
Frontal fibrosing alopecia: A review of 60 cases

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Background: Frontal fibrosing alopecia (FFA) is a variant of lichen planopilaris primarily affecting postmenopausal women, with a predilection for the frontotemporal hairline.

Objectives: We sought to examine possible causal associations and review the clinical features, natural history, and response to treatment of patients with FFA attending a specialist hair clinic.

Methods: This was a case note review of 60 patients with FFA.

Results: The number of patients with FFA seen has increased over the last decade. All were Caucasian women, with significantly above-average affluence scores and were less likely to be smokers. The mean age at presentation was 64 years and average disease duration was 3.4 years (range: 6 months-30 years). Three patients were premenopausal. All patients had frontotemporal involvement, with follicular hyperkeratosis, scarring, and variable perifollicular erythema. Several patients had more unusual patterns: 8 had extensive parietal involvement, 4 had occipital involvement, 1 had asymmetric frontal involvement, and 5 had typical FFA associated with diffuse scalp lichen planopilaris. Eyebrow loss was documented in 73%, eyelash loss in 3%, and body hair loss in 25%. Almost all patients had been treated with superpotent topical steroids. Other treatments included topical calcineurin inhibitors; intralesional triamcinolone acetate; phototherapy; hydroxychloroquine; lymecycline; and prednisolone. Although some treatments may reduce inflammation, their efficacy in controlling the progress of the alopecia was uncertain.

Limitations: This is a retrospective review.

Conclusions: FFA is a clinically distinctive condition, the prevalence of which appears to be increasing. It has a generally poor response to treatment. The origin remains uncertain. (J Am Acad Dermatol 2012;67:955-61.)

Key words: affluence; alopecia; autoimmunity; frontal fibrosing alopecia; lichen planopilaris; origin; prognosis; treatment.

Frontal fibrosing alopecia (FFA) is a relatively recently recognized condition, first described in 1994.¹ It is a cicatricial alopecia characterized by progressive recession of the frontotemporal hairline. FFA typically affects postmenopausal women and is generally considered a clinical variant of lichen planopilaris (LPP).² FFA is usually diagnosed clinically,³ with perifollicular erythema, follicular hyperkeratosis, and scarring affecting the frontotemporal hairline. Eyebrow loss is frequently recorded (50%-83% of cases)³⁻⁵ but body hair loss

Abbreviations used:

ACEI:	angiotensin-converting enzyme inhibitors
FFA:	frontal fibrosing alopecia
LP:	lichen planus
LPP:	lichen planopilaris
NSAID:	nonsteroidal anti-inflammatory drug

elsewhere has been less commonly reported (0%-77%).^{4,6,7} The histologic features of FFA and LPP are similar: both demonstrate a follicular lichenoid

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Funding sources: None.

Conflicts of interest: None declared.

Accepted for publication December 9, 2011.

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Published online April 16, 2012.

0190-9622/\$36.00

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doi:10.1016/j.jaad.2011.12.038

inflammatory infiltrate involving the isthmus and infundibulum, apoptotic keratinocytes in the external root sheath, perifollicular fibrosis, and fibrous tracts.^{2,8} Origin is uncertain, although an androgen-driven hypothesis is speculated,⁹ given the strong association with postmenopausal status. The natural history of FFA is unknown but slow progression and spontaneous remission may be seen in some cases.^{2,3} We present a series of 60 cases that extends previous reports¹⁰ and to our knowledge represents the largest series to date.

METHODS

Case records of 60 patients with FFA attending a specialist hair clinic in Glasgow, United Kingdom, from January 2000 to June 2010 were examined. The diagnosis was made clinically in most and supported by histology in 15 cases.

RESULTS

Patient demographics and history

All patients were Caucasian women. The mean age at presentation was 64 years (range: 36-87 years) and mean duration at presentation was 3.4 years (range: 3 months-30 years). Four patients were given a diagnosis incidentally at general dermatology clinics. Mean age at onset was 60.4 years (range: 31-86 years). Most women were postmenopausal at onset, but 3 (5%) were not (age of onset of 34, 43, and 45 years). Two patients reported sudden-onset hair loss after bereavement. Table I shows the proportion of patients given a diagnosis of FFA annually compared with total hair loss referrals, highlighting a 10-fold increase in the numbers of patients seen with the condition.

The socioeconomic status of patients was assessed by the Carstairs¹¹ Deprivation scores (derived from patients' postcodes). The Carstairs and Morris index is a commonly used indicator of socioeconomic status in health research in the United Kingdom,¹² with Deprivation score 1 being the most affluent and Deprivation score 7 the least affluent. The distribution of Deprivation scores for our patients is illustrated in Fig 1 and contrasted with 80 age- and sex-matched control subjects attending with other types of alopecia. These data suggest

patients with FFA were a more affluent group ($P < .001$). Patients with FFA were also found to be more affluent than Greater Glasgow National Health Service patients generally ($P = .001$). Data regarding smoking status were available for 52 patients; 37 patients (71%) had never smoked, 5 patients (10%) were current smokers, and 10 patients (19%) were ex-smokers. These data show a significant preponderance of nonsmokers within our cohort, compared with national data regarding smoking status of Scottish women¹³ ($P = .01$) (Table II).

Fourteen patients (23%) had confirmed hypothyroidism and two had borderline hypothyroidism. Of these, one also had pernicious anemia. One further patient had Sjögren syndrome and one had patchy alopecia areata copresenting with FFA. Thus, 18 patients (30%) had associated autoimmune disease, whereas two further patients (3%) gave a family history.

Only one patient had previous lichen planus (LP), involving the oral mucosa 20 years earlier and recurring shortly after the onset of FFA. None had concurrent cutaneous LP. One patient had vulval lichen sclerosus. Nine patients (15%) had an atopic background. At diagnosis, 73% of patients were taking systemic medication: beta-blockers 11% ($n = 7$); nonsteroidal anti-inflammatory drugs (NSAIDs) 11% ($n = 7$) or 28% ($n = 17$) if aspirin included, and 5% ($n = 3$) angiotensin-converting enzyme inhibitors (ACEI). There was no clear association of specific medications with the onset of the condition.

Clinical features

Frontotemporal recession was present in all cases, with perifollicular erythema and follicular hyperkeratosis described in most. The degree of erythema was variable: marked in some but minimal in others, in whom perifollicular depression was the most prominent feature (Fig 2). All patients were of Fitzpatrick skin types I to III and the distinction between normal-appearing skin and area of hairline recession was sometimes subtle. A striking feature was the unnatural appearance of the hairline caused by loss of both terminal and vellus hairs. Although the hairline generally regressed in a relatively linear

CAPSULE SUMMARY

- Frontal fibrosing alopecia is an uncommon scarring alopecia of unknown origin, affecting the frontal hairline of postmenopausal women.
- Frontal fibrosing alopecia was seen with increasing frequency over the last decade. The condition may affect the entire hairline and commonly involves hair-bearing skin elsewhere. Higher levels of affluence were demonstrated and patients were frequently nonsmokers. In all, 30% of patients had associated autoimmune disease.
- An effective treatment remains elusive. Some treatments may reduce inflammation but impact on progression of alopecia is uncertain.

Table I. Number of new patients presenting with frontal fibrosing alopecia annually to hair clinic 1999 through 2011, with proportion of frontal fibrosing alopecia referrals compared with total number of new referrals annually highlighted

Year	Total No. of new patients seen	No. of patients with FFA	Patients with FFA within new referrals, %
2011 (to May)	57	10	17
2010	220	24	11
2009	220	13	6
2008	161	11	6.8
2007	175	6	3.4
2006	133	3	2.2
2005	71	4	5.6
2004	87	3	3.4
2003	83	5	6
2002	44	1	2.3
2001	56	1	1.7
2000	61	1	1.6
1999	13	0	0

FFA, Frontal fibrosing alopecia.

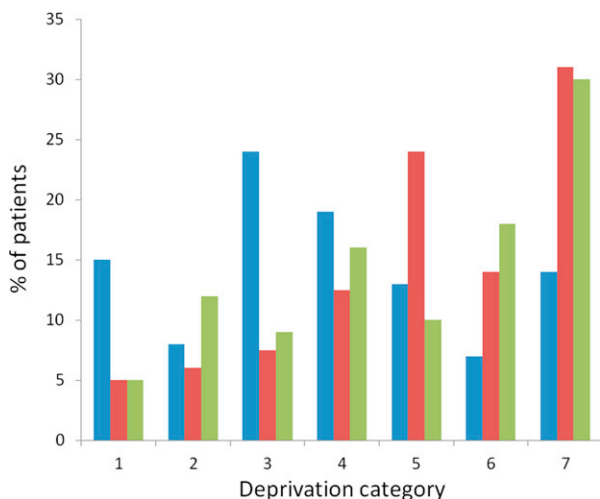


Fig 1. χ^2 Test of proportions revealed that affluence differed in patients attending with frontal fibrosing alopecia (blue columns) compared with age- and sex-matched control subjects attending hair clinic for other conditions (red columns) ($P < .001$); and Greater Glasgow National Health Service patients generally (green columns) ($P = .001$).

fashion, sparing of isolated hairs within the band of alopecia was noted. Although involvement of the frontotemporal hairline was universal, the periauricular hairline was involved in many cases, sometimes discontinuous with the affected frontotemporal hairline. Occipital hairline disease (Fig 3) was documented in 4 cases and significant parietal involvement in 8 cases, with an asymmetric pattern

Table II. Smoking status for patients with frontal fibrosing alopecia ($n = 52$) compared with Scottish female population (age 55-64 years and 65-74 years; $P = .013$, and $P = .00$, respectively, by χ^2 test)

	Patients with FFA, % (n = 52)	Scottish women, % (age 55-64 y)	Scottish women, % (age 65-74 y)
Never smoked	71	53	50
Ex-smokers	19	23	31
Current smokers	10	24	29

FFA, Frontal fibrosing alopecia.



Fig 2. Degree of inflammation along hairline is variable. **A**, perifollicular erythema is evident. **B**, Perifollicular erythema is absent with perifollicular depression being marked.

in two cases. Two patients had minimal frontal loss with significant biparietal loss and one had markedly asymmetric involvement of the frontal hairline (Fig 4). Five patients had diffuse LPP throughout the scalp in addition to FFA at the frontotemporal hairline (Fig 5). Only one patient (1.6%) had significant documented concurrent female pattern hair loss. The condition was generally asymptomatic, although one patient reported itch and one reported pain



Fig 3. Marked occipital involvement.



Fig 4. Biparietal hair loss (**A**), and asymmetric frontal involvement (**B**).

affecting the frontal scalp and crown, which improved with superpotent topical steroids.

Eyebrow loss was documented in 44 patients (73%). Nine patients stated this had preceded scalp involvement, in one case by 8 years. Only one had documentation of eyebrow erythema but otherwise this was clinically noninflammatory without frank scarring. Two patients had loss of eyelashes. Fifteen patients (25%) reported body hair loss (axillary, pubic, and limb). Facial and body hair loss appeared to be permanent, with no spontaneous regrowth reported.



Fig 5. Diffuse lichen planopilaris throughout scalp, in addition to typical changes at frontotemporal hairline.

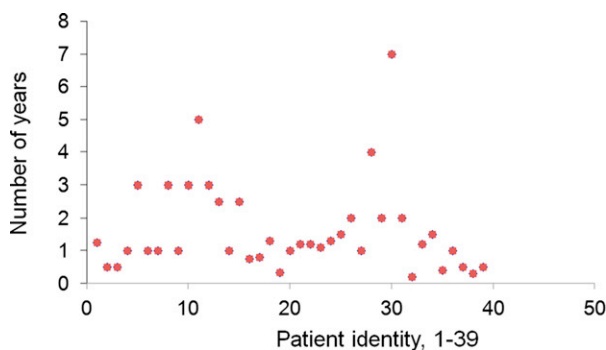


Fig 6. Scatterplot graph of follow-up duration (years).

Treatment

Almost all patients had tried potent or superpotent topical steroids. Many reported this reduced inflammation, however, this did not necessarily correlate with control of alopecia. Several patients developed follicular pustules and focal purpura secondary to topical steroid use. Other treatments included intralesional triamcinolone acetate (10 mg/mL) (n = 8); topical calcineurin inhibitors (n = 22); hydroxychloroquine (n = 9); phototherapy (n = 3); lymecycline (n = 2); prednisolone (n = 1); and topical minoxidil (n = 3). A further 3 patients declined hydroxychloroquine and 3 patients declined cyclosporin, citing potential toxicity as a deterrent.

As most patients were seen within the last 2 years, the mean follow-up time for the cohort is relatively short. Follow-up data are available for 39 patients (mean follow-up period 0.5 years; range: 0-7 years) (Fig 6). In all, 22 patients had no further significant hair loss after presentation despite ongoing erythema in 8 cases (mean follow-up duration 1.4 years; mean disease duration at presentation 4.5 years). Seventeen patients had ongoing hair loss despite resolution of erythema in two cases. In two further cases, hair loss was static at the frontal hairline but progressed at the temporoparietal hairline.

Sequential measurements are available for 11 patients. For this group, mean recession of the frontal

hairline was 1.4 cm (range 0.1–4 cm). For 9 patients, sequential data allowed a calculation of hair loss per year, which ranged from 0.1 to 2.5 cm (mean 0.95 cm). None had hairline recession beyond the crown of the scalp.

Patients were distressed by their alopecia and found it difficult to camouflage. With frontotemporal loss, partial wigs were effective in 3 cases, whereas 8 patients with more extensive loss required full wigs. Eyebrow loss was also distressing and 3 patients were referred for eyebrow tattooing.

DISCUSSION

FFA may be underrecognized,³ supported by incidental presentation in 4 patients, however our impression of increasing incidence was confirmed on analysis of the proportion of cases seen annually (Table D). The cause for this apparent increase in incidence is unknown.

Origin

The origin of FFA is uncertain but most consider it a clinical variant of LPP.² It is postulated that LPP represents a hair-specific autoimmune disorder characterized by a cell-mediated immune reaction against follicular keratinocytes.¹⁴ Eighteen of our patients (30%) had associated autoimmune disease, more in keeping with the prevalence reported in LPP¹⁵ than previously reported for FFA (16.5%),³ and significantly higher than levels of thyroid dysfunction expected in the general female population (3%–10%).^{16,17}

Interestingly, a recent report by Clayton et al¹⁸ suggested an association between mucosal LP and both beta-blockers and NSAIDs, with a possible protective effect of ACEI. Of our cases, 11% were on beta-blockers, 11% on NSAID (28% if aspirin is included), and 5% on ACEI. Compared with the control female population described by Clayton et al¹⁸ (mean age 67 years), a similar proportion of patients with FFA were taking beta-blockers, but a higher proportion were taking NSAIDs (11%, or 28% if aspirin included, vs 4%, $P < .001$). A smaller proportion of patients with FFA were taking ACEI compared with this control population (5% vs 12%, $P < .0010$).

FFA usually occurs in postmenopausal women although 3 patients (5%) were premenopausal. Occurrence in premenopausal women has been described but is considered rare.^{3,4,5,19,20} The clinical presentation and outcome of our patients did not differ from the remainder of the cohort.

Only one of our patients had evidence of clinically notable concomitant female pattern hair loss. This association has been reported more frequently in smaller case series (0%–50%).^{2,4,9} The prevalence of

female pattern hair loss in the UK population has been estimated at approximately 36% in women aged 60 to 69 years,²¹ much higher than the prevalence in our patients (1.6%).

Comparison of Carstairs¹¹ Deprivation scores suggests those with FFA had higher levels of affluence than expected, which may be a surrogate marker for an unknown risk factor associated with affluence. We are unaware of data regarding socioeconomic status in FFA or LPP although other dermatologic conditions are associated with affluence.²² Of note, there were a preponderance of nonsmokers within our cohort, compared with national data and this merits further investigation.

Clinical presentation

Although all cases demonstrated typical features of FFA, namely a band of scarring alopecia affecting the frontotemporal hairline, a number of patients had a less typical pattern of distribution, indicating that FFA may variably involve the entire hairline. Five patients (8%) had evidence of coexistent diffuse LPP affecting nonmarginal scalp, a feature reported infrequently,^{2,23} although Samrao et al⁵ described this appearance in 14% of 36 patients. The condition was generally asymptomatic, with symptoms reported in only 3%, compared with 60% to 70% of cases in multifocal LPP, in whom severe itching, burning, and tenderness are commonly encountered.^{24,25} Eyebrow involvement in FFA is common (73%), consistent with previous reports,^{3,4} whereas eyelash involvement is rare (3%), this feature reported only once previously.² Body hair loss was reported in 25%, although this may be an underestimate of the true prevalence.⁷ It is reported that the histologic features of eyebrow and body hair loss are identical to those at the frontal hairline,^{7,26} suggesting FFA is a generalized alopecia. The lack of clinically apparent scarring or inflammation of eyebrows and body hair, and the apparently low incidence of diffuse scalp LPP, are intriguing and highlight FFA as a clinically distinct variant of LPP.

Compared with LPP, few patients had a history of LP at other sites. Although both cutaneous and oral LP have been reported coexistent with FFA, the association seems uncommon.^{3,20} Only one of our patients (1.6%) gave a history of LP affecting the mucosa. In LPP, typical cutaneous or mucosal LP is reported in 28% to 50% of cases.^{15,24} Thus, extra-scalp involvement with typical LP seems to be less common in FFA than in LPP.

Treatment and prognosis

Currently there are no clinical trials of treatment for FFA and treatments are generally those used in

the management of LPP,²⁷ mostly based on small trials and case series.^{24,25,27,28} Our patients were treated with several different modalities, none consistently effective. Potent topical steroids and calcineurin inhibitors reduced inflammation but without clear benefit in slowing the alopecia, consistent with previous reports.^{2,4,9,29} The most frequently used systemic medication, hydroxychloroquine, was without consistent benefit. Reports of the benefits of hydroxychloroquine in LPP are mixed although a recent review of 40 cases suggested benefit in both LPP and FFA,³⁰ and a significant reduction in signs and symptoms was found by Samrao et al.⁵ The number of patients treated with other modalities (tetracycline, intralesional triamcinolone, and UVB), preclude any conclusion regarding efficacy. Recently, mycophenolate mofetil has been added to the therapeutic armamentarium for LPP.³¹

Follow-up data are available for 65% of our cases (n = 39), however, the mean length of follow-up was short, as most patients were seen more recently. Our impression is that FFA often progresses slowly but may remain static for periods of time. Whether this is as a result of treatment is debatable.

FFA is a fascinating condition. Clinical and histologic similarities with LPP indicate it is a clinical variant of this disorder but the cause of the distinctive "marginal march" is unknown. Involvement of other body hair occurs very frequently and indeed may be universal. Like LPP, autoimmune associations occur more frequently than expected. The association of affluence in our cohort perhaps hints at an as yet unidentified environmental trigger. The role of androgens remains uncertain: although generally affecting a postmenopausal population, no evidence for androgen excess have been demonstrated previously and the involvement of nonandrogen-dependent hair (parietal and occipital hairline, eyebrows and lashes, and limb hair) would also counter this. In our hands, a range of both topical and systemic treatments have been disappointing. Effective management of FFA would best be established by multicenter randomized controlled trials. However, foreseeable difficulties would be assessment of disease activity and progression, and a prolonged time frame for observation would be required. Until then, management of this fascinating disorder will remain unsatisfactory.

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