Dupilumab as a Therapeutic Approach in Alopecia Universalis

Michael J. Visconti, DO; Adam Richardson, DO; Ann A. LaFond, MD

PRACTICE **POINTS**

- Practicing dermatologists should be aware of the shared pathophysiology of alopecia areata and atopic dermatitis and the relief patients with these conditions can experience when treated with dupilumab.
- As molecular-directed biologic therapies emerge in the marketplace, their potential for targeting one atopic disease may offer notable benefits for use in the treatment of other atopic diseases.

To the Editor:

Atopic diseases, specifically atopic dermatitis (AD) and alopecia areata (AA), are at the forefront of a new era in dermatology involving molecular-directed therapy. Dupilumab is one specific example, having received US Food and Drug Administration approval in March 2017 for the treatment of adults with moderate to severe AD.[1] It currently is being investigated for use in pediatric AD. The most commonly reported side effects associated with the use of dupilumab include headaches, conjunctivitis, keratitis, blepharitis, nasopharyngitis, and injection-site reactions.[2] We discuss a case of hair regrowth in a patient who was previously diagnosed with AA after treatment with dupilumab for refractory AD.

A 65-year-old White man presented with a history of AD since childhood. Additional medical history included hyperlipidemia; herpes simplex virus infection; asthma; and a diagnosis of AA 6 years prior, which eventually progressed to alopecia universalis. Physical examination demonstrated scattered erythematous lichenified plaques with excoriations involving the arms, legs, and trunk. The patient's face and scalp were spared of lesions. Complete loss of body hair including the eyelashes and eyebrows also was noted, which was consistent with alopecia universalis.

The patient was started on dupilumab for refractory AD after multiple courses of topical and systemic steroids failed. Prior treatment for AD did not include immunosuppressive or light therapy. The standard dosage of dupilumab was administered, which consisted of a 600-mg subcutaneous loading dose, followed by 300 mg every 2 weeks. There was no concurrent topical corticosteroid or topical calcineurin inhibitor prescribed. After 1 month of treatment with dupilumab, near-complete resolution of the patient's AD was noted, and after 10 months of treatment, the patient experienced regrowth of the eyelashes, terminal hairs of the beard area (Figure), and vellus hairs of the eyebrows. This hair regrowth persists today with continued dupilumab treatment, and the patient has experienced no additional side effects.

Multiple retrospective and meta-analysis studies have demonstrated a high occurrence of AD comorbid with AA, which strongly suggests a common pathogenesis.[3,4] Atopic dermatitis is an inflammatory skin disease mediated by IL-4, IL-5, and IL-13 of the helper T-cell type 2 (T_H2) pathway.[1] Dupilumab is a human monoclonal antibody that binds to IL-4Rα, which also is found in IL-13 receptors. Dupilumab prevents T_H2 pathway-related downstream signaling effects of both cytokines. Although this effect was originally utilized to suppress the

From the Department of Dermatology, St. Joseph Mercy Health System, Ypsilanti, Michigan.

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Correspondence: Adam Richardson, DO, Department of Dermatology, St. Joseph Mercy Health System, 5333 McAuley Dr, Ste 5003, Ypsilanti, MI 48197 (adamsr00@gmail.com).

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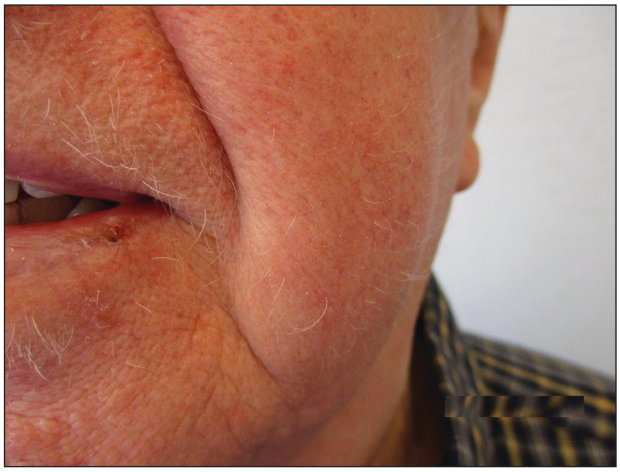

Terminal hair regrowth of the beard area 10 months after starting dupilumab therapy for refractory atopic dermatitis.

T_H2-mediated signaling in AD, our patient and others have demonstrated successful hair regrowth with dupilumab, which likely stems from a similar T_H2-related antagonism in AA.[5,6]

The cause of AA is unknown, but IL-4 and IL-13 of the T_H2 pathway have been implicated, which renders support for the therapeutic effect of dupilumab in the treatment of AA. Scalp samples of patients with AA have demonstrated upregulation of T_H2, helper T-cell type 1 (T_H1), and IL-23 cytokines, suggesting efficacy with the use of anti-T_H2, anti-T_H1, and anti–IL-23 therapies.[7] Polymerase chain reaction testing performed on serum samples in patients with AA displayed marked elevation of T_H2 cytokines, notably IL-13, which were reduced following intralesional corticosteroid treatment.[8] It also has been demonstrated that multiple T_H2-related genes contribute to the genetic susceptibility of developing AA, specifically IL-4 and IL-13.[9,10]

Prior case reports have shown contradicting effects (dupilumab-induced AA), which are speculated to be caused by a stronger T_H1 response from T_H2 suppression.[11,12] In one report, dupilumab was initiated for AD refractory to multiple topical and oral interventions. New-onset hair loss to the scalp was noted after 18 weeks of therapy. Twenty-six weeks into therapy with dupilumab, full hair regrowth was then reported.[11] Despite this report, our patient's hair regrowth after the use of dupilumab for refractory AD further strengthens support for the use of dupilumab as a potential therapy for alopecia universalis and other lymphocyte-mediated hair loss conditions. However, a large disparity in response time and an overall slower progression of hair regrowth reported in our case separate it from other reports of rapid voluminous hair regrowth.[5,6] Our findings support the potential use of dupilumab in the treatment of patients with AA.

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