INTRODUCTION

Alopecia areata (AA) is a common disorder that accounts for 1%-3% of patients visiting dermatology clinics (1). Although it usually presents as asymptomatic localized hair loss (patch AA), it is a disease of very broad spectrum. The hair of the entire scalp and the whole body can be affected, which are called alopecia totalis (AT) and alopecia universalis (AU), respectively. AT and AU are severe forms of AA and only 10% of patients with AT/AU experience full recovery (2, 3).

AA is characterized by a variety of clinical courses, and it is not easy for clinicians to predict prognosis and clinical outcome of each patient. However, several epidemiologic studies on clinical presentation of AA have reported that onset before adolescence is one of the important prognostic factors (4). The extent of involvement, ophiasis pattern of hair loss, long duration of hair loss, a positive family history, nail involvement, atopic diseases and other autoimmune diseases are also known as predictors of poor prognosis in patients with AA (1, 2, 5-8). However, their correlations were identified mainly based on patients with patch AA, and AT/AU has rarely been studied separately although these severe forms of AA show different characteristics and clinical features from patch AA.

In this study, we investigated the clinical characteristics of AT/AU retrospectively by review of medical records and telephone-interview. Patients with AT/AU were classified into the early- or late-onset group by the onset-age (< or ≥ 13 yr), and demographic data, type of AA, family history of AA, concomitant disorders, treatment modalities and the present state of hair loss were assessed and compared in these groups.

MATERIALS AND METHODS

Participants

A total of 287 patients diagnosed as AT or AU in Seoul National University Hospital (SNUH) from 1999 to 2010 were enrolled in this study. The medical records were reviewed retrospectively and the patients were interviewed by telephone. All subjects were classified into the early-onset or late-onset group based on the age at onset of < or ≥ 13 yr, respectively, and the clinical profiles of these two groups regarding alopecia and associated conditions were then compared.

Clinical profiles

Clinical details including type of alopecia, age at onset, family history of AA, concomitant disorders, and treatment history were
obtained from the review of medical records. Treatment modalities were classified as follows: application of topical steroids, intralesional injection of triamcinolone, immunotherapy with diphencyprone or squaric acid dibutyl ester, and oral administration of corticosteroids or systemic immunosuppressant like cyclosporine. Information on the present state of AT/AU was obtained from medical records for a total of 161 patients; 83 patients who recently visited our clinic and from telephone interviews for the other 78 patients; we could not follow-up the other 126 patients. We compared the present state with the state at the first visit and graded the disease state as described above: aggravation or no improvement (< 25%), partial improvement (25%-75%) and much improvement (> 75%). In case of telephone interview, we checked the compartment of hair re-growth (frontal, parietal, occipital, temporal, vertex) and percentage of that compartment (7). If the patient could not answer as percentage, we asked about the subjective assessment of their current scalp status.

Statistical analysis
Using the statistical package program (SPSS Inc., Chicago, IL, USA), the chi-square test was performed to identify differences between groups; P values of < 0.05 were considered significant.

Ethics statement
Verbal informed consents were obtained from patients or their parents in case of under ages by the interviewer before conducting the interview. The present study was approved by the institutional review board of SNUH (IRB H-1005-066-319).

RESULTS

Demographics and clinical profiles
Clinical profiles of 287 patients (154 males, 133 females) with AT/AU were assessed. Among them, 137 patients had AT and the other 150 patients had AU. Their age of onset ranged from 1 yr to 61 yr (mean 19.7 ± 14.1 yr). Based on the age at onset of < or ≥ 13 yr, 108 patients were classified to the early-onset group and the other 179 patients to the late-onset group, respectively. Regarding gender and type of AA, no significant difference was found between the early- and late-onset groups. However, significantly more patients in the early-onset group had family history of AA, concomitant nail dystrophy, and history of atopic dermatitis than in the late-onset group (Table 1). These clinical differences were more prominent in patients with AU than in those with AT. Analysis of patients with AU showed that family history of AA (P = 0.007), nail dystrophy (P = 0.058), and history of atopic dermatitis (P < 0.001) were more frequently seen in the early-onset group than in the late-onset group. These tendencies were similarly observed in patients with AT but were not statistically significant (Fig. 1).

Concomitant disorders in study population
Fifty-seven patients (38.4%) in the study population had a medical history of concomitant disorders, most of which were previously unknown. The most frequent disorder was atopic dermatitis (45.1%), followed by nail dystrophy (20.9%). Other disorders included bacterial or fungal infection, psoriasis, urticaria, eosinophilic cellulitis, and melanocytic naevus (1.9%).

Table 1. Demographic data and clinical presentations (n = 279)

| Parameters               | Early-onset (n = 108) | Late-onset (n = 179) | P value |
|--------------------------|-----------------------|----------------------|---------|
| Gender                   |                       |                      |         |
| Male                     | 62 (57.4%)            | 92 (51.4%)           | 0.324   |
| Female                   | 46 (42.6%)            | 87 (48.6%)           |         |
| Type of AA               |                       |                      |         |
| AT                       | 55 (50.9%)            | 82 (45.8%)           | 0.402   |
| AU                       | 53 (49.1%)            | 97 (54.2%)           |         |
| Family history of AA     |                       |                      |         |
| Negative                 | 66 (85.7%)            | 132 (94.3%)          | 0.001   |
| Positive                 | 11 (14.3%)            | 8 (5.7%)             |         |
| Nail dystrophy           |                       |                      |         |
| Negative                 | 69 (83.1%)            | 91 (92.9%)           | 0.042   |
| Positive                 | 14 (16.9%)            | 7 (7.1%)             |         |
| History of atopic dermatitis |                 |                      | 0.001   |
| Negative                 | 68 (82.1%)            | 126 (95.5%)          |         |
| Positive                 | 15 (17.9%)            | 6 (4.5%)             |         |

**Fig. 1.** Assessment of clinical characteristics of AT and AU by onset-age. *P < 0.1, †P < 0.01.
Table 2. Comorbid disorders with alopecia areata

| Concomitant disorders       | Early-onset (n = 72) | Late-onset (n = 77) |
|----------------------------|----------------------|---------------------|
| Atopic dermatitis          | 15 (20.8%)           | 6 (7.8%)            |
| Allergic rhinitis          | 8 (11.1%)            | 6 (7.8%)            |
| Thyroid disease            | 5 (6.9%)             | 4 (5.2%)            |
| Psoriasis                  | 2 (2.8%)             | 2 (2.6%)            |
| Vitiligo                   | 1 (1.4%)             | 2 (2.6%)            |
| Asthma                     | 2 (2.8%)             | 0 (0.0%)            |
| Nephrotic syndrome         | 0 (0.0%)             | 2 (2.6%)            |
| Inflammatory bowel disease | 0 (0.0%)             | 1 (1.3%)            |
| Behcet disease             | 0 (0.0%)             | 1 (1.3%)            |
| No concomitant disorder    | 39 (54.2%)           | 53 (68.8%)          |

ures were seen in the two groups. It has been known that AT/AU had taken by 13 yr because previous epidemiologic studies have generally considered the onset-age of puberty as around 13 yr (12, 13). There was no significant difference in gender and ratio of AT and AU between groups. Interestingly, some clinical features, such as family history, atopic disorders, and nail changes, showed significant differences between early- and late-onset groups only in patients with AU, a more severe type of AA than AT.

As mentioned, several autoimmune diseases and atopic disorders are generally thought to be associated with AA (6, 7, 11). According to Goh et al. (6), 56% of AA patients had comorbidities other than AA and the proportion was higher in AT/AU than in patch AA. However, some studies reported that the incidence of concomitant disorders was not higher either in patients with severe type AA or in patients in whom AA had developed during childhood (7, 14). In our study, 38.4% of AT/AU patients had concomitant disorders and atopic dermatitis was most common, which was more prominent in the early-onset group.

The second most common comorbidity was thyroid disorder in both groups. Thyroid disease, including Grave’s disease, Hashimoto’s thyroiditis and simple goiter, are reported in 8% to 28% of AA patients (1). In one Korean report, 1.4% of AA individuals had autoimmune thyroid disease (15). Compared with those in a previous report, a relatively high rate (6.0%) of AT/AU individuals had thyroid diseases in this study, but no differences were seen in the two groups. It has been known that AT/AU is less favorable than patch AA and fewer than 10% of AT/AU patients recover spontaneously (16), which was consistent with our result that 16.9% of AT patients and 5.6% of AU patients showed > 75% improvement.

The most common therapy used in AA is intralesional injection of corticosteroids and 64%-97% of AA sites exhibit hair growth (17, 18). In this study, topical application and oral administration of steroid were the most frequently used treatment modalities for AT/AU. However, all treatment modalities including steroid failed to show any association with the present hair condition of patients in this study, which suggested that they cannot alter the long-term clinical course of the disease. In previous studies, several poor prognostic factors were reported, including the extent of hair loss, long duration of hair loss, atopy, a positive family history, the presence of other autoimmune
diseases, nail involvement, and young age of onset (1). However, in the cases of AT/AU, the present state of disease was associated with the type of AA and a family history of AA only in the early-onset group, while no associated factors with disease progression were found in the late-onset group. The earlier age of onset and family history suggest a relationship with personal genetic susceptibility as previously reported (19-21).

Our study has certain limitations. First, this study was retrospectively performed and recall bias might be involved because some clinical data were obtained by telephone interview. Secondly, a larger number of subjects would be helpful to statistically confirm the association between age at onset and clinical characteristics of AT/AU. For example, early-onset patients with AT seemed to be more associated with family history of AA, nail dystrophy, and history of atopic dermatitis than late-onset patients with AT, but this finding was not statistically significant. Data from more patients may be useful to demonstrate statistical significance. Thirdly, in the chart review we checked the presence of any comorbid disorders when diagnosed by primary physicians of the patients. Therefore, some patients would not be included in rhinitis or asthma group even though they developed any suggestive symptom of rhinitis or asthma. Finally, this study was cross-sectional study and reviewed non-standardized treatment method. Therefore, prospective standardized study would be executed to investigate progress of the disease or treatment efficacy.

In summary, early-onset of AU was associated with family history of AA, atopic dermatitis, nail changes, and young age of onset (1). Howev-

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In summary, early-onset of AU was associated with family history of AA, atopic dermatitis, and nail changes. Comorbid disorders, especially allergic disorders, were also more common with early-onset AT/AU than with late-onset disease. Assessment of the present hair state suggests that patients with AU or family history of AA make worse progress in the early-onset group than in the late-onset group.

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