INTRODUCTION

Frontal fibrosing alopecia (FFA) and fibrosing alopecia in a pattern distribution (FAPD) represent two distinct patterns of cicatricial pattern hair loss. Both share a patterned distribution and histological evidence of a lichenoid follicular inflammation with fibrosis. FFA is characterized by a marginal alopecia along the frontotemporal hairline, and FAPD by a progressive alopecia of the centroparietal scalp. Since the original reports, evidence has accumulated that there exists considerable clinical overlap among FFA, FAPD, and lichen planopilaris, with coexistence of features of the three conditions within the same individual. Moreover, familial cases of FFA have been reported, pointing to a possible genetic background to the condition. Our observation of familial occurrence of FFA and FAPD in daughter and mother, respectively, further underscore a nosologic relationship between the two conditions with respect to both an androgenetic background and the (lichenoid) inflammatory reaction pattern.

Key words: Cicatricial pattern alopecia, familial occurrence, fibrosing alopecia in a pattern distribution, frontal fibrosing alopecia

Familial Cicatricial Alopecia: Report of Familial Frontal Fibrosing Alopecia and Fibrosing Alopecia in a Pattern Distribution

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ABSTRACT

Frontal fibrosing alopecia (FFA) and fibrosing alopecia in a pattern distribution (FAPD) as originally reported by Kossard in 1994 and by Zinkernagel and Trüeb in 2000, respectively, represent two distinct patterns of cicatricial pattern hair loss. Both share a patterned distribution and histological evidence of a lichenoid follicular inflammation with fibrosis. FFA is characterized by a marginal alopecia along the frontotemporal hairline, and FAPD by a progressive alopecia of the centroparietal scalp. Since the original reports, evidence has accumulated that there exists considerable clinical overlap among FFA, FAPD, and lichen planopilaris, with coexistence of features of the three conditions within the same individual. Moreover, familial cases of FFA have been reported, pointing to a possible genetic background to the condition. Our observation of familial occurrence of FFA and FAPD in daughter and mother, respectively, further underscore a nosologic relationship between the two conditions with respect to both an androgenetic background and the (lichenoid) inflammatory reaction pattern.

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In 2000, Zinkernagel and Trüeb\[13\] reported yet another peculiar cicatricial pattern hair loss with histopathological features of LPP and named it FAPD. Patients developed progressive fibrosing alopecia of the central scalp area, without the multifocal areas of involvement typical for LPP. Histopathology of early lesions demonstrated hair follicle miniaturization and again a lichenoid inflammatory infiltrate targeting the upper follicle region, while advanced lesions showed perifollicular lamellar fibrosis and completely fibrosed follicular tracts. Due to the specific distribution and evidence of associated AGA, the authors speculated whether the lichenoid tissue reaction leading to follicular destruction may be pathogenetically related to the events underlying AGA. As yet, familial occurrence of FAPD has not been reported.

Herein, we report the familial occurrence of FFA and FAPD underscoring a nosologic relationship between the two conditions.

CASE REPORTS

**Patient 1**

A 45-year-old woman presented with the complaint of a receding frontal hairline and loss of eyebrows accompanied by redness and fine scaling. The primary attending physician suspected traction alopecia, but the patient denied any respective hair style. Clinical examination revealed a symmetric, cicatricial band of frontal hairline recession with lonely hairs [Figure 1], rarefaction of sideburns and of lateral eyebrows. The distance between the eyebrows and frontal hair line was 7 cm. Dermoscopic examination revealed perifollicular erythema, mild perifollicular scaling, and loss of follicular openings. A diagnosis of FFA was made, and the patient was prescribed 1% pimecrolimus cream b.i.d. for the frontal hairline, sideburns area, and eyebrows, and 5% minoxidil solution once daily for the crown area.

**Patient 2**

The 75-year-old mother of patient 1 presented with a 3-year history of pruritus of the central scalp area with progressive loss of hair. A biopsy performed by her primary attending dermatologist revealed AGA with histological evidence of follicular inflammation and fibrosis. Treatment was started with 0.05% clobetasol propionate foam. Clinical examination revealed a follicular inflammatory scarring alopecia of the central scalp area [Figure 2] with obliteration of follicular orifices, perifollicular erythema, and follicular keratosis limited to the respective area of AGA on close clinical and dermoscopic examination. Notably, the frontal hairline was preserved. A diagnosis of FAPD was made, and the patient was prescribed a compound of 5% minoxidil and 0.2% triamcinolone acetonide b.i.d. for the crown area.

DISCUSSION

Our observation of familial occurrence of FFA with FAPD points to possible common pathogenic pathways on a genetic background of AGA with a lichenoid inflammatory reaction pattern.

Conventionally, AGA or patterned hair loss is understood to represent a hereditary and androgen-sensitive, progressive thinning of the scalp hair with a polygenic hereditary background and peculiarities of androgen-metabolism.
The limited success rate of respective treatment modalities, specifically oral antiandrogens, 5-alpha-reductase inhibitors, and topical minoxidil, implies that additional pathogenic factors must be considered. The implication of a follicular inflammation and fibrosis associated with patterned hair loss has emerged from several independent studies: an early study referred to an inflammatory infiltrate of activated T-cells and macrophages in the upper third of the hair follicles, associated with an enlargement of the follicular dermal sheath composed of collagen bundles in regions of actively progressing alopecia.[3,4] Subsequently, Whiting[25] demonstrated in morphometric studies in patients with male pattern AGA treated with minoxidil that 55% of patients with microinflammation had regrowth in response to treatment, in comparison to 77% of those without inflammation and fibrosis. Finally, Mahé et al.[18] proposed the term microinflammation, as in much as the process involves a slow, subtle, and indolent course, in contrast to the inflammatory and destructive process in the classical inflammatory scarring alopecias.

Following the original reports of FFA and FAPD, it was pointed out that both may represent the end of a continuum reaching from AGA with histological evidence of follicular microinflammation and fibrosis to clinically perceptible forms of patterned inflammatory scarring alopecia.[17] Moreover, considerable overlap exists among FFA, LPP, and FAPD: FFA has been described in association with lichen planus elsewhere, including the oral cavity[15] and the nails,[14] and FFA-type changes have also been observed in patients with FAPD, including facial papules.[8] Other authors have referred to mid-frontal scalp hair loss in patients with FFA and clinical features of AGA,[19] while alternatively, we might rather be dealing with FAPD extending to involve the frontal hairline.

Ultimately, the question arises how the lichenoid tissue reaction pattern is generated around the individual androgenetic hair follicle. Follicles with some form of damage or malfunction might express cytokine profiles that attract inflammatory cells to assist in damage repair or the initiation of apoptosis-mediated organ deletion. Alternatively, an as yet unknown antigenic stimulus from the damaged or malfunctioning hair follicle might initiate a lichenoid tissue reaction in the immunogenetically susceptible individual.[13]

Remarkably, in healthy murine skin clusters of perifollicular macrophages have been described as perhaps indicating the existence of a physiological program of immunologically controlled hair follicle degeneration by which malfunctioning follicles are removed by programmed organ deletion.[20]

Various forms of clinically perceptible, permanent alopecia might represent a pathological exaggeration of this type of programmed organ deletion, resulting in a lichenoid tissue reaction pattern and true scarring alopecia. Further studies are required in patients with FFA and FAPD to elucidate a presumable role of androgenetic factors in addition to that of the lymphohistiocytic infiltrate, perifollicular lamellar fibrosis, and apoptosis-mediated follicular regression.

Harries et al.[21] ultimately provided the first evidence that LPP may result from an immune privilege collapse of the hair follicle’s epithelial stem cell niche. Due to its analogies with lichen planus, graft versus host disease (GvHD) constitutes a valid model for a better understanding of the pathophysiological features underlying both lichen planus and LPP. Miyazaki et al.[22] reported the first case of GvHD with follicular involvement. Moreover, GvHD may present on the scalp as FAPD (personal observation), as originally reported by Basilio et al. as permanent alopecia after bone marrow transplantation.[23]

While studies on cicatricial pattern hair loss have so far primarily focused on androgenetic factors and on the lymphohistiocytic infiltrate, perifollicular lamellar fibrosis, and apoptosis-mediated follicular regression, the role of environmental factors and hair grooming practices have so far not found the appropriate attention, specifically in relation to the pattern of hair loss, whether FFA or FAPD.

Originally considered to be an uncommon condition, in the recent past, the number of cases of FFA has exploded exponentially. A questionnaire-based study on FFA suggested a possible association with the use of facial skin care products, particularly sunscreens,[24,25] but the causality of this relationship remains to be confirmed since the study may have been biased through patient and question selection, as well as confounding factors that were not included in the patient questionnaire. Moreover, there is evidence that FFA was described well before Kossard’s original report and the use of modern sunscreens.[26]

Hot comb alopecia represents yet another type of cicatricial pattern hair loss that was originally considered to be associated with the excessive use of hot combs, oil pomades and other hair care chemicals among African American women.[27] It was thought that the oils applied to the hair and heated by the hot comb would travel down the hair shaft into the hair follicular unit opening, and cause inflammation around upper follicles. However, it was later recognized that, while hot combing might elicit the condition in some individuals, the condition can also present in the absence of a history of the respective
cosmetic procedure. Subsequently, the condition was renamed central centrifugal cicatricial alopecia (CCCA) and included by the North American Hair Research Society in 2003 within the lymphocytic group of primary scarring alopecia in their respective working classification.[28] The condition presents in the 20s with a quasi-symmetrical alopecia centered on the crown/vertex of the scalp and progresses centrifugally over the following 20–30 years. A considerable amount of hair is often lost before the alopecia and scarring are recognized. Therefore, it has been recommended to consider the possibility of the diagnosis in women of African origin with what appears to be female-pattern AGA.[29] The etiopathogenesis of CCCA has remained elusive and is probably multifactorial and heterogeneous. Histopathologic features include again a perifollicular lymphocytic infiltrate, concentric lamellar fibrosis, and sebaceous gland loss. To investigate medical and environmental risk factors for CCCA, Kyei et al.[30] performed a population study involving a quantitative cross-sectional survey of risk factors. Diabetes mellitus type 2 was significantly higher in those with CCCA, as were bacterial scalp infections, and hair styles associated with traction. Ultimately, Miteva and Tosti found in their samples of CCCA evidence of a high proportion of hair follicle miniaturization on histopathology,[31] and hair shaft variability together with peripilar white halo on dermoscopy,[32] strikingly similar to the findings in FAPD. This ultimately raises the question whether CCCA may at least in part not represent FAPD in patients of African origin, while Zinknagel and Trüeb’s[13] original observations on FAPD involved Caucasians exclusively.

In summary and conclusion, the observation of familial occurrence of FFA and FAPD underscores a nosologic relationship between the two conditions with respect to both the androgenetic background and the (lichenoid) inflammatory reaction pattern. Whether differences in environmental factors and/or hair grooming habits, either the use of sunscreens or hair styles associated with traction, would explain the different patterns of cicatricial alopecia in mother and daughter could not be elucidated.

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Conflicts of interest
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Missio, et al.: Familial cicatricial pattern hair loss

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