

Frontal fibrosing alopecia, clinical and histopathological characteristics of Mexican patients: an original research study and review of literature

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Abstract

Background: Frontal Fibrosing Alopecia (FFA) was described at twenty-century, and cases increased exponentially. FFA has a great impact on patient's quality life.

Objective: Thus, the aim of this work was report FFA cases attended during a fifteen-year period.

Material and methods: A retrospective study was carried out, including patients with FFA diagnosis treated at Dermatology department. Data were obtained from the clinical files, and tissue slices were reviewed.

Results: Thirty-seven patients FFA were identified. Ninety-seven percent (n= 36) were women, with an average age of 57.8 years (range between 35 to 86 years). Eighty-one percent presented with recession of implantation line as the main clinical manifestation; the predominant histological pattern was scarring alopecia, presented in 34 patients (91.8%).

Discussion: Increased of the pathology was observed in the last five years, since 2017. FFA is a newly diagnosed disease with increased prevalence in Mexico, where it occurs predominantly in postmenopausal women.

Conclusion: Mexican patients presented in late stages of the disease, with mean ages lower than other series, so in our country the challenge is to identify the FFA in early stage and prevent disease progression and the irreversible alopecia.

Keywords: Frontal Fibrosing Alopecia, Cicatrized Alopecia, Scar Alopecia, Menopause

Abbreviations

FFA: Frontal Fibrosing Alopecia.

Introduction

Frontal Fibrosing Alopecia (FFA) was first described as a type of lymphocytic scarring alopecia in 1994, by Kossard [1]. It is characterized by selective affected frontotemporal implantation line and eyebrows [2]. Currently, FFA is considered a variant of lichen planopilaris, whose incidence is unknown. But it is described mostly in Caucasian, postmenopausal women [2,3]. Hundreds of cases have been documented around the world, especially in the last decade. The rise in reported cases have been associated with surges incidence, plus increase recognition of this pathology by dermatologists [3,4].

Patients usually presented with progressive and symmetrical

recession of the frontotemporal implantation hair line, a sign called "the doll hairline"; also, few terminal hairs could remain in the original implantation hair line, which is named "solitary hair" sign. In addition, facial involvement could be represented by decrease or loss of eyebrows, and facial papules [1,4,5]. In some patients, elevated titers of ANA and anti-SSA-60/52 (Ro) autoantibody have been reported; suggesting that the disease is not limited to the scalp, on the contrary it can affect other topographies such as eyelashes, armpits, pubis, extremities, or trunk [6]. Also, patients usually described symptoms such as itching, burning sensation, and hypersensitivity in the affected regions [3,7].

In Europe and United States has been reported case or cases series where the clinical presentation and treatment response were documented [1,2,8-11]. Whereas in Latin-American, Asia, Africa, and Australia we did not find databases or cohorts that describe

and analysed the epidemiological, clinical, trichoscopy and histopathological characteristics of patients with FFA, just reports of single case or few cases [12-16]. Therefore, the objective of this study was to describe the epidemiological, clinical, trichoscopy and histopathological characteristics of FFA patients, in a large group recollected during a fifteen-year period; with the aim of know the FFA characteristic presented in Mexican patients.

Case Reports

This retrospective study included patients with clinical and histopathology diagnosis of FFA [17], who were attended at Dermatology Service of a third-level reference center between 2005 and 2020. This work was approved and register by the institutional ethic committee with the number 06-24-2021 and performed according to human rights established on Helsinki declaration. Information of each case was reviewed, including clinical images, histopathological reports, and tissue slices; to select those that met the current diagnostic criteria for FFA. According to the information available in the records, the epidemiological variables analysed were age, sex, occupation, place of birth and residence, and date of diagnosis. In addition, tissue sections were re-evaluated, and histopathological characteristics were collected in the database. Epidemiologic data was analysed using descriptive statistical, and x2 Pearson.

Ninety-eight patients with a FFA clinical diagnosis were identified in dermatopathology records between 2005 and 2020. Nevertheless, just 37 patients met FFA histopathology criteria for diagnosis. In the remaining 61 cases other diagnoses were concluded as lichen planopilaris, centrifugal central alopecia, late alopecia areata and follicular degeneration syndrome. In patients with FFA diagnosis 97.2% (n=36) affected were women. Patients have a 57.8 years-old average age at diagnosis time, range between 35 to 86 years. Twenty-seven (72.9%) were housewife. The records do not mention other factors that literature considered as possible causal agents.

Regards clinical findings, hair implantation line recession was observed in 30 patients (81%; Figure 1a and 1b). Concomitant eyebrow loss was evident in 21 patients (56.7%, figure 1a to 1d) and follicular facial papules affected 6 patients (16.2%; Figure 1d). Pseudo-fringed pattern was present in three cases (Figure 1d); whereas diffuse pattern was displayed by four FFA cases (10.8%; Figure 1e). One case presented loss of eyelashes. Other symptoms as pruritus were mentioned by 13 patients (35.1%) representing the prevalent associated symptom; also, four patients reported trichodynia and other four denied any symptoms. Unfortunately, in most cases (n=18, 48.6%) the clinical records did not mention the presence or absence of accompanying symptoms.



Figure 1: Fibrosing frontal alopecia with hairline recession (1a, 1b); FFA with eyebrow loss (1c and 1d); FFA with pseudo-fringed pattern and facial papules (1d); FFA with diffuse pattern (1e); Trichoscopy: observe erythema and peripheral scales, white and yellow dots, unique follicular units (1f, 1g and 1h).

Trichoscopy evaluation reveal white spots in 30 patients (81%), peripheral erythema and single follicular units in 29 cases (78.3%); yellow spots were in 22 patients (59.45%) and peripheral hyperkeratosis occurred in 19 patients (51.3%, figures 1f to 1j). Unfortunately, seven cases (18.9%) did not have an iconographic record of trichoscopy evaluation, or this was not available.

Histological analysis displayed signs of scar alopecia in 34 patients (91.8%), including concentric fibrosis as most frequent hallmark, followed by vacuolar interface damage and lichenoid interface folliculitis. Moreover 3 patients (8.1%) presented mixed alopecia, composed by scar alopecia and miniaturization of the hair follicle, being the second pattern in frequency (Table 1 and Figure 2).

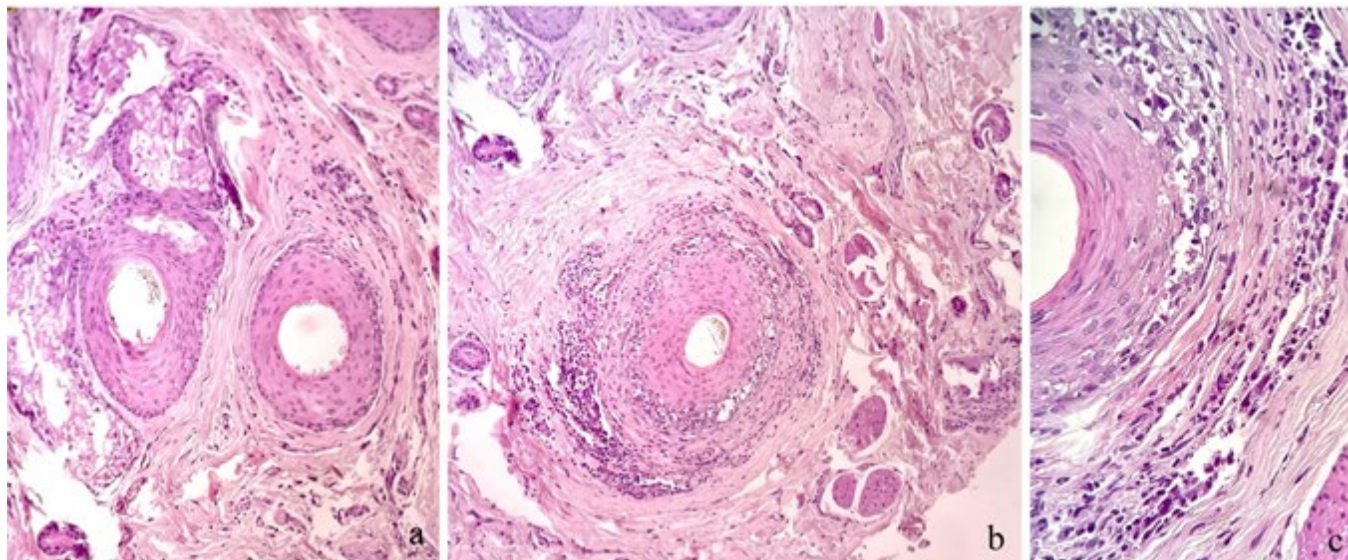


Figure 2: Histological sections with FFA features, hematoxylin, and eosin stain: 2a. (10x) Follicles with concentric fibrosis and absence of sebaceous glands. 2b. (10x) Follicle with lichenoid inflammatory infiltrate and concentric fibrosis. 2c. (40x) Approach of lymphocytic infiltrate producing interface damage in the follicular epithelium.

Most of the patients were both Mexico City native (81%; n= 30) and residents (91.80%; n=34). Associated endocrine diseases were found in 16.2% (n=7), including polycystic ovary syndrome (n=2,5.4%), hypothyroidism (n=3,8.1%), thyroiditis, and parathyroid adenoma (n=1,2.7% each one), thyroid problems presented significant statistical association with FFA, $p < 0.02$. Also, chronic degenerative diseases were presented in four patients (10.8%), such as diabetes mellitus type 2 and arterial hypertension. Additionally, other dermatological conditions were presented in

four patients (10.8%), counting lichen planus pigmented in two patients, one patient with Cinderella dermatitis and another with a history of lupus erythematosus discoid.

Interestingly most FFA cases (n=33; 89.1%) included in this study were recorded from 2017 and 2022, indicating an increases diagnosis of FFA on the last five years, thus that fact could be reflect the growths knowledge about this pathology or a real rise in the presence of FFA in Mexican population, or both.

Table 1: Histopathological characteristics of AFF cases.

Scar alopecia	34
Lichenoid interface damage	2
Vacuolar interface damage	7
Vacuolar and lichenoid interface damage with fibrosis	3
Concentric fibrosis	14
Lichenoid interface folliculitis	6
Ciliary region	1
Mixed alopecia	3
Scarring and miniaturisation	3

Table 2: Cases reporting in Latin-america.

Country	Clinical characteristic	Age	N	Histology	Asociateded diseases	Treatment	Ref.
Argentina	Alopecia in the frontotemporal (88.88%)	69	18	Dense lymphocytic infiltrate with lichenoid pattern at the level of the infundibue, isthmus and bulb	Hipoparatiroidism (33.33%) Depression Hepatitis Diabetes mellitus type 2 Breast cancer Colon cancer Linfoma	Esteroids topics or intralesinal (Clobetasol, mometasone, triancinolone) Finasteride Minoxidil Metotrexate	[24]
Colombia	Alopecia in the frontotemporal Partial or total alopecia of the eyebrows Facial lesions:	50	12	NR	Lichen planus pigmentosus 100%	NR	[20]
Chile	Alopecia in the frontotemporal Difusse alopecia Alopecia of the eyebrows	45	8	Lymphocytic infiltrate with concentric fibrosis	NR	NR	[19]
Ecuador	Alopecia frontotemporal Retraction of the hairline Sign of solitary hair Alopecia of the eyebrows and partial eyelashes. There was no nail or mucosal involvement	58	1	Interface vacuolar dermatitis	Lichen planus pigmentosus Early ovarian failure Glaucoma Allergic rhinitis	Minoxidil Finasteride	[25]
Mexico	Alopecia frontotemporal Alopecia axilar	43	17	Lymphocytic infiltrate with fibrosis	NR	Esteroids topics Tacrolimus	[18]
Mexico	Alopecia frontotemporal Retraction of the hairline Partial or total alopecia of the eyebrows ollicular facial papules	58	37	Lymphocytic infiltrate with fibrosis	Hipoparatiroidism Polycystic ovary syndrome parathyroid adenomachronic degenerative diseases (Diabetes mellitus type 2 and arterial hypertension). Lichen planus Cinderella dermatitis Lupus erythematosus discoid	Minoxidil Steroids	This work

A: Age or Mean Age; N: Number of Patients Included; Ref: References.

Discussion

As was expected, Mexican FFA patients were mostly postmenopausal women, most patients were housewife, and no association was found with a specific professional activity, the place of origin or residence. Nevertheless, average age at onset was lower than reported in other series, including patients around thirties years old. In a big European series, average age was 61 years. The clinical characteristics were consistent with previous descriptions; Being the hair implantation line recession pattern the most frequent phenotype reported. Whereas facial papules were presented in Mexican population like reported in other groups. Still, eyebrow affectation has been reported in 73% to 80% of FFA cases [9]; these number is very high compared to our study. The trichoscopy findings in a study group of 249 patients, highlighting peripheral hyperkeratosis as the prevalent characteristic, followed by peripheral erythema, and white and yellow spots [8]. In contrast white spots, solitary hairs and peripheral erythema were more frequent in Mexican patients, these results are associated with the scar stage, and correlate with a FFA late phase presented in Mexican patients [13,18]. Thus, these finding suggests that FFA diagnosis in Mexican patients has been delayed. Consequently, some difference found in this FFA Mexican case series are probably associated to the fact that most patients were diagnosis in scar stage. Hence considered the shorter age at diagnosis time, the FFA in Mexican women is initiated early in life or it is presented a faster evolution or both. According with Cardona et al. in 17 cases of Mexican patients the mean age at diagnosis was 43 years old [13]. Moreover, in Chile and Colombia studies of AFF patients the median age reporter was in Chile, was 45 years old, and 50% of patients initiated before menopause, whereas in Colombia was 50 years old (Table 2) [19,20]. The AFF actual etiopathogenesis hypothesis considering that environmental triggers act over a genetic predisposition patient driving Th1/JAK-STAT profile of inflammation. Thus, in Mexicans the early start could be related with immune characteristic of Mexican patients; HLA-DRB1*01:01 and HLA-DRB1*01:02 have been associated with statistically significant values in FFA patients compared to healthy controls (personal communication Dr. Granados J). Furthermore, it is also possible that the early start in Latin America could be related with environmental factors such as the growing fashion use of hair straighteners containing phenol (formaldehyde) [21]; Such products are regulated in Europe and the permitted concentration most be lower than 0.05% until to 2022 (European Cosmetics Regulation No 1223/2009), but in Latin-American exist a poor control of “cosmetic products” in consequences formaldehyde concentration frequently are much higher.

In relation to the histological study, all the original reports were available in the database. However, only 15 tissue slices were found in good condition, out of a total of 37 patients with histopathological diagnosis of FFA. Of these, ten tissue samples (66.6%) displayed inflammatory lichenoid infiltrate by lymphocytes at the level of the follicular epithelium and 14 (93.33%) exhibited peripheral concentric fibrosis, findings compatible with the histological diagnosis of FFA (Figure 2). Furthermore nine (60%) presented

both histological characteristics. Also, vacuolar interface damage and/or lichenoid lymphocytic infiltrated; presence of alopecia (decrease in the number of terminal follicles); absence of annexes (mainly sebaceous glands); the presence of dilated eccrine glands with spraying fibrosis as well as abundant fibrous trails were reported in histological data and corroborated in tissue samples available [22,23].

Associated symptoms as pruritus followed by trichodynia were the most reported in our patients, in agreement with previous publications [2]. Comorbidities most mentioned in literature associated with FFA are Hashimoto's thyroiditis and autoimmune diseases such as Sjögren's syndrome [2,8,15]. But any of these specific diagnoses were found in the records of this series of patients. Nevertheless, thyroid problems were reported in four patients, three cases presented hypothyroidism and other referred a thyroiditis of unspecified origin. Hypothyroidism in Mexico is reported between 0.1-2% in general population, and in 2% of postmenopausal women, thus in this series the frequency is more than five times higher, so these four patients represented 10.81%, (considering that thyroiditis usually evolve to hypothyroidism) values with statistical significance $p < 0.02$ of cases. Furthermore, in South American patients, association with hypothyroidism was higher, reported in 33.33% [24]. Thus, clinical data plus HLA association reports supports the immunologic role in disease pathogenesis. Other disease associated is lichen planus; in contrast this disease was reported in two of our patients with FFA [20]. Information regarded previous treatments were collected, but only use of minoxidil 5% lotion in four patients, topical steroid in three patients, different commercial shampoos in other three was recorded, and three patients denied previous treatments.

Conclusion

FFA is a newly diagnosed disease with increased prevalence in Mexico, where it occurs predominantly in postmenopausal women, but in Mexico disease started at younger age compared with Caucasian series and in similarity with disease presentation in other Latin-American countries. The dominant clinical presentation includes recession of the frontotemporal implantation line, with presence of white spots and solitary hairs at trichoscopy evaluation. Accordingly, scar alopecia with peripheral concentric fibrosis represented the prevalent histological pattern. These findings indicate late stages of the disease, so the challenge is to identify the FFA in early stage and prevent disease progression and the irreversible alopecia. Also, trichoscopy studies need to be properly performed and reported, which will allow better analysis. In the future studies should be carried out to delve into the causes of the disease, pathophysiology, the associated diseases; as well as the evolution of patients comparing the different treatments.

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Declarations

Conflict of Interest

The authors declare that they have no conflict of interest in preparing this article.

Etic Declarations

Clinical images included in this article were authorized by the patient's written consent, according to the Helsinki declaration, 1975.

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