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A Case of New-Onset Vitiligo in a Healthy Volunteer After Administration of Adalimumab

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Dear Editor:

A 22-year-old male was referred to the Dermatology Department for two pruritic achromic patches on his neck and chest that had appeared 2 weeks ago. Previously, he had enrolled as a healthy volunteer in a bioequivalence test of adalimumab. The achromic patches appeared 7 weeks after he received a single subcutaneous injection of 40 mg adalimumab (Humira). The patient denied a personal or family history of vitiligo. There was no evidence of premature hair graying, hair loss, autoimmune diseases, or atopic diathesis, factors associated with vitiligo.

Physical examination showed two relatively well-demarcated whitish patches of longest diameters 5 and 6 cm, respectively (Fig. 1A, B). Under Wood's lamp, the lesions turned bright blue with fluorescence. Laboratory tests, including complete blood count, anti-nuclear antibody titer, and concentrations of rheumatoid factor, glucose, thyroid stimulating hormone, free T4, and anti-thyroid peroxidase antibody, were all within normal ranges.

Two 3-mm punch biopsies were obtained, one from an achromic site and the other from an adjacent, normally-pigmented site. Histopathologic examination of the achromic skin lesion revealed basal hypopigmentation and loss of melanocytes. Immunohistochemical staining was negative for Fontana Masson and Melan A, which are findings consistent with vitiligo (Fig. 2A～C). Examination of the perilesional normally-pigmented skin sample revealed scattered melanophages with hydropic degeneration. Immunohistochemical staining showed appreciable melanin pigment and melanocytes (Fig. 2D～F).

The patient was treated with a combination of weekly excimer laser and twice per day application of topical tacrolimus. After 3 months, he started to show a partial response with perifollicular repigmentation (Fig. 1C). Further improvements were observed at 4 (Fig. 1D) and 5 (Fig. 1E) months.

Adalimumab is a fully human monoclonal antibody targeting tumor necrosis factor-α (TNF α).

The role of TNF α inhibitors in vitiligo is unclear. Treatment with TNF α inhibitors has shown improvement or clearance of vitiligo in some cases. The success may be due to the elevation of TNF α levels in active vitiligo lesions[1]. *In vitro*, TNF α was shown to reduce the level of tyrosinase, a rate-limiting enzyme in melanin biosynthesis[2]. Clinically, treatment with TNF α inhibitors was found to stabilize progressive vitiligo[3].

By contrast, several studies have reported that treatment with TNF α inhibitors induces new vitiligo lesions and exacerbates pre-existing vitiligo[4]. TNF α inhibitors may induce or enhance vitiligo by increasing the numbers of nucleosomes, major autoantigens released during apoptosis. This can lead to induction of autoantibodies and cause vitiligo. Alternatively, TNF α inhibitors may interfere with the suppression of autoreactive B-cells by cytotoxic T-cells[5].

New vitiligo lesions following the use of adalimumab have been reported in patients with other underlying diseases, such as inflammatory bowel diseases and rheumatoid arthritis[4]. Because our patient had none of these diseases, vitiligo in this patient was likely an adverse effect of adalimumab.

This report describes a patient without an underlying immune or inflammatory disease who developed vitiligo, strongly suggesting that adalimumab itself plays a role in inducing vitiligo. Moreover, the finding that this patient devel-

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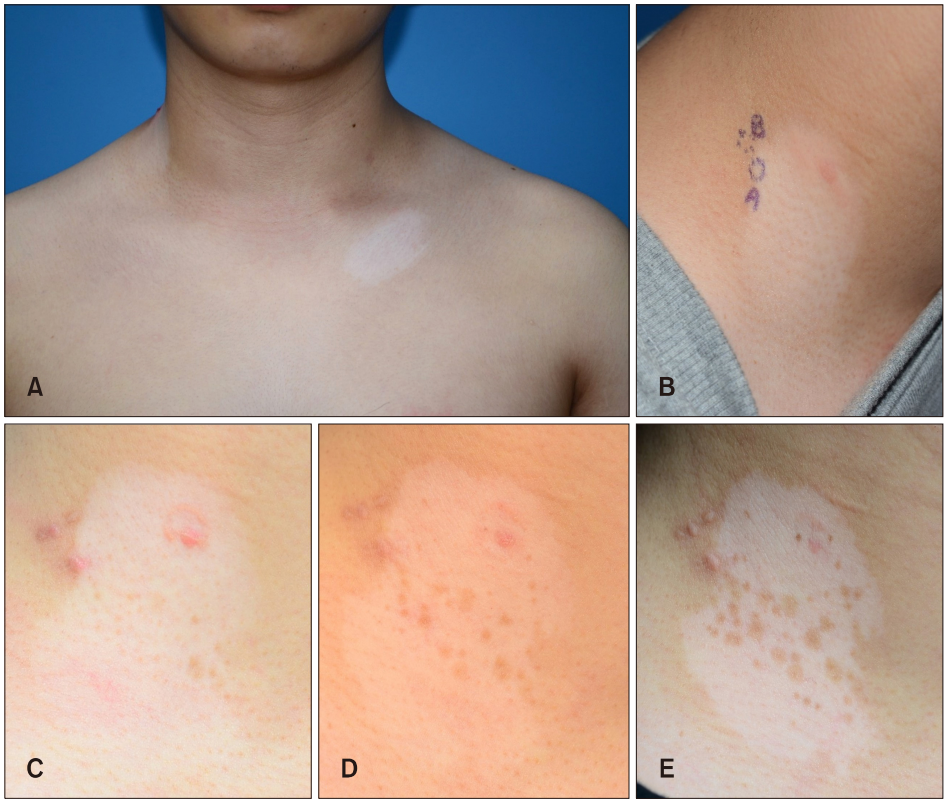

Fig. 1. Clinical features of vitiligo in the patient. Photographs showing (A, B) two relatively well-demarcated patches on the anterior chest and right neck. (C) Three months of treatment with excimer laser and topical tacrolimus resulted in partial perifollicular repigmentation. At 4 (D) and 5 (E) months, further improvements were seen.

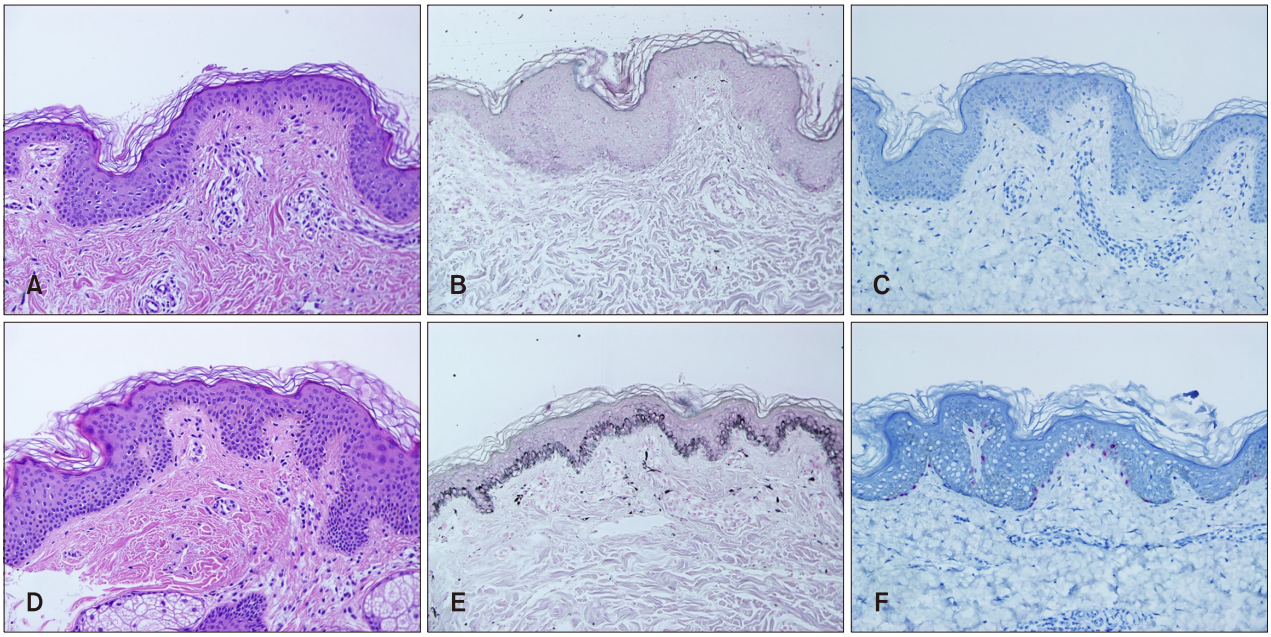

Fig. 2. Histopathological and immunohistochemical features of the patient. (A) Examination of lesional skin, showing basal hypopigmentation and loss of melanocytes, along with mild inflammation in the papillary dermis (H&E, ×400). (B, C) Immunohistochemical staining of lesional skin was negative for Fontana Masson (×400) (B) and Melan A (×400) (C). (D) Examination of perilesional normally-pigmented skin, showing scattered melanophages with hydropic degeneration, along with mild inflammation in the superficial dermis (H&E, ×400). (E, F) Immunohistochemical staining showing appreciable melanin pigment on Fontana Masson staining (×400) (E) and melanocytes on Melan A antibody staining (×400) (F).

oped vitiligo after a single injection of 40 mg adalimumab suggests the need for careful initiation and thorough monitoring after initiation.

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

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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