Facial Papules in Frontal Fibrosing Alopecia: Beyond Vellus Hair Follicle Involvement

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Keywords

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Abstract

Background: Frontal fibrosing alopecia (FFA) is considered a variant of lichen planopilaris affecting mainly the frontotemporal hairline. Since the first report in 1994, several other clinical features have been associated with the disease, such as facial papules (FP). Even though FP have been linked to facial vellus hair follicle involvement, how this finding alone could lead to the formation of clinically evident FP in FFA patients had not yet been addressed. **Objective:** To describe histopathological findings of FP in the context of FFA and to highlight features that may be linked to their clinical formation. **Methods:** Cutaneous FP biopsies of FFA patients performed between January 2016 and May 2017 were retrieved from our pathology database and reexamined by 2 pathologists. **Results:** Histological sections of thirteen 3.0-mm punch biopsy specimens (2 horizontally and 11 vertically oriented) were collected from 7 patients. Eleven specimens demonstrated prominent sebaceous glands and 10 dilated sebaceous ducts. Pinkus acid orcein staining revealed reduction and fragmentation of the elastic fibers in 12 samples and, in

7 of these, this finding was observed in both the papillary and reticular dermis, particularly around sebaceous lobules. Vellus hair follicle involvement was only seen in 2 samples. **Conclusions:** Prominent sebaceous lobules with dilated ducts associated with an abnormal elastic framework seem to be the main explanation for the formation of FP in the context of FFA.

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Introduction

Frontal fibrosing alopecia (FFA) was first described in 1994 as a variant of lichen planopilaris affecting mainly the frontotemporal hairline and eyebrows of postmenopausal women [1]. Since then, several features have been associated with FFA, such as glabellar red dots [2], body hair involvement [3], lichen planus pigmentosus (LPPigm) [4], depression of the frontal veins [5], and facial papules (FP) [6]. The disease is now regarded by many authors as a generalized skin condition [7].

FP as a sign of facial vellus hair follicle involvement in FFA was first recognized by Abbas et al. [6] in 2007. In 2011, Donati et al. [8] also found lichenoid perifollicular inflammation and fibrosis in biopsies of papules from 4

FFA patients, corroborating involvement of facial vellus hairs in the disease. Despite their seminal contribution, such reports as well as later ones [9] did not address how facial follicular involvement alone could lead to the formation of clinically evident FP in FFA patients. In this paper, we aim to describe histopathological findings of FP in FFA patients and to highlight features that may be linked to their clinical formation.

Patients and Methods

Cutaneous FP biopsies of FFA patients performed between January 2016 and May 2017 were retrieved from our pathology database. All cases were seen in a single center. Inclusion criteria required that patients had histopathological evidence of FFA. Cutaneous FP specimens were obtained through a 3-mm punch biopsy and stained with hematoxylin and eosin and Pinkus acid orcein staining. The histological examination was performed by 2 pathologists (T.C. and D.C.Q.) and the histological features analyzed included: (i) presence and pattern of inflammation; (ii) involvement of vellus hairs; (iii) involvement of sebaceous glands; (iv) changes in elastic fibers; and (v) severity of solar elastosis. Additional findings were also documented. Patient demographics (age, gender, skin type, menopausal status) and clinical data were also recorded.

Results

Thirteen biopsies (2 horizontally and 11 vertically oriented) from 7 patients were retrieved. Six patients were female and 1 male; ages ranged from 30 to 61 years; 4 had skin type III, 2 type IV, and 1 type V. Disease onset was postmenopausal in 4 of the females. Prominent FP and eyebrow involvement were noted in all patients (Fig. 1) and body hair loss in 4. Of note, facial LPPigm was clinically present in 5 patients.

In the histologic sections of the FP, vellus hair follicles were visualized in 7 specimens. Perifollicular lichenoid inflammation was only seen in 2 cases (Fig. 2d). Prominent sebaceous glands were present in 11 specimens (Fig. 2a). In addition, dilated sebaceous ducts were seen in 10 cases (Fig. 2c), while in 4, scarce lymphocytic inflammatory infiltrate focally surrounded sebaceous lobules. Only in 1 case was the sebaceous gland mostly obscured and degenerated due to permeation of the inflammatory infiltrate, forming an inflammatory nodule (Fig. 2e). Pinkus acid orcein staining revealed reduction and fragmentation of elastic fibers in 12 (out of 13) samples. In 7 of these, this finding was observed in both the papillary and reticular dermis, especially around sebaceous lobules (Fig. 2b).

Fig. 1. Male patient with frontal fibrosing alopecia presenting prominent facial papules and eyebrow loss.

Additional features in most samples included: vacuolar alteration of the epidermal basal layer, pigmentary incontinence with the presence of melanophages, fibroplasia in the papillary and high reticular dermis, and discrete superficial perivascular lymphocytic infiltrate. Basophilic degeneration of the collagen was also observed (refer to Table 1 for a complete description of the histological findings).

Discussion

FFA was only recently described and its exact pathogenesis remains unknown. Sebaceous glands have been considered possible primary targets in scarring alopecias and their early destruction is a hallmark of this group of disorders [10, 11]. FP in the context of FFA were first noted in 2007 [6] and, in the largest series of FFA patients, have been reported in 14% of cases [12]. It is worth noting that, even though FP have been linked to facial vellus hair follicle involvement in the context of FFA, sebaceous glands were present in the majority of our specimens (from FP), differently from the picture one might expect in scalp biopsies.

In fact, FP presence seems to be better explained by the relatively large sebaceous glands. We hypothesize that this is a late residual finding of an inflammatory process

Fig. 2. Biopsy of facial papules revealed prominent sebaceous glands (H&E, $\times 40$) (a) and reduction of elastic fibers in the papillary and reticular dermis, particularly around the sebaceous lobules (Pinkus acid orcein staining, $\times 40$) (b). c Dilated sebaceous ducts were also a prominent feature. d Vellus hair follicle involvement was only observed in 2 cases. e Degeneration of the sebaceous gland in 1 case.

that is clinically unapparent, insufficient to cause sebaceous gland destruction or extensive fibrosis at this particular anatomical site when compared to the scalp. There are signs of prior inflammation: pigment incontinence and destruction of elastic fibers. This abnormal elastic framework would be responsible for the “pop out” of sebaceous glands and the formation of FP.

Structural differences between facial vellus hair and scalp terminal hair may account for a distinct intensity of the inflammatory process, resulting in different histopathological features and clinical presentations.

One could argue that sebaceous glands were evident because biopsies were performed too early. However, in some of our cases, FP had been present for at least 2 years

Table 1. Histopathological findings of facial papules in frontal fibrosing alopecia

Patient	Sample	Area	SG	SGDD	LISG	VHF	PFLI	EA	VABLE	Fibro-plasia ^a	PI	PSLI	Reduction and fragmentation of EF			SE ^b
													PD	RD	ASG	
A	1	Lateral chin	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	1+
B	2	Lateral chin	Yes	Yes	Yes	No	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	1+
	3	Lateral chin	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	No	2+
C	4	Jowl	Yes	Yes	No	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	No	1+
	5	Jowl	Yes	Yes	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	1+
D	6	Lateral chin	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	No	No	2+
	7	Jowl	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	No	Yes	2+
E	8	Jowl	Yes	Yes	No	No	No	No	Yes	Yes	No	Yes	Yes	Yes	Yes	3+
	9	pre-auricular	Yes	No	No	No	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	3+
F	10	Lateral chin	No	No	No	Yes	Yes	No	No	Yes	Yes	No	Yes	No	No	1+
	11	Lateral chin	Yes	No	No	Yes	Yes	No	No	Yes	Yes	No	Yes	No	No	1+
G	12	Temple	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	1+
	13	Temple	Yes	Yes	No	No	No	No	No	No	Yes	Yes	Yes	Yes	Yes	1+

SG, presence of prominent sebaceous glands; SGDD, sebaceous glands dilated ducts; LISG, Lymphocytic infiltrate around sebaceous glands; VHF, visualization of vellus hair follicles; PFLI, perifollicular lichenoid inflammatory infiltrate; EA, epidermal atrophy; VABLE, vacuolar alteration of the basal layer of the epidermis; PI, pigmentary incontinence; PS LI, perivascular superficial lymphocytic infiltrate; EF, elastic fibers; PD, papillary dermis; RD, reticular dermis; ASG, around sebaceous gland; SE, solar elastosis. ^a Fibroplasia in the papillary dermis or papillary and high reticular dermis. ^b 1+, few elastotic fibers can be seen in high magnification (×400); 2+, elastotic fibers can be easily observed in high magnification (×400); 3+, elastotic fibers are observed in low magnifications (×40); 4+, amorphous aggregates of elastotic material easily seen in low magnification (×40).

prior to biopsy. Additionally, sebaceous glands do not cause papules in normal facial skin whereas they were associated with an overhead shape of the epidermis in the samples studied.

Influenced by our observations, we performed a proof-of-concept study that was recently published [13], in which we proposed a 3-month therapeutic regimen of oral isotretinoin for 3 patients with FFA and prominent FP. At the end of this period, the FP had either completely disappeared or were considered minimal. We believe that improvement of FP was due, at least in part, to sebaceous gland atrophy and improvement of the elastic fiber framework, which are well-known effects of the drug [14, 15]. It is not our conclusion that sebaceous glands seem prominent merely because of the biopsied site (face). The response to oral isotretinoin may corroborate our proposition that architecture derangement of sebaceous glands with relatively prominent lobules contribute to the formation of clinical papules and that they may be the only histopathologic substrate of FP seen in FFA patients.

One possible bias in this study is the concomitance of LPPigm in most patients. Larger studies, particularly with patients without coexisting LPPigm, are necessary to confirm our findings.

To date, FP have been described as a sign of lichenoid inflammation of facial vellus hair follicles [1–3]. Histologic features presented herein, in association with the previously described good response to oral isotretinoin, suggest that prominent sebaceous lobules with dilated ducts associated with an abnormal elastic framework are the main explanation for the formation of FP in the context of FFA.

Statement of Ethics

All patients have given oral consent for their details to be described.

Disclosure Statement

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

References

- 1 Kossard S: Postmenopausal frontal fibrosing alopecia. Scarring alopecia in a pattern distribution. *Arch Dermatol* 1994;130:770–774.
- 2 Pirmez R, Donati A, Valente NS, Sodre CT, Tosti A: Glabellar red dots in frontal fibrosing alopecia: a further clinical sign of vellus follicle involvement. *Br J Dermatol* 2014;170:745–746.
- 3 Miteva M, Camacho I, Romanelli P, Tosti A: Acute hair loss on the limbs in frontal fibrosing alopecia: a clinicopathological study of two cases. *Br J Dermatol* 2010;163:426–428.
- 4 Pirmez R, Duque-Estrada B, Donati A, Campos-do-Carmo G, Valente NS, Romiti R, Sodré CT, Tosti A: Clinical and dermoscopic features of lichen planus pigmentosus in 37 patients with frontal fibrosing alopecia. *Br J Dermatol* 2016;175:1387–1390.
- 5 Vaño-Galván S, Rodrigues-Barata AR, Urech M, et al: Depression of the frontal veins: a new clinical sign of frontal fibrosing alopecia. *J Am Acad Dermatol* 2015;72:1087–1088.
- 6 Abbas O, Chedraoui A, Ghosn S: Frontal fibrosing alopecia presenting with components of Piccardi-Lassueur-Graham-Little syndrome. *J Am Acad Dermatol* 2007;57:S15–S18.
- 7 Chew AL, Bashir SJ, Wain EM, Fenton DA, Stefanato CM: Expanding the spectrum of frontal fibrosing alopecia: a unifying concept. *J Am Acad Dermatol* 2010;63:653–660.
- 8 Donati A, Molina L, Doche I, et al: Facial papules in frontal fibrosing alopecia: evidence of vellus follicle involvement. *Arch Dermatol* 2011;147:1424–1427.
- 9 Laniauskaite I, Ezmerli M, von Braunmühl T, Ruzicka T, Flaig MJ, Wolff H: Frontal fibrosing alopecia with facial papules – three cases. *J Eur Acad Dermatol Venereol* 2017;31:e69–e71.
- 10 Stenn KS: Insights from the asebia mouse: a molecular sebaceous gland defect leading to cicatricial alopecia. *J Cutan Pathol* 2001;28:445–447.
- 11 Sundberg JP, Boggess D, Sundberg BA, et al: Asebia-2J (Scd1^{ab2J}): a new allele and a model for scarring alopecia. *Am J Pathol* 2000;156:2067–2075.
- 12 Vaño-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.
- 13 Pirmez R, Duque-Estrada B, Barreto T, Quintella DC, Cuzzi T: Successful treatment of facial papules in frontal fibrosing alopecia with oral isotretinoin. *Skin Appendage Disord* 2017;3:111–113.
- 14 Rademaker M: Isotretinoin: dose, duration and relapse. What does 30 years of usage tell us? *Australas J Dermatol* 2013;54:157–162.
- 15 Bravo BSF, Azulay DR, Luiz RR, Mandarin-De-Lacerda CA, Cuzzi T, Manela-Azulay M: Oral isotretinoin in photoaging: objective histological evidence of efficacy and durability. *An Bras Dermatol* 2015;90:478–486.