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SHORT COMMUNICATION

Clinical and Histopathological Features of Itch in Patients with Alopecia Areata

Takako Yamakoshi[1], Tsugunobu Andoh[2]*, Teruhiko Makino[1], Yasushi Kuraishi[2] and Tadamichi Shimizu[1]*
Departments of [1]Dermatology, and [2]Applied Pharmacology, Graduate School of Medicine and Pharmaceutical Sciences, University of Toyama, 2630 Sugitani, Toyama 930-0194, Japan. E-mail: shimizut@med.u-toyama.ac.jp, andoht@pha.u-toyama.ac.jp
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Alopecia areata (AA) is commonly characterized by patchy areas of hair loss on the scalp. AA has been considered as a tissue-specific and T cell-mediated autoimmune disease of the hair follicles with a genetic predisposition to hair loss (1, 2). Patients with AA sometimes report experiencing itch on the scalp at the same time as an increase in hair loss activity. However, the relationship between the mechanism of itch and hair loss in patients with AA is unclear. We report here clinical and histopathological features of patients with itchy AA, focussing on mast cells and the expression of 5-lipoxygenase (5-LOX), a key enzyme for the production of the itch mediator leukotriene B_4 (LTB_4).

RESULTS

A total of 156 patients with AA (92 females and 64 males, age range 4–80 years) attending our clinic between August 2009 and April 2011 were enrolled in this study. The subtypes of AA were as follows: 34 simplex (22%), 64 multiplex (41%), 39 totalis (25%), 9 universalis (6%), 8 ophiasis (5%), and 2 acute diffuse and total alopecia of the female scalp (ADTAFS) (1%). Out of these 156 patients with AA, 14 (11 females and 3 males, 11–68 years) reported experiencing itch, represented by tickling or an ant-like crawling sensation, on the lesion at the same time as the increase in hair loss, when the hair was lost suddenly. The patients with itch were diagnosed as 5 AA multiplex (36%), 5 totalis (36%), 2 ophiasis (14%) and 2 ADTAFS (14%). In 12 out of 14 patients with AA with itch, the intensity of itch was decreased in tandem with the decrease in hair loss.

In the histopathological study of the scalp, we compared 2 AA patients with itch (male 72 years; female 43 years) with 2 normal subjects (male 40 years; female 37 years) and 2 patients with androgenetic alopecia (AGA) without itch (males 43 and 32 years). We were not able to obtain skin tissues from patients with AA without itch. Compared with normal subjects and patients with AGA, epidermal thinning and massive lymphocytic infiltration around the hair follicles were shown in the lesional skins of patients with AA and itch (Fig. 1). Toluidine blue staining of skin sections showed a high number of both total and degranulated mast cells around the hair follicles and hair bulbs in patients with AA (Table I).

5-LOX was highly expressed in epidermis and around the hair follicles of patients with AA having itch (Fig. 2). These immunoreactivities were seen at high density around nuclei, including the nuclear membrane, and at low density in cytosol. In particular, immunoreactivity for 5-LOX was observed in the epidermal basal layer. The expression of 5-LOX in the skin of AGA patients and normal subjects was low.

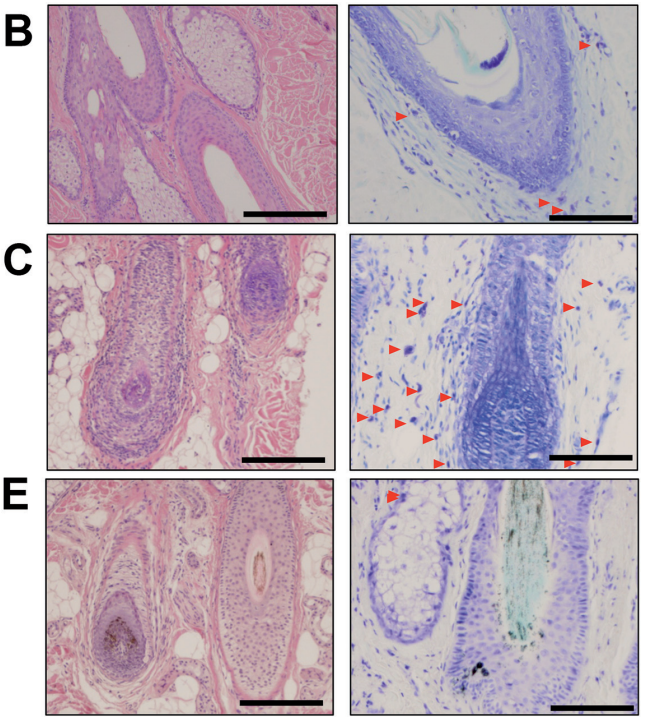

Fig. 1. Histopathology of the scalp: (B) normal skin, (C) alopecia areata, (E) androgenetic alopecia. *Left panel*: haematoxylin-eosin stain, scale bar: 200 μm; *right panel*: toluidine blue stain, scale bar: 100 μm. Arrowhead indicates mast cells. (Complete Fig. 1 available from: http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-1613.)

DISCUSSION

The present study showed that 9% (14/156) of patients with AA reported having itch on the lesional scalp. The

Table I. *Number of mast cells (MC) (per 0.2 mm²) around hair follicles in two patients each with alopecia areata (AA) and androgenetic alopecia (AGA), and in healthy controls*

	AA, mean ± SD		AGA, mean ± SD			
	Case 1	Case 2	Case 1	Case 2	Control 1	Control 2
Total MC	17.4 ± 3.6	13.6 ± 7.3	0.6 ± 0.9	7.2 ± 6.9	9.6 ± 5.7	4.8 ± 1.8
Degranulated MC	11.8 ± 3.5	9.8 ± 5.2	0	1.4 ± 1.3	0	0

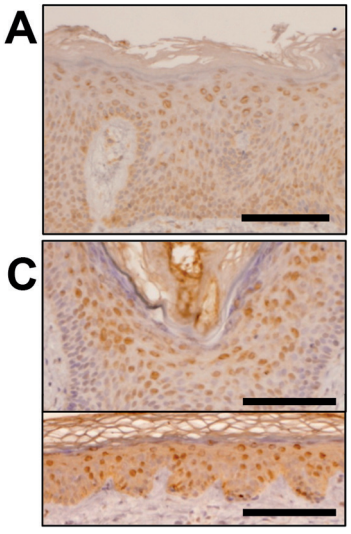

Fig. 2. Distribution of the expression of 5-lipoxygenase in the scalp: (A) normal skin, (C) alopecia areata. Scale bar: 100 µm. (Complete Fig. 2 available from: http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-1613).

itch arose at the same time as the hair loss (early stage of AA). The patients also reported that itch occurred at the time of sudden hair loss. Most of patients with itch were diagnosed with AA multiplex (36%) and AA totalis (36%), suggesting that itch may be related to AA subtype. Histopathologically, epidermal thinning was observed in patients with AA with itch, compared with normal subjects and AGA patients. Infiltration of lymphocytes around the hair follicles and hair bulbs was shown in patients with itch, but not in normal subjects or AGA patients without itch. T lymphocytes have been shown to be distributed around the hair follicles and hair bulbs in patients with AA (3). The current study suggests that T lymphocytes may be involved in the induction of itch through the production of pruritogens, such as IL-31 (4).

Numerous mast cells were observed around hair bulbs in patients with AA and itch. Mast cells release several mediators, well-known to induce itch (5). Histamine and tryptase act mainly on H_1-receptor and proteinase-activated receptor 2 (PAR_2), respectively. Numerous nerve fibres are present around the hair follicles in the scalp of patients with AA (6). It has been shown that histamine and PAR_2 agonist affect different neurones (7). The mechanisms of activation and degranulation of mast cells are not fully understood. Substance P (SP) is shown to activate mast cells and elicits itch through histamine (8). In patients with AA, neurones containing SP are distributed around the hair follicles (6), and might be involved in the activation of mast cells causing itch in patients with AA.

The present study also detected the expression of 5-LOX, which is involved in the production of LTB_4 (9). 5-LOX is distributed at high density around nuclei, including the nuclear membrane, and at low density in cytosol, as also reported elsewhere (10, 11). In patients with AA and itch, the expression level of 5-LOX was increased in the epidermis and around the hair follicles, suggesting the possibility of the involvement of LTB_4 in itch. LTB_4 elicits itch through BLT1 LTB_4 receptor expressed in primary afferents (9) and lymphocytes (12) producing some pruritogens (e.g. IL-2 and IL-31) (4, 13).

The present study demonstrates that the increase in pruritogen-releasing cells (e.g. mast cells, lymphocytes) around the hair follicles and the enzymes for the production of pruritogens (e.g. LTB4) may be involved in the induction of itch in patients with AA. Since the patients with AA reported that itch occurred at the time of sudden hair loss, not only pruritic mechanisms, but also emotional mechanisms, may be involved in the induction of itch in patients with AA. A Further study of biopsy material from both itchy and non-itchy AA scalps is warranted.

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