Single-center analysis of patients with frontal fibrosing alopecia: evidence for hypothyroidism and a good quality of life

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Abstract

Objective: Frontal fibrosing alopecia (FFA) is an underestimated scarring alopecia. This study aimed to examine epidemiological information, as well as predilection sites, associated diseases, and responses to therapy of patients with FFA. We also aimed to determine whether the extent or duration of disease correlated with the quality of life (QoL).

Methods: Twelve outpatients with FFA for > 2 years were analyzed. The Erlanger atopic score and the Functional Assessment of Non-life-threatening Conditions (FANLTC) for QoL-assessment were used as scoring systems.

Results: All patients were women with a mean age of 70.3 years. Most patients did not have any symptoms during their disease progression and no therapy that was used showed any significant effects. FFA was associated with hypothyroidism. There were no correlations between hairline regression, duration of disease, atopic disposition, and QoL. The overall QoL was good.

Conclusions: The present study shows that there is no correlation between the extent of FFA and QoL or atopic predisposition. There is a strong correlation between the incidence of thyroid disease and FFA.
Introduction

Frontal fibrosing alopecia (FFA) was first described in 1994 by Steven Kossard as “postmenopausal frontal fibrosing alopecia”.\(^1\) He documented frontal regression of the hairline with perifollicular erythema and a loss of hair follicles in postmenopausal women. Some of these patients also reported rarefication or total loss of the eyebrows. The histological picture was characterized by lymphocytic infiltrate, perifollicular fibrosis, and loss of follicles. Although most described cases of FFA are postmenopausal, a limited number of cases in men and premenopausal women have been reported.\(^2,3\) FFA typically involves slow, progressive retraction of the fronto-temporal hairline with complete loss of hair and follicular ostia (Figure 1a, b). Parietal, occipital, and/or supra- and retroauricular regions may also be affected (Figure 1c, d). Patients occasionally report symptoms, such as itching, distension, pain, and burning.\(^3\)

The pathogenesis of FFA remains unclear. FFA may be difficult to distinguish from lichen planopilaris based on histology. Comparative analysis of immunopathological findings did not show any groundbreaking differences in direct immunofluorescence and/or immunohistochemistry that would allow for histological differentiation of these two diseases.\(^4\) However, other authors defined FFA as an independent entity, with a unique distribution pattern and sex- and age-specific manifestations.\(^5\)

Therapy for FFA is empirical; neither prospective, controlled trials nor guideline recommendations have been established.\(^6\) All published treatment options of FFA involve preparations that are used to treat many forms of alopecia. The leading therapeutic goal of FFA is to prevent progression of hair loss and renewed hair growth is rare. This study aimed to analyze a group of patients with FFA to characterize disease signs and comorbidities, and to measure quality of life (QoL) in this patient population.

Materials and methods

We screened our outpatient registry for patients who had FFA for >2 years and identified 16 patients. Among these, 12 patients agreed to participate in the study. Written informed consent was obtained from these patients to participate in this study and for its publication and any accompanying images. All of the patients were examined by two investigators (MDM and MM). Sex, age at diagnosis, date of first onset, ethnicity, duration of illness, pattern of hair loss, clinical symptoms, comorbidities, therapies administered, responses to treatment, and the extent of frontal hairline regression were determined when patients visited our clinic for the study.

The Erlanger atopic score was determined. Finally, patients completed the Functional Assessment of Non-life-threatening Conditions (FANLTC) questionnaire for determining QoL. The FANLTC is a questionnaire from the Functional Assessment of Chronic Disease
Therapy Measurement System (www.facit.org) that measures the QoL of patients with chronic diseases.

The study was approved by the ethical committee of Goethe University, Frankfurt (ethical reference number: 223/14) and is in accordance with the Helsinki Declaration of 1975, as revised in 1983.

**Results**

**Sex, age, ethnicity, and association of FFA with menopause**

All 12 patients were women. The mean age at first onset of FFA was 64.7 years and the mean age at the time of the study visit was 70.3 years. The mean duration of disease was 5.67 years. One patient was of black ethnicity and the other patients were white. Seven patients remembered the timing of the onset of menopause. Among these patients, the mean age at the onset of menopause was 51.3 years. One patient developed the first signs of FFA before the onset of menopause. In all of the other patients, the first signs of FFA appeared after menopause (Table 1).

**Distribution pattern of hairline regression**

Frontal hair line regression was observed in 91.7% (n = 11) of patients. Mean frontal hair line regression was 3.91 cm. Rarefication and/or eyebrow loss affected 75% of patients. Temporal and parietal

![Figure 1. Characteristics and pattern of hair loss. Frontal hairline regression with perifollicular erythema at disease onset in 2010 (a) and in 2014 (b); lateral hairline regression in 2010 (a) and in 2014 (b)](image)
regions were affected in 91.7% of cases, axillae in 50%, pubic hair in 41.7%, the retroauricular area in 50%, and eyelashes in 25% (Table 2).

**Symptoms and clinical signs**

We differentiated symptoms that were experienced during disease onset from those observed during the study visit. Pruritus was the most common symptom during disease onset (33%) and 58% of patients did not report any symptoms during disease onset. At the time of the study visit, 83% of patients reported not having any symptoms (Table 3). With regard to clinical characteristics, perifollicular erythema was observed in 75%, hair follicle loss in 100%, and hyperkeratosis in 50% of patients.

**Comorbidities**

Hypothyroidism was observed in 58% of patients. Rheumatic disease was observed in 33% of patients. Two patients had history of prolactinoma. Among these patients, underlying disease occurred at rates similar to those observed in the age-matched general population (Table 4). Dermatological comorbidities are also shown in Table 4. There was no increase in risk for any particular dermatological illness. All of the patients were negative for a family history of FFA.

**Therapy**

Most patients had previously attempted various therapies, which were often prescribed by numerous physicians (Table 5). None of the treatments that were attempted resulted in regrowth. Delayed progression was reported by two patients who were treated with local minoxidil and one patient who was treated with tacrolimus cream.

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**Table 1.** Demographic data, ethnicity, and menopausal status

| Variable                  | n = 12 |
|---------------------------|--------|
| Female                    | 12 (100%) |
| Mean age at disease onset (years) | 64.7 |
| Mean age at study visit (years) | 70.3 |
| Mean duration of disease (years) | 5.67 |
| Ethnicity                 |        |
| White                     | 11 (91.7%) |
| Black                     | 1 (8.3%) |
| Menopausal status         |        |
| Premenopausal             | 1 (8.3%) |
| Postmenopausal            | 647 (84.14%) |
| Mean age at menopause     | 51.3 (n = 7) |

**Table 2.** Distribution pattern of hair loss

| Distribution of hair loss at the study visit | n = 12 |
|----------------------------------------------|--------|
| Frontal                                     | 11 (91.67%) |
| Temporal                                    | 11 (91.67%) |
| Parietal                                    | 11 (91.67%) |
| Occipital                                   | 3 (25%) |
| Retroauricular                              | 6 (50%) |
| Supra-auricular                             | 1 (8.33%) |
| Axillae                                     | 6 (50%) |
| Upper and/or lower limb                     | 3 (25%) |
| Pubic region                                | 5 (41.67%) |
| Eyebrows                                    | 9 (75%) |
| Eyelashes                                   | 3 (25%) |
| Mean frontal regression                     | 3.91 cm |

**Table 3.** Symptoms at the study visit and disease onset

| Symptoms at the study visit | n = 12 | Symptoms at disease onset | n = 12 |
|-----------------------------|--------|---------------------------|--------|
| Perspiration at the head    | 1 (8.33%) | Pruritus                  | 4 (33.33%) |
| Pain                        | 1 (8.33%) | Inflammation              | 1 (8.33%) |
| None                        | 10 (83.33%) | Feeling of tension of the scalp | 1 (8.33%) |
|                             |         | None                      | 7 (58.33%) |
Correlation between duration of disease and QoL

To analyze whether the duration of disease was correlated with QoL, we asked our patients to fill out the FANLTC. Among our patients, the mean FANLTC score was 83.4 (range, 65.3–104), which indicated an overall good QoL. Regression analysis showed no significant linear correlation between QoL and duration of disease ($P = 0.16$; coefficient of determination, 0.02; t-value, –0.5) (Figure 2).

Correlation between maximal hairline regression and QoL

We also analyzed whether maximal hair regression was correlated with QoL. Regression analysis showed no significant linear correlation between maximal hair regression and QoL ($P = 0.07$; coefficient of determination, 0.005; t-value, –0.21) (Figure 3).

Correlation between the Erlanger Atopic Score and maximal hairline regression

The atopic score was determined for all 12 patients. The mean atopic score was 6.8, which suggested minimal atopic predisposition. Regression analysis showed no significant linear correlation between maximal hair regression and the atopic score among our patients ($P = 0.12$; coefficient of determination, 0.01; t-value, 0.4) (Figure 4).

Discussion

Our clinical and epidemiological data add to current knowledge about FFA. A previous study reported a predominance of FFA among women, but up to 3% of patients with FFA were men.7,8 All of the patients included in our study were women. Among our patients, the mean age at first manifestation was 64.7 years, which is older than that reported in the literature. Banka et al.9 reported that the mean age of patients with FFA was 63 years (62 patients) and Vano-Galvan et al.7 reported a mean age of 56 years (355 patients). The number of patients in our study (n = 1) who reported

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**Table 4.** Dermatological and internal comorbidities

| Dermatological comorbidities                  | n = 12 |
|----------------------------------------------|--------|
| Psoriasis                                    | 2 (16.66%) |
| Rosacea                                      | 1 (8.33%) |
| Lichen ruber mucosae                        | 1 (8.33%) |
| Vitiligo                                     | 1 (8.33%) |
| lichen sclerosus et atrophicans genitalis    | 1 (8.33%) |
| Atopic dermatitis                            | 1 (8.33%) |
| Internal comorbidities                       |        |
| Hypothyroidism                               | 7 (58.33%) |
| Hypertension                                 | 6 (50%) |
| Dyslipidemia                                 | 2 (16.66%) |
| Undifferentiated collagenosis                 | 1 (8.33%) |
| Hemochromatosis                              | 1 (8.33%) |
| Rheumatoid arthritis                         | 3 (25%) |
| Prolactinoma                                 | 2 (16.66%) |
| Allergies                                    | 7 (58.33%) |

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**Table 5.** Therapies and therapy combinations and their response

| Therapy                  | Progressive hair loss | Stable situation n |
|--------------------------|-----------------------|--------------------|
| Minoxidil                | 6                     | 2                  | 8                  |
| Diphenylcyclopropenone   | 1                     | –                  | 1                  |
| Mometasone               | 3                     | –                  | 3                  |
| Clindamycin              | 1                     | –                  | 1                  |
| Clobetasol               | 2                     | –                  | 2                  |
| Triamcinolone            | 1                     | –                  | 1                  |
| Tacrolimus               | –                     | 1                  | 1                  |
| Resorcin                 | 1                     | –                  | 1                  |
| Fusidic acid + betametasone | 1                  | –                  | 1                  |
| GKL-02 (thymus extract)  | 1                     | –                  | 1                  |
Premenopausal onset of symptoms is similar to that reported in the literature. Among the patients who were included in our study, the mean onset of menopause was at 51.3 years. This finding suggests a time gap of almost 14 years between menopause and the first manifestation of FFA. Therefore, menopause alone might not lead...
to FFA. In contrast to other reports, we analyzed the distribution pattern of hair loss in more detail.7–9 Interestingly, almost half of our patients showed hair loss in the axillae and genital regions, and loss of eyelashes was observed in 25% of patients. This finding might be explained by the fact that our cohort was older (mean age of 70.3 years at the study visit) and had a longer duration of disease (5.7 years) compared with previous studies.7–9 In line with this observation, Vano-Galvaono et al. showed that the severity of FFA was correlated with the duration of disease.7 Therefore, the extent of hair loss observed in older patients may be more extensive than that in younger patients, who have a shorter duration of disease.

The most common clinical signs identified in our study were perifollicular erythema (75%), hyperkeratosis (50%), and hair follicle loss (100%). These rates of perifollicular erythema and hair follicle loss are higher than those previously reported.7–9 This discrepancy between studies may reflect the fact that we prospectively obtained clinical data from our patients at the time of the study visit using a preformed questionnaire, rather than retrospectively analyzing outpatient records, as in most other studies. However, the dual nature of our study (retrospective as well as prospective) allowed us to compare symptoms that were observed during the onset of disease with those observed after many years at the study visit. We found that pruritus was often reported soon after disease onset (33%). This frequency of pruritus is in line with that reported by other studies.3 Trichodynia was reported by one patient (8%) compared with 5% to 20% in the literature.7 Approximately 60% of our patients did not report any symptoms at the time of disease onset. At the study visit, many years after onset of FFA, more than 80% of patients reported a lack of symptoms.

The most common comorbidity that was observed among the patients in our study was hypothyroidism (58%). The incidence of thyroid disease in our patients with FFA was much higher than that in the general population (6%–10%).10 In a retrospective study with 32 patients with FFA, Meinhard et al.11 observed a lower incidence of thyroid disease (31%) than that reported in the current study. Control of thyroid levels, including organ ultrasonography, is recommended when confirming the diagnosis of FFA. Other internal diseases, such as hypertension (50%) and diseases of the rheumatic spectrum (33%), were common among our patient population. The fact that these diseases appear to be underrepresented in other studies most likely results from the retrospective methodology used and the fact that these diseases were only partially investigated.7 No dermatological comorbidity showed a significant prevalence in our study.

To determine whether there is a correlation between QoL and the duration of disease or maximum hairline regression, our patients completed the FANLTC. The overall QoL of our patients was good. Interestingly, there was no significant correlation between QoL and either of the variables investigated. After completion of our study, Saceda-Corralo et al.12 developed the Frontal Fibrosing Alopecia Severity Score (FFASS) to quantify the severity of FFA. The FFASS asks for information related to clinical signs and symptoms, such as hairline regression, inflammation, pruritus, and pain. During validation of the FFASS, the authors found no correlation between the severity index and QoL. This finding is in line with our results for maximal hairline regression and disease duration. A recent publication analyzed the health-related QoL in approximately 80 patients by using three questionnaires and analyzed different aspects of anxiety and depression, illness perception, or dermatology life...
In our population, the FANLTC had a score of 83 (maximum score = 104), which we interpreted as an overall good, but not excellent, QoL. Therefore, there might be a slightly negative correlation between FFA and QoL. This is comparable with the findings of Saceda-Corralo et al. who found that 84% of patients with FFA demonstrated no or mild impairment of QoL. Additionally, these authors could not demonstrate any association between the severity of alopecia and QoL, which is in line with our results. Notably, changes in QoL may have been less noticeable among our patient population, with a mean age of 70 years and extended disease duration, compared with younger patients and/or those with newly diagnosed illnesses. A positive correlation between QoL and severity of the disease or early onset was observed in patients with alopecia areata, who are typically younger than patients with FFA (mean age: 30–36 years). Finally, we showed the absence of a correlation between atopic predisposition and FFA, which is in line with observations for patients with other types of alopecia.

In summary, our analysis of a small cohort of patients with FFA confirmed several known aspects of FFA. We also identified hypothyroidism as an important comorbidity that should be considered upon diagnosis of FFA. There does not appear to be a correlation between hairline regression or duration of disease and QoL, and these patients show an overall good QoL.

The main limitation of our study is that statistical correlations were difficult to identify because of the small number of patients who were included in the study. Nonetheless, this study represents the first attempt to identify a correlation between QoL and duration of FFA or maximum hairline regression. This analysis adds to the current store of knowledge about FFA.

**Availability of data and materials**
The datasets analyzed in the current study are available from the corresponding author on reasonable request.

**Authors’ contributions**
EMV designed the study, performed data analysis, and wrote and approved the manuscript. MDM performed data collection and statistical analysis, and approved the manuscript. RK performed data analysis and approved the manuscript. MM designed the study, performed data and statistical analysis, and wrote and approved the manuscript.

**Declaration of conflicting interest**
The authors declare that there is no conflict of interest.

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