PRACTICAL DERMATOLOGY

Diagnostic and Therapeutic Assessment of Frontal Fibrosing Alopecia

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Abstract. Frontal fibrosing alopecia is a clinical entity characterized by recession of the frontotemporal hairline in middle-aged and older women. Since it was first described in 1994, more than 100 cases have been reported describing other clinical manifestations such as eyebrow and axillary alopecia, and perifollicular inflammation that help in the diagnosis of the disease and the differential diagnosis with other scarring alopecias. Histopathology reveals an inflammatory infiltrate and perifollicular lamellar fibrosis. Although numerous therapeutic options have been tested, including corticosteroids, finasteride, and minoxidil, none have shown clear benefits in terms of halting the progression of the alopecia.

Key words: frontal fibrosing alopecia, postmenopause, postmenopausal, scarring alopecia.

Diagnostic Assessment of Frontal Fibrosing Alopecia

Frontal fibrosing alopecia is a disease that is diagnosed clinically in most cases and for which a histopathological study is indicated in patients for whom the clinical diagnosis...
is not conclusive, taking into consideration a number of recommendations that will be described below. Further tests have not provided any benefit in the diagnosis of frontal fibrosing alopecia.

**Clinical Diagnosis**

Frontal fibrosing alopecia is characterized by the recession of the frontal hairline with scarring of the alopecic skin, often accompanied by alopecia of the eyebrows, and usually occurs in postmenopausal women\(^1,2\) (Figure 1). It is therefore a clinically well-differentiated entity. However, with the exception of the receding hairline present in 100% of patients, the other clinical manifestations reported for frontal fibrosing alopecia appear with variable frequency and are therefore of varying interest in clinical diagnosis (Table 2).

Scarring of the alopecic skin, onset after menopause, presence of perifollicular papules, and eyebrow alopecia appeared in more than 60% of patients with frontal fibrosing alopecia in the clinical series reviewed (Table 2). Other manifestations, such as follicular hyperkeratosis, associated female androgenetic alopecia, axillary alopecia, pruritus, and lichen planus or lichen planopilaris, were identified in less than 30% patients with frontal fibrosing alopecia (Table 2). Following are the clinical manifestations reported in patients with frontal fibrosing alopecia:

**Recession of the Frontal Hairline**

The progressive recession of the frontal and parietal hairline is the most constant and characteristic clinical manifestation of frontal fibrosing alopecia. It is present in all patients and is therefore a requisite condition for diagnosis. Onset of hairline recession usually occurs symmetrically and bilaterally, giving rise to a band of alopecia between 0.5 cm and 8 cm from the original hairline (Figure 1). Alopecia progresses slowly and ceases spontaneously several years after onset. However, some cases of long-term progression may lead to a total loss of hair from the frontoparietal area, giving rise to a “clown” pattern of alopecia (Figure 2). In 1 of the reviewed series, a case where the patient also presented...
recession of the occipital hairline was also included as frontal fibrosing alopecia.\textsuperscript{7}

**Scarring Alopecia**

Changes in the alopecic area consisting of pale skin with destruction of the follicular openings and skin atrophy are described in 96\% of published cases of patients with frontal fibrosing alopecia. This scarring is usually mild and no induration or clinically evident sclerosis has been reported. The affected scalp area has an unusual appearance that is clearly different from hyperpigmentation of the forehead due to chronic sun damage. These changes are common to other entities associated with scarring alopecia and are therefore not useful for the differential diagnosis.

**Onset in Postmenopausal Women**

The slow progression of the disease and the mildness of the initial stages make it difficult to estimate the exact age at which onset of the disease occurs, with delays in diagnosis of between 1 and 18 years.\textsuperscript{2,6}

In the published studies, the age at onset of frontal fibrosing alopecia varied between 45 and 82 years of age, with a mean age for all reviewed cases of 63.15 years.

Frontal fibrosing alopecia was initially described in postmenopausal women and this led to coining the term "postmenopausal frontal fibrosing alopecia."\textsuperscript{5} Onset after the menopause is reported in 94.87\% of patients in the published studies. Therefore, onset of frontal fibrosing alopecia occurred in premenopausal women in 5.13\% of cases. Despite the fact that onset is postmenopausal in a significant majority of cases and that hormone replacement therapy has no effect on the course of the alopecia, some authors prefer to dissociate the term frontal fibrosing alopecia from any reference to the hormonal status of the patient.\textsuperscript{5,7}

**Erythema, Papules, and Perifollicular Inflammation**

Inflammatory papules and follicular or perifollicular erythema in the line of progression of the alopecia have been reported in 72\% of patients with frontal fibrosing alopecia (Figure 3). These manifestations, which are usual in lichen planopilaris, are present particularly in the initial stages of frontal fibrosing alopecia and correlate with the inflammatory phase of the disease. The presence of these lesions, together with the usual signs, led to frontal fibrosing alopecia being classified under the term "frontal fibrosing alopecia."
alopecia being considered a clinical subtype of lichen planopilaris.8

Eyebrow Alopecia

The thinning or partial or total loss of eyebrow hair has been reported in 62.82% of patients with frontal fibrosing alopecia. Hair-loss from the lateral third of the eyebrows is characteristic and, in some cases, there may be total loss of eyebrow hair (Figures 2 and 3A). In other cases, however, diffuse thinning of the eyebrows occurs, giving them a sparse appearance. Eyelash loss was observed in a patient in the series published by Kossard et al.2 Eyebrow alopecia is also a frequent characteristic of alopecia areata; several patients with frontal fibrosing alopecia from the reviewed studies were initially diagnosed with alopecia areata due to the total or partial loss of eyebrow hair.

Follicular Hyperkeratosis

Follicular keratotic plugs or hyperkeratotic papules have been reported in 30.77% of patients with frontal fibrosing alopecia and should be distinguished from the lesions that occur in widespread form on the trunk and limbs of patients with Graham-Little-Piccardi-Lassueur syndrome.

Female Androgenetic Alopecia

Of the patients with frontal fibrosing alopecia included in the reviewed series, 20% presented different degrees of female pattern baldness. This association, which is a consequence of the age of the patient with frontal fibrosing alopecia, gives rise to a clinical pattern of recession of the frontal hairline and diffuse alopecia on the rest of the scalp.5

Axillary Alopecia

Generalized thinning of the hair on other parts of the body, particularly the axillae, was reported in 14.10% of the cases from the reviewed series. This loss of axillary hair may be accompanied by reduced hair density in other areas (pubic area, limbs etc) and this may, in some cases, be accompanied by mild skin atrophy and diffuse follicular erythema.2,6 In some cases, this loss of hair from the axillae and limbs was interpreted as being compatible with Piccardi-Lassueur-Graham-Little syndrome, especially in cases with follicular keratotic papules—a finding present in all patients with this syndrome. However, recession of the frontal hairline points towards frontal fibrosing alopecia rather than a diagnosis of multifocal scarring alopecia.2

Pruritus

Pruritus of the scalp was reported by 8% of patients with frontal fibrosing alopecia.

Associated Dermatoses

Unlike lichen planopilaris, which is associated with lichen planus lesions in up to 50% of patients, only 5% of patients with frontal fibrosing alopecia presented lesions compatible with lichen planus in other locations. Some patients with frontal fibrosing alopecia have tested positive for antinuclear antibodies, although patients with lupus erythematosus or other autoimmune diseases were not described in the reviewed studies.

Histopathological Diagnosis

The histopathological signs originally described by Kossard1,2 and confirmed in subsequent studies consisted of the presence of a lichenoid perifollicular infiltrate at the level of the isthmus and infundibulum, with perifollicular fibrosis in onion-skin layers and lamellar fibrosis at the same location as the inflammatory infiltrate. These histopathological manifestations—shown in the 16 patients of the series of Kossard et al2—were indistinguishable from the histopathological changes in the cases of multifocal lichen planopilaris. However, in the clinical series reported by Poblet et al7 dermatological abnormalities were described that may allow for a differential diagnosis between the 2 entities (Figure 4 and Table 3).

Figure 4. Histopathology of frontal fibrosing alopecia. The images show a mild perifollicular inflammatory infiltrate (hematoxylin–eosin, ×40) (A), with lamellar fibrosis around the follicular isthmus and infundibulum (hematoxylin–eosin, × 100) (B).
Therefore, in cases where the clinical manifestations are not sufficient to diagnose frontal fibrosing alopecia, the following recommendations should be followed to provide an adequate histopathological study:

1. Perform 6-8 mm punch biopsies in the area of progression of the alopecia where hair still exists, including follicles and, if evident, perifollicular papules.
2. Transverse sections should be prepared to facilitate observation of the infiltrate and perifollicular fibrosis.
3. It should be remembered that biopsies in patients with long-term frontal fibrosing alopecia will present fibrous tracts with no follicles and no inflammatory infiltrate. These biopsies should therefore be reported as “scarring alopecia,” which, from a pathological point of view, is indistinguishable from other diseases.

### Additional Tests

Several further tests were performed in the published studies, including a complete blood count and general biochemistry, liver function tests, thyroid hormones (thyrotropin, triiodothyronine, thyroxine), serology for hepatitis C virus, antinuclear antibodies, sex hormones (luteinizing hormone, follicle stimulating hormone, androgens, and estradiol), and prolactin.\(^1\) Results were normal in most patients, with isolated cases of positive results for antinuclear antibodies at low titers.\(^7\)

Therefore, based on the results of the reviewed studies, further tests are not required in patients with clinical symptoms compatible with frontal fibrosing alopecia who present no other dermatosis or associated systemic disease and no other clinical manifestations of hyperandrogenism.

### Differential Diagnosis

Frontal fibrosing alopecia is a form of primary scarring alopecia. This is a large group of diseases characterized by the irreversible loss of hair due to a scarring process that leads to the thinning and destruction of the hair follicles—generally in the scalp. The distribution pattern of the alopecia (single plaque, multifocal, hairline recession), the involvement of other hairy areas (eyebrows, axillae, body hair), and the presence of other associated cutaneous manifestations (signs of lichen planus, discoid lupus, etc) will allow for a clinical differential diagnosis with these diseases in a large number of cases. Histopathological findings may be of help, especially in the initial stages where each of the diseases being considered will show a more or less typical inflammatory infiltrate, whereas the final stages of scarring alopecia are characterized by the presence of fibrosis of the follicle and absence of inflammatory infiltrate.

Frontal fibrosing alopecia should also be differentiated from other forms of nonscarring alopecia that may have similar clinical symptoms and course (progressive recession of the frontal hairline).

Table 4 shows the clinical characteristics of diseases that may pose problems in the differential diagnosis with frontal fibrosing alopecia.

### Treatment

The fact that frontal fibrosing alopecia presents the symptoms of scarring alopecia in the final stages and that progression is slow, with spontaneous cessation of the disease years after onset makes both treating the disease...
and assessing the effectiveness of the administered treatment difficult.

The available evidence on the treatment of frontal fibrosing alopecia comes from retrospective observational studies that described the clinical manifestations of the disease. There are no randomized clinical trials or quasi-experimental studies that make it possible to reach conclusions regarding the most appropriate treatment options. Table 5 describes the treatment regimens and combinations used, along with the results obtained. Each of these alternatives was tried in less than 10 patients, making the level of evidence insufficient to establish recommendations for each of the options described below.

### Corticosteroids

Corticosteroids may be considered a rational approach in the initial stages of the disease, characterized by the presence of perifollicular papules and lymphocytic infiltrate. The relationship between frontal fibrosing alopecia and lichen planopilaris and lichen planus would also support the use of corticosteroids in these patients. Of the patients...
### Table 5. Treatment Regimens Administered to Patients With Frontal Fibrosing Alopecia

<table>
<thead>
<tr>
<th>Study</th>
<th>Therapeutic Regimen</th>
<th>No.</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kossard1 1994 and Kossard et al 1997</td>
<td>Oral prednisone 25-50 mg/d for 1 month</td>
<td>4</td>
<td>2 cases of temporary slowing of hair loss (50%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 cases with no response and slow progression (50%)</td>
</tr>
<tr>
<td></td>
<td>Chloroquine phosphate 150 mg/d for 3-9 months</td>
<td>3</td>
<td>1 case of temporary response (33.3%) 2 cases with no effect</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>on progression of alopecia (66.6%)</td>
</tr>
<tr>
<td></td>
<td>Moderate-potency topical corticosteroid</td>
<td>9</td>
<td>No therapeutic effect</td>
</tr>
<tr>
<td></td>
<td>2% minoxidil solution</td>
<td>2</td>
<td>No therapeutic effect</td>
</tr>
<tr>
<td></td>
<td>Intralesional corticosteroid</td>
<td>1</td>
<td>No therapeutic effect</td>
</tr>
<tr>
<td>Naz et al 2003</td>
<td>0.05% fluocinolone acetonide cream twice daily for 1 year</td>
<td>1</td>
<td>No therapeutic effect</td>
</tr>
<tr>
<td></td>
<td>Oral prednisone 1 mg/kg/d for 3 months</td>
<td>1</td>
<td>Hair-loss was halted, though it did continue after suspension</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>of the oral prednisone</td>
</tr>
<tr>
<td></td>
<td>2% minoxidil solution twice daily for 6 months</td>
<td>1</td>
<td>No therapeutic effect</td>
</tr>
<tr>
<td></td>
<td>0.025% triamcinolone acetonide cream twice daily for 6 months</td>
<td>1</td>
<td>No therapeutic effect</td>
</tr>
<tr>
<td>Vaisse et al 2003</td>
<td>Topical corticosteroid (potency I-II) for 2-16 months</td>
<td>8</td>
<td>No therapeutic effect</td>
</tr>
<tr>
<td></td>
<td>Topical corticosteroid (potency I-II) + hydroxychloroquine</td>
<td>2</td>
<td>No therapeutic effect</td>
</tr>
<tr>
<td></td>
<td>Topical corticosteroid (potency I-II) + chloroquine</td>
<td>2</td>
<td>No therapeutic effect</td>
</tr>
<tr>
<td></td>
<td>Topical corticosteroid (potency I-II) + 2% minoxidil solution</td>
<td>1</td>
<td>No therapeutic effect</td>
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<tr>
<td></td>
<td>2% minoxidil solution</td>
<td>2</td>
<td>No therapeutic effect</td>
</tr>
<tr>
<td></td>
<td>Acitretin 30-40 mg/d for 3-6 months</td>
<td>4</td>
<td>No therapeutic effect</td>
</tr>
<tr>
<td></td>
<td>Oral prednisone 0.5 mg/kg/d for 6-18 weeks</td>
<td>2</td>
<td>No therapeutic effect</td>
</tr>
<tr>
<td>Moreno-Ramírez et al 2005</td>
<td>Intralesional triamcinolone acetonide 20 mg/mL (1 mg/2 cm², 1/10 dilution on eyebrows) every 3 months</td>
<td>9</td>
<td>Rapid stabilization of frontal recession in 4 patients (44%)</td>
</tr>
<tr>
<td></td>
<td>Intralesional triamcinolone acetonide + finasteride 2.5 mg/d + 5% minoxidil solution twice daily</td>
<td>7</td>
<td>Rapid stabilization of frontal recession in 1 patient (14%)</td>
</tr>
<tr>
<td></td>
<td>Regimen applied to patients with associated androgenetic alopecia</td>
<td></td>
<td>General improvement in 6 patients (86%) with increased hair density, but with no effect on the degree of frontal fibrosing alopecia</td>
</tr>
<tr>
<td>Tosti et al 2005</td>
<td>Intramuscular triamcinolone acetonide 40 mg every 3 weeks</td>
<td>3</td>
<td>No response. Slow progression of alopecia</td>
</tr>
<tr>
<td></td>
<td>+ 2% minoxidil solution twice daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Finasteride 2.5 mg/d + 2% minoxidil solution twice daily</td>
<td>8</td>
<td>Progress halted in 4 patients (50%) after between 12 and 18 months of treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>No response. Slow progression of alopecia in 4 patients (50%) after between 6 and 9 months of treatment</td>
</tr>
</tbody>
</table>
reviewed, 60% were treated with corticosteroid monotherapy and 73% of patients were treated with corticosteroids alone or in combination with another drug.

**Systemic Corticosteroids**

Administration of oral prednisone halted hairline recession in 42.9% of patients treated. However, in the cases where this treatment was beneficial, the disease continued to progress when administration of corticosteroids was suspended. The administered dosages were 0.5–1 mg/kg/d for a period of 3 to 18 months.\(^3,4\) However, administration of 25–50 mg/d of oral prednisone in short cycles of 1 month was the regimen that provided the greatest, if transient, benefit.\(^1,2\)

**Topical Corticosteroids**

As shown in Table 5, topical administration of medium to high-potency corticosteroids (I-II) did not halt progression of the alopecia in any of the patients in the reviewed studies. The treatment regimens described consisted of administering 0.05% fluocinolone acetonide or 0.025% triamcinolone acetonide twice daily for 2 to 6 months. The studies reviewed reported no adverse effects due to the topical application of corticosteroids despite prolonged administration on moderately atrophied skin, which is potentially more sensitive to the local effects of corticosteroids.\(^1-6\)

**Intralesional Corticosteroids**

Intralesional administration of triamcinolone acetonide provided a response rate of 40% (Table 5). This response was obtained in patients in whom the biopsy revealed an active inflammatory infiltrate. The administration regimen consisted of triamcinolone acetonide at a dose of 1 mg/cm\(^2\) every 3 months using a solution of 20 mg/mL for administration in the scalp and a solution of 2 mg/mL (10%) for administration in the eyebrows, as this location is more susceptible to atrophy.\(^5\)

Once alopecia has advanced to the fibrotic phase, intralesional corticosteroids provide no benefit and may even worsen the fibrosis and atrophy that characterize the advanced stages of frontal fibrosing alopecia.

**Minoxidil**

The pathogenic mechanism of frontal fibrosing alopecia (inflammation and fibrosis) is different from that of androgenetic alopecia (miniaturization). Nevertheless, minoxidil, which has a known effect on reducing the rate of follicle miniaturization, has been tried in patients with frontal fibrosing alopecia. Approximately a third of the patients in the reviewed studies received minoxidil.

A 2% solution of minoxidil was applied twice daily for 6 months as monotherapy in 5 patients and did not slow the progression of the frontal alopecia.\(^1-6\)

**Finasteride**

Finasteride is an inhibitor of 5#-reductase and prevents the follicular miniaturization that characterizes androgenetic alopecia by blocking the conversion of testosterone to dihydrotestosterone. For this reason, in the cases where finasteride was administered to patients with frontal fibrosing alopecia, the improvement obtained was related to the improvement in the level of the associated androgenetic alopecia.\(^5,6\) Finasteride was not used as monotherapy in any of the patients with frontal fibrosing alopecia. Of the patients who did receive this treatment (n = 15), 8 were administered 2.5 mg/d of finasteride in association with a 2% solution of minoxidil. Progression of the alopecia was halted in 4 of these patients (50%) after 12-18 months, whereas the other 4 patients (50%) showed no response. Administration of the same dosage of finasteride in association with minoxidil and intralesional triamcinolone acetonide to 7 patients provided general improvements with increased hair density in 86% of patients (n = 6) but had no effect on the degree of frontal fibrosing alopecia.\(^5,6\) There is no risk of feminization of male fetuses in these cases due to the mean age of the patients with frontal fibrosing alopecia (more than 60 years of age).

**Antimalarial Drugs**

In the original studies by Kossard et al,\(^1,2\) administration of 150 mg/d of chloroquine phosphate for 3–9 months in 3 patients obtained a temporary response in 1 patient. In the study by Vaisse et al,\(^4\) the association of hydroxychloroquine and topical corticosteroids provided no response in either of the 2 patients treated.

**Other Treatments**

There are anecdotal cases in which a small number of patients with frontal fibrosing alopecia were treated with griseofulvin, isotretinoin, tacrolimus, pimecrolimus, cyclosporine etc. These treatments were not shown to be effective in halting the progression of alopecia in any of the cases.

**Conclusions**

1. Diagnosis of frontal fibrosing alopecia is primarily clinical in the case of a middle-aged or elderly woman with a receding frontal hairline.
2. The existence of other manifestations (scarring alopecia, eyebrow alopecia, axillary alopecia, or perifollicular papules) will allow for greater certainty in the clinical diagnosis and differential diagnosis with other forms of scarring alopecia.

3. Histopathology is characterized by a perifollicular lymphocytic infiltrate surrounding the upper parts of the follicle, with lamellar fibrosis in advanced stages.

4. There are no therapeutic options to date that have proven to be effective with an appropriate level of evidence in the treatment of frontal fibrosing alopecia.

Conflicts of Interest
The authors declare no conflicts of interest.

References