

Gut instinct: Using tofacitinib to treat alopecia areata in the context of comorbid inflammatory bowel disease



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INTRODUCTION

Alopecia areata (AA) is an autoimmune form of hair loss characterized by T-cell-mediated damage to hair follicles.¹ Inflammatory bowel disease (IBD) is an autoimmune disease of the bowel characterized by dysregulation of T cells, increased production of proinflammatory cytokines (eg, interleukin [IL] 6, IL-23, IL-12, and IL-21), and intestinal epithelial dysfunction.² Genome-wide association studies, performed separately in AA and IBD populations, reveal overlapping susceptibility loci in AA and Crohn disease (PRDX5 and IL-2RA) and AA and ulcerative colitis (UC) (IL-2/IL-21).^{3,4} The incidence of comorbid AA and IBD is unknown. Despite the success of biologics for the treatment of IBD, it may be that some biologics, in particular tumor necrosis factor α inhibitors, precipitate AA. The Janus kinase (JAK) inhibitor tofacitinib is approved for the treatment of UC, and there are several ongoing trials of other JAK inhibitors for IBD. JAK inhibitors are an emerging treatment for AA.^{1,5} In this study, we describe the results of treatment of patients with comorbid IBD and AA with tofacitinib.

CASE SERIES

We conducted a retrospective chart review of patients aged ≥ 18 years seen in the clinic of B.A.K. between July 2014 and August 2019 who had a diagnosis of both AA and either UC or Crohn disease

Abbreviations used:

AA:	alopecia areata
IBD:	inflammatory bowel disease
IL:	interleukin
JAK:	Janus kinase
UC:	ulcerative colitis

and who underwent treatment with tofacitinib. The patients had been referred for AA. Physician notes documenting patient encounters were reviewed. After discussing treatment options with the patients and their gastroenterologists, tofacitinib was started. Information regarding age, gender, disease course, and therapies was obtained. The patients' IBD status (ie, controlled or not) during treatment with tofacitinib was determined by the gastroenterologist.

A total of 9 patients with both AA and IBD underwent treatment with tofacitinib (Table I). The average age of onset of AA was 21.8 years (standard deviation, 13.2). The median severity of alopecia tool score was 100 (range, 45-100). Eight patients had a diagnosis of UC, and 1 had a diagnosis of Crohn disease. The onset of AA relative to that of IBD and vice versa was mixed (IBD developed prior to AA in 55.6% of the patients, AA developed first in 33.3%, and the order of the onset was unknown in 11.1%). Six of 7 patients with active IBD (85.7%) achieved remission of both IBD and AA with tofacitinib; 3 of

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Table I. Characteristics and outcomes of patients with comorbid AA and IBD treated with tofacitinib

Patient	Dx	Sex	Age (years) (at the time of chart review)	Onset of AA relative to IBD	IBD control with tofacitinib (Y/N)	Dose of tofacitinib, duration of tofacitinib treatment	Concomitant IBD therapies	SALT scores (prior to tofacitinib/ during tofacitinib)	Other comorbidities
1	UC	F	21	AA then UC	Y	Tofacitinib 10 mg BID, 34 months	None	100/0	
2	Crohn disease	F	36	Crohn disease then AA	Y	Investigational JAK inhibitor (for 6 months) followed by tofacitinib 5 mg BID, 10 months	None	100/0	
3	UC	F	22	AA then UC	Y	Tofacitinib 5 mg BID, 30 months	Mesalamine	45/0	
4	UC	M	53	UC then AA	N/A – UC in remission for years prior to tofacitinib for AA	Tofacitinib 5 mg BID, 42 months	None	100/5	
5	UC	F	35	Unknown	N	Tofacitinib 15 mg QD, 5 months	None	100/100	Atopic dermatitis, juvenile RA
6	UC	F	62	UC then AA	N/A – UC inactive prior to tofacitinib for AA (s/p colectomy)	Tofacitinib 5 mg BID, 31 months (taking for RA)	None	100/100	Atopic dermatitis, celiac disease, hypothyroidism, RA
7	UC	F	21	UC then AA	Y	Tofacitinib 5 mg QD (tapered from 10 mg BID), 27 months*	Vedolizumab	100/0	Atopic dermatitis
8	UC	M	50	AA then UC	Y	Tofacitinib 5 mg BID (tapered from 10 mg BID), 24 months	None	50/0	
9	UC	M	37	UC then AA	Y	Tofacitinib 10 mg BID, 14 months*	Infrequent mesalamine	99/15	Vitiligo

AA, Alopecia areata; BID, twice a day; Dx, diagnosis; F, female; IBD, inflammatory bowel disease; JAK, Janus kinase; M, male; N, no; N/A, not available; QD, daily; RA, rheumatoid arthritis; SALT, severity of alopecia tool; s/p, status post; UC, ulcerative colitis; Y, yes.

*Patient 7 was treated with intralesional triamcinolone as needed, and patient 9 was treated with minoxidil 2.5 mg twice daily plus intralesional triamcinolone as needed.

these patients received concomitant therapy for their IBD, and 2 received concomitant therapy for their AA (Table 1). One patient (patient 5) did not experience control of either her UC or AA with tofacitinib.

This study was limited by the relatively small number of patients, possible selection bias, and generalizability, as the patients came from a single provider clinic.

DISCUSSION

Autoimmune comorbidities are common in patients with AA. While it is unknown how often IBD and AA co-occur in the same patient, in our experience IBD (UC, in particular) is not rare in patients with AA. Indeed, the pathobiology of AA and IBD may overlap,¹⁻⁴ and data support a therapeutic role for JAK inhibitors in the treatment of both diseases.^{1,2,5} Indeed, our data show successful treatment of both IBD and AA in a small cohort of patients. It is notable that the majority of the patients had UC, and clinical trial data supports use of tofacitinib for patients with UC. The one patient with Crohn disease also responded, but, in general,

there is conflicting evidence regarding the treatment of Crohn disease with tofacitinib.

Therapeutic decision-making can be complex in patients with multiple autoimmune diseases, such as AA and IBD. In such patients, it would be preferable to treat more than 1 disease with a single agent. Toward this end, JAK inhibitors should be considered in patients with comorbid AA and IBD.

REFERENCES

1. Xing L, Dai Z, Jabbari A, et al. Alopecia areata is driven by cytotoxic T lymphocytes and is reversed by JAK inhibition. *Nat Med*. 2014;20(9):1043-1049.
2. Salas A, Hernandez-Rocha C, Duijvestein M, et al. JAK-STAT pathway targeting for the treatment of inflammatory bowel disease. *Nat Rev Gastroenterol Hepatol*. 2020;17(6):323-337.
3. Festen EAM, Goyette P, Scott R, et al. Genetic variants in the region harbouring IL2/IL21 associated with ulcerative colitis. *Gut*. 2009;58(6):799-804.
4. Petukhova L, Duvic M, Hordinsky M, et al. Genome-wide association study in alopecia areata implicates both innate and adaptive immunity. *Nature*. 2010;466(7302):113-117.
5. Liu LY, Craiglow BG, Dai F, King BA. Tofacitinib for the treatment of severe alopecia areata and variants: a study of 90 patients. *J Am Acad Dermatol*. 2017;76(1):22-28.