Relationship of Hair Regrowth Pattern in Alopecia Areata Patches According to DIMT Classification with Treatment Modalities and Patch Size: A Retrospective Cross-Sectional Analysis

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Background: The morphology of hair regrowth in alopecia areata (AA) patches could be classified into four types, namely diffuse, irregular, marginal, and targetoid patterns, according to the DIMT classification. However, factors affecting hair regrowth patterns have not been investigated.
Objective: We investigated whether the DIMT-classified hair regrowth patterns of AA patches are associated with treatment modality and patch size.
Methods: We conducted a retrospective, cross-sectional study of 152 AA patches with hair regrowth.
Results: The associations between the diffuse pattern and patch size >2 cm (*p*=0.006; odds ratio [OR]: 0.36, 95% confidence interval [CI]: 0.17~0.74), between the irregular pattern and triamcinolone acetonide intralesional injection (*p*<0.001; OR: 274.87, 95% CI: 25.75~2,933.56), between the marginal pattern and systemic and topical corticosteroid (*p*=0.018; OR: 4.89, 95% CI: 1.31~18.27), and between the targetoid pattern and patch size >2 cm (*p*=0.028; OR: 2.50, 95% CI: 1.10~5.68) were statistically significant.
Conclusion: Treatment modalities and patch size are the factors affecting hair regrowth patterns in AA patches.

Keywords: Alopecia areata, DIMT classification, Hair regrowth, Therapeutics

INTRODUCTION

We previously suggested DIMT classification as the morphological classification system for hair regrowth patterns in alopecia areata (AA) patches; it includes diffuse (D), irregular (I), marginal (M), and targetoid (T) patterns (Fig. 1)[1]. It has been speculated that such hair regrowth patterns are influenced by various factors, such as the clinical subtypes of AA, treatment modalities, and demographics[1,2]. However, factors affecting hair regrowth patterns have not been investigated. Because hair regrowth patterns could vary depending on the treatment modalities or AA patch size, the objective of the present study was to investigate whether the DIMT-classified hair regrowth patterns in AA patches are associated with treatment modality and patch size.

MATERIALS AND METHODS

We conducted a retrospective cross-sectional study of patients with AA who attended the outpatient clinic of the Department of Dermatology at Wonju Severance Christian Hospital, Wonju, Korea, between December 2016 and February 2019. We reviewed serial clinical photographs of the scalps of AA patients, and those with hair regrowth on AA patches were included in our study. The inclusion criteria for our study was as follows: 1) patients who first visited the clinic during the included pe-

riod; 2) patients who visited two times or more; and 3) patients who had taken serial photos for regrowth evaluation. The hair regrowth pattern was determined by comparing the baseline and follow-up photographs and by agreement of four different dermatologists (SH, HI, JW, and SH). The hair regrowth morphologies were classified into four types, diffuse, irregular, marginal, and targetoid, according to DIMT classification. The patients' electronic medical records were reviewed for relevant clinical and demographic data. The AA treatment modalities were classified into four types: topical corticosteroid only (TCS), diphenylcyclopropenone contact immunotherapy (DPCP), systemic and topical corticosteroid (SCS), and 5 mg/ml of triamcinolone acetonide intralesional injection (TA ILI). The AA patches were classified into two groups according to size: ≤2 cm and >2 cm. The cut-off defining smaller and larger lesions was determined as 2 cm to ensure balance between the two groups.

Ethics statement

This study was conducted in accordance with the Declaration of Helsinki and International Conference on Harmonization and Good Clinical Practice Guidelines. This study was approved by the institutional review board of Wonju Severance Christian Hospital (CR318309). Written informed consent was obtained from all subjects before study enrollment.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics ver. 20.0 (IBM Corp., Armonk, NY, USA). Univariate and multivariate analyses were performed to determine the relationships between hair regrowth patterns and treatment modality and AA patch size. $p<0.05$ was considered statistically significant.

RESULTS

Of the 99 patients, 51 were included in our study: 31 were male, and 20 were female, and the mean age was 40.1 years. Most of the excluded patients were lost to follow-up. All the patients had patchy-type AA[3,4], which is defined by one or
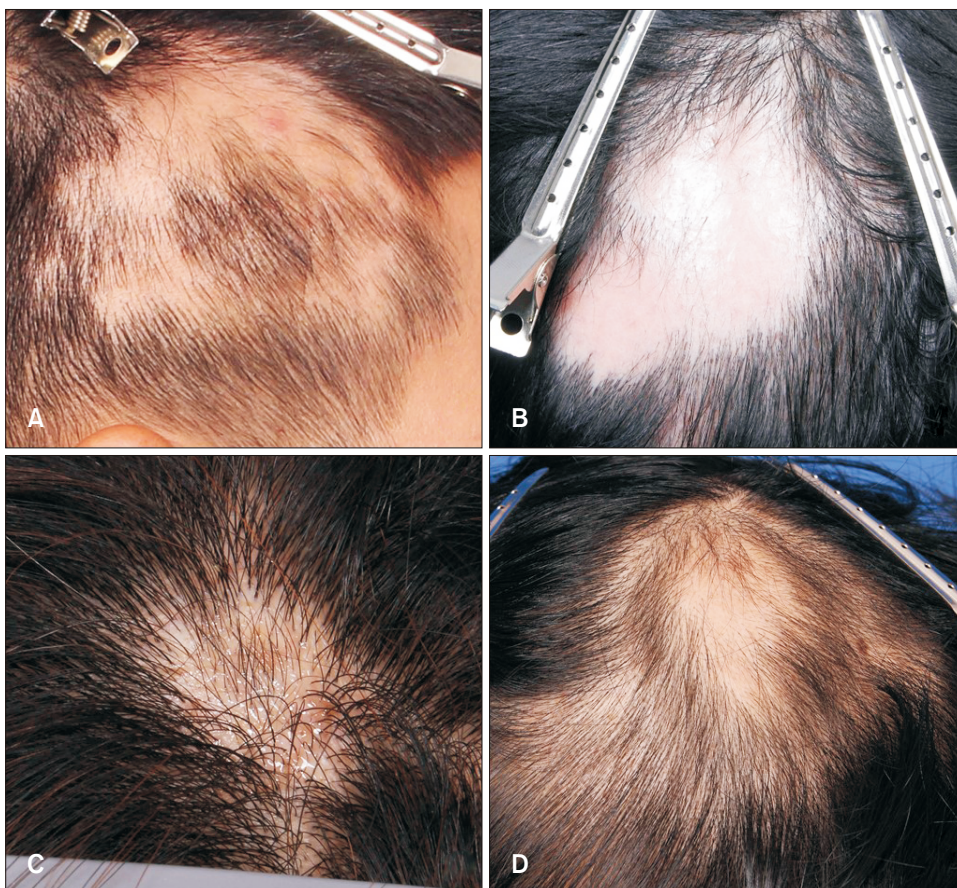

Fig. 1. Hair regrowth patterns according to treatment modalities and patch size. (A) Irregular hair regrowth pattern after treatment with triamcinolone acetonide intralesional injection. (B) Marginal hair regrowth pattern after treatment with systemic and topical corticosteroid. (C) Diffuse hair regrowth pattern in alopecia areata patches ≤2 cm in diameter. (D) Targetoid hair regrowth pattern in alopecia areata patches >2 cm in diameter.

more circumscribed AA patches. The clinical and demographic data of the study population are shown in Table 1. There were significant differences in age (p=0.016), number of total patches (p=0.01), and mean patch size (p=0.023) between the treatment subgroups. In total, 152 AA patches showing hair regrowth were analyzed (Table 2). Overall, a diffuse hair regrowth pattern was the most frequently observed (n=57, 37.5%), followed by the marginal (n=43, 28.3%), targetoid (n=36, 23.7%), and irregular hair regrowth patterns (n=16, 10.5%). TCS was the most common treatment modality used (n=34, 66.7%), followed by TA ILI (n=10, 19.6%), DPCP (n=4, 7.8%), and SCS (n=3, 5.9%) in this order (Table 1). No other types of treatment were prescribed or performed for AA management. The univariate analysis revealed that an irregular hair regrowth pattern was more frequently observed in AA patches treated with TA ILI than in those treated by any other modality (all p<0.001). Moreover, the marginal hair regrowth pattern was more frequently observed in the AA patches treated with SCS than in those treated with TA ILI (p=0.013). The diffuse hair regrowth pattern was more frequent in AA patches ≤2 cm (p=0.008). In contrast, the irregular hair regrowth pattern was more frequent in AA patches >2 cm (p=0.045). The multivariate analysis revealed that the diffuse hair regrowth pattern was less frequent in the patches >2 cm (p=0.006; odds ratio [OR]: 0.36, 95% confidence interval [CI]: 0.17~0.74). The associations between the irregular pattern and TA ILI (p<0.001; OR: 274.87, 95% CI: 25.75~2,933.56), between the marginal pattern and SCS (p=0.018; OR: 4.89, 95% CI: 1.31~18.27), and between the targetoid pattern and patch sizes >2 cm (p=0.028; OR: 2.50, 95% CI: 1.10~5.68) showed higher ORs.

DISCUSSION

This is the first study to investigate factors affecting hair regrowth patterns. This retrospective study demonstrated that the treatment modality used on the AA patch and its size are associated with the hair regrowth pattern. TA ILI is likely to induce an irregular hair regrowth pattern (Fig. 1A), which could indicate that hair regrowth occurred at the area where the triamcinolone was injected[2]. SCS is likely to induce a marginal hair regrowth pattern (Fig. 1B), which requires a higher level of interpretation, considering AA pathogenesis and systemic immunosuppression by SCS. An earthquake theory of AA has been proposed in which a wave of immunologic insult to hair follicles propagates from a focal point, enlarging the area of alopecia[5]. In this respect, marginal hair regrowth in response to systemic administration of corticosteroid implies differences in disease activity between the center and the periphery of AA patches and provides additional evidence that a focal point serves as the beginning center of AA patches.

The sizes of AA patches are also an important factor determining the hair regrowth pattern. Our results showed that smaller AA patches have greater tendencies to show diffuse hair regrowth patterns (Fig. 1C). This might be a limitation of morphological determination of hair regrowth patterns. In other words, when any hair regrowth occurs in smaller AA patches, investigators could interpret it as a diffuse hair regrowth pattern owing to the difficulty in discriminating between the area of hair regrowth and non-regrowth. Furthermore, in smaller patches, intermittent observation would likely only permit observation at a later stage of regrowth; therefore, a diffuse pattern would be observed, even though

Table 1. Clinical and demographic data of the study population

Characteristic	TCS (n=34)	DPCP (n=4)	SCS (n=3)	TA ILI (n=10)	p-value
Age (yr)	43.1±13.1	48.3±15.8	30.3±13.2	29.2±13.2	0.016
Sex					0.595
Male	19 (55.9)	2 (50.0)	2 (66.7)	8 (80.0)	
Female	15 (44.1)	2 (50.0)	1 (33.3)	2 (20.0)	
Duration of disease (mo)	9.4±17.0	4.3±3.6	4.0±3.5	5.1±3.4	0.835
No. of total patch	3.1±2.1	8.0±2.4	7.0±5.0	2.5±1.2	0.01
Mean size of patches					0.023
≤2 cm (n=23)	19 (55.9)	1 (25.0)	2 (66.7)	1 (10.0)	
>2 cm (n=28)	15 (44.1)	3 (75.0)	1 (33.3)	9 (90.0)	

Values are presented as mean±standard deviation or number (%). TCS: topical corticosteroid, DPCP: diphenylcyclopropenone contact immunotherapy, SCS: systemic and topical corticosteroid, TA ILI: triamcinolone acetonide intralesional injection, AA: alopecia areata.

Table 2. Univariate and multivariate analyses of the relationships between alopecia areata patches with a particular hair regrowth pattern and their sizes and treatment modalities

Variable	Total	Diffuse	Irregular	Marginal	Targetoid	Univariate analysis p	Multivariate analysis Diffuse OR (95% CI)	p	Irregular OR (95% CI)	p	Marginal OR (95% CI)	p	Targetoid OR (95% CI)	p
Treatment modality						<0.001								
TCS	91 (100)	41 (45.1)	1 (1.1)*	24 (26.4)	25 (27.5)		Reference		Reference		Reference		Reference	
DPCP	31 (100)	12 (38.7)	1 (3.2)*	10 (32.3)	8 (25.8)		1.05 (0.43~2.54)	0.915	1.95 (0.12~32.91)	0.642	1.33 (0.53~3.33)	0.539	0.70 (0.26~1.84)	0.466
SCS	11 (100)	1 (9.1)	0 (0)*	7 (63.6)†	3 (27.3)		0.13 (0.02~1.07)	0.058	0.0 (0.0)	0.999	4.89 (1.31~18.27)	0.018	0.87 (0.21~3.66)	0.848
TA ILI	19 (100)	3 (15.8)	14 (73.7)*	2 (10.5)†	0 (0)		0.29 (0.08~1.08)	0.065	274.87 (25.75~2,933.56)	<0.001	0.33 (0.07~2.55)	0.160	0.0 (0.0)	0.998
Size of the AA patch						0.003								
≤2 cm	74 (100)	37 (50.0)‡	3 (4.1)§	21 (28.4)	13 (17.6)		Reference		Reference		Reference		Reference	
>2 cm	78 (100)	20 (25.6)‡	13 (16.7)§	22 (28.2)	23 (29.5)		0.36 (0.17~0.74)	0.006	7.33 (0.98~54.97)	0.053	0.99 (0.47~2.12)	0.987	2.50 (1.10~5.68)	0.028

Values are presented as number (%). OR: odds ratio, CI: confidence interval, TCS: topical corticosteroid, DPCP: diphenylcyclopropenone contact immunotherapy, SCS: systemic and topical corticosteroid, TA ILI: triamcinolone acetonide intralesional injection, AA: alopecia areata. *The irregular hair regrowth pattern was more frequent in AA patches treated with TA ILI than in those treated with any other treatment modalities (all $p<0.001$, chi-square test). †The marginal hair regrowth pattern was more frequent in AA patches treated with SCS than with TA ILI ($p=0.013$, chi-square test). ‡The diffuse hair regrowth pattern was more frequent in AA patches ≤2 cm ($p=0.008$, chi-square test). §The irregular hair regrowth pattern was more frequent in AA patches >2 cm ($p=0.045$, chi-square test).

other types of hair regrowth had occurred in between. The treatment modality was determined mainly by the disease activity rather than patch size. In the acute exacerbation phase, SCS treatment was preferred. However, there are possible effects of patch size itself on the regrowth patterns. The clinical and demographic data revealed significant differences in patch size between treatment groups. Thus, this could be a confounding factor for the regrowth pattern of AA patches. By contrast, larger AA patches tend to show a targetoid hair regrowth pattern (Fig. 1D). Several case reports have described targetoid hair regrowth[6-8]. However, there is disagreement about the pathogenesis of targetoid regrowth in AA patches. One of the proposed mechanisms was the earthquake theory[5,6], which is mentioned previously. We hypothesize that as the lesion progresses, a treatment-sensitive focal area may form, leading to targetoid regrowth. The precise mechanism has yet to be identified. We believe there is a possibility that the earthquake theory could explain both marginal and targetoid regrowth patterns. Another suggested mechanism is centrifugal accumulation of TCS by vigorous massage[8]. Our results also indicated that a large proportion of patients who received TCS treatment exhibited targetoid and marginal regrowth patterns. This implies that the way a patient applies TCS may affect the regrowth pattern.

In this study, the no-treatment control group was not included because there were no eligible cases in the outpatient clinic retrospective data. In addition, morphology of natural hair regrowth in AA patches has not been reported in the literature. In studying the natural history of AA, the morphology of hair regrowth had been rarely focused compared to its extent[9]. However, it deserves further study to increase our understanding about the natural history of AA.

Our study is limited by its single-center, retrospective nature, small sample size, and lack of control group. Also, the demographic data already revealed significance differences in age, number of total patches and mean size of patches between the treatment groups. These could be the confounding factors for interpreting the results. Moreover, we did not include patients treated with systemic immunosuppressive agents, such as methotrexate, azathioprine, and cyclosporin. Long-term use of systemic immunosuppressive agents has many adverse effects with limited therapeutic effects compared with other treatment modalities; thus, such agents were not preferred by our institution.

In conclusion, treatment modality and AA patch size affect hair regrowth patterns in AA. Additional studies are required to investigate other factors associated with hair regrowth patterns and to reveal clues about AA pathogenesis.

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CONFLICTS OF INTEREST

The authors have nothing to disclose.

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REFERENCES

1. Lee H, Lee S, Lee WS. Morphological classification system of hair regrowth patterns in alopecia areata patches: DIMT classification. J Eur Acad Dermatol Venereol 2019;33:e96-e97.

2. Li J, Sinclair R. Clinical observations in alopecia areata: implications and hypotheses. Australas J Dermatol 2016;57:e29-e31.

3. Finner AM. Alopecia areata: clinical presentation, diagnosis, and unusual cases. Dermatol Ther 2011;24:348-354.

4. Lee H, Choe SJ, Lee WS. Method for describing patterns and distributions of alopecia areata which may be helpful for patient characterization and predicting prognosis. J Dermatol 2019;46:739-740.

5. Eckert J, Church RE, Ebling FJ. The pathogenesis of alopecia areata.

Br J Dermatol 1968;80:203-210.

6. Del Río E. Targetoid hair regrowth in alopecia areata: the wave theory. Arch Dermatol 1998;134:1042-1043.

7. Delorenze LM, Gavazzoni-Dias MF, Teixeira MS, Aide MK. Concentric polycyclic regrowth pattern in alopecia areata. Int J Trichology 2016;8:35-37.

8. Tan RS, Delaney TJ. Letter: circular regrowth in alopecia areata. Br J Dermatol 1975;92:233-234.

9. Vestey JP, Savin JA. Natural history of severe alopecia areata. Br J Dermatol 1987;117:531.