Refractory moderate-to-severe paediatric-onset alopecia areata with elevated serum IgE treated by JAK inhibitors

Dear Editor,

The management of refractory moderate-to-severe paediatric alopecia areata (AA) is challenging because of the high recurrence and ineffectiveness of the current therapeutic strategies. Although multiple therapeutic strategies have been explored in AA, no treatments have been completely effective. Baricitinib has been approved for the treatment of adult moderate-to-severe AA. However, the efficacy and safety of JAK inhibitors need to be evaluated in children.

Here, we report five cases of refractory moderate-to-severe paediatric-onset AA successfully treated either by baricitinib or tofacitinib. Refractory AA was defined as patients who had no response to standard therapies for at least 6 months, including minoxidil liniment, pilatory, oral glucocorticoids, enteric-coated thymopeptides, and Chinese medicines. Detailed medical information was obtained, and necessary laboratory tests were conducted to rule out contraindications (blood disorders, cancers, active infections, and a history of active tuberculosis, etc.) before the initiation of JAK inhibitors. These patients were treated with baricitinib 2 mg/day or tofacitinib 10 mg/day and underwent monthly follow-up. Since tofacitinib is more commonly used in children below 10 years than baricitinib, as per the previous reports, we preferred to choose tofacitinib in this age group.[1] Two dermatologists assessed the severity of alopecia using the SALT (Scoring of Alopecia Tool) and AASIS (Alopecia Areata Symptom Impact Scale) scores at baseline and every month. Complete blood count, C-reactive protein, fasting lipid profile, liver and kidney functions, and blood coagulation tests were conducted for all patients at baseline and every 3 months during the treatment course. Serum IgE levels were determined in all patients before treatment using chemiluminescence assay (Siemens AG, Germany). Normal reference values for serum IgE were identified as follows: 1–5 years: 0–60 IU/mL, 6–9 years: 0–90 IU/mL, and 10–15 years: 0–200 IU/mL.

The characteristics of study patients have been summarised in Table 1. The age of onset ranged from 4 to 15 years, with

Table 1: The characteristics of 5 alopecia areata teenage patients

Case	Onset age(y)/ gender/ duration	body weight (kg)	Previous treatment	Allergic history	Accompanying disease	Treatment and course (m)	Adverse event	Initial SALT score	Latest SALT score	baseline IgE(IU/ mL)
1	10/M/1 y	46.5	Minoxidil, Chinese medicine	N	N	Tofacitinib 5 mg BID, twice a day for 6 m, tapered to 5 mg QD, once a day for 2 m	N	85	4	232
2	11/F/2 y	48.5	Minoxidil, Ciclosporin	N	CHD, thyroid nodule	Tofacitinib 5 mg BiD for 6 m	N	88	55	57.5
3	4/M/4 y	45	systemic glucocorticoids, ILCSs, Chinese medicine	allergic rhinitis	N	Tofacitinib 5 mg BiD for 8 m, tapered to 5 mg QD for 3 m	elevated liver transaminase	100	10	200
4	10/M/5 y	62.5	minoxidil liniment, thymopeptide capsule, pilatory	N	N	Baricitinib 2 mg QD for 8 m	N	100	9	>1130
5	15/M/6 m	65	minoxidil liniment, Pilatory, Chinese medicine	N	N	Tofacitinib 5 mg BID for 15 m, tapered to 5 mg QD for 2 m	N	100	0	25.7

M: male, F: female, y: year, m: month, N: none, CHD: congenital heart disease, ILCSs; Intralesional glucocorticosteroid.

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a male-to-female ratio of 4:1, and all patients received JAK inhibitors (4 received tofacitinib, and 1 received baricitinib) for at least 6 months, with a median therapeutic course of 8 months (range 6–15 months). By the end of the study period, all five patients had achieved SALT 75 improvement, and 80% patients experienced 90% hair regrowth. Dynamic changes in SALT and AASIS scores from baseline and during the treatment are shown in [Figure 1]. Photos of the patients before and after treatment are shown in [Figure 2]. No significant adverse effects were observed during the administration. Two patients relapsed 7–10 days after the discontinuation of JAK inhibitors, but the condition ameliorated again after JAK inhibitors were resumed. Three patients had the tofacitinib dose reduced to 5mg/day after achieving cosmetically acceptable hair regrowth, as recommended by the physician, and no AA flares were observed during the following 2 to 3 months' surveillance period. Around 80% of patients are still on therapy with JAK inhibitors and are followed up monthly.

Interestingly, we noted that 71.4% patients exhibited high serum IgE levels, which may contribute to the intractable and severity of the disease. Elevated serum IgE levels in AA have been elaborated in several studies, which were considered to be involved with Th2 immune responses.[2] JAK inhibitors can reduce inflammation by preventing signal transduction and reduce the phosphorylation and activation of signal transduction and transcription factors (STAT) by blocking JAK. Furthermore, we noted that among the three patients, one exhibited a reduction in serum IgE levels within the normal range following 3 months of oral tofacitinib administration.

To date, only five reports including 59 cases documented baricitinib in paediatric AA. The majority of paediatric AA cases were treated with tofacitinib, with an estimated 95 cases from one prospective, single-centre study, one retrospective study, and case reports.[3,4] Upadacitinib (2 cases), Ritlecitinib (105 cases), and Ruxolitinib (4 cases) were also prescribed in paediatric AA in previous reports. Hair regrowth was

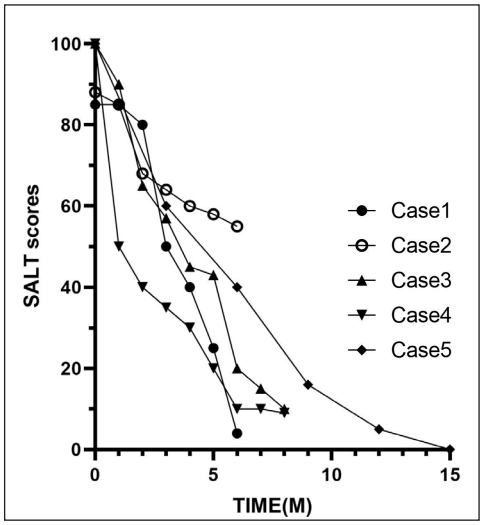

Figure 1a: All 5 patients had an improvement in the SALT scores throughout the treatment.

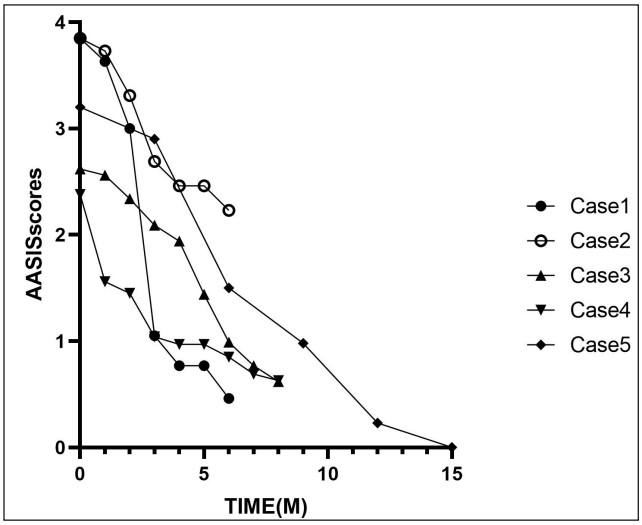

Figure 1b: All 5 patients had a decrease in AASIS scores throughout the treatment.

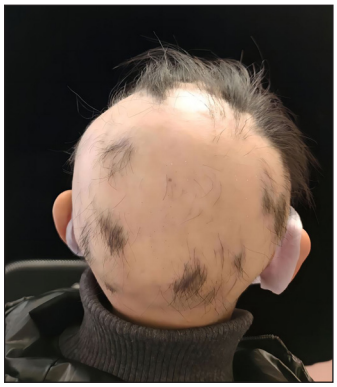

Figure 2a: Case 1 before treatment.

Figure 2b: After treatment of tofacitinib for 6 months, Case 1 showed rapid hair recovery and the SALT score decreased from 85 to 4.

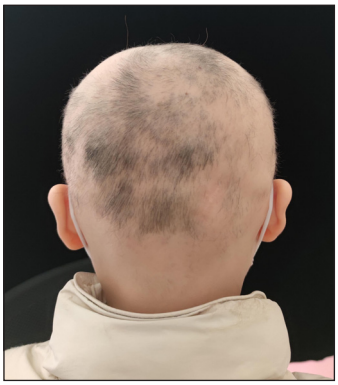

Figure 2c: Case 2 before treatment.

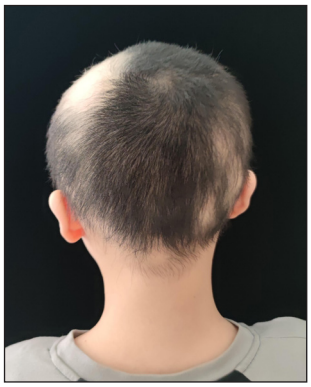

Figure 2d: Case 2, an 11-year-old girl, achieved obvious hair regrowth after 6 months of tofacitinib treatment, with an improvement in the SALT score from 88 to 55.

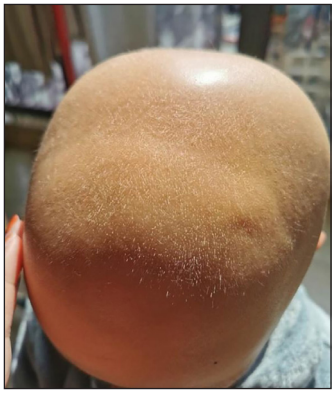

Figure 2e: Case 3 before treatment.

Figure 2f: After treatment of tofacitinib for 8 months, Case 3 showed significant hair recovery and the SALT score decreased from 100 to 10.

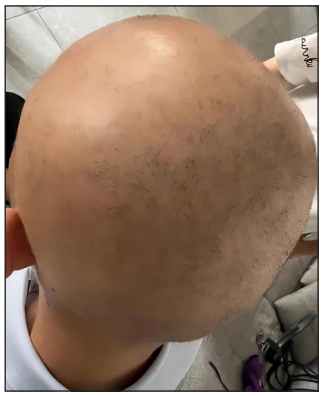

Figure 2g: Case 4 before treatment.

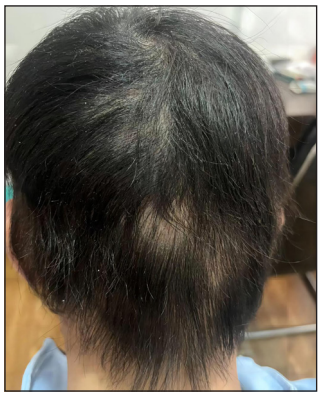

Figure 2h: Case 4 after 8 months of tofacitinib treatment showed an improvement in the SALT score from 100 to 9.

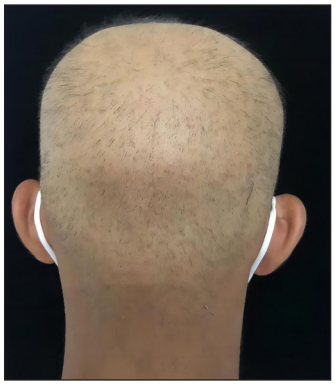

Figure 2i: Case 5 before treatment.

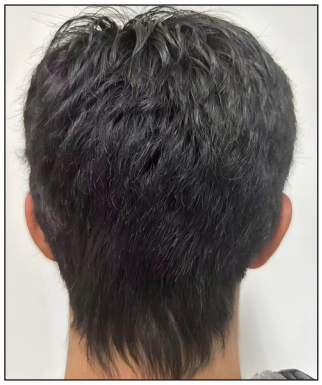

Figure 2j: Case 5 after treatment. He had a complete response after 15 months of baricitinib treatment.

achieved in most patients after oral JAK inhibitors with an estimated efficiency of 88.21% (95% CI 88.13–88.29%).[1] Adverse effects were mild and well tolerated. However, there is no long-term follow-up data on the treatment of JAK inhibitors in paediatric AA, and no standardised guidelines were formulated for the maintenance therapy and tapering of dosage.

A systematic review of tofacitinib in paediatric AA demonstrated an overall incidence rate of adverse events of 21%, most of which were mild and self-limiting.[5] Therefore, JAK inhibitors have been considered to be promising agents with a low incidence of adverse events in the treatment of refractory paediatric AA. However, long-term surveillance studies with a larger sample size are required to evaluate the overall safety and adverse events in clinical settings.

Ethical approval

This study was approved by the Institutional Review Board of Jinling Hospital, Medical School of Nanjing University, Nanjing, number 2023DZGZR-055, dated 2023-03-10.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)–assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)–assisted technology for assistance in the writing or editing of the manuscript, and no images were manipulated using AI.

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