Focal atrichia: A diagnostic clue in female pattern hair loss

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Background: Focal atrichia is a common clinical finding in female pattern hair loss, the specificity and histologic findings of which need further clarification.

Objective: To determine the frequency of focal atrichia in various types of hair loss and its histologic characteristics in female pattern hair loss.

Methods: Part 1 of the study was a review of 250 consecutive female patients seen with hair loss for the presence of focal atrichia, and part 2 examined paired biopsy specimens from haired areas versus those from areas with focal atrichia in 18 subjects with female pattern hair loss.

Results: Focal atrichia was seen in 46 of 104 of women with female pattern hair loss (44%), including 67% of those with the late-onset subtype versus 15% of those with the early-onset subtype, compared with in 3 of 146 of those with other hair disorders (2%). Biopsy findings of focal atrichia in female pattern hair loss showed primarily a more progressive miniaturization process than that of haired areas of the scalp.

Limitations: Some women with female pattern hair loss may have had concomitant chronic telogen effluvium.

Conclusions: When present, focal atrichia is a clinical clue to the diagnosis of female pattern hair loss, particularly the late-onset subtype. (J Am Acad Dermatol 2019;80:1538-43.)

Key words: anagen; biopsy; female pattern hair loss; focal atrichia; telogen; terminal; vellus.

Female pattern hair loss (FPHL) is characterized histologically by miniaturization of affected hair follicles and clinically by the phenotype of central with or without parietal scalp hair loss in postpubertal females.[1] There are 3 patterns of hair loss in FPHL[2]: diffuse central (Ludwig[3]), central with frontal accentuation or a Christmas tree pattern (Olsen[4]), and male pattern (Hamilton[5]), the latter with frontal and vertex accentuation. Only the first 2 patterns are common; both are more likely to show a diminution in hair density versus the frank baldness seen in men with male pattern hair loss (MPHL). Unlike MPHL, in which the diagnosis is relatively simple to make clinically, the diagnosis of FPHL can sometimes be difficult to separate out from chronic telogen effluvium (CTE), which may occur in concert with or independent of FPHL.[6] Clinical clues are

Abbreviations used:

ATE:	acute telogen effluvium
CTE:	chronic telogen effluvium
EFPHL:	early onset female pattern hair loss
FA:	focal atrichia
FFA:	frontal fibrosing alopecia
FPHL:	female pattern hair loss
LFPHL:	late onset female pattern hair loss
MPHL:	male pattern hair loss
TE:	telogen effluvium

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important to help in this process, as histology alone is rarely diagnostic (especially in older patients).

In 2001 Olsen reported the presence of areas about 4 mm in diameter that were devoid of any emerging hairs in the involved scalp of 13 of 63 women with FPHL, areas that she named *focal atrichia* (FA) (in a paper on FA associated with fibrosis in FPHL that was presented at the World Congress of Hair Disorders in Tokyo, Japan, in 2001).[7] The underlying scalp of these areas of FA is normal, without atrophy or erythema and with preservation of ostia. Areas of FA are notable on close inspection of the scalp (Fig 1) or with the irregularity that they cause in a central part of the hair.

The current article reports the results of a study that assessed the presence of FA in a larger group of female patients with a variety of hair disorders and evaluated the histology of FA in comparison with that of haired areas of the scalp in the same subject with FPHL.

CAPSULE SUMMARY

- Focal atrichia (FA) is the finding of small (~4 mm diameter) areas in the scalp devoid of emerging hairs.
- We found that FA is much more common in female pattern hair loss than in other types of hair loss.
- FA is a helpful clue in the diagnosis of female pattern hair loss.

METHODS

This study was designed in 2 parts. It was approved by the Duke University Institutional Review Board, and all subjects gave consent before participation. In Part 1, a total of 250 consecutive female patients age 18 years or older who were seen by and whose disease was diagnosed by one of the authors (E.O.) had the presence or absence of FA noted as part of a routine scalp examination. In all cases, diagnosis was based not on the presence or absence of FA but on specific clinical criteria. The criteria used for the diagnosis of FPHL included widening of the central and/or frontal scalp part width, with decreased hair density in the central scalp compared with the hair density in the occiput. Subjects with telogen effluvium (TE) had a positive hair pull from the occiput and at least 3 other areas of the scalp, with CTE vs acute telogen effluvium (ATE) being determined by duration of the hair loss process (>6 vs <6 months' duration). If a patient had obvious patterning in the central or frontal scalp but also had increased shedding as documented by hair pull, she was recorded as having FPHL. Thus, there may have been patients with FPHL who also had ATE or CTE. The clinical diagnosis of alopecia areata was based on patchy or diffuse hair loss with intact follicular ostia with or without exclamation point hairs and/or a readily positive hair pull for broken, telogen, and/or dystrophic anagen hairs at the periphery of remaining areas of hair growth. Patients with cicatricial alopecia had loss of follicular ostia in areas of hair loss; specific categorization of type of cicatricial alopecia was determined by clinicopathologic correlation. Patients with FPHL were further divided into those with early-onset FPHL (EFPHL) (defined as onset immediately after puberty through the third decade) versus late-onset FPHL (LFPHL) (defined as onset in the fourth decade and beyond) according to prior recommendations by a multidisciplinary conference on FPHL.[1]

Continuous variables are reported by using the mean, standard deviation, median, and range, as determined by the variable distribution. Categoric data are shown using counts and percentages of subjects with the various types of hair loss. The relationship between the type of hair disorder and FA was evaluated by using the chi-square test or Fisher's exact test (expected cell counts <5). A P value less than .05 was considered statistically significant.

After demonstration of a potential relationship of FA with FPHL in Part 1, pathologic assessment of FA in FPHL was performed in Part 2. A total of 20 subjects who had both FA and a clinical diagnosis of FPHL had two 4-mm punch biopsy specimens taken of the central scalp (1 from an area of FA and 1 from a nearby area of FPHL with remaining but decreased density of terminal hair). Each subject had her clinical pattern of FPHL (central vs central/frontal accentuation) confirmed on review of standardized global photographs taken at clinic visits; the severity of hair loss was assigned on the basis of a 3-point scale, with 1 indicating minimal hair loss, 2 indicating moderate hair loss, and 3 indicating severe hair loss. Each biopsy specimen was preserved in formalin and sent in a de-identified, blinded fashion to 1 of the authors (D.W.) for histologic examination as detailed previously.[8] The biopsy specimens were divided horizontally, processed routinely, and stained with hematoxylin and eosin. Both the upper and lower sections of the biopsy specimens were examined. All terminal and vellus hairs and follicular units were counted, and the anagen-to-telogen ratio was determined. The degree of inflammation and fibrosis and number of stelae were recorded (stelae are the streamers or residual fibrous tracts left behind when

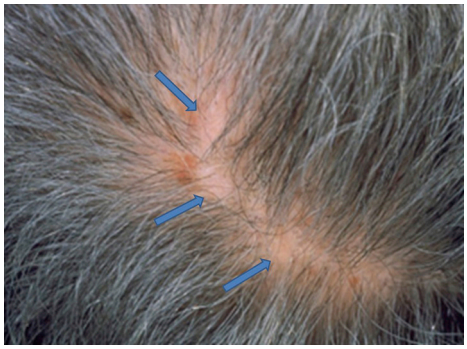

Fig 1. Example of clinical appearance of focal atrichia in female pattern hair loss. Arrow points to focal atrichia.

the hair cycles upward through catagen into telogen[9]). Pathologic criteria for FPHL included a reduced terminal-to-vellus ratio lower than the normal (7:1 or 8:1)[8,10,11] and an increased percentage of telogen hairs; only those who also met this criteria were included in the final analysis. The results of examination of the paired biopsy specimens from haired areas versus those from areas of FA in 18 subjects with FPHL were compared by using a paired *t* test or Wilcoxon signed rank test. A *P* value less than .05 was considered statistically significant. In addition, the results were compared with data generated by this same author (D.W.) on 4-mm biopsy specimens from control subjects,[6] patients with CTE,[6] and patients with FPHL. The control data included the results for biopsy specimens of the vertex of the scalp from 22 subjects (13 male and 9 female), who had no alopecia and were 18 to 70 years old (average age, 43).

RESULTS

Part 1

The 250 consecutive female subjects with hair loss had a mean age when seen in the clinic of 47.2 years (31.2 years for EFPHL and 58.5 years for LFPHL), and their racial breakdown was as follows: white, 76.4%; African American, 18.4%; and Asian/East Indian, 5.2%. The percentage of subjects with various types of hair loss is shown in Table I. Ninety-four percent of all FA (46/49) were seen in FPHL with the majority of these (39/45 or 85%) occurring in LFPHL. FA was seen in 44% of cases of FPHL, including in 67% (39/58) of those with LFPHL ($P < .001$) and 15% (7 of 46) of those with EFPHL. FA was not seen in ATE or CTE uncomplicated by FPHL. FA was seen in only 3 other hair loss conditions: 1 case each of central centrifugal cicatricial alopecia (1 of 26), frontal fibrosing alopecia (FFA) (1 of 1), and scarring alopecia not otherwise specified (1 of 1).

Part 2

Of the 20 subjects with FPHL and FA who had scalp biopsies performed, 18 also met the pathologic criteria for FPHL (Supplemental Table I; available at http://www.jaad.org). Of these 18 subjects, all were white. The mean duration of hair loss was 12 years (range, 0.5-43). The mean age of all 18 subjects at the time of the study was 55.8 years. Of the 18 subjects, 5 had EFPHL and 13 had LFPHL; 6 subjects had a central-only pattern of FPHL (2 with grade 1, 3 with grade 2, and 1 with grade 3 severity) and 12 had a central/frontal accentuation pattern of FPHL (6 with grade 1 and 6 with grade 2 severity). Twelve women were postmenopausal; 3 subjects were actively using topical minoxidil but had been receiving a steady dose for at least 6 months.

Histologically, the 4-mm punch biopsy specimens from the areas of FA versus from the haired areas of FPHL showed a trend toward a lower mean follicular density (22.9 vs 25.3 [$P = .070$]) and a significantly lower mean number of terminal follicles (13.3 vs 17.7 [$P < .001$]), lower mean terminal-to-vellus ratio (1.2:1 vs 2.4:1 [$P = .005$]), and higher median number of stelae in the areas of FA versus in the haired areas of FPHL (4.5 vs 3.0 [$P = .005$]). Though not significant, a lower mean number of follicular units (11.8 vs 12.9 [$P = .147$]) and a lower mean percentage of hairs in anagen (85% vs 86% [$P = .371$]) was observed. These findings are indicative of a more progressive miniaturization process in FA versus in haired scalp in the same subject with FPHL. The degree of lymphohistiocytic infiltrate in the upper dermis was not different in the biopsy specimens from areas of FA and those from haired areas, and inflammation in the lower dermis was absent in most cases of both biopsy specimens. Fibrosis was not significantly different between biopsy sites, and if present, it was higher in the upper versus lower dermal sections of the follicle. Representative photomicrographs of biopsy specimens from haired areas and areas of FA are shown in Fig 2. The biopsy specimens from the 3 subjects using topical minoxidil had a slightly higher percentage of anagen hairs (89% for the haired areas and 90% for the areas of FA) from those not using topical minoxidil but were not significantly different in other aspects on histologic examination. A comparison of the histologic results seen in this study with those seen in specimens from biopsies performed at the Dallas Hair Center on controls, patients with CTE, and a large series of patients with FPHL is shown in Table II.

DISCUSSION

Unger in the 1988 textbook on hair transplantation noted small (2-mm) areas without hair scattered in the scalp of women with hair loss who were being evaluated for potential

Table I. FA in 250 consecutive patients with hair disorders

	Total No. of subjects	Subjects with FA	Subjects with no FA	
Hair disorder	**250**	**49**	**201**	***P* value**
FPHL	104 (42%)	46/104 (44%)	58/104 (56%)	<.001
Early onset	46 (18%)	7/46 (15%)	39/46 (85%)	.407
Late onset	58 (23%)	39/58 (67%)	19/58 (33%)	<.001
Alopecia areata	58 (23%)	0/58 (0%)	58/58 (100%)	<.001
Primary cicatricial alopecia	47 (19%)	3/47 (6%)	44/47 (94%)	.011
CCCA	26	1/26 (4%)	25/26 (96%)	.033
LPP	7	0/7 (0%)	7/7 (100%)	.351
Pseudopelade	3	0/3 (0%)	3/3 (100%)	1.000
FAPD	2	0/2 (0%)	2/2 (100%)	1.000
DLE	2	0/2 (0%)	2/2 (100%)	1.000
Other*	7	2/7 (29%)	5/7 (71%)	.006
Chronic TE	24 (10%)	0/24 (0%)	24/24 (100%)	.006
Acute TE	4 (2%)	0/4 (0%)	4/4 (100%)	1.000
Miscellaneous†	13 (5%)	0/13 (0%)	13/13 (100%)	.078

Data are presented as count (percentage).
CCCA, Central centrifugal cicatricial alopecia; *DLE*, discoid lupus erythematosus; *FA*, focal atrichia; *FAPD*, fibrosing alopecia in a pattern distribution; *LPP*, lichen planopilaris; *TE*, telogen effluvium.
**Other* primary cicatricial alopecia includes folliculitis decalvans, scarring alopecia not otherwise specified, dissecting cellulitis, sarcoid, acne miliaria necrotica, and frontal fibrosing alopecia.
†Includes hair breakage, marginal alopecia, folliculitis, tinea capitis, postchemotherapy alopecia, and trichotillomania.

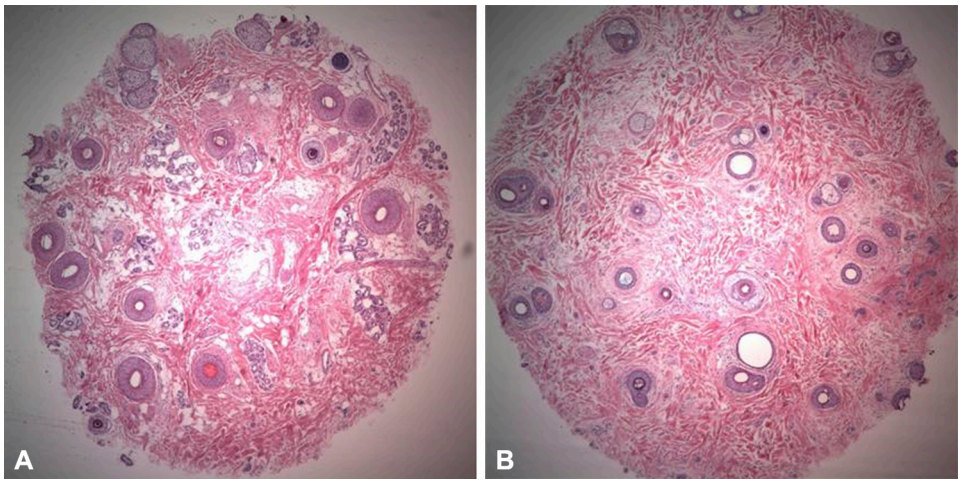

Fig 2. Representative histopathologic findings based on scalp biopsy samples of haired area and focal atrichia in a patient with female pattern hair loss. **A**, Biopsy specimen of haired area: 16 follicular units, 19 terminal hairs, anagen-to-telogen ratio of 79:21, and telogen-to-vellus ratio of 1.9:1. **B**, Biopsy specimen of focal atrichia: 15 follicular units, 9 terminal hairs, anagen-to-telogen ratio of 78:22, and telogen-to-vellus ratio of 0.9:1.

hair transplant.[12] Both Guarrera and Rebora[13] and Courtois et al,[14] using phototrichograms, showed that there were empty spaces for certain periods after telogen in patients with FPHL and MPHL, suggesting a "lag phase" after telogen in these conditions. This lag phase has more recently been confirmed and renamed *kenogen*.[15] Empty spaces have also been noted on dermoscopy in pattern hair loss.[16] However, Guarrera et al also reported a few empty follicles in a young boy without hair loss,[17] which may indicate that these empty spaces can be seen during normal cycling, perhaps because of early ejection of a telogen hair.

The areas of FA seen in the subjects in this study, like those earlier reported by Olsen[4], are larger than the 2 mm empty spaces noted by Unger and Nordstrom,[12] instead being approximately 4 mm in diameter. Areas of FA are easiest to see in the "bites"

Table II. Findings on pathologic review of 4-mm punch biopsy samples taken of subjects with FPHL (haired area vs FA in central scalp area of FPHL) and comparison with nonstudy cohorts of patients with FPHL, patients with CTE, and controls seen at Dallas Hair Center

	Current study		Dallas Hair Center		
Histologic findings	**Haired areas adjacent to FA**	**FA**	**FPHL***	**Controls[6]**	**CTE[6]**
No. of subjects	18	18	950	22	355
Total hairs	25.3 ± 6.5 (10-34)	22.9 ± 6.1 (12-36)	33	40	39
Total terminal hairs	17.7 ± 5.2 (7-28)	13.3 ± 5.6 (4-28)	22	35	35
% anagen	86 (69-100)	85 (25-100)	86	93.5	89
Terminal-to-vellus ratio	2.4:1 (1.1:1 to 5.0:1)	1.2:1 (0.3:1 to 5.0:1)	2:1	7:1	9:1
No. of follicular	12.9 ± 2.4 (10-17)	11.8 ± 2.8 (7-17)		13	13
No. of stelae	3.0 (0-18)	4.5 (0-22)		1-2	3

CTE, Chronic telogen effluvium; *FA*, focal atrichia; *FAPD*, fibrosing alopecia in a pattern distribution.
*All histologic assessments performed by D. Whiting. Data are presented as mean plus or minus standard deviation (range) or as median (range).

that appear to be taken out of a central part of the scalp hair, but they are also seen when separating the hair over the central scalp. The number of follicular units seen in the 4-mm punch biopsy specimens from both the haired areas and areas of FA of the subjects in this study was close to the reported range of 10 to 12 follicular units per 4 mm-punch biopsy specimen from the normal scalp.[9] The mean number of total hairs seen in biopsy specimens from both haired areas and areas of FA (25.3 and 22.9, respectively) were lower than the normal range of 35 to 40 reported per 4-mm biopsy specimen in whites,[6,8,10] which is reflective of the underlying FPHL and the decrease in follicular density seen in the late stage of FPHL, called cicatricial FPHL.[18] There was no significant difference in the lympho-histiocytic infiltrate or fibrosis in the haired areas versus in the areas of FA, both being representative of what is typically seen in FPHL. In these subjects with FPHL, the major difference between the biopsy specimens from areas of FA and those from adjacent scalp areas with hair was the greater degree of miniaturization in the biopsy specimens from areas of FA, as demonstrated by a decrease in terminal hairs, decrease in terminal-to-vellus ratio, and increased number of stelae. On a practical note, in addition to providing a clinical clue to the diagnosis of FPHL, areas of FA, if present, may represent the preferred biopsy site for histologic confirmation of FPHL.

The surprising finding was the presence of no hair shafts emerging from the scalp in areas of FA but the histologic presence of terminal anagen hairs. We did not follow these patients over time to determine whether these areas of FA eventually produced a visible hair. However, the results of examination of the 4-mm biopsy specimen results would mean that for no hairs to be projecting from the scalp surface in FA, all the follicular units in the area of FA would be simultaneously involved in the process. This would imply synchrony of suspension of hair growth in multiple follicular units in a given area. A selective hierarchy of androgen sensitivity within follicular units that leads to selective miniaturization and a reduction in the number of terminal hairs per follicular unit has been suggested to explain the mosaic pattern of hair loss in FPHL versus in MPHL.[19] Our results would suggest that this androgen sensitivity, and its effect on anagen hair growth, may be inherent in specific follicular units with local spread to adjacent follicular units.

FA appears to be a relatively specific clinical marker for FPHL given that 94% of all FA in our series was observed in FPHL ($P < .001$). Within FPHL cases, FA was seen significantly more frequently in LFPHL than in EFPHL (67% versus 15% of cases, respectively), which was also clinically and statistically significant ($P < .001$). FA was not seen in patients with CTE without obvious concomitant FPHL and may serve as a marker to help distinguish the 2 hair disorders unless they exist in concert. The only time FA was seen in other hair loss conditions in our study was in central centrifugal cicatricial alopecia and FFA, both of which have a potential relationship to FPHL,[18,20] and in 1 case of scarring alopecia not otherwise specified. The presence of FA in FFA should be sought to determine its true incidence.

CONCLUSION

FA appears to be a reliable marker of FPHL when present and is more commonly seen in LFPHL than in EFPHL. In FPHL, the histologic findings of FA are those with a more progressive miniaturization than that of the surrounding haired areas. The reason for the lack of visible hair growth in the areas of FA in

which terminal anagen hairs are clearly present in biopsy specimens is unclear but may reflect synchronization of the androgen-sensitive process in FPHL with suspension of hair growth in a grouping of follicular units.

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Supplemental Table I. Part II of study: Clinical characteristics of subjects with scalp biopsy specimens

Pt	Age	Type of FPHL	Duration of FPHL (y)	Pattern severity*	Menopausal
1	55	Late	5	CF-1	Yes
2	64	Late	1	CF-2	Yes
3	55	Early	25	CF-1	Yes
4†	70	Late	4	CF-1	Yes
5†	43	Late	3	CF-2	No
6	52	Late	6.5	CF-2	Yes
7	41	Late	3	CF-1	No
8	67	Late	20	C-3	Yes
9	73	Early	43	C-2	Yes
10	51	Late	14	CF-1	No
11	52	Late	12.5	C-2	Yes
12	71	Late	0.5	C-2	Yes
13	37	Early	5	CF-2	No
14	51	Late	2	CF-1	No
15	63	Late	10	CF-2	Yes
16	56	Early	43	C-1	Yes
17	67	Late	3	C-1	Yes
18†	36	Early	20	CF-2	No

C, Central pattern of FPHL; *CF*, central/frontal accentuation pattern of FPHL; *FPHL*, female pattern hair loss.
*Numerals 1, 2, and 3 indicate severity of hair loss, with 1 indicating mild hair loss, 2 indicating moderate hair loss, and 3 indicating severe hair loss.
†Use of topical minoxidil for at least the past 6 months.