

# Imiquimod in the Treatment of Alopecia Universalis

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*Imiquimod is used topically in the treatment of numerous dermatologic conditions. Imiquimod modifies the immune response through cytokine induction of the T-cell helper subset, correlating with the expression of interferon  $\alpha$ , tumor necrosis factor  $\alpha$ , interferon  $\gamma$ , and interleukins (ILs) 1 and 12. Reciprocal inhibition of  $T_H2$  immune response occurs via up-regulation of interferon  $\gamma$  and down-regulation of  $T_H2$ -associated cytokines, including IL-4, IL-5, IL-6, IL-10, and IL-13. Alopecia universalis is a severe form of alopecia thought to arise from T-cell mediated autoimmune disease of the hair follicle. There have been no case reports noting a beneficial effect of topical imiquimod in the treatment of alopecia universalis. We present a case of a 15-year-old adolescent girl with alopecia universalis since age 8 who experienced transient hair growth after topical application of imiquimod.*

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## Case Report

A 15-year-old Japanese American adolescent girl presented to the dermatology clinic with a history of cyclic total body hair loss. The patient's medical history was significant only for infantile eczema that was well-treated with several short courses of topical steroids. She denied use of medications other than

those prescribed for her alopecia during this time. Her family history was negative for alopecia, other hair disorders, and autoimmune disease. Laboratory evaluation was negative for inflammatory, thyroid hematologic, and infectious etiologies.

The patient reported her first episode of spontaneous hair loss at age 8. The hair loss initially occurred in patches from the scalp and eventually led to total body hair loss, including the eyebrows, over 6 months. Throughout this episode, her overall health was unchanged, and she denied illness or increased stress. The patient then experienced complete spontaneous hair regrowth over 18 months. Two years later, she reported another 6-month episode of spontaneous total body hair loss similar to the first episode (Figure, A). The hair loss continued for approximately 2 years. During this time, tazarotene cream 0.1% was applied to the scalp without hair regrowth. When the patient was 14 years old, topical imiquimod cream 5% was applied to the scalp, initially 3 times weekly for 1 week and eventually increased to nightly for 4 months. During these 4 months, the patient noticed hair regrowth on treated areas of the scalp (Figure, B), as well as untreated areas of the body, including the eyebrows, bilateral axillae, upper lip, and pubis. The regrowth remained for approximately 1 year when she once again experienced spontaneous total body hair loss, despite continued nightly use of the topical imiquimod cream. During this time, she reported increased stress caused by family relocation and had stopped application of imiquimod. Three months later, she restarted applying imiquimod cream to the scalp once to twice weekly. After 2 months, there was little hair regrowth. Imiquimod cream application then was increased to twice daily and the patient again noted some hair regrowth on the scalp and untreated areas, including the eyebrows and eyelashes.

## Comment

Alopecia universalis is a condition characterized by total body hair loss, including scalp, eyebrow, axillary, and pubic hair. It is a severe form of alopecia areata of unknown etiology; however, autoimmune reactions

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Patient with spontaneous hair loss on the scalp before (A) and after (B) 4 months of treatment with topical imiquimod cream 5%.

have been suspected as the cause of hair loss. Anagen hair follicles develop a  $T_H2$  immune response-mediated perifollicular T-cell infiltrate.<sup>1</sup> This condition results in abnormal keratinization of the hair follicle and leads to premature entry of the hair follicle into the telogen or late catagen phases and eventual hair loss.<sup>2</sup>

Numerous treatment attempts aimed at immune suppression have resulted in varied success. Intralesional corticosteroid injection,<sup>3</sup> topical minoxidil,<sup>4</sup> sulfasalazine,<sup>5</sup> contact sensitizers,<sup>6</sup> oral steroids,<sup>7</sup> and oral cyclosporine<sup>8</sup> have yielded modest results in patients with alopecia areata. To date, few

published studies have observed benefit in patients with alopecia universalis. One exception is a study by Tosti and colleagues<sup>9</sup> in which topical steroids were used under occlusion.

Imiquimod is an immune response modifier commonly used for the treatment of external genital, perianal, and plantar warts, and more recently for the nonsurgical treatment of actinic keratosis and basal cell carcinoma. It is well-tolerated and has a well-documented safety profile.<sup>10,11</sup> Imiquimod activates the innate and cell-mediated immune pathways. Cytokine activation eventually leads to the drug's antiviral, antitumor, and antiproliferative

properties. One of the indirect effects of imiquimod resulting from topical application is the proliferation of interferon  $\gamma$  by  $T_H1$  and the suppression of interleukins 4 and 5 by  $T_H2$ .<sup>12</sup> Since alopecia areata is proposed to be mediated through  $T_H2$  immunity, imiquimod has been considered as a possible agent for treatment.

In a case series by Sommerfeld and Poppova,<sup>13</sup> partial or total hair regrowth was observed in 5 patients with alopecia areata after topical application of imiquimod. Poor hair growth was seen in a prospective study conducted in 2002 of 15 patients with either alopecia totalis or alopecia universalis. In this study, only 3 of 15 treated patients reported growth of vellus hair with regression after suspension of therapy.<sup>14</sup> These are the only known reported cases of imiquimod treatment in patients with alopecia universalis.

In our patient, noticeable hair growth to the patient's baseline occurred during 4 months of topical imiquimod application, with eventual hair loss after 1 year of continued use. Regrowth also was noted after reapplication of imiquimod subsequent to a 3-month interruption in use.

It is feasible that this patient's hair regrowth would have occurred regardless of treatment. In fact, even before application of imiquimod, the patient had experienced an episode of slow spontaneous hair regrowth after a 6-month period without hair. During imiquimod therapy, growth also was observed in nontreated areas of the patient's body (ie, eyebrows, axillae, upper lip, and pubis); however, regrowth of hair on the scalp was temporary and apparently related to restarting topical imiquimod therapy.

### Conclusion

As observed in this patient, imiquimod is a possible therapeutic avenue for patients with alopecia universalis, though the effect is temporary. Because an effective permanent cure does not yet exist, topical imiquimod offers a potential treatment for this frustrating disease in some patients. Additional studies will be needed to help determine the extent of efficacy of imiquimod in patients with alopecia universalis.

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