Alopecia areata after dupilumab for atopic dermatitis

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INTRODUCTION

Dupilumab is the first targeted biologic therapy approved for the treatment of atopic dermatitis (AD).[1] More than 1,000 adult patient exposures formed the basis of its approval in March 2017 for the treatment of moderate-to-severe AD not well controlled with topical therapies or when other therapies are inadvisable. A reassuring safety profile was established, with conjunctivitis being the most significant safety signal.[2] We describe our experience in a patient treated with dupilumab for AD that developed alopecia areata (AA) within 5 weeks of first exposure (3 doses).

CASE REPORT

A 29-year-old Indian male with no significant medical history presented with a 3-year history of poorly controlled, biopsy-proven AD. He was treated previously with phototherapy, topical corticosteroids, methotrexate, cyclosporine, and tofacitinib with only mild improvement. The patient's AD had a clinically psoriasiform appearance, and, because it was nonresponsive to treatment for AD, trials of prednisone, ustekinumab, apremilast, and secukinumab were implemented later in the treatment course (Table I). Prednisone induced osteopenia, ustekinumab resulted in generalized pruritus, and apremilast resulted in diarrhea. Tofacitinib helped partially. Workup for these medications yielded a positive γ-interferon release assay, prompting the successful completion of a 12-week course of weekly isoniazid, 600 mg, and rifapentine, 900 mg.[3]

Abbreviations used:

AA: alopecia areata
AD: atopic dermatitis
IL: interleukin
Th: T helper

Table I. Timeline of failed therapies secondary to poor response or complication before dupilumab

Date of therapy	Therapy
Before 7/18/16	Methotrexate, cyclosporine, tofacitinib, topical corticosteroids
7/18/2016–7/26/2016	Cyclosporine
Before first appointment–11/22/2016	Prednisone
7/26/2016–8/30/2016	Adalimumab
8/16/2016–9/15/2016	Ustekinumab
8/30/2016–9/15/2016	Apremilast
10/11/2016–4/5/2017*	Secukinumab

*Secukinumab was discontinued and dupilumab was initiated 4/5/2017.

After it was approved by the US Food and Drug Administration, he was started on dupilumab at 600 mg subcutaneously on day 0 followed by 300 mg subcutaneously every 2 weeks beginning on day 15. After 6 weeks of treatment, his AD improved significantly; however, he noted several patches of hair loss on his posterior scalp that appeared after 5 weeks of treatment (Fig 1). He was seen in our clinic, and AA was diagnosed clinically (no biopsy was taken). He is currently being treated with

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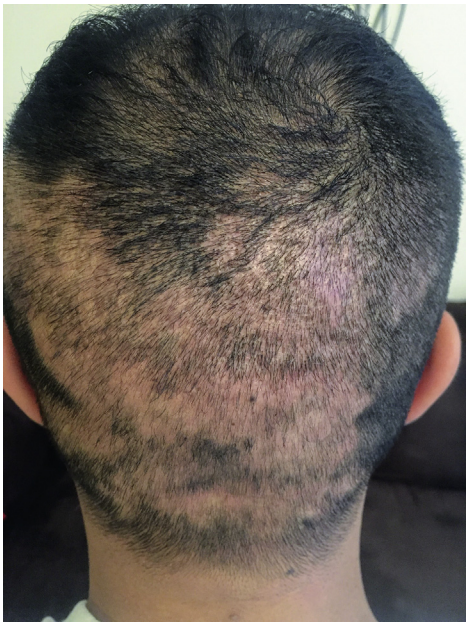

Fig 1. Development of AA during dupilumab treatment. Clinical photograph of AA after 5 weeks of treatment with dupilumab and before treatment with intralesional triamcinolone acetonide, 5 mg/mL.

intralesional triamcinolone acetonide, 5 mg/mL every 4 weeks, and his AA is gradually improving.

DISCUSSION

We report a temporal relationship between dupilumab and the subsequent development of AA. Of course, temporal cannot be interpreted as causal; however, we cannot rule out this possibility. Reports of AA in patients on dupilumab therapy are absent in the existing medical literature. AA is commonly associated with atopic dermatitis.[4] AD is primarily a type 2 T helper (Th2)-driven disease with increased interleukin (IL)-4, IL-5, IL-13, and IL-31.[5] The pathogenesis of AA is not completely understood, but several studies found a heterogeneous process involving T-cell autoantigens, type 1 T helper (Th1)/interferon-γ, Th2, PDE4, IL-23, and IL-9.[4] Because of the similar Th2 cytokine profile between AA and AD, dupilumab may actually be of clinical utility in AA and AD.[4] Yet, the involvement of other immune system mediators, such as Th1, combined with the downregulation of Th2 pathways, may amplify the Th1 pathway and promote the development of AA with dupilumab use.[4] As dupilumab moves into phase IV monitoring, clinicians will need to be aware of any potential adverse reactions that may arise. Despite the associated complication of AA, our patient remains on therapy satisfied with the outcome dupilumab provides and reports overall improved quality of life.

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