

Unique Treatment for Alopecia Areata Combining Epinephrine With an Intralesional Steroid

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PRACTICE POINTS

- Patients with alopecia areata that is refractory to first-line treatments may benefit from intralesional triamcinolone acetonide (ILTA) diluted to 2.5 mg/mL in 1% lidocaine and epinephrine 1:100,000 in place of normal saline.
- Local vasoconstriction due to epinephrine may potentiate ILTA effects and play an independent role.

Alopecia areata (AA) is an autoimmune disorder characterized by well-demarcated patches of hair loss with preservation of the hair follicle (HF). It generally is a nonscarring alopecia that can be extensive and refractory to treatment. We propose modification to an already widely used first-line treatment by diluting intralesional triamcinolone acetonide (ILTA) to 2.5 mg/mL in 1% lidocaine and epinephrine 1:100,000 in place of normal saline (NS). Our 2 cases of severe AA are among many in our practice that responded with seemingly permanent hair regrowth using this novel combination regimen. We hypothesize that local vasoconstriction due to epinephrine potentiates the ILTA and that epinephrine also may play an independent role.

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Alopecia areata (AA) is an autoimmune disorder characterized by transient hair loss with preservation of the hair follicle (HF). The lifetime incidence risk of AA is approximately 2%,¹ with a mean age of onset

of 25 to 36 years and with no clinically relevant significant differences between sex or ethnicity.² Most commonly, it presents as round, well-demarcated patches of alopecia on the scalp and spontaneously resolves in nearly 30% of patients. However, severe disease is associated with younger age of presentation and can progress to a total loss of scalp or body hair—referred to as alopecia totalis and alopecia universalis, respectively—thus severely impacting quality of life.^{3,4}

First-line treatment options for AA include potent topical steroids^{5,6} and intralesional (IL) steroids, most commonly IL triamcinolone acetonide (ILTA). Intralesional steroids have been found to be more effective than topicals in stimulating hair growth at the injection site.^{7,8} A recent systemic therapy—the Janus kinase inhibitor baricitinib—was approved by the US Food and Drug Administration for AA.⁹ Other systemic therapies such as oral corticosteroids have been studied in small trials with promising results.¹⁰ However, the risks of systemic therapies may outweigh the benefits.^{9,10}

Another less common topical therapy is contact immunotherapy, which involves topical application of an unlicensed non-pharmaceutical-grade agent to areas affected with AA. It is reported to have a wide range of response rates (29%–87%).¹¹

We report 2 cases of extensive AA that were treated with a novel combination regimen—2.5 mg/mL of ILTA diluted with lidocaine 1% and epinephrine 1:100,000 in place of normal saline (NS)—which is a modification to an already widely used first-line treatment.

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The authors report no conflict of interest.

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Case Reports

Patient 1—An 11-year-old girl presented with nonscarring alopecia of the vertex and occipital scalp. Three years prior she was treated with topical and IL corticosteroids by a different provider. Physical examination revealed almost complete alopecia involving the bottom two-thirds of the occipital scalp as well as the medial eyebrows (Figures 1A and 1B). Over the span of 1 year she was treated with betamethasone dipropionate cream 0.05% and several rounds of ILTA 2.5 mg/mL buffered with NS, with minimal improvement. A year after the initial presentation, the decision was made to initiate monthly injections of ILTA 2.5 mg/mL buffered with 1% lidocaine and epinephrine 1:100,000. Some hair regrowth of the occipital scalp was noted by 3 months, with near-complete regrowth of the scalp hair and eyebrows by 7 months and 5 months, respectively (Figures 1C and 1D). During this period, the patient continued to develop new areas of alopecia of the scalp and eyebrows, which also were injected with this combination. In total, the patient received 8 rounds of IL injections 4 to 6 weeks apart in the scalp and 6 rounds in the eyebrows. The treated areas showed resolution over a follow-up period of 14 months, though there was recurrence at the right medial eyebrow at 5 months. No localized skin atrophy or other adverse effects were noted.

Patient 2—A 34-year-old woman who was otherwise healthy presented with previously untreated AA involving the scalp of 2 months' duration. Physical examination revealed the following areas of nonscarring alopecia: a 10×10-cm area of the right occipital scalp with some regrowth; a 10×14-cm area of the left parieto-occipital scalp; and a 1-cm area posterior to the vertex (Figure 2A). Given the extensive involvement, the decision was made to initiate ILTA 2.5 mg/mL buffered with 1% lidocaine and epinephrine 1:100,000 once monthly. Appreciable hair regrowth was noted within 1 month, mostly on the

parietal scalp. Substantial improvement was noted after 3 months in all affected areas of the hair-bearing scalp, with near-complete regrowth on the left occipital scalp and greater than 50% regrowth on the right occipital scalp (Figure 2B). No adverse effects were noted. She currently has no alopecia.

Comment

Alopecia Pathogenesis—The most widely adopted theory of AA etiology implicates an aberrant immune response. The HF, which is a dynamic “mini-organ” with its own immune and hormonal microenvironment, is considered an “immune-privileged site”—meaning it is less exposed to immune responses than most other body areas. It is hypothesized that AA results from a breakdown in this immune privilege, with the subsequent attack on the peribulbar part of the follicle by CD8⁺ T lymphocytes. This lymphocytic infiltrate induces apoptosis in the HF keratinocytes, resulting in inhibition of hair shaft production.¹² Other theories suggest a link to the sympathetic-adrenal-medullary system and hypothalamic-pituitary-adrenal axis.¹³

Therapies for Alopecia—Topical and IL corticosteroids are the first-line therapies for localized AA in patients with less than 50% scalp involvement. Triamcinolone acetonide generally is the IL steroid of choice because it is widely available and less atrophogenic than other steroids. Unlike topicals, ILTA bypasses the epidermis when injected, achieving direct access to the HF.¹⁴

High-quality controlled studies regarding the use of ILTA in AA are scarce. A meta-analysis concluded that 5 mg/mL and 10 mg/mL of ILTA diluted in NS were equally effective (80.9% [$P<.05$] vs 76.4% [$P<.005$], respectively). Concentrations of less than 5 mg/mL of ILTA resulted in lower rates of hair regrowth (62.3%; $P=.04$).¹⁵ The role of diluents other than NS has not been studied.

FIGURE 1. A, An 11-year-old girl with alopecia areata of the occipital scalp before treatment. B, Alopecia of the eyebrows before treatment. C, Near-complete regrowth of hair on the occipital scalp was seen after 7 months of treatment with intralesional triamcinolone acetonide 2.5 mg/mL plus 1% lidocaine and epinephrine 1:100,000 at monthly intervals. D, Near-complete regrowth of the medial eyebrows was seen after 5 months of this combination regimen.





FIGURE 2. A, A 34-year-old woman with alopecia of the right occipital scalp before treatment. B, Partial regrowth (>50%) of hair on the right occipital scalp was seen after 3 months of treatment with intralesional triamcinolone acetonide 2.5 mg/mL plus 1% lidocaine and epinephrine 1:100,000 at monthly intervals.

Patients Treated With ILTA in 1% Lidocaine and Epinephrine 1:100,000

Patient characteristics	Patient 1	Patient 2	Patient 3	Patient 4
Age, y/Gender	11/F	34/F	13/M	50/F
Location(s) affected	Vertex, inferior two-thirds of occipital scalp, medial eyebrows	Right occipital scalp, left parieto-occipital scalp, posterior to the vertex	6×4 cm of vertex of scalp, 2×4 cm of left parietal scalp, and 2 cm of right temporal scalp	Alopecia totalis
Prior therapies	Betamethasone dipropionate cream 0.05% plus ILTA 2.5 mg/mL buffered with NS	None	Minoxidil 5% and betamethasone dipropionate cream 0.05% for 3 mo	ILTA 5 mg/mL buffered with NS (2 rounds)
Concentration of ILTA	2.5 mg/mL	2.5 mg/mL	2.5 mg/mL	2.5 mg/mL
No. of rounds	Scalp, 8; eyebrows, 6	3	5	5
Interval between rounds, wk	4–6	4	4–6	4
Regrowth, %	Scalp, 90–100; eyebrows, 80–90	80–90	80–90	90–100
Side effects	None	None	None	None
Remission duration, mo	Scalp and eyebrows, 14+; right medial eyebrow, 5+ (with recurrence)	11+	9+ (no recurrence in treated areas but new lesions occurred)	28+

Abbreviations: F, female; ILTA, triamcinolone acetonide; M, male; NS, normal saline.

Benefits of Epinephrine in ILTA Therapy—The role of epinephrine 1:100,000 is to decrease the rate of clearance of triamcinolone acetonide from the HF, allowing for a better therapeutic effect. Laser Doppler blood flowmeter studies have shown that epinephrine 1:100,000 injected in the scalp causes vasoconstriction, thereby decreasing the blood flow rate of clearance of other substances in the same solution.¹⁶ Also, a more gradual systemic absorption is achieved, decreasing systemic side effects such as osteoporosis.¹⁷

Another potential benefit of epinephrine has been suggested in animal studies that demonstrate the important role of the sympathetic nervous system in HF growth. In a mouse study, chemical sympathectomy led to diminished norepinephrine levels in the skin, accompanied by a decreased keratinocyte proliferation and hair growth. Conversely, norepinephrine was found to promote HF growth in an organotypic skin culture model.¹⁸ Topically applied isoproterenol, a panadrenergic receptor agonist,

accelerated HF growth in an organotypic skin culture. It also has been shown that external light and temperature changes stimulate hair growth via the sympathetic nervous system, promoting anagen HF growth in cultured skin explants, further linking HF activity with sympathetic nerve activity.¹⁹

In our experience, cases of AA that at first failed ILTA 5 mg/mL in NS have been successfully treated with 2.5 mg/mL ILTA in 1% lidocaine and epinephrine 1:100,000. One such case was alopecia totalis, though we do not have high-quality photographs to present for this report. The 2 cases presented here are the ones with the best photographs to demonstrate our outcomes. Both were treated with 2.5 mg/mL ILTA in 1% lidocaine and epinephrine 1:100,000 administered using a 0.5-in long 30-gauge needle, with 0.05 to 0.1 mL per injection approximately 0.51-cm apart. The treatment intervals were 4 weeks, with a maximal dose of 20 mg per session. In addition to the 2 cases reported here, the Table includes 2 other patients in our practice who were successfully treated with this novel regimen.

Prior to adopting this combination regimen, our standard therapy for AA was 5 mg/mL ILTA buffered with NS. Instead of NS, we now use the widely available 1% lidocaine with epinephrine 1:100,000 and dilute the ILTA to 2.5 mg/mL. We postulate that epinephrine 1:100,000 enhances therapeutic efficacy via local vasoconstriction, thus keeping the ILTA in situ longer than NS. This effect allows for a lower concentration of ILTA (2.5 mg/mL) to be effective. Furthermore, epinephrine 1:100,000 may have an independent effect, as suggested in mouse studies.¹⁸

Our first case demonstrated the ophiasis subtype of AA (symmetric bandlike hair loss), which has a poorer prognosis and is less responsive to therapy.²⁰ In this patient, prior treatment with topical corticosteroids and ILTA in NS failed to induce a response. After a series of injections with 2.5 mg/mL ILTA in 1% lidocaine and epinephrine 1:100,000, she entered remission. Our second case is one of alopecia subtotalis, which responded quickly, and the patient entered remission after just 3 months of treatment. These 2 cases are illustrative of the results that we regularly get and have come to expect with this treatment.

Conclusion

Our novel modified regimen of 2.5 mg/mL ILTA diluted with 1% lidocaine and epinephrine 1:100,000 has yielded a series of excellent outcomes in many of our most challenging AA cases without any untoward effects. Two cases are presented here. Higher-powered studies are needed to validate this new yet simple approach.

A split-scalp or split-lesion study comparing ILTA with and without epinephrine 1:100,000 would be warranted for further investigation.

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