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The Use of Direct Immunofluorescence in Frontal Fibrosing Alopecia

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Keywords
Cicatricial alopecia · Diagnosis · Hair disorder · Hair loss

Abstract
Background: Frontal fibrosing alopecia (FFA) differs from lichen planopilaris (LPP) in many clinical aspects, but histology fails to distinguish between these entities. Direct immunofluorescence (DIF) is a diagnostic technique used for autoimmune diseases, including those affecting skin and hair. ***Objective:*** To characterize DIF patterns in patients with FFA. ***Method:*** Data was collected retrospectively from FFA cases presenting to the Centre de Santé Sabouraud Hair Clinic in Paris from November 2013 to November 2014. ***Results:*** Of 149 patients with FFA, 44 cases underwent DIF. Thirteen cases showed positive results with DIF. Patterns characteristic of LPP and lupus erythematosus were observed, with nearly half showing nonspecific staining. ***Conclusion:*** DIF patterns in patients with FFA were variable. This diagnostic technique should be used with caution in cases of cicatricial alopecia, particularly FFA.

Introduction

Frontal fibrosing alopecia (FFA) is a primary lymphocytic cicatricial alopecia that affects predominantly the frontotemporal hairline [1]. Histology shows perifollicular lichenoid or lymphohistiocytic infiltrate with variable perifollicular fibrosis and follicular dropout, depending on the stage of the disease [2]. Due to histological similarities, FFA is considered a clinical variant of lichen planopilaris (LPP) [1].

Direct immunofluorescence (DIF) is used to detect autoantibodies deposits on lesional and perilesional tissue. It has been shown to be useful for differential diagnosis of cicatricial alopecias [3]. DIF patterns in LPP consist of numerous globular deposits of immunoglobulins, particularly IgM (colloid bodies), and deposits of C3 in the papillary dermis. Granular deposits in the dermoepidermal junction, comprising IgG, IgM, and C3, are typical of DIF results observed in lupus erythematosus (LE). While most cases of cicatricial alopecia may be differentially diagnosed using histopathology, there are cases that can be aided by the use of DIF [3].

The clinical presentation of FFA, together with the likelihood of affecting postmenopausal women, often leads to clinical diagnosis without the use of laboratory results. However, many clinics may obtain routine sam-

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Table 1. Demographics, ANA positivity, and DIF staining of 13 patients with positive results

Patient No.	Sex	Age, years	ANA	DIF staining			
				BMZ		colloid bodies	pattern
1	F	71	negative	E: – F: C3	granular		ns
2	M	47	negative	E: IgG, IgA, C3 F: –	moderate		LE
3	F	58	negative	E: IgM, C3 F: –	continuous	IgM	LP
4	M	77	negative	E: IgG, IgA, C3 F: IgG, IgA, C3			LE
5	F	71	negative	E: – F: –		IgG, IgA, C3	LP
6	F	67	negative	E: IgM F: –			ns
7	F	39	negative	E: - F: –		IgG, IgA, C3	LP
8	F	86	na	E: IgA F: –		C3	LP
9	F	63	negative	E: – F: C3	microgranular, discontinuous		ns
10	F	72	1/160 nuclear homogeneous	E: IgA, IgG F: –			ns
11	F	na	negative	E: IgG F: –	continuous, moderate		ns
12	F	74	negative	E: IgG, IgA, C3 F: –	homogenous		LE
13	F	80	negative	E: IgM F: –			ns

ANA, antinuclear antibodies; DIF, direct immunofluorescence; BMZ, basal membrane zone; E, epidermis; F, follicular epithelium; Ig, immunoglobulin; LP, lichen planopilaris; LE, lupus erythematosus; ns, nonspecific; na, not available.

ples for histopathological and DIF testing. The utility of performing such diagnostic tests in cases of FFA is unknown. DIF results in FFA cases have rarely been reported [2, 4, 5]. To our knowledge, the current study reports DIF findings from the largest sample of FFA cases to date.

Method

A retrospective analysis of all cases of FFA presenting between November 2013 and November 2014 at the Centre de Santé Sabouraud Hair Clinic in Paris was performed. Informed consent was not necessary due to the retrospective nature of the study. Clinical and epidemiological data was retrieved from patient charts. Patients with the diagnosis of systemic LE were excluded and antinuclear antibodies of the included cases were studied.

Staining of vertical slides with commercially available fluorescein-labeled antisera to human IgG, IgA, IgM, and C3 had been performed as routine investigation for skin autoimmune diseases. Based on previous studies [3], globular deposits (colloid bodies) of immunoglobulins or C3 on the papillary dermis or around the hair follicles were considered characteristic of LPP. All other findings were considered nonspecific, and the absence of staining was considered a negative finding.

Results

During the study period, FFA was clinically diagnosed in 149 patients. Histology confirmed the diagnosis in 69 patients, while DIF was performed in 44 cases. Thirteen patients (29.5%) showed positive DIF results, and the remaining 31 showed negative DIF results. Eleven of 13 patients were female, with a mean age of 67 ± 13.5 years (range 39–86, data on 1 patient were unavailable).

Table 2. Results of DIF findings in our study and in previous reports

	FFA (+/total)	DIF pattern
Kossard, 1994 [2]	1/3 (33%)	IgA, IgM, and IgG in CB
Poblet, 2006 [4]	0/2	na
Chew, 2010 [5]	0/13	na
Current study, 2017	13/44 (30%)	Any positivity
	4/44 (9%)	LP pattern: Ig or C3 in CB
	3/44 (7%)	LE pattern: ≥2 Ig and C3 in epidermal or follicular BMZ

BMZ, basal membrane zone; CB, colloid bodies; DIF, direct immunofluorescence; FFA, frontal fibrosing alopecia; Ig, immunoglobulins; na, not available.

Table 1 characterizes the staining results in these 13 cases of FFA. Eleven patients showed negative ANA titers, including those patients with a typical LE DIF pattern. Four cases (9%) presented a typical LPP pattern, with globular deposits of immunoglobulins and/or C3. Three cases (7%) presented deposits of all immunoglobulins and C3 over the epidermal or the follicular epithelial basal membrane zone (BMZ), resembling LE. FFA presenting an LE DIF pattern did not have clinical or histological evidence of LE at the time of diagnosis. The remaining 6 cases showed positive staining, but with nonspecific patterns of immunoglobulins or C3.

Discussion

FFA was first described in 1994 in 6 postmenopausal Caucasian women [2]. Since its first reports, FFA has been considered a form of LPP; however, there are differences such as more frequent involvement of eyebrows and body hair [5]. Histologically, FFA cannot be distinguished from LPP even though there are slight differences on the degree of apoptosis of the external root sheath, interfollicular and perifollicular inflammatory infiltrate density, and interfollicular epidermal involvement [4].

There are 3 previous reports of DIF results in FFA patients (Table 2). One of 3 women studied in FFA's first description presented globular deposits of immunoglobulins at the BMZ [2], while a second report described negative DIF results in 2 FFA scalp biopsies [4]. Lastly, histopathological analysis of FFA patients with scalp, eyebrow, and body hair loss yielded negative scalp DIF findings [5]. In the literature, only limited attention has been given to FFA and DIF; however, DIF as used for characterizing LPP and other cicatricial alopecias may be on the radar as a diagnostic tool for physicians and specialists.

Histological similarities generally confer FFA with the classification of clinical variants of LPP [1]. However, as we recall FFA's epidermal involvement [6–8] with clear predilection for sun-exposed areas associated to DIF findings, FFA would be better placed in the middle of a spectrum of primary cicatricial alopecias between LPP and LE and thus considered a stand-alone form of primary cicatricial alopecia.

To our knowledge, this is the largest sample of FFA patients in whom the utility of DIF for scalp biopsies has been investigated. Our study confirms previous results and suggests that DIF will likely be negative in FFA cases. Moreover, a typical LPP (9%) or LE (7%) pattern is rarely seen in FFA, suggesting that the same value that DIF may have for differentially diagnosing pathologically ambiguous cases of LPP from LE is not present for FFA. DIF is an expensive tool and should be sparingly used when diagnosing cicatricial alopecias. Despite histological similarities, DIF findings and clinical presentation of FFA are distinct enough so that it may be accurate to describe FFA as a separate disease process.

Statement of Ethics

Informed consent was not necessary due to the retrospective nature of the study.

Disclosure Statement

The authors have no conflicts of interest to disclose. There was no funding source for this work.

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