

Successful Treatment of Alopecia Universalis With Alefacept: A Case Report and Review of the Literature

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Alopecia universalis often responds poorly to standard therapies. We report how a novel treatment option, alefacept, was successfully used in the management of a 21-year-old woman with alopecia universalis. The patient responded with complete regrowth of scalp and body hair after a single 12-week treatment course of alefacept. In addition, a review of the literature was performed pertaining to the use of biologic agents in the treatment of alopecia areata/universalis to determine which agents have a potential role in the treatment of this often refractory disease.

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Case Report

A 21-year-old woman presented with hair loss of 7 months' duration that started as a small patch on the scalp and rapidly progressed to involve the rest of the scalp within 3 weeks. There was no hair loss on any other areas except her scalp at presentation; the patient's eyebrows and eyelashes were spared. Findings of a review of systems were unremarkable, and she had a prior medical history of asthma. Physical examination results yielded widespread alopecia with few patches of hair on the occiput and right temple. Initial complete blood count, comprehensive metabolic panel, and thyroid-stimulating hormone values were within reference range, and the VDRL test result was negative. Treatment with anthralin, betamethasone valerate foam 0.12%,

and psoralen plus UVA were unsuccessful, and the condition worsened. By 2 months after initial presentation, the patient's hair loss had progressed to her eyebrows, eyelashes, arms, legs, and pubic area, and a diagnosis of alopecia universalis was made.

Alefacept was discussed as the next treatment option. Baseline laboratory assessments at this visit, including CD4⁺ T-lymphocyte count, were within reference range. At approximately one year after the onset of alopecia, the patient was administered alefacept intramuscularly at a dosage of 15 mg once weekly. Seven days after treatment was initiated, the patient began noticing hair regrowth. Her CD4⁺ T-lymphocyte count remained within reference range, and diffuse hair regrowth on the scalp and body was apparent after each week of therapy. At 8 weeks of treatment, fine gray hair almost completely covered the scalp and eyebrows, though eyelash regrowth remained sparse. At 10 weeks, dense hair regrowth on the scalp was noted. After the 12-week treatment course, the patient had nearly complete resolution, with some lack of density on certain regions of the scalp (Figure). At 8 weeks after the final injection of alefacept, the patient's alopecia had completely resolved, with dense natural-colored hair with no discoloration or thinning and no evidence of alopecia. At the time of this report (one year after treatment), she had maintained hair growth.

Comment

Alefacept shows promise as a potential treatment of alopecia universalis and other severe forms of alopecia areata. The patient received a single 12-week course of the biologic agent and dramatically responded, with full and sustained regrowth of scalp, eyebrow, and body hair. The patient experienced no adverse events with the therapy. Further studies enrolling larger numbers of patients are needed to assess the

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Complete regrowth of scalp hair after a 12-week treatment course of alefacept (A and B).

true efficacy of alefacept in the treatment of alopecia areata. Reports of the use of alefacept and other biologic agents in the treatment of alopecia areata and its more severe subtypes can be found throughout the literature. We review the literature on the use of biologic agents in alopecia areata to determine which agents show the most promise.

A PubMed search was performed using the words *alefacept*, *efalizumab*, *infliximab*, *adalimumab*, *etanercept*, and *biologics*, each combined with the word *alopecia*. Seven relevant articles were found: 1 each pertaining to adalimumab, alefacept, efalizumab, and infliximab; 2 pertaining to etanercept; and 1 pertaining to both efalizumab and infliximab. No reports were identified concerning the use of adalimumab to treat alopecia, though one report was found on a patient who developed alopecia areata while on therapy with adalimumab for rheumatoid arthritis. The reports are summarized in the Table.

Alefacept—Alefacept was approved by the US Food and Drug Administration (FDA) in 2003 for the treatment of adults with moderate to severe chronic plaque psoriasis. It is a dimeric fusion protein that consists of the extracellular CD2-binding portion of the human leukocyte function-associated antigen 3 (LFA-3) linked to the Fc region of

human IgG1. It interferes with T-lymphocyte activation by inhibiting LFA-3/CD2 interaction, which plays a role in the pathophysiology of chronic plaque psoriasis and also may play a role in the pathogenesis of alopecia areata. Treatment with alefacept results in a reduction in circulating total CD4⁺ memory T cells. This T-cell population has been shown to be present in the peribulbar inflammatory infiltrate that characterizes alopecia areata.

A review by Heffernan et al² of 4 patients with alopecia areata for more than one year noted a decrease in scalp alopecia after 12 weeks of therapy with alefacept. Furthermore, 2 of 4 patients had involvement of 100% of the scalp surface area (alopecia universalis), with only 10% and 50% residual scalp involvement at follow-up. The authors pointed out that the medication was well-tolerated in all patients and may be a promising agent to offer patients, even those patients with a poor prognosis. We agree with their conclusion that larger randomized controlled studies are needed to establish the true efficacy of alefacept in the treatment of alopecia areata.²

Efalizumab—Efalizumab was approved by the FDA in 2003 for the treatment of adults with moderate to severe chronic plaque psoriasis.

Case Reports on Biologic Agents and Alopecia Areata/Universalis

Biologic Agent	Reference	No. of Patients	Effect
Adalimumab	Garcia Bartels et al ¹	1	Induced alopecia universalis
Alefacept	Heffernan et al ²	4	Improved alopecia areata in all 4 patients, with 50%–90% regrowth in 2 patients
Efalizumab	Kaelin et al ³	1	90% regrowth in 1 patient with alopecia universalis
	Tosti et al ⁴	1	Induced progressive alopecia areata
Etanercept	Strober et al ⁵	17	No substantial regrowth in 17 patients
	Posten and Swan ⁶	1	Induced recurrence of alopecia areata
Infliximab	Ettefagh et al ⁷	1	Induced alopecia areata
	Tosti et al ⁴	1	Induced alopecia areata

It binds to CD11a, the α subunit of leukocyte function–associated antigen 1 (LFA-1), which is expressed on all leukocytes, and inhibits lymphocytes to use LFA-1 to bind to intercellular adhesion molecule-1, thereby inhibiting the adhesion of leukocytes to other cell types. Interaction between LFA-1 and intercellular adhesion molecule-1 is important in multiple processes, including activation of T lymphocytes, adhesion of T lymphocytes to endothelial cells, and migration of T lymphocytes to sites of inflammation, including psoriatic skin. It has been proposed that efalizumab also may prevent the migration of lymphocytes to the area surrounding the hair follicle and therefore may demonstrate efficacy in the treatment of alopecia areata.

Kaelin et al³ reported the successful reversal of alopecia universalis in the treatment of a 19-year-old man. After 6 months of therapy with efalizumab, 90% regrowth was achieved, with scalp hair responding more readily than body hair. The treatment was well-tolerated with no reported side effects. The authors concluded that efalizumab is a safe treatment and larger trials are needed to determine its place in the treatment of alopecia areata.³ This excellent success can be countered, however, in a

report by Tosti et al⁴ that discussed the development of progressive alopecia areata in a patient treated with efalizumab for psoriatic arthropathy. Clearly, further study is necessary.

Etanercept—Etanercept is FDA approved for the treatment of moderately to severely active rheumatoid arthritis, active ankylosing spondylitis, adults with chronic moderate to severe plaque psoriasis, and moderately to severely active polyarticular juvenile idiopathic arthritis. It is a fusion protein receptor consisting of 2 human tumor necrosis factor (TNF) receptors and the Fc region of human IgG1. Etanercept binds soluble TNF- α and inactivates it.

In the dermatologic literature, there are no reports of successful treatment of alopecia areata with etanercept. There is a suggestion that TNF- α gene polymorphisms may underlie the pathogenesis of the patchy form of alopecia areata.⁸ Research into the various effects of cytokines on hair follicle growth has shown that TNF- α can prohibit hair follicle growth.⁹ Clinically, however, blockade of TNF- α activity does not promote resolution of the disease and may actually induce or worsen the condition. In a large open-label study reported by Strober et al,⁵ 17 patients were treated with etanercept and none showed

improvement in severity of alopecia tool scores greater than 10% after 8 to 24 weeks of therapy. The authors concluded that etanercept shows no efficacy in the treatment of alopecia areata and may actually worsen the disease, and they suggested that TNF- α may not play a role in the pathogenesis of the disease.⁵ This argument is further supported by a report from Posten and Swan⁶ that described the recurrence of alopecia areata in a patient with rheumatoid arthritis. Although some research into the pathogenesis of alopecia areata has identified a possible role for TNF- α , clinical experience argues to the contrary.

Infliximab—Infliximab is approved by the FDA for the treatment of moderately to severely active Crohn disease, moderately to severely active rheumatoid arthritis, active ankylosing spondylitis, adults with chronic severe plaque psoriasis, psoriatic arthritis, and moderately to severely active ulcerative colitis. Infliximab inhibits the biological activity of TNF- α by binding with high affinity to the soluble and transmembrane forms as well as by forcing apoptosis of cells that express TNF- α on their surface.

Similar to etanercept, there are no reports of success with the use of infliximab to treat alopecia areata. Furthermore, Etefagh et al⁷ reported the development of alopecia areata in a patient being treated with infliximab for Sjögren syndrome. The authors concluded that TNF- α does not necessarily have a role in the pathogenesis of alopecia areata.⁷ Tosti et al⁴ reported a case of alopecia areata in a 43-year-old man being treated with infliximab for pustular psoriasis. These case reports argue that there is no role for infliximab in the treatment of alopecia areata.

Adalimumab—Adalimumab is indicated by the FDA for the treatment of adults with moderately to severely active Crohn disease, adults with moderately to severely active rheumatoid arthritis, psoriatic arthritis, moderately to severely active polyarticular juvenile idiopathic arthritis, adults with moderate to severe chronic plaque psoriasis, and ankylosing spondylitis. Adalimumab is a recombinant human IgG1 monoclonal antibody specific for human TNF- α . Its mechanism of action, like infliximab, is through the binding of TNF- α and the prevention of its interaction with TNF receptors.

This TNF- α inhibitor, like etanercept and infliximab, has not been reported to be a successful treatment for alopecia areata. In fact, adalimumab was reported by Garcia Bartels et al¹ to have induced

alopecia universalis in a patient being treated for rheumatoid arthritis. This report lends further support to the argument against the use of TNF- α inhibitors in the treatment of alopecia areata.

Conclusion

Reports in the literature have indicated that alefacept shows the most promise among biologic therapies as a potential treatment for all types of alopecia areata. Clearly, larger randomized, double-blind, placebo-controlled trials are needed. Efacept was found to demonstrate success in the treatment of alopecia universalis as well as induce alopecia areata in some patients. Etanercept, infliximab, and adalimumab were not shown in this literature review to be possible treatment options. On the contrary, the present literature argues that TNF- α inhibitors should be abandoned from the therapeutic armamentarium for alopecia areata.

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