Treatment of alopecia universalis with oral alitretinoin: A case report

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Key words: alitretinoin; alopecia areata; alopecia universalis.

INTRODUCTION

Alopecia areata (AA) is an autoimmune disease distinguished by the appearance of nonscarring hair loss. Initially characterized by oval or round patches of hair loss, the disease can progress to multiple clinical presentations, including the alopecia universalis (AU) subtype in which there is a complete loss of scalp and body hair. We report the case of a patient with AU who had prompt regrowth of hair after treatment with alitretinoin.

Abbreviations used:

AA:	alopecia areata
AU:	alopecia universalis
IL:	interleukin
SALT:	Severity of Alopecia Tool

CASE REPORT

A 52-year-old woman presented to the dermatology clinic with a 2-month history of rapidly progressing total body hair loss. She had been taking adalimumab for Crohn's disease for 4 years, which was in clinical and endoscopic remission. Other medications included montelukast, venlafaxine, pantoprazole, hydrochlorothiazide, and amlodipine. Family history included AU in 2 maternal uncles. Dermatologic examination found 100% hair loss of the scalp based on the Severity of Alopecia Tool (SALT) Score[1] with no erythema or scaling (Fig 1). The patient's eyebrows, eyelashes, and body hair were also completely absent. Skin biopsy found an increased number of catagen and telogen follicles with a peribulbar lymphocytic infiltrate. Results of laboratory tests, including thyroid function tests and complete blood count, were normal. Adalimumab was stopped, and she was initially prescribed prednisone (20 mg once daily for 2 weeks followed by 15 mg once daily for 1 week). Corticosteroid treatment was stopped after 3 weeks because of proximal lower limb weakness and creatinine kinase elevation compatible with a steroid-induced myopathy. Methotrexate, 10 mg, was prescribed orally once per week. However, treatment was ceased after 2 weeks, as the patient complained of fatigue and malaise. Topical immunotherapy with diphenylcyclopropenone and ultraviolet A1 phototherapy were discussed, but these time-consuming treatments were not suitable with the patient's schedule. The patient was then started on oral alitretinoin (30 mg once daily). After 2 months of treatment, 45.2% of hair regrowth was noted based on the SALT score

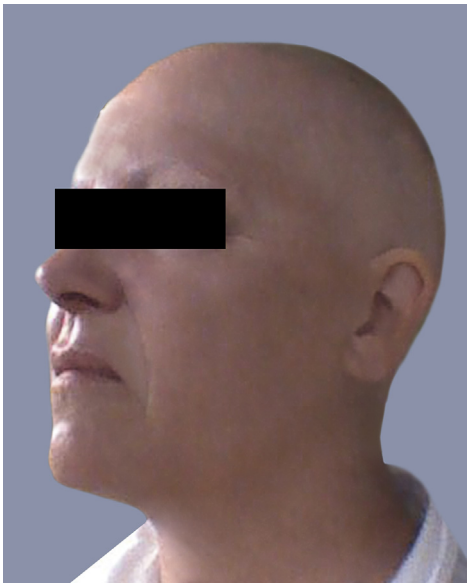

Fig 1. Complete loss of hair, eyebrows, and eyelashes (SALT score 100).

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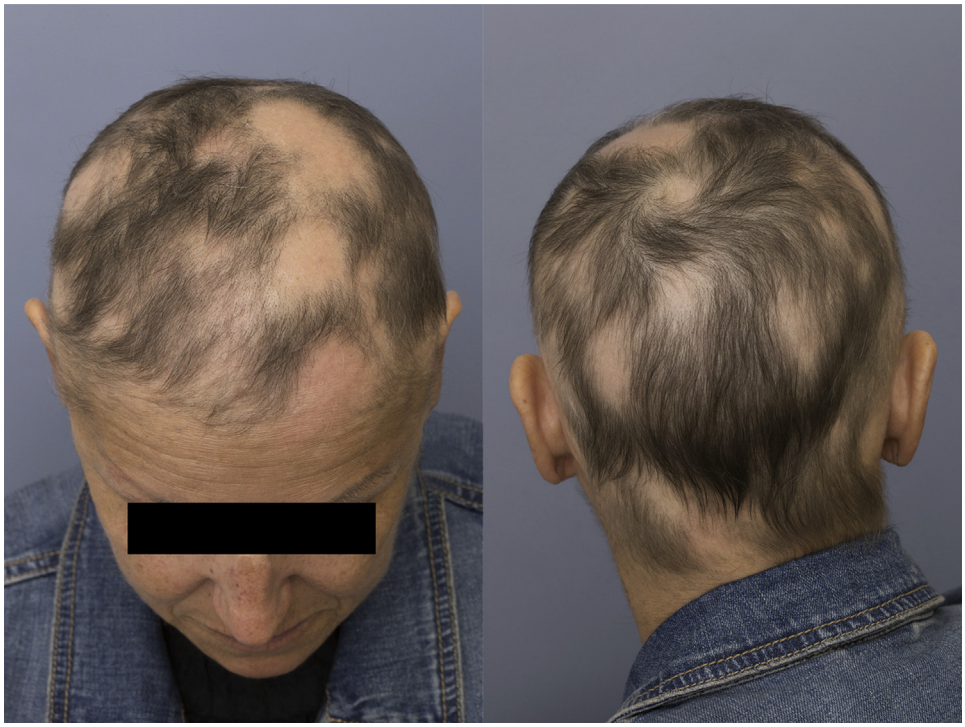

Fig 2. Hair regrowth after 2 months of treatment with oral alitretinoin, 30 mg daily (SALT score 54.8).

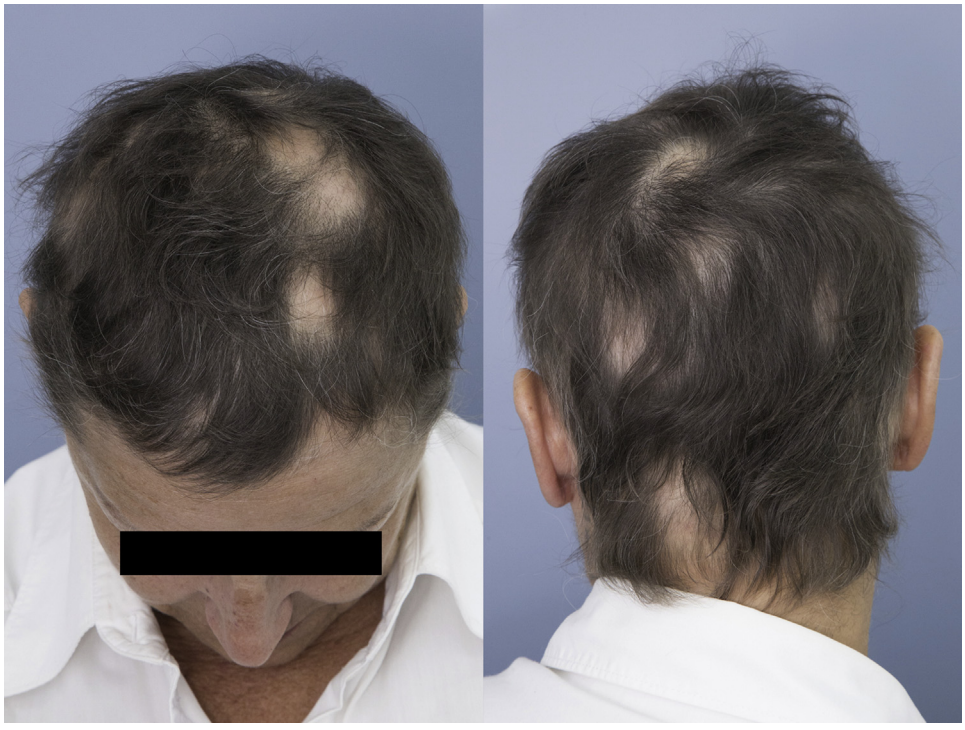

Fig 3. Hair regrowth after 4 months of treatment with oral alitretinoin (SALT score 13.2).

(Fig 2). We lowered the dose to 10 mg once daily because of headaches refractory to conventional therapy. After another 2 months of treatment, 86.8% of hair regrowth was observed when compared with baseline SALT score, along with significant regrowth of eyebrows and eyelashes (Fig 3). We are now considering an additional 8 months of alitretinoin at 10 mg daily, for a total of 1 year.

DISCUSSION

AA is characterized by a T-cell–mediated immune response that targets hair follicules.[2,3] In this hair disorder, there is a disruption in the hair cycle, especially in the anagen phase where a peribulbar inflammation leads to dystrophic follicles.[3] The autoimmune hypothesis is reinforced by the presence of perifollicular and intrafollicular inflammatory CD4+ and CD8+ lymphocytes, along with antigen presenting cells.[2,3] Moreover, several cytokines, especially interferon-γ and other T helper 1 and 2 cytokines, are implicated in a cascade, resulting in an inflammatory response.[2,3] Clinically, autoimmunity is suggested by multiple associated autoimmune diseases, including thyroid disease, vitiligo, and, more rarely, lupus erythematosus, pernicious anemia, celiac disease, ulcerative colitis, and multiple sclerosis.[2,3] Genetic factors with human leukocyte antigen suggest that genetics play a role in the development of AA.[2,3] Treatment of extensive AA or AU is usually disappointing, and many patients experience relapse after therapy.[2,4] Several systemic therapies have been reported with varying success, such as systemic corticosteroids, cyclosporine, and methotrexate.[2,4]

Alitretinoin (9-cis retinoic acid) binds both the retinoid acid receptor and the retinoid X receptor, suppressing the expression of cytokine-induced dermal cells, lymphocytes, and antigen-presenting cells; it has anti-inflammatory and immunomodulating effects.[5] More precisely, there is a suppression of various cytokine and chemokine receptors, including tumor necrosis factor-α, interleukin (IL)-4, IL-1β and IL-12p40.[5] Common side effects of oral alitretinoin include headache, xerosis, and hyperlipidemia.[5,6] Only one case of AA has been reported in the literature to have total regrowth of hair with alitretinoin treatment.[7] The exact mechanism for hair regrowth with alitretinoin remains unknown. Although a remission owing to the natural course of the disorder could not completely be ruled out, there is evidence in mouse models that retinoids could reduce the cytokines implicated in the pathogenesis of AA, thus regulating the immune response to halt the progression of this hair disorder.[8] These findings support the theory that alitretinoin is effective in helping hair regrowth in our AU patient. Moreover, sharing the same retinoid X receptor ligand receptor with alitretinoin and oral and topical bexarotene showed regrowth of hair in mycosis fungoides alopecic lesions.[9] A randomized, controlled trial with topical bexarotene 1% gel applied to one side of the scalp for AA patients found that there is a possible positive effect on hair regrowth; 12% of patients exhibited at least 50% hair regrowth on the treated side of the scalp with an additional 14% of patients that had regrowth on both sides.[9]

This is the first case report, to our knowledge, of hair growth recovery in an AU patient treated with oral alitretinoin. This finding suggests the potential therapeutic benefit of this medication in a difficult-to-treat dermatologic condition with profound psychological effects. It is worth noting that topical alitretinoin gel, which has a good safety profile, has never been reported in the literature for the treatment of AA. Its use may become a potential therapeutic avenue for this condition.

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