Trichoscopic features of frontal fibrosing alopecia: Results in 249 patients

To the Editor: Currently, dermoscopy constitutes an essential noninvasive tool for dermatologists. It helps discern between different types of alopecia, it provides a more precise follow-up, and it can be used to identify an adequate biopsy site.[1] Frontal fibrosing alopecia (FFA) is a primary lymphocytic scarring alopecia with a distinctive clinical pattern of progressive frontotemporal hairline recession and eyebrow loss that mainly affects postmenopausal women.[2] The main objective of our study was to describe the trichoscopic features of FFA in a large series of patients and to correlate these findings with several relevant parameters of FFA.[2,3]

We performed a descriptive, retrospective, observational, multicenter study of digital trichoscopic images, obtained between 1994 and 2013, of 238 women with FFA at 12 Spanish centers.[4] Diagnostic criteria included typical clinical signs and/or histopathologic features consistent with FFA.[2] Images were obtained with either a nonpolarizing or a polarizing dermoscope. Two dermatologists expert in dermoscopy evaluated the images if the registered trichoscopic features of FFA (cicatricial white patches, perifollicular erythema, follicular hyperkeratosis, lonely hairs, and hair diameter diversity) and yellow dots typical of androgenetic alopecia were present on the frontotemporal hairline.[3] Both a descriptive and an analytic study to correlate these parameters with the degree of severity and other clinical variables were performed using SPSS 15.0 software. Clinical and severity variables included female pattern hair loss (FPHL), presence or absence of menopause, FFA severity (I: 1 cm, II: 1-2.99 cm, III: 3-4.99 cm, IV: 5-6.99 cm, and V: >7 cm), and years of evolution, pruritus, trichodynia, facial papules, occipital involvement, eyebrow and eyelash loss, pubis hair loss, and body hair involvement. A bivariate analysis including trichoscopic findings and the aforementioned variables was carried out, and those variables with statistical significance in X^2 test were included in a multivariate logistic regression analysis adjusted for age and excluding lost cases. No new dermoscopic signs were found. Descriptive dermoscopic results are listed in Table I. Both the intraobserver and interobserver agreement for the assignment of a dermoscopic pattern for each lesion were excellent ($\kappa = 0.82$, $P < .001$; $\kappa = 0.80$, $P < .001$, respectively). The trichoscopic features that were statistically significantly associated ($P < .05$) with some clinical parameters in the bivariate and multivariate logistic regression analysis are listed in Table II.

Dermoscopic features of FFA have previously been described in some isolated studies.[2,3] Toledo-Pastrana et al[5] retrospectively analyzed the dermoscopic images of 79 patients with FFA. They found that 100% of the patients showed no follicular openings, 72.1% showed follicular hyperkeratosis, 66.3% showed perifollicular erythema, and 44.8% showed follicular plugs. Interestingly, they also found that perifollicular erythema was statistically associated to the activity of FFA. In our study, we correlated the dermoscopic features with another outcome: the severity of the disease in terms of extension of the hairline.[4] Remarkably, we found that the presence of cicatricial white patches was statistically associated with the severity of FFA. This dermoscopic feature correlates with the histopathologic findings of hair follicle destruction and severe tissue fibrosis.[3] Therefore, it

Table I. Frequency of trichoscopic features of patients diagnosed with FFA: Relationship between trichoscopic features and FFA severity, pruritus, and trichodynia

	FFA severity (X^2 test*)		Pruritus (X^2 test*)		Trichodynia (X^2 test*)	
Trichoscopic features	Mild (I-II)	Severe (III-V)	No	Yes	No	Yes
Follicular hyperkeratosis	89.6%	90.9%	85.2%	96% (P = .007)	88.6%	94.3%
	NS	NS				NS
Perifollicular erythema	77%	65.9%	68.3%	83% (P = .01)	75.1%	73.6%
	NS	NS				NS
Lonely hair	67.9%	77.3%	54.9%	78% (P = .001)	54.9%	83% (P = .001)
	NS	NS				
Hair diameter diversity	45%	56.8%	32.8%	64% (P = .001)	36%	81.1% (P = .001)
	NS	NS				
Cicatricial white patches	22.3%	43.2% (P = .018)	24.4%	29%	24.1%	34%
	NS			NS		NS
Yellow dots	21.9%	20.5%	19.7%	24%	21.3%	22.6%
	NS	NS		NS		NS

FFA, Frontal fibrosing alopecia; *NS*, nonsignificant.
*P value calculated with X^2 test with P values. Differences were considered significant at $P \leq .05$.

Table II. Trichoscopic features statistically significantly associated with clinical parameters in the bivariate and multivariate logistic regression analysis

Trichoscopic features	Bivariate analysis (X^2 test*)	Multivariate logistic regression analysis (IC: 95%) (X^2 test*)
Follicular hyperkeratosis (213/238 patients)	Pruritus (P = .007) and menopause (P = .05)	Pruritus P = .12 OR = .24
Perifollicular erythema (173/238 patients)	Pruritus (P = .01)	Pruritus P = .02 OR = .47
Lonely hair (212/238 patients)	Pruritus (P = .001), trichodynia (P = .001)	Pruritus P = .007 OR = .41
Hair diameter diversity (110/238 patients)	Pruritus (P = .001), trichodynia (P = .001), FPHL (P = .001) and severity (P = .001), axillary hair loss (P = .001), pubic hair loss (P = .004)	FPHL severity P = .04 OR = .11
Cicatricial white patches (59/238 patients)	FPHL (P = .01) and severity (P = .023), FFA severity (P = .018), occipital (P = .04), axillary (P = .01) and pubis hair loss (P = .001)	FFA severity P = .047 OR = .24 and pubic hair loss P = .03 OR = .20
Yellow dots (48/238 patients)	FPHL (P = .001), occipital (P = .03), and pubic hair loss (P = .05)	FPHL P = .0001 OR = .29, occipital P = .024 OR = .39

FFA, Frontal fibrosing alopecia; *FPHL*, female pattern hair loss.
*P value calculated with X^2 test with P values. Differences were considered significant at $P \leq .05$.

is understandable that severe FFA presents cicatricial white patches more frequently than mild FFA, reflecting the increased number of hair follicles destroyed. Another interesting finding was the association between perifollicular erythema and follicular hyperkeratosis with pruritus, supporting the hypothesis that the erythema is produced by the lichenoid infiltrate seen on histopathological examination, producing pruritus and representing a marker of activity of FFA.[5] The yellow dots and hair diameter diversity were observed in patients with associated FPHL, with hair diameter diversity being related to Ludwig's classification. Patients with pubic hair loss presented more cicatricial white patches.

Our study presents three main limitations: the retrospective design, the presence of only 2 observers evaluating each patient, and the fact that neither the treatment for alopecia nor the activity of the disease was included in the analysis.

In conclusion, the presence of perifollicular erythema and cicatricial white patches is independently associated with pruritus and the severity of FFA, respectively. Trichoscopy is a valuable tool not only in the diagnosis of FFA, but also in estimating the activity, symptoms, and severity of the disease.

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REFERENCES

1. Miteva M, Tosti A. Dermoscopy guided scalp biopsy in cicatricial alopecia. *J Eur Acad Dermatol Venereol*. 2013;27:1299-1303.
2. Moreno-Ramírez D, Ferrándiz L, Camacho FM. Diagnostic and therapeutic assessment of frontal fibrosing alopecia. *Actas Dermosifiliogr*. 2007;98:594-602.
3. Miteva M, Tosti A. Hair and scalp dermatoscopy. *J Am Acad Dermatol*. 2012;67:1040-1048.
4. Vañó-Galván S, Molina-Ruiz AM, Serrano-Falcón C, et al. Frontal fibrosing alopecia: a multicenter review of 355 patients. *J Am Acad Dermatol*. 2014;70:670-678.
5. Toledo-Pastrana T, García Hernández MJ, Camacho Martínez FM. Perifollicular erythema as a trichoscopy sign of progression in frontal fibrosing alopecia. *Int J Trichology*. 2013;5:151-153.

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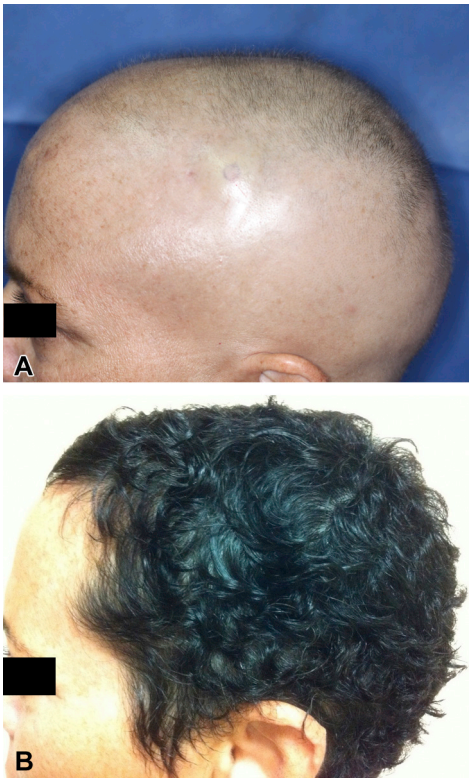

Fig 1. Alopecia areata. Patient 23 before (**A**) and 40 weeks after (**B**) treatment.

Treatment of alopecia areata with simvastatin/ezetimibe

To the Editor: In addition to their lipid-lowering effects, statins are powerful lymphocytic modulators and could therefore be part of the armamentarium of anti-inflammatory agents in dermatology.[1] It was observed in 2 case reports that simvastatin/ezetimibe (Vytorin, Merck & Co) successfully treated alopecia areata totalis and universalis.[2,3] This prospective pilot study aimed to further delve into the combination of simvastatin and ezetimibe in a larger cohort of patients with alopecia areata.

After approval by the internal review board of the University of Miami, we recruited 29 patients with alopecia areata older than 18 years, with 40% to 70% of scalp involvement using the North American Hair Research Society (NAHRS) scale. The patients had not received systemic treatment for 3 months, or topical treatment for 2 weeks. Patients were given only simvastatin/ezetimibe 40 mg/10 mg daily for 24 weeks. At baseline and every 8 weeks, global photography and standard laboratory tests were performed. Patients were also evaluated for adverse effects. Subjects who showed more than 20% hair regrowth on week 24 using the NAHRS scale were considered positive responders.

Of the 29 enrolled patients, 19 completed 24 weeks of treatment, and 14 of 19 were judged responders. Hair regrowth was evident after 16 to 24 weeks of treatment (Fig 1). The remaining 10 patients were lost to follow-up (Table I). No side effects were observed.

Upon completion of the initial 24 weeks of treatment, the 14 responders were randomized into 2 groups: in group A, 7 of 14 patients continued treatment for an additional 24 weeks; and in group B, 7 of 14 patients stopped medication but were evaluated every 8 weeks.

In group A, 5 of 7 continued with hair growth/stable disease, 1 of 7 had new patches, and 1 of 7 was lost for follow-up.

In group B, 5 of 7 patients relapsed, 1 of 7 had no change, and 1 of 7 was lost for follow-up.

Statistical analysis of the data between groups A and B was performed using the Fisher exact test (1-tailed). The association between being on therapy and stable remission is statistically significant ($P = .0400$).

The results of our study could be explained by the previously reported effects of the statins on the immune system. Such effects include inhibition of major histocompatibility complex class II and CD1d-mediated antigen presentation,[1] blockage of lymphocyte function-associated antigen 1 and intercellular adhesion molecule 1 interaction,[1] decreasing