

# Case report of novel combination of anthralin and calcipotriene leading to trichologic response in alopecia areata



Loren Krueger, MD, Erik Peterson, BS, Jerry Shapiro, MD, and Kristen Lo Sicco, MD  
New York, New York

**Key words:** alopecia; alopecia areata; anthralin; calcipotriene; hair; topical immunomodulatory therapy.

## INTRODUCTION

Alopecia areata (AA) is an autoimmune, non-scarring alopecic disorder with a lifetime prevalence of about 2%.<sup>1</sup> This disorder presents with varying amounts of hair loss, ranging from focal patchy loss to entire scalp and body hair loss as in alopecia totalis (AT) and alopecia universalis (AU), respectively. Severe subtypes are difficult to treat and contribute to significant patient burden. Current treatment strategies center on immunomodulation, both systemically and topically.

Systemic therapies such as oral corticosteroids, cyclosporine, and methotrexate can be efficacious, with regrowth rates between 30% and 76%.<sup>2</sup> However, side-effect profiles, lengthy treatment durations, and relapse rates after discontinuation of therapy limit their use.<sup>2</sup> Newer Janus kinase (JAK) inhibitors appear promising, yet patients relapse after treatment cessation, and cost is often prohibitive.<sup>3</sup>

Topical glucocorticoids offer variable efficacy; 17.8% of patients with AT or AU had long-term regrowth with clobetasol use.<sup>4</sup> Topical calcineurin inhibitors have not demonstrated efficacy, perhaps because of insufficient depth of penetration.<sup>5</sup> Intralesional triamcinolone at concentrations of 2.5 to 5 mg/mL are considered first-line therapy with regrowth seen in 61% of subjects with AT at 6 weeks and minimal side effects.<sup>2,6</sup> An additional therapeutic option used for more severe forms of AA is the topical immunomodulator, diphenylcyclopropenone (DPCP). Although the exact mechanism of DPCP is unknown, its resultant allergic contact dermatitis is thought to cause antigenic competition

### Abbreviations used:

|       |                        |
|-------|------------------------|
| AA:   | alopecia areata        |
| AT:   | alopecia totalis       |
| AU:   | alopecia universalis   |
| DPCP: | diphenylcyclopropenone |

and an alteration of the inflammatory cytokine milieu.<sup>2,7</sup> In one retrospective study of 50 patients treated with DPCP, terminal hair regrowth of 50% or more was seen in 56% and 71% of those with AU and AT, respectively.<sup>7</sup>

Anthralin (dithranol), available in 0.25% to 1% concentrations, is another topical treatment option. Anthralin functions via the production of a localized irritant dermatitis with resultant pruritus, erythema, and scale. Patients who do not have a robust inflammatory response to anthralin may not achieve significant therapeutic response.<sup>2</sup> Response rates with anthralin in AA and AT are between 25% and 75%.<sup>2</sup> Combination treatment strategies may provide a more robust therapeutic response, such as the combination of minoxidil with topical glucocorticoids and anthralin with DPCP.<sup>2,8</sup>

Calcipotriol/calcipotriene is a topical vitamin D<sub>3</sub> analogue commonly used in plaque psoriasis. Recently, a significant benefit of combination therapy with calcipotriol and 5-fluorouracil has been identified in the treatment of actinic keratoses.<sup>9</sup> When used together, these medications show a synergistic mechanism of action, perhaps because of calcipotriol's induction of antitumor immunity and allergic skin inflammation via thymic stromal

The Ronald O. Perelman Department of Dermatology, New York University School of Medicine.

Funding sources: None.

Conflicts of interest: None disclosed.

Correspondence to: Kristen Lo Sicco, MD, FAAD, The Ronald O. Perelman Department of Dermatology, 240 East 38<sup>th</sup> Street, 11th Floor, New York, New York 10016. E-mail: [Kristen.LoSicco@nyumc.org](mailto:Kristen.LoSicco@nyumc.org).

JAAD Case Reports 2019;5:258-60.

2352-5126

© 2019 by the American Academy of Dermatology, Inc. Published by Elsevier, Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<https://doi.org/10.1016/j.jidcr.2019.01.006>



**Fig 1.** Before therapy. Frontal and temporal scalp with patchy alopecic patches without loss of follicular ostia.

lymphopoietin cytokine.<sup>9</sup> The efficacy of this combination offers a potential corollary for the treatment of additional dermatologic conditions in which immunomodulation plays a key role. The combination of anthralin and calcipotriene may likewise demonstrate synergistic effects in the treatment of AA.

### CASE REPORT

A 39 year-old woman presented with a 20-year history of hair loss involving the scalp and eyebrows. Her personal medical history was significant only for eczema, and she had no family history of AA or other autoimmune disorders. The diagnosis of AA was made by physical examination, which found diffuse patchy alopecia of the scalp without erythema, scaling, or loss of follicular ostia (Figs 1 and 2). Near complete loss of eyebrow hair was noted. Nail pitting was present.

She was previously treated with intralesional triamcinolone (2.5-5 mg/mL) over the course of 5 years with minimal improvement. She was started on whole scalp anthralin 1% shampoo for 15 minutes nightly, increased to 90 minutes nightly for more than 2 months, but she denied the development of any scalp irritation or regrowth. Next, a combination of anthralin 1% cream with calcipotriene 0.005% cream was applied topically with duration of application increased from 5 minutes to 90 minutes as tolerated for 5 days per week. The anticipated side effect of scalp irritation with associated pruritus, erythema, and scale then developed. Physical examination found increased hair density with background scalp erythema. Eyebrow hair regrowth was not seen. Clinical response is illustrated in Figs



**Fig 2.** Before therapy. Temporal, vertex and occipital scalp with patchy alopecic patches without loss of follicular ostia.



**Fig 3.** After therapy. Frontal and temporal scalp with increased hair density. Mild erythema and scaling of the scalp are seen.

3 and 4). The combination of anthralin and calcipotriene resulted in visible hair regrowth with satisfactory cosmetic results that were maintained through follow-up at 8 months. There were no adverse or unanticipated events.

### DISCUSSION

We theorize that the combination of anthralin and calcipotriene promotes a robust inflammatory response that may be useful in treatment-refractory



**Fig 4.** After therapy. Temporal, vertex, and occipital scalp with increased hair density.

AA. Anthralin functions by inducing an irritant dermatitis, shifting T lymphocyte inflammation away from hair follicles to the epidermis. It is well established that calcipotriene also causes an irritant dermatitis; therefore, its concomitant use may bolster the resultant irritant dermatitis, potentially hastening and/or amplifying clinical responses. However, calcipotriene can also cause an allergic contact dermatitis, likely via expression of cytokine thymic stromal lymphopoietin, which adds an additional mechanism of immunomodulation.<sup>9,10</sup> This patient's response can likely be attributed to combination therapy, as previous treatment did not provide satisfactory regrowth, and diffuse AA is severe and thus less likely to spontaneously remit. Further studies are needed to better understand concomitant

use of anthralin and calcipotriene in the promotion of hair regrowth in AA, which may provide an attractive option for patients preferring topical over systemic therapy.

#### REFERENCES

1. Alkhalifah A, Alsantali A, Wang E, McElwee KJ, Shapiro J. Alopecia areata update: part I. Clinical picture, histopathology, and pathogenesis. *J Am Acad Dermatol*. 2010;62(2):177-188.
2. Alkhalifah A, Alsantali A, Wang E, McElwee KJ, Shapiro J. Alopecia areata update: part II. Treatment. *J Am Acad Dermatol*. 2010;62(2):191-202.
3. Shivanna C, Shenoy C, Priya R. Tofacitinib (selective Janus kinase inhibitor 1 and 3): a promising therapy for the treatment of alopecia areata: a case report of six patients. *Int J Trichology*. 2018;10(3):103-107.
4. Tosti A, Piraccini B, Pazzaglia M, Vincenzi C. Clobetasol propionate 0.05% under occlusion in the treatment of alopecia totalis/universalis. *J Am Acad Dermatol*. 2003;49(1):96-98.
5. Rigopoulos D, Gregoriou S, Korfitis C, et al. Lack of response of alopecia areata to pimecrolimus cream. *Clin Exp Dermatol*. 2007;32(4):456-457.
6. Abell E, Munro D. Intralesional treatment of alopecia areata with triamcinolone acetonide by jet injector. *Br J Dermatol*. 1973;88:55-60.
7. Chiang K, Mesinkovska N, Piliang M, Bergfeld W. Clinical efficacy of diphenylcyclopropenone in alopecia areata: retrospective data analysis of 50 patients. *J Investig Dermatol Symp Proc*. 2015;17(2):50-55.
8. Durdu M, Ozcan D, Baba M, Seckin D. Efficacy and safety of diphenylcyclopropenone alone or in combination with anthralin in the treatment of chronic extensive alopecia areata: a retrospective case series. *J Am Acad Dermatol*. 2015;72(4):640-650.
9. Cunningham TJ, Tabacchi M, Eliane JP, et al. Randomized trial of calcipotriol combined with 5-fluorouracil for skin cancer precursor immunotherapy. *J Clin Invest*. 2017;127(1):106-116.
10. Li M, Hener P, Zhang Z, Ganti K, Metzger D, Chambon P. Induction of Thymic Stromal lymphopoietin expression in keratinocytes is necessary for generating an atopic dermatitis upon application of the active vitamin D3 analogue MC904 on mouse skin. *J Invest Dermatol*. 2009;129(2):498-502.