Alopecia areata in 2 patients treated with dupilumab: New onset and worsening

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INTRODUCTION

Atopic dermatitis (AD) is a chronic inflammatory skin disorder that can be comorbid with the autoimmune disease alopecia areata (AA).[1,2] Dupilumab is a novel treatment for moderate-to-severe AD that may have implications in AA therapy given its role in inhibiting the helper T cell 2 response at the level of interleukin-4 receptor α subunit.[3] This mechanism might target AA of the scalp where there can be upregulation of helper T cell 2 via interleukin-13 among other cytokines.[3,4] Here we present 2 cases of patients with hair loss while on dupilumab for AD—1 with new onset and subsequent improvement of alopecia universalis (AU), and one with worsening of previously diagnosed alopecia totalis (AT) while on treatment.

Abbreviations used:

AA: alopecia areata
AD: atopic dermatitis
AT: alopecia totalis
AU: alopecia universalis

CASE REPORTS

Case 1

A 51-year-old woman with asthma and allergic rhinitis, presented with lifelong AD that started at a few months of age and significantly worsened in her early 20s. Previous treatments included topical corticosteroids, intramuscular corticosteroid injections, narrowband-ultraviolet B therapy, and cyclosporine.

After completing 24 months of open-label dosing in clinical trials of dupilumab for AD, she transitioned to commercial dosing of dupilumab, 300 mg every 2 weeks. At month 26, she noted generalized thinning of her hair. Initially, no discrete patches of hair loss were appreciated, and iron deficiency–induced telogen effluvium was considered as a possible etiology given her ferritin of 22, vitamin D of 28.6, and normal thyroid studies. Despite successful supplementation of iron (ferritin 54) and vitamin D (49.2), her hair loss progressed to discrete alopecic patches, now more clearly consistent with AA by month 28. The role of dupilumab in her hair loss remained unclear, but given the rapid progression of her AA, dupilumab was discontinued. During month 29, she self-administered 1 dose of dupilumab for an AD flare and started minoxidil 5% with some hair regrowth. At month 30, her hair loss then rapidly progressed to nonscarring AU despite consistent use of betamethasone solution, ezetimibe, and simvastatin. She remained hesitant to resume regular dosing of dupilumab given her AU, but she required another single dose of dupilumab in month 33 for another AD flare. At month 34, she was encouraged to resume regular dosing given concern that ongoing intermittent dosing may lead to development of resistance to the drug. She resumed dupilumab at monthly dosing with dramatic regrowth of the hair on her frontal, vertex, and parietal

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Table I. Timeline of events for case 1

Month	Main events
0-24	Dupilumab, clinical trial dosing
25	Transition to dupilumab commercial dosing
26	Generalized hair thinning
28	Progression to AA Discontinued regular dupilumab dosing
29	First rescue shot of dupilumab
30	Progression to AU
33	Second rescue shot of dupilumab
34	Resumed dupilumab at monthly dosing
35	Dramatic regrowth of AU
44	90% scalp regrowth

scalp shortly after and 90% regrowth of scalp hair 10 months later (Table I).

Case 2

A 25-year-old white man presented with a history of lifelong AD that began as a child, cleared as a teenager, and then flared at age 18 with severe AD that has since remained severe with ongoing erythrodermic flares. AA developed at age 21, which gradually progressed toward AT with rare small patches of scalp hair. He has asthma and seasonal allergies. He denied a family history of AD or AA.

Previous treatments for his AD included topical corticosteroids, topical tacrolimus, oral prednisone, narrow-band ultraviolet B, and mycophenolate mofetil. For his AT, he attempted topical clobetasol, minoxidil, and intralesional triamcinolone acetonide. A trial of cyclosporine, intended to target both AD and AT, was only successful in improving his AD (Fig 1).

Dupilumab provided initial improvement in his AD, but after 6 to 8 weeks (4-5 doses), he experienced his most severe erythrodermic flare, with loss of his few remaining patches of scalp hair (Fig 2). Both conditions failed to improve despite adding methotrexate, so dupilumab was discontinued.

Since then, he has attempted another round of cyclosporine, which improved his AD and provided some facial hair regrowth, and tofacitinib, with patchy improvement of his AT within 6 weeks of treatment and significant improvement in his erythroderma.

DISCUSSION

We present 2 cases in which dupilumab has been associated with new-onset or worsening AA. It is important to note that AA is a comorbidity of AD; therefore, a causal association with dupilumab cannot be made.

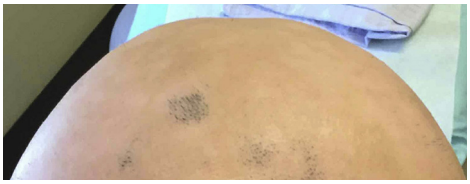

Fig 1. AT before dupilumab therapy.

In our first case, dupilumab plays an unclear role in the sudden occurrence of new-onset AA. Given her conflicting experiences of hair loss and hair regrowth while on dupilumab, it remains difficult to determine if dupilumab contributed to her AA or if her AA began de novo. Furthermore, it is possible that resuming regular dosing of dupilumab contributed to her hair regrowth. One possibility is that AU de novo was going to develop; however, treatment with dupilumab initially slowed the onset of hair loss, as she initially experienced generalized thinning without discrete patches of hair loss, more consistent with telogen effluvium or vitamin deficiencies. This possibility is worth considering given onset at 26 months into treatment and her improvement upon resuming regular dosing of dupilumab. Our patient chose to remain on dupilumab given the excellent control of her AD and steadily improving hair regrowth with her current monthly dosing regimen.

In our second case, the patient reported complete loss of his few remaining patches of hair by his fifth dose of dupilumab. It is unclear whether dupilumab caused this hair loss or failed to prevent an independent worsening of his AT. Regardless, dupilumab did not appear to be a treatment for AT in this case. He currently remains on tofacitinib given great improvement of his scalp and facial hair while on this medication.

To date, 6 reports exist in the literature of AA and dupilumab. Four case reports describe patients with new-onset AA after the third,[5,6] fourth,[7] and ninth[8] doses of dupilumab. Meanwhile, 2 case reports support the improvement of preexisting alopecia as early as 6 weeks[9] and 3 months[10] of dupilumab therapy. Therefore, more investigation in dupilumab trials is necessary to determine whether the medication can cause, worsen, or treat AA. Discussion with patients before starting dupilumab for AD should include the possibilities of new-onset AA and improving or exacerbating preexisting AA. Although dupilumab can provide great relief of AD, its effects on AA are unclear and, if negative, could significantly affect the patient's quality of life and self-esteem, which are important factors to consider in determining the treatment plan.

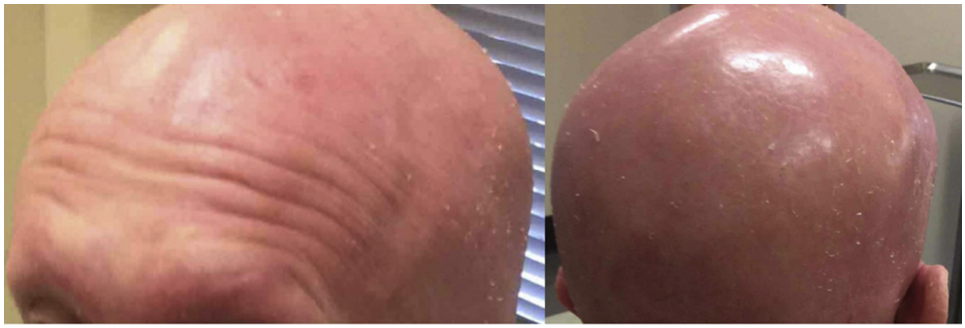

Fig 2. AT after dupilumab therapy.

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