

Successful Treatment of Severe Alopecia Areata With Oral or Topical Tofacitinib

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ABSTRACT

Alopecia areata is an autoimmune disease involving the hair follicle with a chronic, relapsing course. Tofacitinib is Janus kinase inhibitor approved for treatment of rheumatoid arthritis that has been shown to be effective in treatment of alopecia areata. We present a case series of 11 patients with severe alopecia areata on longstanding, regular to high dose oral tofacitinib with marked hair regrowth. Additionally, we present a case of moderate to severe alopecia areata successfully treated with topical tofacitinib cream.

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INTRODUCTION

Alopecia areata (AA) is a chronic autoimmune disease involving the hair follicle with a high relapse rate and variable response to traditional therapies that nonspecifically target the immune system. Janus kinase (JAK) inhibitors are targeted immunosuppressants shown to improve hair loss in alopecia areata and are available in oral and topical formulations.[1-10] Patients with more severe and longstanding disease have shown poorer response to tofacitinib, a JAK 1/3 inhibitor, therapy.[9,10] We present a case series of eleven patients with alopecia areata universalis or totalis treated with standard to high dose oral tofacitinib and four patients treated with a compounded topical tofacitinib cream.

METHODS

Eleven patients diagnosed with AA universalis or totalis treated with oral tofacitinib were identified (Table 1). Oral tofacitinib treatment was started at 5 mg once daily, 5 mg twice daily, or 11 mg extended release once daily. Dosage was titrated based on response, tolerability, and insurance coverage. Adjuvant intralesional Kenalog (ILK) was administered at the physician's discretion. Additionally, we identified four patients with severe AA who were treated with 2% tofacitinib cream twice daily. Notably, two of these patients were treated with oral tofacitinib either prior to or after topical tofacitinib, but not concurrently with topical tofacitinib (Table 2). This case series was approved by the University of California, Los Angeles Institutional Review Board. The review spanned April 1, 2015 to August 20, 2017.

Treatment response was evaluated by patient reported time to initial response (defined as time to first documented sign of any hair regrowth) and the validated Severity of Alopecia Tool (SALT) score, with a higher score indicating more severe disease. The SALT score was calculated prior to initiation of treatment and throughout follow-up by a combination of in office physician evaluation and retrospective photographic evaluation. The % SALT score change from baseline was calculated as (initial SALT score - best SALT score on treatment)/initial SALT score x 100%.

RESULTS

Oral Tofacitinib

Patient characteristics are summarized in Table 1. We identified 10 patients with alopecia areata universalis and one patient with alopecia areata totalis with mean duration of disease of 5.23 years (range, 3-11 years). Patients were treated with oral tofacitinib (range 5 mg once daily to 11 mg extended release twice daily) for a mean treatment duration of 14.4 months (range, 4.5-27 months).

The mean time to first response was 1.36 months (range 4 days to 3 months). The mean SALT score improvement from baseline was calculated to be 61.18% (n=10, range, 0%-100%). One patient was not included because she was lost to follow up. Of the ten patients with documented follow-up SALT scores, five patients achieved complete disease resolution (SALT score <=5%), three of whom were treated with adjuvant ILK treatment (5-10 mg/ml) to recalcitrant patches.

Five patients temporarily ceased treatment and were observed to have gradual patchy loss of hair regrowth. One patient developed hyperlipidemia and weight gain while on 11 mg extended release twice daily, which improved with exercise and diet changes while remaining on treatment. Other side effects included gastrointestinal symptoms and mild acne. One patient stopped treatment due to new-onset multiple sclerosis.

Topical Tofacitinib

Patient characteristics are summarized in Table 2. We identified 4 patients (3 men, 1 woman) diagnosed with AAU with

TABLE 1.

Oral Tofacitinib Patient Characteristics and Treatment Regimen

Age/ Gender	Duration disease (years)	Diagnosis	Medication trials	Lowest dose tofacitinib	Highest dose tofacitinib	Treatment duration (months)	Time to first effect (months)	Adjuvant ILK	Initial SALT score	Best SALT score achieved	Change SALT score	Adverse effects
50M	7	AAU	ILK, tacrolimus, SADBE, oral steroids, topical steroids	5 mg BID	11 mg ER BID	22	3	Y	50%	<5%	90%	Hyperlipidemia
56M	2	AAU	Contact immunotherapy, ILK, clobetasol, topical tofacitinib 2%	5 mg BID	5 mg BID	7	1	N	100%	0%	100%	n/a
42F	11	AAU	DNCB, topical steroids	5 mg BID	5 mg BID	13	1	N	100%	100%	0%	n/a
58F	2	AAU	ILK, latisse, drithrocreme, anthracycline, minoxidil, SADBE	11 mg ER daily	11 mg ER daily	5	3	N	100%	5%	5%	n/a
45F	10	AAT	ILK, SADBE, tacrolimus, desonide	5 mg BID	11 mg ER BID	12	3	Y	100%	5%	95%	n/a
23F	2	AAU	ILK, IM steroid, MTX, SADBE	5 mg BID	11 mg ER daily	16	1	N	100%	12%	88%	Knee soreness
41F	3.5	AAU	Oral steroid, ILK, contact immunotherapy, minoxidil, topical steroid	5 mg BID	15 mg daily	4.5	n/a	Y	100%	100%	0%	Weight gain, mild joint aches
27F	6	AAU	ILK, oral steroid, diphencyprone	5mg daily	5 mg BID	26	1	Y	100%	0%	100%	n/a
34F	3	AAU	MTX, entanercept, topical and oral steroids	5 mg BID	11 mg ER qd	27	1	Y	100%	5%	95%	n/a
24M	6	AAU	Oral steroids, entanercept, hydroxychloroquine, topical steroid	5 mg BID	5 mgTID	18	1	N	100%	0%	100%	none
21F	5	AAU	ILK, topical steroids, cyclosporine	5 mg daily	5 mg BID	8	4 days	N	100%	n/a	n/a	Multiple sclerosis
Average	5.23					14.4	1.36				61.18%	

mean age 42.5 (range, 28-58 years) and mean duration of disease 5.6 years (range 3-10 years). Each was treated with 2% tofacitinib cream twice daily for a mean duration of 7 months (range, 3-11 months). One patient was observed to have excellent results with a 93.3% change in SALT score from baseline (initial SALT 100%, SALT after treatment 6.5%). In this patient, CBC, CMP, and lipids remained at baseline. Two of the four patients saw no improvement or progressive loss of hair (patient was previously treated with oral tofacitinib with robust results, but oral treatment was discontinued due to lack of insurance coverage). One patient was concurrently treated with methotrexate 25 mg weekly and prednisone 10 mg daily. Hair regrowth in this patient was reported at application site of tofacitinib cream, but no photographs or SALT scores were recorded. No adverse events were reported in any patient.

DISCUSSION

Our results suggest that oral tofacitinib may be an effective option for patients with severe alopecia areata and that higher dose treatment may be necessary in some patients with unsatisfactory results on standard dose oral tofacitinib. Compared to previous studies, we found our patients to have a shorter time to first response (1.36 mos vs 4.2 mos), though this was patient reported, and greater percent improvement in SALT score (61.18% vs 44.3%).[10] Most patients noticed at least mild regrowth within the first three months, but some required more time to see significant growth. Five of our eleven patients

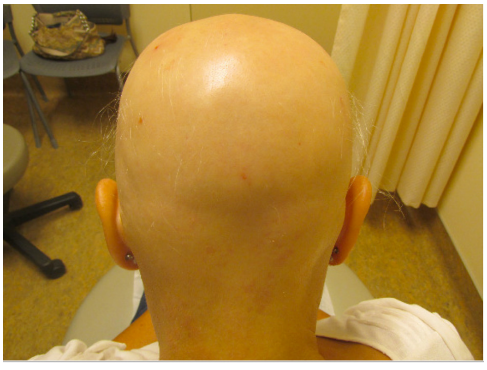
TABLE 2.

Topical Tofacitinib Patient Characteristics and Treatment Regimen

	Age (years)	Gender	Disease duration (years)	Concurrent treatments	Previous treatments	Initial SALT Score	Treatment time (months)	Time to first effect	Post-treatment SALT score	Change SALT score
1	28	M	3.5	10 mg pred, 25 mg MTX	ILK, oral prednisone, methotrexate	n/a	11	n/a	n/a	n/a
2	28	M	7	n/a	ILK, SADBE, acupuncture clobetasol 0.05% solution, minoxidil	75%	9	1 month	6.70%	91.10%
3	56	M	2	n/a	Contact immunotherapy, ILK, clobetasol, oral tofacitinib 5mg BID	100%	3	n/a	100%	0%
4	58	F	10	n/a	ILK, latisse, drithrocreme, anthracycline, minoxidil, SADBE, oral tofacitinib 11mg ER qd	20%	5	n/a	99%	-395%
Average	42.5		5.625				7	n/a		

FIGURE 1. Occipital scalp of patient prior to treatment (A), 11 months after treatment with oral tofacitinib (10 mg daily for 2 months followed by 15mg daily for 7 months followed by 22mg daily for 2 months followed by 11mg daily) (B).

(A)



(B)

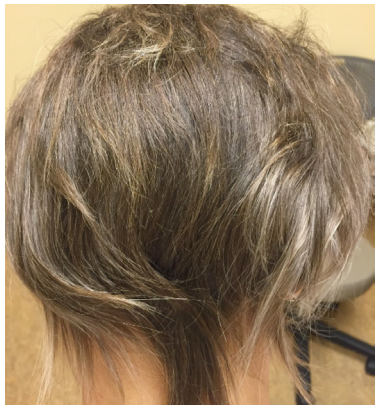
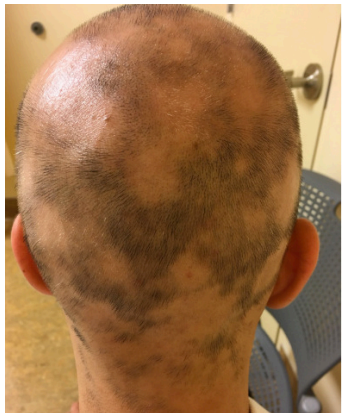
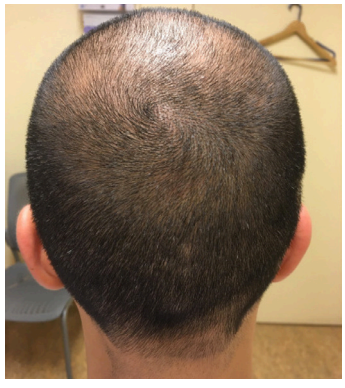


FIGURE 2. (A) Occipital scalp of patient 1.5 months after starting topical tofacitinib cream twice daily (A), 9 months after treatment with topical tofacitinib cream twice daily (B).

(A)



(B)



were trialed on significantly higher doses of tofacitinib (15-22 mg once daily) with only one patient unresponsive to both high and low dose treatment (15 mg once daily). This suggests that if no growth is seen after 3 months, the patient may be a

non-responder. If possible, higher dose treatment may be helpful in these patients. Three other studies have documented use of high dose tofacitinib (>5 mg twice daily),[7, 9-10] which demonstrated similar results.

In addition, our study indicates that judicious use of ILK in combination with tofacitinib may be helpful in attaining complete disease resolution as four of five patients with adjuvant ILK achieved >90% change in SALT score. (Figure 1A/B) Finally, we observed lack of treatment durability following cessation of treatment, similar to previous reports.[6,10]

Evidence for the use of topical JAK inhibitors in alopecia areata remains sparse. Currently, there exists a case series of pediatric patients treated with topical tofacitinib[11] and two case reports in literature of patients with AAU treated with topical ruloxitinib[12,13] 0.6%, one reporting 10% hair regrowth[12] and another reporting treatment failure.[18] Only one of our four patients treated with topical tofacitinib 2% cream was observed to have hair regrowth (Figure 2A/B). However, the patient's regrowth was robust with near complete resolution (post treatment SALT score 6.5%, 91.1% improvement in SALT score). During this period, the patient remained on several natural supplements which he had been taking prior to initiation of topical tofacitinib. No adverse effects were reported in this group.

This study also shows that most patients tolerated the medication well. While there is increased risk of serious infection and increased malignancy with higher dose oral tofacitinib, the safety of tofacitinib at 10 mg twice daily dosing has been demonstrated to be comparable to standard dosing in several clinical trials including phase IIa and IIb trials in psoriasis.[14] Notably, several of our patients were trialed on slightly higher doses (11 mg extended release twice daily). Of our patients on higher dose regimens, only one experienced an adverse effect (hyperlipidemia), which was mild. Notably, one patient developed multiple sclerosis (MS). Whether this can be attributable to the drug is unclear, particularly as the JAK/STAT pathway has been identified as a possible therapeutic target in animal models of MS.[15]

Tofacitinib administered orally and topically are exciting and promising treatment options for patients with longstanding, refractory AA. Additional studies are necessary to evaluate the safety and efficacy of JAK inhibitor treatment at both standard and higher doses. Topical tofacitinib may be an option for patients who cannot afford systemic tofacitinib treatment or tolerate the adverse effects. Given the apparent lack of durability following treatment cessation, long term studies of safety will be particularly important.

DISCLOSURES

The authors have no conflicts of interest to declare.

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