# Evidence for a possible dosage effect of Dupilumab-induced alopecia areata

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## Introduction

Atopic dermatitis is one of the most common chronic skin conditions worldwide, affecting more than 15% of children and 2% of adults [1]. This disorder can be a significant burden to individuals afflicted, causing skin lesions that are often described as erythematous, pruritic, and weeping. While atopic dermatitis has traditionally been treated with emollients and topical corticosteroids, the development of new immune-modifying drugs like dupilumab, an IL-4/IL-13 receptor antagonist has been added to the arsenal of treatment options [2].

Our case report provides a scenario in which dupilumab use was associated with alopecia areata, a rare autoimmune condition in which patients experience hair loss usually involving the scalp. Although this phenomenon has been reported before [3], our case report remains unique in that our patient demonstrated clinical improvement of his atopic dermatitis without hair loss when dupilumab was restarted at a modified dosage [2].

## Case Report

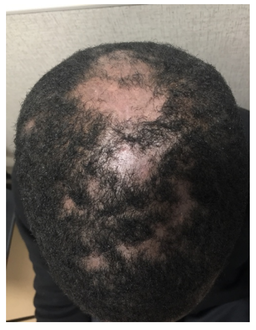

Figure 1. 3 Months on Dupilumab

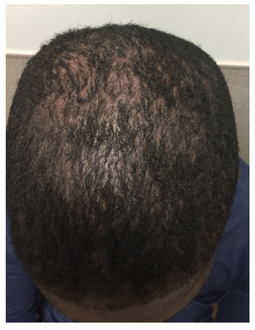

Figure 2. 5 Months After Stopping Dupilumab

Figure 3. 4 Months After Starting 300 mg Dupilumab

- 22-year-old African American male who has had atopic dermatitis since infancy. Past treatment of topical corticosteroids, a janus kinase inhibitor, and mycophenolate mofetil with minimal improvement of atopic dermatitis as measured by EASI scores.
- Past medical history with IgE level > 5000 IU/mL and a positive skin scratch test result to dogs, cats, dust mites, mold, and peanuts. Positive family history of atopic dermatitis.
- With an EASI of 30.6 and body surface area involvement of 61%, he was considered to have moderate to severe atopic dermatitis and qualified for dupilumab treatment.
- Per clinical guidelines, the patient was given a 600 mg loading dose of dupilumab subcutaneous injection followed by 300mg subcutaneous injections every two weeks.
- The patient noted significant clinical improvement of his atopic dermatitis within four months of starting dupilumab with an EASI of 5.6 and BSA of 17%.
- Also demonstrated significant patchy hair loss of the vertex scalp during this time period as seen in Figure 1.
- Biopsy results showing spongiotic dermatitis with loss of hair follicles and perifollicular inflammation consistent with the clinical picture of alopecia areata. Subsequently administered intralesional triamcinolone to the scalp, topical clobetasol ointment, and a short course (10 days) of oral prednisone. When hair growth did not return after a month, he was given another intralesional steroid injection. Dupilumab was stopped and he was started on 500 mg mycophenolic acid mofetil twice daily for 3 months.
- Within the next 6 months, his scalp hair slowly returned as seen in Figure 2. During this time course, he received another one month treatment with mycophenolate mofetil. Although improved from baseline, his atopic dermatitis worsened compared to when on dupilumab. Six months after stopping dupilumab, the patient's EASI score was 21.9 and BSA was 35%.
- Restarted on the dupilumab at lower dose, 300mg every month. 4 months after starting this new regimen, he showed significant improvement of his atopic dermatitis with an EASI of 1.8 and a BSA of 3%. These values represent the best therapeutic response he ever experienced. He did not experience any additional hair loss with the new regimen, and his scalp hair returned to baseline (Figure 3). **The patient has remained without evidence of alopecia areata one year as of restarting the lower dosage of dupilumab.**

## Discussion

- Available treatment options for atopic dermatitis aim to address components of the proposed pathophysiology of the disease: poor integrity of the epidermal barrier and an exaggerated Th2 immune response [3].
- Dupilumab is a monoclonal antibody that interferes with IL-4 and IL-13 signaling. These pathways are thought to play a key role in the pathogenesis of atopic dermatitis, being responsible for the release of several downstream cytokines as well as the production of IgE [4].
- Dupilumab is a relatively new treatment option, being approved by the FDA for use in moderate to severe atopic dermatitis in 2017. Additionally, cost and need for injections might act as barriers for clinical use making its clinical data sparse. E.g., while commonly reported adverse side-effects—like reactions at the injection site, conjunctivitis and reactivation of latent infections—are well known, very little is known about more rare adverse events due to dupilumab [4].
- This report documents a rare case of autoimmune hair loss, alopecia areata with dupilumab. Besides a few case reports concerning autoimmune endocrine and dermatologic conditions with dupilumab use, current literature reviews yield very little information [2,5,6]. Support for this relationship comes from clinical observation that other biologics are associated with autoimmune conditions [7].

**Learning Points**

1. We propose that the ability of dupilumab to effectively block Th2 responses can lead to an increased incidence of autoimmunity by dysregulating other Th1/Th17 pathways.
2. The patient maintained remission of his alopecia areata despite restarting dupilumab. This supports a dose-dependent effect on the various aspects of autoimmunity involving IL-4 and IL-13 blockade.
3. An investigation that looks at dupilumab dosage, therapeutic response, and adverse events is essential to optimize patient care.

## References

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