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NEWS, VIEWS, & REVIEWS

Highlighting the Link Between Lichen Planus Pigmentosus and Frontal Fibrosing Alopecia

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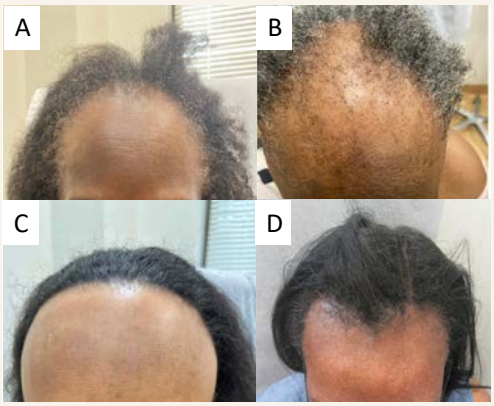
BACKGROUND

Frontal fibrosing alopecia (FFA) is a primary lymphocytic cicatricial alopecia, considered a variant of lichen planopilaris due to histological similarities.[1] Clinically, FFA causes gradual hair loss of the frontotemporal hairline and is commonly associated with loss of eyebrows and body hair. FFA may occur in conjunction with lichen planus pigmentosus (LPPigm), another lichenoid condition (Figure 1). LPPigm is a macular variant of lichen planus that presents as diffuse or reticulated grey to brown macules on sun-exposed areas and in flexures, eventually evolving into large hyperpigmented patches.[2] LPPigm mainly affects the face and neck but can sometimes progress to the trunk and upper limbs and may be associated with a burning sensation or itch.[3] There is limited data regarding the association between these two conditions, though various reports have documented a link.[4-8]

Figure 1. Typical clinical presentations of frontal fibrosing alopecia, with band-like recession of the frontotemporal hairline, and lichen planus pigmentosus, with hyperpigmented patches affecting the forehead **(A, B, C, D)**.



Epidemiology

Concomitant FFA and LPPigm most commonly affects dark skinned individuals, with one case series describing its occurrence in 5 women with skin phototypes II and III.[9] The first study associating both conditions evaluated 24 patients from South Africa, with 91% of patients identifying as African.[4] Subsequent reports similarly noted its association in dark skinned patients.[6,7,10] More recently, a multicenter retrospective descriptive analytical study involving 104 patients with combined FFA and LPPigm found that most affected patients had skin phototypes IV, V, and VI (74.1%).[5] Data regarding whether LPPigm precedes FFA is conflicting. In the patient cohorts evaluated by Dlova et al and Romiti et al, LPPigm preceded FFA in all patients, with an average lag time of 14 and 10 months respectively between each diagnosis.[4,7] These case series consisted of smaller cohorts, involving 24 and 16 patients respectively. The observed trend was less pronounced in the larger, multicenter study, with LPPigm preceding FFA in 56.8% of cases[5] and 51% of cases in another case series of 37 patients.[6] Though there is inconsistent evidence elucidating the temporal relationship between LPPigm and FFA, LPPigm appears to precede FFA in some patients, and is thus a proposed risk factor for FFA.[4] Most studies have reported a larger frequency of concomitant FFA and LPPigm in post-menopausal women,[5-7] which is consistent with the general FFA epidemiology.[5] In Dlova et al's study, most patients were premenopausal. Increased mechanical trauma associated with hair grooming styles is a potential explanation for the relatively early manifestation of FFA in African patients.[4]

Pathophysiology

A continual inflammatory response and breakdown of immune privilege of the epithelial hair follicle stem cells is pivotal in the pathogenesis of FFA. CD8+ T-lymphocytes and IFN-γ are key mediators of the associated inflammatory processes.[11,12] The pathogenesis of LPPigm remains unclear, though it is known that CD8+ T-lymphocytes and mediators such as interferon-gamma, tumor necrosis factor-alpha, interleukin 6, and lymphocyte function-associated antigen 1 play a role.[11,3] The clinical parallelism and progression between LPPigm and FFA, and their histological associations suggest that LPPigm and FFA represent distinct stages within the spectrum of the same underlying disease,[4] though more research is necessary to evaluate the association.

Treatment

FFA is a chronic condition, requiring long-term treatment, often with a combination of therapies. Commonly prescribed topical

medications include corticosteroids, minoxidil, and calcineurin inhibitors. Topical treatment involves the whole scalp due to possible follicular inflammation in the unaffected scalp.[13] Systemic treatments include 5-alpha reductase inhibitors, hydroxychloroquine, and retinoids. Table 1 highlights treatments supported by published data, though smaller studies have highlighted the utility of pioglitazone, methotrexate, naltrexone, and hair transplantation.[14] There are currently no approved or validated treatments due to a paucity of randomized trials. Topical treatments for LPPigm include high potency steroids, tacrolimus, and skin lightening creams. Systemic treatments include isotretinoin, tranexamic acid, and vitamin A. Laser treatments and chemical peels are another option, though expensive. Notable studies are highlighted in Table 2. A combination of topical and systemic treatments, robust sunscreen application, and trigger avoidance is likely to yield the best outcomes.[15] Treatment for both FFA and LPPigm centers around slowing or preventing progression, and there is a low threshold for starting systemic therapies for patients who prefer an aggressive approach.

Table 1. Efficacy of Treatment Approaches for Frontal Fibrosing Alopecia[14]

Treatment	Study Type	Patients (n)	Treatment Regimen	Duration	Response
Topical steroids	Retrospective cohort study[16]	48	Clobetasol propionate or betamethasone valerate 3 times per week, pimecrolimus 1% 3 times per week	20 months	Improvement 39.6%, stabilized 25%, no improvement 22.9%
Topical minoxidil	Retrospective cohort study[17]	2	Topical 2% minoxidil solution	Unspecified	No improvement
Intralesional Steroids	Retrospective cohort study[18]	130	Injections every 3 to 6 months, average of 8 injections per patient	Unspecified	Regrowth 34%, stabilized 49%, no improvement 5%, unavailable results 12%
Hydroxychloroquine	Retrospective cohort study[18]	54	Hydroxychloroquine 200-400 mg/day with nonspecific therapies	Unspecified	Regrowth 15%, stabilized 59%, no improvement 22%, unavailable results 4%
Finasteride	Retrospective cohort study[18]	102	Finasteride 2.5-5 mg/day	Unspecified	Regrowth 47%, stabilized 53%
Dutasteride	Retrospective cohort study[19]	13	Dutasteride 0.5 mg/day	12 months	Regrowth 15%, stabilized 46%, slow progression 38%; no recurrence in responders at 18 months
Systemic retinoids	Retrospective cohort study[20]	29	Isotretinoin 20 mg/day	12 to 16 months	Stabilized 79%

Table 2. Efficacy of Treatment Approaches for Lichen Planus Pigmentosus

Treatment	Study Type	Patients (n)	Treatment Regimen	Duration	Response
Tacrolimus ointment	Open label, non-randomized, prospective study[22]	13	Topical tacrolimus 0.03% twice daily	6 to 12 weeks	Cessation of disease progression and reduction of pigmentation in all patients
Tacrolimus ointment + dapsone	Retrospective cohort study[23]	5	Topical tacrolimus 0.1% ointment twice daily and oral dapsone 100mg/day	Unspecified	Partial improvement 50%, no improvement 15%, reduced pruritus 45%, lost to follow up 35%
Oral tranexamic acid	Prospective study[24]	20	Oral tranexamic acid 250 mg/day; sunscreen strongly encouraged	4 to 6 months	Moderate improvement 55.7% (26-50%), good improvement 21.8% (>50%), and mild improvement 6.2% (<25%) in intensity and progression of pigmentation; 11% without improvement
Isotretinoin	Open label, non-randomized, prospective study[25]	27	Oral isotretinoin 20 mg/day and sunscreen	6 months	1-3 courses (n=44): Good improvement 11.4%,
Vitamin A	Prospective pilot study[26]	140	Vitamin A 100,000 units/day daily	15 days, followed by a 15 day washout period; treatment course then repeated with variable frequency	4-6 courses (n=19): good to excellent improvement 31.6%,
Nd:YAG laser	Prospective pilot study[27]	9	1064 nm Q-switched Nd:YAG laser 6mm spot, fluence 3 J/cm^2 and 10-Hz frequency plus toning every 2 weeks	6 sessions	7-9 courses (n=15): good to excellent improvement 44.4%,
Nd:YAG laser	Open label, non-randomized prospective pilot study[27]	13	1064 nm Q-switched Nd:YAG laser 5 mm spot, fluence 3-4.6 J/cm^2 and 5-Hz frequency, with periodic fluence increase	Every 4 to 8 weeks, 5 to 6 sessions on average	10 or more courses (n=12): good to excellent improvement 75%,
Phenol peels	Retrospective cohort study[28]	17	Croton oil free phenol combination every 3 weeks	6 sessions	35.7% lost to follow-up

Clinical Considerations

FFA and LPPigm are difficult to treat and can be distressing for patients, especially when coexisting. The loss of follicular ostia in FFA is irreversible, and thus dermatologists need to diagnose and treat it early. Clinicians should be aware of the overlap between FFA and LPPigm and examine patients with LPPigm for FFA and vice versa, especially in patients with darker skin tones.[10] As LPPigm frequently precedes FFA, its presence may serve as an early indicator of FFA onset and should prompt further evaluation. When coupled with other severity indicators of FFA, such as facial papules and the loss of eyebrows and eyelashes, concurrent LPPigm can be regarded as an adverse prognostic factor.[5]

Disclosure

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