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Letter to the Editor

Dupilumab therapy rapidly improved alopecia areata associated with trichotillomania in an atopic dermatitis patient

Dear Editor,

Alopecia can occur as a serious complication of atopic dermatitis (AD). Dupilumab, an interleukin (IL)-4 receptor subunit alpha antagonist that down regulates T-helper 2 responses, has recently been approved as a treatment for AD. It has subsequently been reported that dupilumab ameliorated alopecia areata (AA) in AD patients in a number of cases.^{1,2} However, in AD patients hair loss can be caused by trichotillomania as well as AA.³ Here, we report a case in which AA complicated with trichotillomania in an AD patient was rapidly ameliorated by dupilumab.

A 33-year-old female presented with severe AD. A physical examination revealed erythema, scaling and lichenification over her entire body (Eczema Area and Severity Index [EASI] score: 46) and multiple alopecia patches on her scalp, which had first appeared 6 months prior to her visit (Fig. 1a). A dermoscopic examination of the marginal part of the alopecia patch demonstrated a mixture of yellow dots, black dots and short vellus hair, coiled hair, and flamed hair (Fig. 2a). AA complicated with trichotillomania was suspected, and a biopsy of the central part of the alopecia patch on her forehead was performed. A histopathological examination revealed catagen and telogen hair dominance with few anagen hairs and mild lymphocytic inflammation around the hair bulbs (Fig. 2b), which were compatible with chronic phase of AA. At her next visit, the patient admitted that she was plucking her hair.

Based on the patient's clinical, dermoscopic, and histopathological findings, a diagnosis of AA complicated with trichotillomania was made. Dupilumab therapy was started as a treatment for the AD. Surprisingly, 3 weeks after the first round of dupilumab therapy, marked hair regrowth and the rapid amelioration of itching were observed (Fig. 1b). Dupilumab was continued, and 19 weeks later the hair loss had almost completely resolved (Fig. 1c). The patient's skin condition had also improved (EASI score: 9.6).

Trichotillomania can be easy to miss in patients with AA complicated with AD, unless the patient discloses it. The amelioration of AA with dupilumab in AD patients has frequently been reported. However, although it is known that trichotillomania can occur in AD patients it was not mentioned in previous reports.^{1,2} Tsuboi *et al.*³ reported that about 15% of trichotillomania patients were complicated with AD. In addition, trichotillomania is known to

occur in AA.⁴ Therefore, clinicians should keep trichotillomania in mind in cases of AA and AD.

Distinguishing between AA and trichotillomania can be difficult based on histological and dermoscopic findings alone. Histologically, the acute phase of AA involves lymphocytic infiltration around anagen hair bulbs in a pattern that resembles a swarm of bees, which is specific to AA. However, in the chronic phase, few "swarms of bees" are seen and catagen/telogen hairs, which are compatible with trichotillomania, predominate.⁵ Regarding dermoscopic findings, tapered hairs and exclamation mark hairs are highly specific to acute phase of AA, and the presence of a combination of yellow dots and short vellus hairs exhibits high sensitivity for diagnosing AA. Flame hairs are highly specific to trichotillomania.⁶ In our case, the histological and dermoscopic features matched both chronic AA and trichotillomania. As catagen/telogen hairs are easier to pull out, the onset of AA might have exacerbated alopecia caused by trichotillomania.

Dupilumab is effective against trichotillomania complicated with AD. The cause of trichotillomania in AD has long been suspected to involve itching and the mental stress associated with the disease.⁴ Our case involved marked and rapid improvements in the patient's alopecia and EASI score. Since it is unusual for hair regrowth to occur within such a short period (3 weeks) in AA, we suggest that this quick response was due to the rapid amelioration of the patient's itching and mental stress, leading to a reduction in trichotillomania, which was disrupting new hair re-growth in chronic phase of AA. Indeed, the patient had stated that soon after the initial dose of dupilumab was administered, her itching was relieved, and she also stopped plucking her hair. The hair plucking might have represented a similar behavior to scratching.

In recent years, studies have shown that oxidative stress is one of the main causes of trichotillomania, and AD is known to involve oxidative stress in the skin.⁷ In addition, N-acetylcysteine, an antioxidant drug, has been reported to be effective against trichotillomania.⁸ Furthermore, neutralization by IL-4 or IL-13 antibodies reduces macrophage-induced oxidative stress.⁹ Therefore, we hypothesize that dupilumab might ameliorate both trichotillomania and AA by decreasing itching and disease-related mental stress, and reducing oxidative stress in AD skin lesions. Trichotillomania can result in scarring alopecia when it is not treated properly for a long period, and prompt diagnosis and treatment are necessary to avoid permanent hair loss.¹⁰ Thus, clinicians should be aware of the possibility of trichotillomania when alopecia occurs in AD patients, and dupilumab might be effective at treating such cases and avoiding permanent hair loss.

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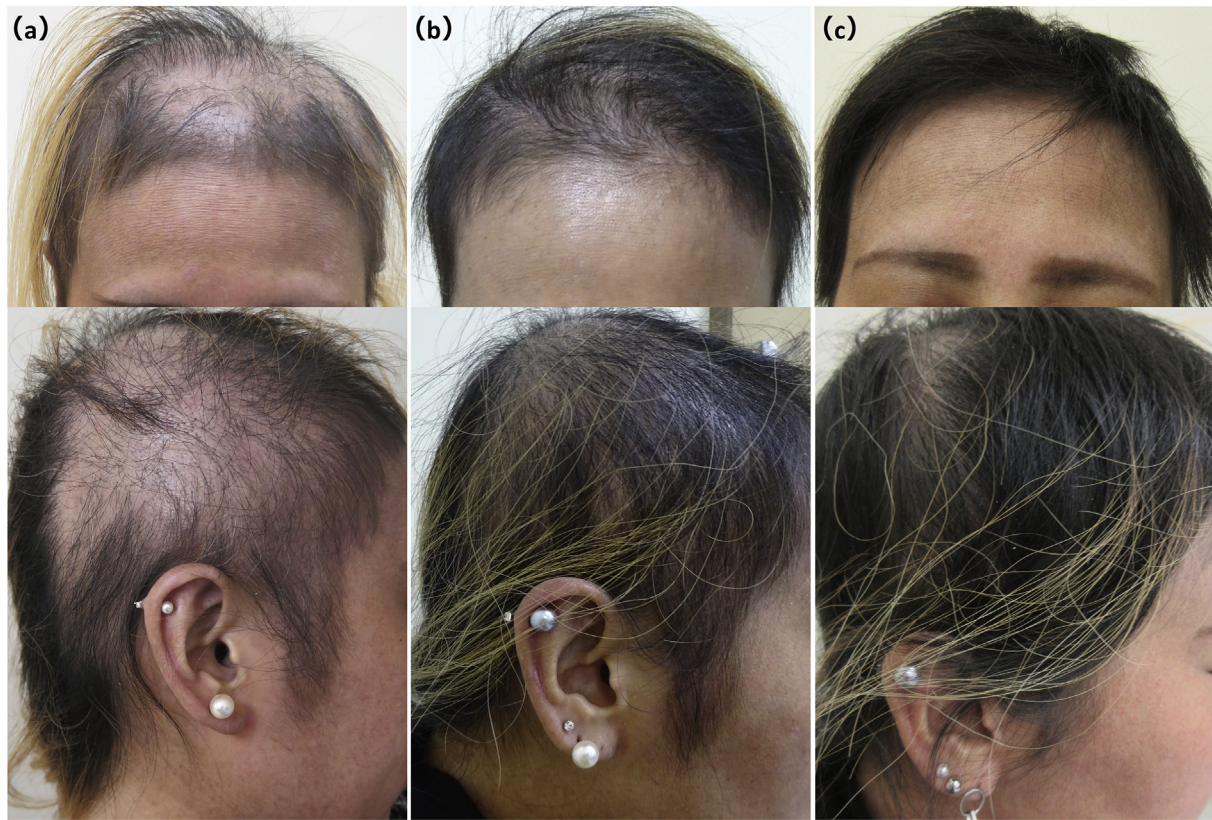


Fig. 1. (a) Before dupilumab therapy was administered, multiple alopecia patches were seen on the scalp. (b) The patient's clinical presentation after the administration of dupilumab for 3 weeks is shown. (c) The patient's clinical presentation after the administration of dupilumab for 19 weeks is shown. For the use of these images, a permission from the patient has been obtained.

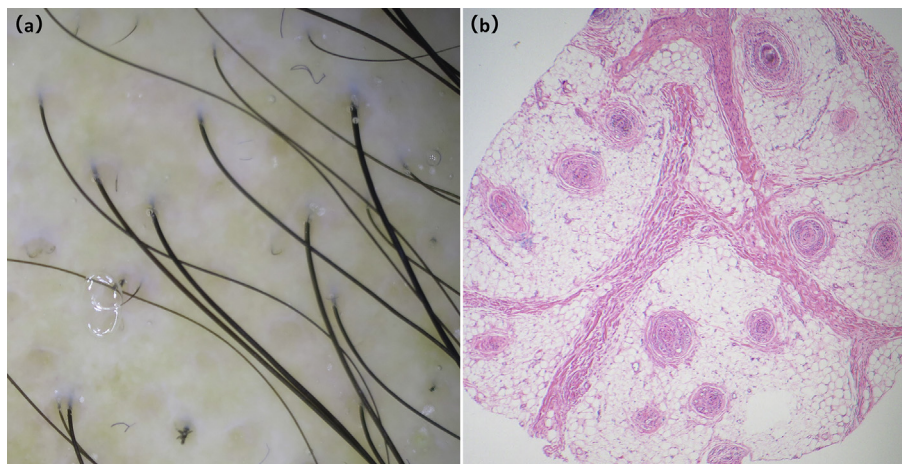


Fig. 2. (a) A dermoscopic examination of the marginal part of the alopecia patch revealed a mixture of yellow dots, black dots, short vellus hair, coiled hair, and flamed hair, prior to dupilumab therapy. (b) A histopathological examination from the central part of the alopecia patch revealed catagen and telogen hair dominance with few anagen hairs and mild lymphocytic inflammation around the hair bulbs.

Conflict of interest

NK has received lecture honoraria and research grants from Regeneron and Sanofi. The rest of the authors have no conflict of interest.

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