Combination of oral tofacitinib and oral mini-pulse with betamethasone (T-OMP) for the successful treatment of long-standing alopecia universalis: A real-world experience in a recalcitrant disease

Dear Editor,

The hair regrowth in alopecia areata (AA) following oral tofacitinib is frequently partial and slow in onset, reportedly after a mean treatment duration of 4 months.[1] Additionally, the regrowth rates are abysmally low in patients with alopecia Universalis (AU) with any therapy.

We report a series of extensive AA/AU patients who had been treated with a combination of oral mini-pulse therapy (OMP) and tofacitinib over the past 4 years (February 2021 to February 2025). All patients with long-standing (>12 months duration), mean SALT (Severity of Alopecia Tool) score of 100 and aged ≥12 years were treated. Patients with a lymphocyte count < 500 cells/mm^3, an absolute neutrophil count < 1,000 cells/mm^3, haemoglobin level < 9 g/dL, pre-existing immunosuppression, active tuberculosis or serious infections, severe hepatic impairment, use of combined oral contraceptives, malignancy, or physiological conditions like pregnancy/lactation, were excluded from this regimen. Out of the examined 10 patients with AU, four met the above criteria and were treated with the combination therapy following detailed laboratory evaluation of complete haemogram, liver and renal function tests, viral markers, lipid profile, chest X-ray, Mantoux test, and electrocardiogram. The regime comprised of OMP using tablet betamethasone (5 mg) on two consecutive days in a week in combination with tablet tofacitinib, which was started with 5 mg on alternate days for the first week followed by once daily for 2 weeks and then hiked to twice daily. Our approach was to taper and stop OMP within the 1st year, following which oral azathioprine or apremilast would be used for maintenance. An attempt would be made for tapering and discontinuing tofacitinib (Twice daily →once daily→alternate day→Stop).

Over a mean follow-up period of 38.25 months (30 to 47 months), the patients received OMP for a mean period of 9 months with a median cumulative prednisolone equivalent dose of 988±653 mg, and they received tofacitinib for an average period of 38.3±7.1 months [Table 1]. The earliest hair regrowth was seen after a mean period of 3.75±1.7 weeks with the mean time to complete hair growth being 23±3.8 weeks [Figure 1 and Table 1]. We noticed that the first areas to show response were frontal and vertex regions, and the last to respond was the occipital area. All our patients were able to discontinue OMP, but none could be weaned off tofacitinib over the study period. In total, three patients had mild to moderate relapse (between 5 to 30% of scalp) with a median time to relapse being 2 weeks after stoppage of tofacitinib and OMP. The increment in the respective drugs (along with the addition of adjuvants in 2 patients) achieved control.

Two patients developed transient nasal stuffiness, gastritis, and transient facial puffiness, which were relieved by symptomatic treatment and OMP tapering (for facial puffiness). One patient developed an acneiform eruption on the face and trunk during the OMP phase only, and it was controlled with topical benzoyl peroxide 2.5%. All patients remained free from any cardiac, haematological, or biochemical abnormalities.

Published literature indicates that patients resistant to systemic corticosteroids may respond to tofacitinib.[2] Furthermore, patients who are resistant to tofacitinib monotherapy could respond to combination therapy of tofacitinib and prednisone.[3] Both the time to initiation of hair regrowth and the proportion of patients with complete regrowth were much higher in our series of AU patients (2 weeks and 100%, respectively) as

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Table 1: General characteristics and details of treatment and clinical response in patients

S.No	Sex	Age (yrs)	Disease duration at presentation in months	AA type	OMP in months and total cumulative dose (prednisolone equivalent)	Tofacitinib in months, current status	Visible regrowth (weeks)	$SALT_{50}$ (weeks)	$SALT_{100}$ (weeks)	Facial and Body hair regrowth	Adjuvant (after stoppage of OMP)	Relapse	Side effects of the combination therapy
1.	F	37	24	Universalis	9 (550 mg)	47, 5 mg once daily	6	12	24	Complete	Apremilast (40 mg/day)	Within 1 week of stoppage of tofacitinib, currently controlled on tofacitinib 5 mg once daily and occasional intralesional triamcinolone.	Pharyngitis, gastritis, transient facial puffiness
2.	M	22	18	Universalis	11 (1638 mg)	36, 5 mg twice daily	4	11	20	Complete	Azathioprine (50 to 100 mg/day), added after relapse	Within 2 weeks of the stoppage of OMP. OMP restarted and stopped over another 3 months. Occasional intralesional triamcinolone.	Facial and truncal acneiform eruption, transient facial puffiness
3.	F	18	72 for universal, 156 for areata	Universalis	3 (300 mg)	40, 5 mg once daily	3	8	28	Facial complete, body negligible	Azathioprine (50 to 100 mg/day)	Within a month of tapering tofacitinib to 5 mg OD, able to maintain in a combination with azathioprine. Occasional intralesional triamcinolone.	Pharyngitis, gastritis
4.	F	15	18	Universalis	12 (1425 mg)	30, 5 mg twice daily and then lost to follow-up	2	12	20	Facial complete, body partial (30-40%)	Apremilast (40 mg/day)	No	None

compared to existing literature on treatment of AA with either tofacitinib monotherapy (2.2 months and 45.7%),[4] OMP monotherapy (1 month and 43.7%)[5] or with combination of tofacitinib and steroids ($SALT_{100}$ in 26.1%).[3] The mean cumulative dose of steroids was also lower in our series than in the study by Zhang *et al*.[3] A small sample size and lack of clearly defined treatment endpoints were limitations of our study. The rationale behind our combination regimen included the resistant nature and immense psychological burden of the disease in our patients, an unmet need with existing therapies, and the general paucity of effective treatment modalities for AU in existing literature.

Achievement and maintenance of complete hair regrowth in AU is a huge challenge, and we tried this combination regimen with gratifying results. We observed rapid and complete hair regrowth without any need for higher dose (>10 mg/day) of oral tofacitinib. This combination is relatively safe, and appears to be a promising treatment alternative.

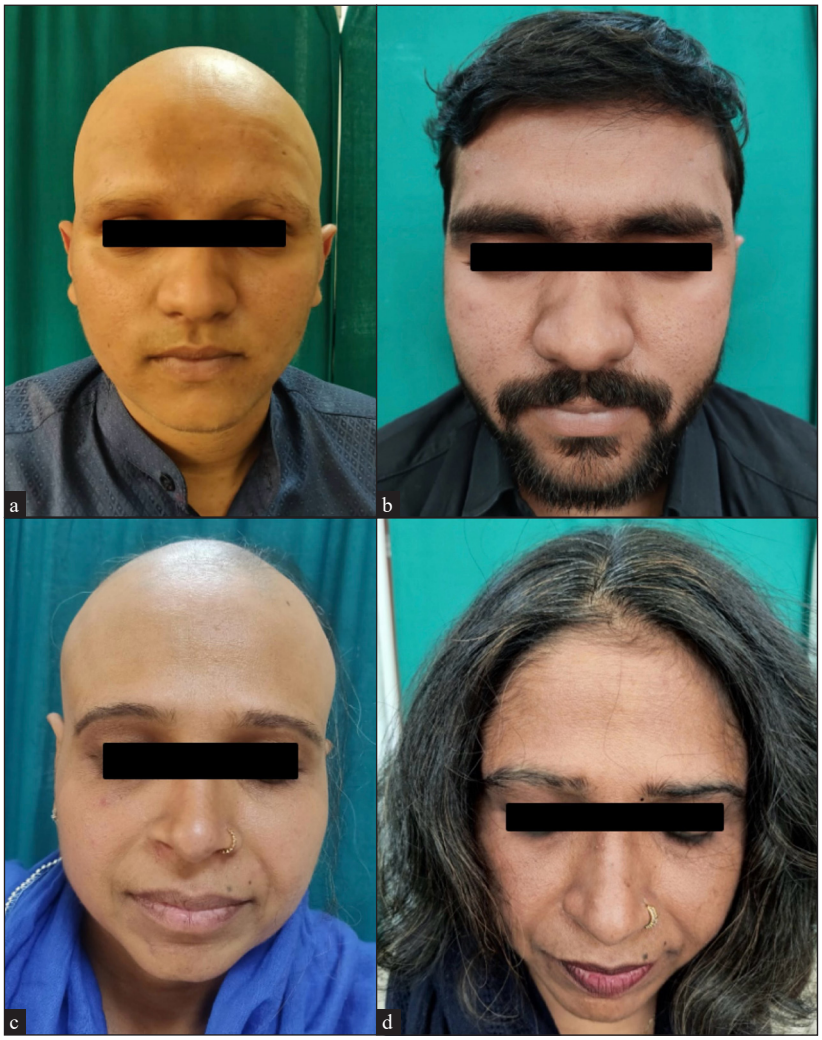

Figure 1: (a) 22-year-old man with alopecia universalis before treatment, (b) complete hair regrowth at 5 months, and (c) 37-year-old woman with alopecia totalis before treatment, (d) complete hair regrowth at 6 months of OMP combined with oral tofacitinib.

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