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REFERENCES

1. Arenas Miras Mdel M, Hidalgo-Tenorio C, Jimenez-Gamiz P, Jiménez-Alonso J. Diagnosis of latent tuberculosis in patients with systemic lupus erythematosus: t.SPOT.TB versus tuberculin skin test. *Biomed Res Int*. 2014;2014:291031.
2. Frequently asked questions for healthcare providers. Available at: https://www.quantiferon.com/us/products/quantiferon-tb-gold-plus-us/provider-resources/provider-faq/. Accessed December 30, 2018.
3. Wallace DJ, Gudsoorkar VS, Weisman MH, Venuturupalli SR. New insights into mechanisms of therapeutic effects of antimalarial agents in SLE. *Nat Rev Rheumatol*. 2012;8:522-533.
4. van den Borne BE, Dijkmans BA, de Rooij HH, le Cessie S, Verweij CL. Chloroquine and hydroxychloroquine equally affect tumor necrosis factor-alpha, interleukin 6, and interferon-gamma production by peripheral blood mononuclear cells. *J Rheumatol*. 1997;24:55-60.

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Tofacitinib therapy for children with severe alopecia areata

To the Editor: Alopecia areata (AA) is a common autoimmune disorder that might progress to alopecia totalis (AT) and alopecia universalis (AU), which significantly affect patients' psychologic well-being and quality of life. The disease can start at any age, but severe forms often start during childhood. Several studies and case reports have shown promising results of using Janus kinase (JAK) inhibitors for the treatment of AA.[1] Previous case series have reported the use of systemic tofacitinib in adolescent patients aged 12 to 19 years and the use of topical tofacitinib and ruxolitinib in pediatric patients aged 3 to 17 years.[2-4] A recent case series showed favorable response to systemic tofacitinib among 4 patients with AA aged 8 to 10 years.[5] In this report, we have presented 3 children aged 5 years or younger with AT and AU treated with systemic tofacitinib.

We reviewed the records of patients with AA, AT, or AU who were treated with tofacitinib in the Taipei Veterans General Hospital between January 2016 and January 2018. The inclusion criteria were patient age less than 12 years, a clinical diagnosis of AA with at least 50% scalp hair loss, AT, AU, stable or worsening disease for at least 6 months, and treatment with tofacitinib for at least 4 months. Disease severity was assessed by dermatologists using the validated Severity of Alopecia Tool (SALT) score. Safety was evaluated by physical examinations; review of systems; and laboratory monitoring, including complete blood count with differential, complete metabolic panel, and fasting lipid panel before treatment, after 4 weeks of treatment and then every 3 months. This study was approved by the institutional review board of Taipei Veterans General Hospital (2018-01-018AC).

The baseline characteristics and treatment response are shown in Table I. We identified 3 pediatric patients who failed previous treatment before tofacitinib therapy. All patients were treated with tofacitinib, 2.5 mg once daily, in the beginning. Patient 3 experienced unsatisfactory hair regrowth (<20% improvement) after 6 months of treatment; thereafter, the patient's dose was adjusted to 2.5 mg once daily for 4 doses and 5 mg once daily for the other 3 doses each week. One patient achieved greater than 90% hair regrowth after 12 months of treatment (Patient 2, Fig 1), and the other 2 patients showed greater than 50% improvement by 6 months and 21 months, respectively. Patient 3 had complete regrowth of the eyebrows and eyelashes and partial regrowth of the scalp hair. Although response was not complete, we decided to continue treatment at the same dose, as there are no safety data for higher-dose tofacitinib in such young children and the parents did not wish to consider other treatments such as systemic corticosteroids because of the potential side effects. The side effects were mild and limited to diarrhea (patients 1 and 3) and upper respiratory tract infection (patient 2). These symptoms resolved completely despite ongoing therapy.

Table I. Baseline characteristics and response to treatment with tofacitinib

Patient	Sex	Age, y	Age of onset, y	Weight, kg	AA subtype	Duration of current episode, mo	Previous treatment	Initial SALT score	Latest SALT score	Tofacitinib dose	Duration of therapy, mo
1	M	4	3	17	AT	6	TCS, ILTAC	100	50	2.5 mg QD	6
2	M	4	3	17	AT	9	TCS, ILTAC	100	6	2.5 mg QD	12
3	F	5	2	19	AU	20	TCS, ILTAC, DPCP	100	41	2.5 mg QD for 6 mo, then 2.5 mg QD for 4 doses and 5 mg QD for the other 3 doses each wk	21

AT, Alopecia totalis; *AU*, alopecia universalis; *DPCP*, diphenylcyclopropenone; *F*, female; *ILTAC*, intralesional triamcinolone; *M*, male; *QD*, once daily; SALT, Severity of Alopecia Tool; *TCS*, topical corticosteroids.

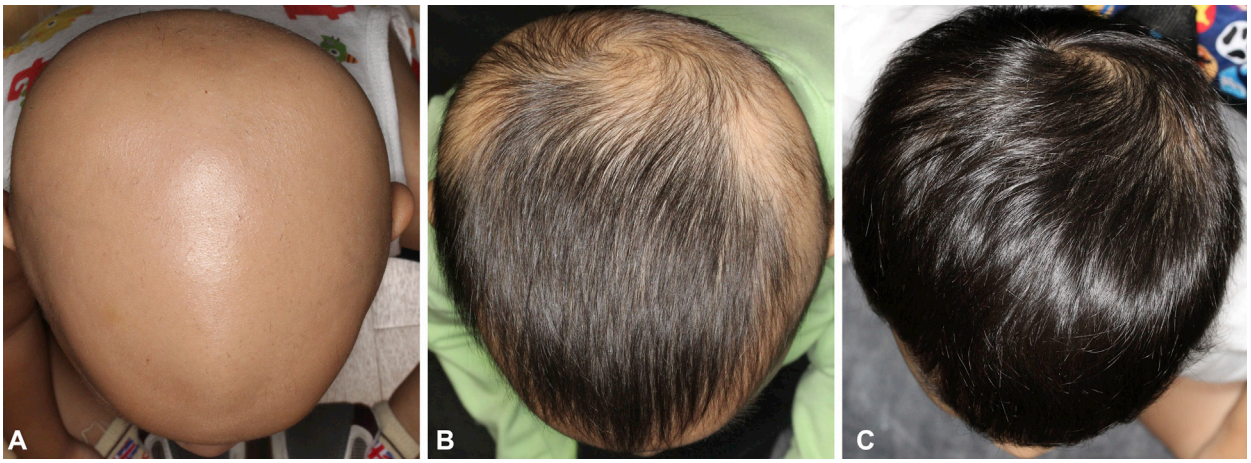

Fig 1. Patient 2 with alopecia totalis at baseline (**A**) and after 6 months (**B**) and 12 months (**C**) of tofacitinib treatment.

All patients are currently continuing to receive tofacitinib therapy.

Although the long-term safety of JAK inhibitors in children is still unknown, tofacitinib is undergoing clinical trials for juvenile idiopathic arthritis in children aged 2 to 18 years (NCT02592434 and NCT01500551). The dose of 2.5 mg daily based on the weight of our patients is lower than the standard dose being used in the aforementioned clinical trials (3.5 mg), whereas the treatment response is satisfactory in our patients. In agreement with previous reports, our experience suggests that tofacitinib may be a therapeutic option for children with severe AA who have failed conventional therapy. However, because of the potential for serious adverse effects with JAK inhibitors, including infection and malignancy, a thorough discussion of risks and benefits is necessary before the initiation of treatment.

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REFERENCES

1. Liu LY, Craiglow BG, Dai F, et al. Tofacitinib for the treatment of severe alopecia areata and variants: a study of 90 patients. *J Am Acad Dermatol*. 2017;76(1):22-28.

2. Bayart CB, DeNiro KL, Brichta L, et al. Topical Janus kinase inhibitors for the treatment of pediatric alopecia areata. *J Am Acad Dermatol*. 2017;77(1):167-170.
3. Liu LY, Craiglow BG, King BA. Tofacitinib 2% ointment, a topical Janus kinase inhibitor, for the treatment of alopecia areata: a pilot study of 10 patients. *J Am Acad Dermatol*. 2018; 78(2):403-404.e401.
4. Craiglow BG, Liu LY, King BA. Tofacitinib for the treatment of alopecia areata and variants in adolescents. *J Am Acad Dermatol*. 2017;76(1):29-32.
5. Craiglow BG, King BA. Tofacitinib for the treatment of alopecia areata in preadolescent children. *J Am Acad Dermatol*. 2019; 80(2):568-570.

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A retrospective review of dupilumab for atopic dermatitis patients with allergic contact dermatitis

To the Editor: Allergic contact dermatitis (ACD) is a delayed hypersensitivity reaction with increased incidence in patients with atopic dermatitis (AD). In studies examining the pathogenesis of AD, the T-cell helper 2 (T_H2) and T_H22 pathways have predominantly been identified, with the T_H17 and T_H1 cells contributing as well.[1] Other studies have shown a role for similar cytokines in ACD (interferon γ, interleukin [IL] 5, IL-9, IL-10, IL-13, and IL-22), with the response varying by allergen.[2,3]

Dupilumab, a monoclonal antibody against the α subunit of the IL-4 receptor, is approved for the treatment of moderate-to-severe AD. It is unknown whether dupilumab will have efficacy in those who have AD with overlying ACD. The purpose of this study was to evaluate the response to dupilumab in these patients.

A retrospective chart review was performed on patients prescribed dupilumab at Tufts Medical Center. We collected information about demographics, diagnosis, treatments, and disease progression during 2017-2018. We excluded patients with diagnoses other than AD and a lack of follow-up information. Of the 126 patients prescribed dupilumab, only 64 patients qualified for inclusion. An analysis was performed with the following patient subsets: those with ACD confirmed by patch testing (n = 17), ACD suspected on the basis of clinical findings (n = 14), and ACD not suspected (n = 33).

Table I summarizes the demographics and dupilumab responses. Overall, an average of 4 different therapies failed before the patients were

Table I. Patient descriptions and dupilumab responses

Category	ACD confirmed	ACD suspected	ACD unsuspected
Demographics	n = 17	n = 14	n = 33
Sex, n			
Male	5	8	20
Female	12	6	13
Age, y, mean ± SD	44 ± 18	44 ± 21	46 ± 19
Race/ethnicity, n			
White, non-Hispanic	10	6	15
Black, non-Hispanic	1	3	3
Hispanic	0	0	4
Asian	5	3	10
Unknown/other	1	2	1
IGA response	n = 14	n = 11	n = 21
Average initial IGA (0-4)	3.2 ± 0.7	3.3 + 0.5	3.4 ± 0.8
Average final IGA (0-4)	1.1 ± 1.2	1.2 ± 1.3	1.9 ± 1.3
% with final IGA of 0 or 1	57	73	48
% with improving IGA	79	73	86
BSA response	n = 16	n = 10	n = 28
Initial BSA involvement, %	32 ± 29	43 ± 37	18 ± 22
Final BSA involvement, %	3 ± 8	7 ± 13	4 ± 7
% with improving BSA	82	83	83
Average % change in BSA	71 + 42	69 ± 39	52 ± 73
Pruritis response, %	n = 13	n = 12	n = 25
Resolved	23	33	24
Improved	100	100	92
Not improved	0	0	6

ACD, Allergic contact dermatitis; *BSA*, body surface area; *IGA*, Investigator's Global Assessment; *SD*, standard deviation.