Examination of clinical and demographic characteristics of 14 cases with frontal fibrosing alopecia

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Abstract

Objective: Frontal fibrosing alopecia (FFA) is a rare type of cicatricial alopecia seen in postmenopausal women characterized with band-type frontal/frontotemporal hair traction and/or significant or complete loss of the eyebrows. We aimed to present the demographic, clinical and laboratory characteristics of female patients diagnosed and followed-up with FFA in our clinic by comparing these with the literature data.

Method: A total of 14 patients who admitted to our outpatient clinic with alopecia on the frontotemporal/frontal hairline and were clinically and/or histopathologically diagnosed with FFA between 2011 and 2016 were evaluated in a retrospective manner. The patients were reviewed in terms of the age of lesion onset, localization, accompanying symptom or disease, and treatment options.

Results: The ages of the patients who were followed-up in our outpatient clinic with FFA were between 52 and 73 (mean 6 years). Eight patients (57%) had total eyebrow loss. Laboratory tests were in normal limits or negative. Comorbidities included thyroid disease, hypertension and coronary artery disease diabetes mellitus. For treatment, all patients were given systemic, intralesional and topical steroid, and topical minoxidil at various times. Four patients received hydroxychloroquine, 2 patients acitretin, 2 patients Vitamin E, 1 patient itraconazole, and 1 patient topical tacrolimus.

Conclusion: FFA should be considered in middle aged and elderly postmenopausal women presenting with hair loss complaints and were detected to have frontal hairline traction and cicatricial alopecia, and the diagnosis should be supported by biopsy. Thereby, the disease progression may be prevented or delayed with early diagnosis and proper treatment.

Keywords: Cicatricial alopecia, frontal fibrosing alopecia

Introduction

Frontal fibrosing alopecia (FFA) was first identified in 1994 (1). FFA is a presentation characterized by symmetrical, progressive traction on frontotemporal hairline and band-type alopecia, predominantly seen in postmenopausal women and frequently also affecting the eyebrows (1-7). The diagnosis is usually made on a clinical basis. Histopathological examination is supportive in diagnosis (2,5,7). While the pathogenesis is not exactly known, its ever-increasing incidence in recent years indicates possible involvement of environmental factors (4). On the other hand, the fact that FFA is seen in more than one individual in some families suggests genetic factors yet to be discovered (8). To date, however, a complete genetic analysis has not been performed. Frequent occurrence in postmenopausal period and successful treatment with 5-alpha reductase inhibitors suggest that a hormone-induced trigger mechanism and androgenetic factors may also be responsible in pathogenesis (2,3,9).

Despite its well-known clinical presentation, clinical studies regarding its treatment are not adequate (2,6). Case reports and series were reported in local and foreign literature (10-19). Here, we aimed to present the demographic, clinical and laboratory characteristics of female patients diagnosed and followed-up with FFA in our clinic by comparing these with the literature data.

Method

A total of 14 patients who admitted to our outpatient clinic with alopecia on the frontal hairline and were clinically and/or histopathologically diagnosed with FFA between 2011 and 2016 were evaluated in a retrospective manner. Photos were taken and patients gave consent form. The patients were reviewed in terms of the age of lesion onset, localization, accompanying symptom or disease, and treatment response. Clinical and demographic characteristics of patients were recorded.
the patients are shown in Table 1. The data is given as mean, percentage, number.

**Results**

The ages of the patients who were followed-up in our outpatient clinic with FFA were between 52 and 73 (mean 62 years). The disease duration varied between 6 months and 10 years (2 years). None of the cases had history of known trauma or hear traction. Comparable clinical characteristics were present in all patients. Symmetrical, band-type traction on the frontal hairline extending to preauricular areas, mild atrophy in the skin, follicles at the hairline margin becoming evident, and perifollicular erythema were detected. While 57% of the patients (8 patients) had total loss of eyebrows, others had partial loss. [Figure1-3]. Eleven patients underwent biopsy. Three patients did not accept biopsy.

One patient had lichen planus pigmentosus on the face supported by biopsy. Skin examination other than the scalp was normal in other patients, mucous membranes and nails were normal in all cases. Punch biopsy was taken from an area containing decreased hair follicles on the frontal region of the scalp from 11 patients. In histopathological examination, decrease in the number and difference in the sizes of hair follicles, perifollicular inflammation, fibrosis in dermis, and decrease in elastic fibers were detected. The patients were regarded as frontal fibrosing alopecia using clinical and/or histopathological findings. In the laboratory studies, complete blood count, routine chemistry tests, thyroid functions, C reactive protein, rheumatoid factor, Anti-dsDNA, Antinuclear Antibody (ANA), hepatitis B and C serology were in normal limits or negative. Comorbidities included thyroid disease in 4 patients, hypertension and coronary artery disease in 3 patients, DM (diabetes mellitus), Vitamin B12 deficiency and iron deficiency anemia in 2 patients each, and Vitamin D deficiency in 7 patients.

For treatment, all patients were given systemic, intralesional and topical steroid, and topical minoxidil at various times. Four patients received hydroxychloroquine, 2 patients acitretin, 2 patients Vitamin E, 1 patient itraconazole, and 1 patient topical tacrolimus.

**Discussion**

FFA is a cicatricial alopecia characterized by the destruction of hair follicles (2-4). Its localization is different than LPP (lichen planopilaris). Presence of band-type cicatricial alopecia on the frontotemporal region of the scalp is typical. As with all our cases, symmetrical and bilateral traction on the frontal and temporal hairline of the patients is explicit. This traction increases even more over time (2,6,7). Traction on the hairline may vary, progresses slowly and spontaneously stop years after onset (6,7,20). The severity of the disease may also be identified by measuring glabellar-frontal distance which is normally 5.9 cm on average (7). Glabellar-frontal distance in FFA patients was reported to be 6.5-12.5 cm on average (7). However, this measurement was not taken in our cases. 96% of the published cases were reported to have paleness in alopecic skin, destruction of follicular orifices, and skin atrophy without clinical induration and sclerosis (1,5,6,20). All our cases had cicatrical alopecia.

FFA is disease of postmenopausal women by 95%, and the mean onset age of the disease is 67 (43-82) (2,3,4). A multi-center study performed by Vano et al., is the study including the largest series with 355 patients on this subject (14). In this study, investigators reported 12 male patients and 40 premenopausal women. Other cases were postmenopausal women. There are also other studies, though low in number, reporting FFA in male cases and premenstrual women (11,21,22). All our cases were female and in postmenopausal period, and their age varied between 58 and 73 (mean 62).

Eyebrow loss and thinning is frequent, and helps to make diagnosis. Thinning or total loss of the eyebrows was reported in 50-95% of the FFA cases (6,12,13,15). Vona et al. stated that eyebrow loss is present in moderate-severe cases (14). In our study, total eyebrow loss was seen in 57% of the cases (8 cases), and others had partial eyebrow involvement. Eyelash loss in FFA is occasional and may indicate poor prognosis. Investigators reported that these cases require systemic treatment (14,20,23). In some studies, eyelash loss was detected in 3-26% of the cases (12,13). In our study, eyelash loss was present in 14.2% of the cases (2 cases), and these cases progressed rapidly and did not respond the treatment at all.

General thinning or loss of hair of the other body parts, especially axillary region, was detected in 14-26, 37.5% of the cases (6,12,13). Our one cases had loss in all body hair, however, no follicular keratotic papule was present. Other cases had normal distribution of body hair.

In the early stages of the disease, presence of perifollicular inflammatory papule or erythema was reported in 31-73% of the cases on the progression region of the disease (6,13,15). While most cases had perifollicular erythema, only 2 cases (14.2%) had perifollicular hyperkeratosis. Symptoms such as itching, burning and pain are seen less compared to lichen planopilaris. Itching on FFA area was reported in 3-67% of the cases in the literature (4,6,11,13,15). Itching was present in 21% of the cases (3 cases).

While the ethiopathogenesis of the FFA is not exactly known, the key role is thought be played by T-cell mediated autoimmune reaction against hair follicles (2,3,5,9,16). Another opinion regarding FFA ethiopathogenesis is the effect of androgen hormonal factors.
Table 1: Clinical and demographic characteristics of the patients

<table>
<thead>
<tr>
<th>P. No</th>
<th>Age</th>
<th>Sex</th>
<th>Localization site</th>
<th>Symptoms</th>
<th>D. period</th>
<th>Concomitant Diseases</th>
<th>Biopsy entity</th>
<th>Lab. findings</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>64</td>
<td>F</td>
<td>F-temporal + eyebrows</td>
<td>pruritus</td>
<td>10 years</td>
<td>Asthma, HT, Thyroid Diseases</td>
<td>-</td>
<td>Vit D level low</td>
<td>TS, ILS</td>
</tr>
<tr>
<td>2</td>
<td>56</td>
<td>F</td>
<td>F-temporal</td>
<td>-</td>
<td>2 years</td>
<td>+</td>
<td>TS, ILS, H</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>67</td>
<td>F</td>
<td>F-temporal + eyebrows</td>
<td>-</td>
<td>3-4 years</td>
<td>Thyroid Diseases</td>
<td>-</td>
<td>Vit D level low</td>
<td>TS, ILS SS, P, H</td>
</tr>
<tr>
<td>4</td>
<td>58</td>
<td>F</td>
<td>F-temporal + eyebrows</td>
<td>+pruritus</td>
<td>1 year</td>
<td>HT, DM,</td>
<td>+</td>
<td>-</td>
<td>TS, ILS, H</td>
</tr>
<tr>
<td>5</td>
<td>64</td>
<td>F</td>
<td>F-temporal + eyebrows</td>
<td>-</td>
<td>3-4 years</td>
<td>HT, Thyroid Diseases, CAD, DM</td>
<td>+</td>
<td>-</td>
<td>TS, ILS</td>
</tr>
<tr>
<td>6</td>
<td>73</td>
<td>F</td>
<td>F-temporal + eyebrows + eyelashes + diffuse alopecia</td>
<td>FH</td>
<td>1 year</td>
<td>Vit D level low</td>
<td>TS, ILS, Etretinat</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>66</td>
<td>F</td>
<td>F-temporal</td>
<td>-</td>
<td>1,5 years</td>
<td>+</td>
<td>TS ILS P</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>64</td>
<td>F</td>
<td>F-temporal</td>
<td>FH</td>
<td>2 years</td>
<td>+</td>
<td>Vit D level low</td>
<td>TS, ILS, H</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>58</td>
<td>F</td>
<td>F-temporal</td>
<td>6 months</td>
<td>+</td>
<td>TS, ILS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>58</td>
<td>F</td>
<td>F-temporal + eyebrows</td>
<td>6 months</td>
<td>+</td>
<td>TS, ILS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>58</td>
<td>F</td>
<td>F-temporal</td>
<td>1 year</td>
<td>+</td>
<td>Vit D level low</td>
<td>TS, ILS, SS, vit E</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>72</td>
<td>F</td>
<td>F-temporal + eyebrows</td>
<td>+pruritus</td>
<td>2 years</td>
<td>Lichen pigmentosus, CAD, HT,</td>
<td>+</td>
<td>Ferritin and vit B12 level low</td>
<td>TS, ILS, Etretinat</td>
</tr>
<tr>
<td>13</td>
<td>59</td>
<td>F</td>
<td>F-temporal</td>
<td>1 year</td>
<td></td>
<td>A (iron-vitB12), Colon Ca</td>
<td>+</td>
<td>TS, ILS, SS, vit D, vit B12</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>52</td>
<td>F</td>
<td>F-temporal + eyebrows</td>
<td>+ pruritus</td>
<td>6 months</td>
<td>Thyroid Diseases,</td>
<td>+</td>
<td>Vit D level low</td>
<td>TS, ILS, SS, vit E</td>
</tr>
<tr>
<td>Total</td>
<td>Med age</td>
<td>F</td>
<td>14 F-temporal, 8 eyebrows, 2 eyelashes, 1 diffuse</td>
<td>3 pruritus</td>
<td>Median period 2 years</td>
<td>1 lichen pigmentosus , 6 vit D deficiency, 4 Thyroid diseases, 2DM, 4HT, 2Anemia (iron, vit b12)</td>
<td>Three no biyopsi, 11 biyopsi</td>
<td>ILS, ILS, FFA</td>
<td></td>
</tr>
<tr>
<td>FFA</td>
<td>62</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2Etreinat, ltracanazol No hormontherapy</td>
</tr>
</tbody>
</table>


Figure 1: Progressive traction on frontotemporal hairline and band-type alopecia.

Figure 2: Diffuse hair and eyebrows loss and pigmented lichen planus lesions on the face.

Figure 3: Progressive traction on frontotemporal hairline.
While the facts that it usually affects postmenopausal women, involves frontal scalp, and responds to antiandrogens such as finasteride or dutasteride in some patients suggest this, a significant relationship is yet to be revealed (4,9,24).

Today, FFA is regarded as a clinical variant of LPP which has selectivity for frontotemporal hairline, primarily affects postmenopausal women and is characterized by lymphocytic cicatricial alopecia (2,3,17). Some authors detected lichen planus lesions in patients with FFA (15,19). Furthermore, due to premenstrual female cases with normal levels of sex hormones with accompanying lichen planus lesions, some authors also supported the opinion that the disease is a clinical variant of LPP rather than being an androgen-based disease (11,17). Also, one of our cases had pigmented lichen lesions.

Histopathologically, lamar fibrosis on perifollicular area and fibrosis of the follicular ducts are frequently seen in FFA. No perivascular and peridnexial inflammation is present. These pathological characteristics are common with LPP. The distinctive pathological characteristic of FFA from LPP is that lymphocytic infiltrate and fibrosis of the FFA selectively affect vellus-like follicles on frontal line and muscles. Although not necessarily, perifollicular localized inflammatory lymphocytic infiltrate may be observed on the upper part of the hair follicle (5,23,25).

Mild to moderate follicular inflammation is the common pathological characteristic of female-type hair loss (FMA). However, inflammatory infiltrate in FMA is not limited to isthmus, and perifollicular fibrosis is not a distinctive characteristic as it is in FFA. The specific involvement of intermediate and vellus-like follicles on frontal line and muscles in FFA is yet to be explained (11,13,23,25).

Histopathological examination is necessary to support diagnosis. However, types of primary fibrosing alopecia may not be distinguished histopathologically (6,25). In cases with long-term FFA, the performed biopsies are only reported as cicatricial alopecia, and fibrous tracts without follicle and inflammatory infiltrate are seen (13). Therefore, while some authors show several clinical presentation, they accept FFA as a special variant of lichen planopilaris (5,20). The histopathological examinations of our cases who underwent biopsy could not be distinguished from LPP. Overall, perifollicular fibrosis and lymphoplasmocytic inflammation, and fibrotic bands in dermis were observed. As the histopathological characteristics of our cases could not be distinguished from LPP and the clinical characteristics suggest FFA, we also thought that FFA might be a different variant of lichen planopilaris. However, there is not sufficient data to accept FFA as a separate entity causing lymphocytic cicatricial alopecia (19).

Laboratory tests do not provide the desired assistance in diagnosis (3). Solely, ANA positivity was reported in some cases (14). As a possible autoimmune mechanism plays a role in the pathogenesis, FFA was reported to have the possibility of co-existing with other autoimmune diseases (14). Banka et al. detected co-existence with autoimmune connective tissue disease in 14% of the cases (15). Also, FFA co-existence with autoimmune diseases such as thyroid disease, vitiligo and psoriasis was reported (13,14,15).

Some authors were detected to have thyroid pathology and DM in 14-16% of the cases (14,19). We detected thyroid pathology in 28% of our cases. Comorbidities including DM, Vitamin B12 deficiency, Vitamin D deficiency were present in some cases.

Moreover, it was also suggested some medications including angiotensin converting enzyme inhibitors, beta-blockers and thiazides may trigger FFA (14). Ozcan et al. detected history of angiotensin converting enzyme inhibitor or beta-blocker use in 24% of the patients (19). In our study, antihypertensive (angiotensin converting enzyme inhibitor) use was present in four cases (28%) and antidiabetic use in two patients (14%).

The identification of the disease 23 years ago and presence of case and case series around 80 suggest that the diagnosis is usually missed rather than the disease being rare (17,23). The incidence of the disease may be more. It may be due to ignoring and not seeking help in the early stages or the fact that these patients are diagnosed differently (24). Thereby, it causes delay in true diagnosis and treatment, and makes the alopecia permanent. A careful dermatological examination may help to avoid this. Two of our cases were previously diagnosed with alopecia areata and treated accordingly.

In the differential diagnosis of FFA, diseases causing primary cicatrical alopecia including discoid lupus erythematosus, multifocal cicatrical alopecia, follicular degeneration syndrome, traction alopecia, pseudopelade, Graham-Little-Piccardi-Lassueur characterized by diffuse follicular plug or papules, and non-cicatrical alopecia causes including alopecia mucinosa, keratosis follicularis decalvans neutrophilic type cicatrical alopecia, alopecia areata, androgenetic alopecia, female-type hair loss, chronic telogen effluvium and familial high hairline should be considered (2,3,6,20).

Very little is known about the natural progression and history of FFA. FFA progresses slowly and the progression stops spontaneously over time, therefore, organizing the treatment and assessing the treatment response may be difficult (2-4). As the alopecia is cicatrical, the aim should be stopping the progression of the disease, preventing more alopecia and decreasing the symptoms (2,26). Also, there is no clear consensus on how to assess the efficacy of FFA treatment. There is no effective option of treatment (3,4,26).

In the literature, preferred treatment options mostly include the use of corticosteroids alone or combined with other medications (26). Steroids may be administered via topical, intralesional or systemic
routes. Oral, intralesional corticosteroid administration was reported to create partial response in 57% of the cases. Most authors considered the steroid treatment as first-line therapy. Intermediate to strong potent topical steroids cannot stop the progression of alopecia in most cases (26). Intralesional steroid administration given in 3-4 weeks intervals was reported to be effective in the early stages of the disease, especially in clinical and histological inflammation stages (3,4). However, as most cases receive combination therapy, the assessment is difficult. Systemic steroid might be effective in rapidly progressing cases with significant inflammatory findings. Hair traction was stopped in approx. half of the cases (42%) using systemic steroid. In some studies, daily administration of oral prednisolone of 25-50 mg in short term was reported to be more beneficial (26). Steroids were found to be less efficacious in FFA than LPP. In our study, we administered firstly intralesional, systemic (intramuscular depot) and topical strong potent steroid treatment to all our cases.

The disease progression stopped, improvement in atrophic skin was observed and a little hair grow was observed in cases who received steroid treatment. While intralesional steroid treatment was found to be successful in 40-97% of the cases with active inflammation in biopsy in the literature, its benefit in cicatrical stage could not be demonstrated (15). We observed slowing down of the progression of the disease with our treatment. We administered intralesional low-dose triamcinolone treatment in patients with eyebrow involvement.

Hydroxychloroquine which is known to be effective LPP is frequently used in FFA. Hydroxychloroquine was demonstrated to considerably decrease the signs and symptoms of the disease and to exert the most effect within the first 6 months (11). Antimalarias stabilize the disease in 30-50% of the patients (7,11,26). We administered hydroxychloroquine treatment as 2x200/day for 6 months in 28% of the cases, however, could not obtain the desired response. Also effective treatment options which are administered in FFA treatment include topical minoxidil, pimecrolimus, tacrolimus, oral acitretin, griseofulvin, doxycycline, mycophenolate mofetil and cyclosporine (4,7,26,28). In our study, we administered acitretin and Vitamin E to 2 cases each, and systemic itraconazole and topical tacrolimus to 1 case each.

In several studies, the most successful medications in FFA were demonstrated to be oral finasteride and dutasteride (12,14,27). However, this effect was also stated to be associated with a possible comorbid androgenetic alopecia. The efficacy of finasteride 2.5 mg use for at least 6 months was demonstrated. In a publication consisting of 111 patients reported in the literature, the most common treatment methods used in FFA patients were reported to be oral finasteride (daily 2.5 mg. for 6-18 months) or dutasteride (daily 0.5 mg for 12 months) (14). Anti-androgenic treatment was demonstrated to be beneficial in 31-47-50% of the cases (27). These agents were often combined with topical minoxidil or intralesional corticosteroids (6, 12,14,15,23,26,27), however, there is still no consensus on how to assess the treatment efficacy in FFA (26).

Conclusion

FFA should be considered in middle aged and elderly postmenopausal women presenting with hair loss complaints and were detected to have frontal hairline traction and cicatrical alopecia, and the diagnosis should be supported by biopsy. FFA may be considered as a special variant of lichen planopilaris. FFA negatively affects the individuals in a psychosocial manner due to progressive and permanent hair loss and decreases the quality of life. Therefore, with proper diagnosis and treatment, the symptoms may be eased and the disease progression may be prevented in most of the patients. In our case series of 14 patients who were diagnosed clinically and histopathologically, general information regarding FFA which is a lesser known cause of cicatrical alopecia was given, its demographic and clinical characteristics, and treatment options were reviewed, and comparison was made to general literature. The limitations of our study include being retrospective, low number of cases, and not being able to observe the true efficacy as we could not administer anti-androgen treatment.

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Ethical issues: All Authors declare that Originality of research/article etc... and ethical approval of research, and responsibilities of research against local ethics commission are under the Authors responsibilities. The study was conducted due to defined rules by the Local Ethics Commission guidelines and audits.

References


