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Research letter

Frontal fibrosing alopecia: a descriptive cross-sectional study of 711 cases in female patients from the UK

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Dear Editor, Frontal fibrosing alopecia (FFA) is an inflammatory primary scarring alopecia of uncertain aetiology that represents a variant of lichen planopilaris.[1] It predominantly, although not exclusively, affects postmenopausal women.[2] Its pathogenesis is characterized by immune-mediated follicular destruction at the level of the hair bulge, which leads to a clinical phenotype of progressive frontotemporal hair and eyebrow loss that is often preceded by widespread body-hair loss.[2] Histologically, a lichenoid inflammatory infiltrate surrounds the isthmus and infundibulum of the hair follicle, and this progresses to follicular scarring and dropout in advanced disease.[2] We recently completed the first genome-wide association study (GWAS) in FFA coupled with transcriptomic and metabolomic analyses, which have provided important insights into its pathogenesis.[3] We have conducted and herein present a descriptive cross-sectional study of the clinical phenotype in women from the FFA UK GWAS Cohort.

Ethical approval was obtained from the Northampton NRES Committee, UK (REC 15/EM/0273). Patients with a formal diagnosis of FFA made by a consultant dermatologist from 20 secondary care dermatology departments across the UK were eligible for inclusion. A diagnosis of FFA was made based on clinical criteria, with histological confirmation if required.[2] Each patient was assessed for multiple clinical variables based on a standardized pro forma. Analysis was limited to female participants of Eurasian ancestry in line with our previous GWAS.[3] Statistical analysis was descriptive and exploratory, estimating frequencies and measures of centrality and spread, and participants for whom data were missing for a given variable were excluded from the analysis. All analyses were conducted using Stata version 15 (StataCorp, College Station, TX, USA).

Phenotypic data were available for 711 UK women with FFA among a total of 1044 participants in the GWAS cohort. Their median age was 66 (interquartile range 59–72) and the median duration of scalp hair loss was 7 years (interquartile range 5–10). In 485 of 663 (73·2%) participants with available data, frontotemporal hairline recession occurred following menopause. Other clinical characteristics and comorbidities are summarized in Table 1. Perifollicular erythema was present in 77·3% and hyperkeratosis in 26·0% of participants. In addition to frontotemporal recession, concomitant occipital recession was noted in 26·0%. Eyebrow loss was noted in 90·6% and eyelash loss in 44·5%. Limb hair loss was also documented in 77·5% and most commonly affected both arms and legs, while concomitant axillary or pubic hair loss was reported in 67·0%. Concurrent multifocal involvement suggesting coexistence of classic lichen planopilaris (14·7%) and nail changes of any type (23·7%) were noted in a smaller proportion of participants. Other forms of lichen planus were seen in 9·5% of participants, with oral (5·1%) and vulval disease (3·5%) being most prevalent.

Only 44·0% of our cohort were prescribed a medication relevant to their FFA. The most frequent treatment was hydroxychloroquine (24·0%), with other treatments such as topical corticosteroids (16·6%), oral tetracycline antibiotics

Table 1 Clinical characteristics of the female participants (n = 711)

Characteristic	n (%)	Missing data
Clinical features		
Perifollicular erythema	508 (77·3)	54
Follicular hyperkeratosis	119 (26·0)	253
Occipital recession	178 (26·0)	27
Eyebrow loss	620 (90·6)	27
Eyelash volume loss	311 (44·5)	12
Limb hair loss	543 (77·5)	10
Arm	15 (3·2)	235
Leg	49 (10·3)	235
Both	254 (53·4)	235
Axillary and pubic hair loss	464 (67·0)	18
Axillary	94 (20·0)	242
Pubic	17 (3·6)	242
Both	129 (27·5)	242
Multifocal scalp hair loss	95 (14·7)	66
Nail changes (any type)	165 (23·7)	16
Comorbidities		
Lichen planus	60 (9·5)	78
Oral	32 (5·1)	78
Vulva	22 (3·5)	78
Skin	7 (1·1)	78
Nails	2 (0·3)	78
Autoimmune disease	141 (20·7)	29
Autoimmune thyroid disease	88 (12·9)	29
Coeliac disease	10 (1·5)	29
Pernicious anaemia	8 (1·2)	29
Previous oestrogen deficiency	38 (5·6)	37
Previous SERM use	15 (2·3)	54
Prior OCP use (> 6 months)	445 (71·2)	86

OCP, oral contraceptive pill; SERM, selective oestrogen receptor modulator.

(10·1%), topical calcineurin inhibitors (3·8%), intralesional steroids (1·7%) and oral corticosteroids (1·3%) being less common. Use of systemic immunosuppressant or antiproliferative agents including retinoids, mycophenolate mofetil, ciclosporin and methotrexate was rare (2·1%).

In keeping with the immune-mediated pathogenesis of FFA, 20·7% of participants reported at least one comorbid autoimmune disease (Table 1). The most common was autoimmune thyroid disease (12·9%), followed by coeliac disease (1·5%) and pernicious anaemia (1·2%). As hormonal aberrations have been implicated in the pathogenesis of FFA, we also examined whether certain endocrine disorders were prevalent in this cohort.[2] A history of oestrogen deficiency secondary to oophorectomy or primary ovarian insufficiency was present in 5·6% of women, while 2·3% reported exposure to selective oestrogen receptor modulators (tamoxifen or clomiphene). With regard to exogenous hormone use, the oral contraceptive pill was used for > 6 months by 71·2% of women.

In summary, this descriptive study outlines the clinical characteristics and treatment modalities in a cohort of 711 women with FFA, recapitulating findings described by other international studies.[4] Analysis of comorbidities revealed that autoimmune disease, thyroid hormone abnormalities and oestrogen deficiency were more prevalent than in the general population, while the frequency of oral contraceptive use was similar.[5–7] These findings accord with other epidemiological studies and the results of our genetic investigation, which implicated causal genetic variation related to antigen presentation and hormone or xenobiotic metabolism in FFA pathogenesis.[3,8]

This investigation is limited by its cross-sectional design, the absence of a control group, and missing data for certain clinical features. Therefore, further detailed clinical and experimental investigations are required to dissect the roles of autoimmunity and hormone metabolism in FFA pathogenesis.

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Conflicts of interest: The authors declare they have no conflicts of interest.

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