SKIN

BRIEF ARTICLE

Adjunctive Dupilumab Therapy in a Partial Responder to Baricitinib for Alopecia Areata

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ABSTRACT

While oral janus kinase (JAK) inhibitors have revolutionized the treatment of severe alopecia areata, the majority of patients in the clinical trials still did not achieve the primary endpoint of SALT 20. There is a paucity of data on using combination immunomodulatory agents to optimize the treatment response in refractory cases. Herein, we report a case of a patient with severe alopecia areata with a predominant ophiasis pattern who partially responded to baricitinib 4 mg daily and oral minoxidil after 15 months of therapy but had near complete hair regrowth just 2 months after adding dupilumab.

INTRODUCTION

While oral janus kinase (JAK) inhibitors have revolutionized the treatment of severe alopecia areata, the majority of patients in the clinical trials still did not achieve the primary endpoint of SALT 20.[1] This is particularly true in patients who had alopecia totalis/universalis and longer disease duration. In the author's experience, certain subtypes of alopecia areata have also been more difficult to treat, specifically those with an ophiasis pattern.[2] Studies have been published on using combination oral minoxidil in patients who were partial responders to oral JAK inhibitors.[3] However, there is a paucity of data on using combination immunomodulatory agents to optimize the treatment response in refractory cases. Herein, we report a case of a patient with severe alopecia areata with a predominant ophiasis pattern who partially responded to baricitinib 4 mg daily and oral minoxidil after 15 months of therapy but had near complete hair regrowth just 2 months after adding dupilumab.

CASE REPORT

A 40-year-old female presented to our clinic for treatment of severe alopecia areata, which started at the age of 29. She initially had localized disease that would respond to intralesional steroids. Over time, her hair loss became more diffuse, often requiring courses of systemic steroids. Other prior treatments included topical corticosteroids, topical minoxidil, and diphenylcyclopropenone. Her past medical history was notable for asthma, which she took montelukast for.

On exam, patient had smooth, confluent patches of non-scarring hair loss involving primarily her temporal and occipital scalp (SALT 30). Eyebrows, eyelashes, and nails were unaffected. Oral baricitinib was discussed at her initial visit but the patient wanted additional time to do research. At her

1-month follow-up, there was evidence of rapid progression as she then had notable hair loss of her vertex with a positive hair pull test (SALT 50). As such, patient was agreeable to start baricitinib 4 mg daily with oral minoxidil 2.5 mg daily.

At her 3-month follow-up, her vertex and occiput had nearly filled in completely making her a SALT 30 responder (at least 30% improvement in SALT score from baseline). By 6 months, her hair regrowth had stagnated so was started on topical tofacitinib 2% cream and intralesional triamcinolone (2.5 mg/cc) every 6 weeks. At 9 months into treatment, oral minoxidil was increased from 2.5 mg to 5 mg daily while continuing with topical tofacitinib cream (patient declined further intralesional steroid injections). Due to scheduling conflicts, the patient was unable to come in for additional follow-up until she had been on baricitinib 4 mg continuously for a total of 15 months (**Figure 1**).

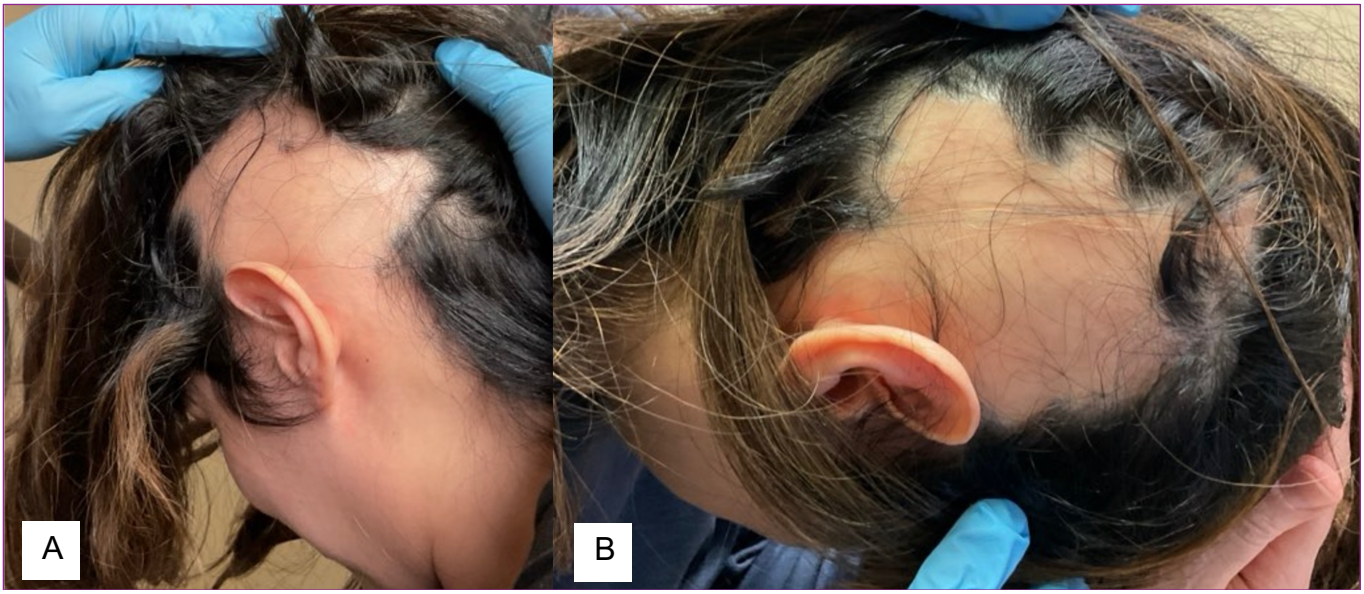

Figure 1. (A and B) 15 months on baricitinib 4 mg daily (SALT 36)

Because she had no appreciable improvement from her visit 6 months earlier, we discussed adjunctive therapy to baricitinib versus changing to ritlecitinib. Given her history of asthma, it was decided to add dupilumab 300 mg subcutaneously (SC) every 2 weeks after a 600 mg loading dose before switching to ritlecitinib.

At her 2-month follow-up after initiating dupilumab, the patient had nearly regrown all her hair and the decision was made not to switch to ritlecitinib (**Figure 2**). Not surprisingly, the patient also noted significant improvement in her asthma. As of today's writing, the patient remains on combination baricitinib 4 mg daily, minoxidil 2.5 mg daily (dosage was decreased due to dramatic response to dupilumab), and dupilumab 300 mg SC every 2 weeks without any notable adverse events, while maintaining a SALT 0.

DISCUSSION

Guttman *et al.* conducted a Phase 2a study to evaluate the efficacy and safety of dupilumab in alopecia areata. While the overall response rates were lower than what has been seen with oral JAK inhibitors,

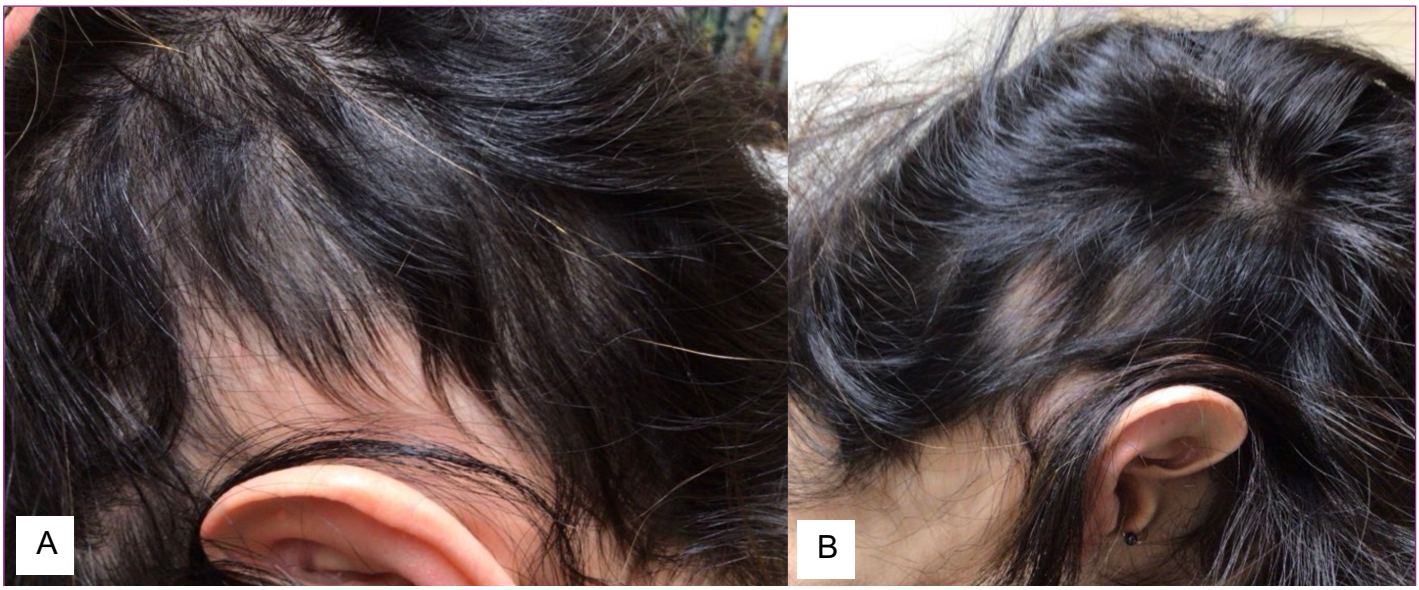

Figure 2. (A and B) 2 months after adding dupilumab 300 mg SC to baricitinib 4 mg daily (SALT 5)

patients with high baseline levels of immunoglobulin E (IgE) and/or an atopic history were the most likely to respond to treatment.[4] On the contrary, there have been case reports of dupilumab causing alopecia areata in patients being treated for atopic dermatitis.[5] Such differences highlight the heterogeneity in the pathomechanism of alopecia areata and the need for further research to subtype these patients due to its implications on treatment selection.

Post-hoc analysis of the BRAVE-AA1/2 trials has demonstrated three distinct treatment trajectories based on when a patient achieved a SALT 30.[6] Generally speaking, the earlier one achieved a SALT 30, the more likely they were to achieve SALT 20, with 83% of "early responders" achieving this endpoint at 52 weeks. In our patient's case, while she would have been considered an "early responder", she still did not achieve a SALT 20 despite 15 months of baricitinib 4 mg once daily therapy.

Given our patient's dramatic response to dupilumab, one can speculate whether dupilumab monotherapy would have been enough to achieve a SALT 20. Although this combination has not been previously reported for alopecia areata, it has been published for atopic dermatitis.[7] Furthermore, disease-modifying anti-rheumatic drugs (DMARDs) such as methotrexate are frequently combined with oral JAK inhibitors in rheumatoid arthritis trials.[8] Such experiences give us a clinical precedent to use these combinations in an array of different chronic inflammatory skin disorders.

In conclusion, we have demonstrated the ability of dupilumab to augment the effects of baricitinib in a partial responder with a history of asthma, which corroborates the findings of earlier studies showing dupilumab to be the most effective in those with an atopic history.

Conflict of Interest Disclosures: BMS, AbbVie, Eli Lilly, Janssen, Novartis, UCB, Pfizer, Amgen, Dermavant, Arcutis, Incyte, SUN, Boehringer Ingelheim, Sanofi & Regeneron, Galderma, Alphyn, MoonLake, Alumis

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