As mentioned before, mitochondrial dysfunction decreases the resistance of melanocytes to oxidative stress and predisposes patients to vitiligo.[5] Therefore, RDV administration might have played a role in vitiligo manifestation in our patient.

In conclusion, the COVID-19 pandemic has been a predisposing factor for autoimmune diseases including vitiligo in many ways including the virus itself, stress and anxiety induced by the pandemic, and the vaccination.

To the best of our knowledge, there have been no previous reports of vitiligo presentation occurring concomitant to RDV administration. Although we cannot definitively determine whether the manifestation of vitiligo in this patient was the consequence of RDV administration, it is worth noting that a mitochondrial defect has been observed in vitiligo cases. Moreover, RDV has been shown to impact mitochondria. Therefore, further investigation is necessary to evaluate this coincidence and explore the potential connection between the effects of RDV on melanocytes.

## AUTHOR CONTRIBUTIONS

**Farideh Beyki:** Conceptualization; data curation; investigation; writing – original draft. **Saba Hasanzadeh:** Writing – review and editing. **Fariba Ghalamkarpour:** Conceptualization; supervision; writing – review and editing.

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None.

## CONFLICT OF INTEREST STATEMENT

The authors state that they have no conflict of interest.

## DATA AVAILABILITY STATEMENT

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

## CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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