

THESIS

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**TRICHOSCOPIC FINDINGS IN FRONTAL FIBROSING
ALOPECIA**

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Declaration

I declare that the submitted manuscript was carried out and written by me without the help of others, that I did not use other than the cited references and that I any copied text is highlighted as such.

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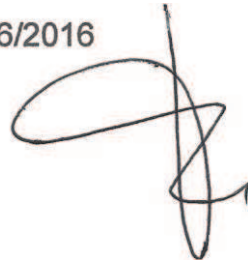
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Table of contents

1. Declaration	2
2. German abstract	4
3. English abstract	6
4. Introduction	9
5. Epidemiology	9
6. Pathogenesis	11
7. Clinical presentation	13
8. Differential Diagnosis	19
9. Histopathology	20
10. Therapy	21
11. Trichoscopy in frontal fibrosing alopecia	24
12. The aim of the study	29
13. Material and method of the study	29
14. Results	34
15. Discussion	48
16. Conclusion	51
17. References	52

German Abstract

Trichoskopische Merkmale der frontal fibrosierenden Alopezie

Hintergrund

Die frontal fibrosierende Alopezie (FFA) ist eine primäre lymphozytäre vernarbende Alopezie, die durch einen progressiven symmetrischen Rückgang der fronto-temporalen Haarlinie, den Verlust der Augenbrauen, der Wimpern und der Körperhaare gekennzeichnet ist. Wegen dem unvorhersehbaren Wesen dieser Krankheit war die Behandlung der FFA bisher frustan. Die Trichoskopie ist eine nützliche, nicht-invasive und kostengünstige Technik um häufige Erkrankungen des Haarapparates von der FFA abzugrenzen. Außerdem sind mit dieser Methode genauere follow-up-Untersuchungen möglich und sie wird in der Wahl einer passenden Stelle für eine Hautprobe eingesetzt.

Material und Methoden

Das Ziel dieser Studie war es die trichoskopischen Merkmale von an einer FFA erkrankten PatientInnen, die das Laboratory of Physiology and Diseases of the Hair am "Andreas Syggros" Krankenhaus in Griechenland besucht haben, zu erforschen und dokumentieren. Der Untersuchungszeitraum lag zwischen September und Dezember 2015. Der Studienablauf enthielt einen Fragebogen, um demographische Daten und Informationen sowohl zur individuellen Krankengeschichte als auch zur Familienanamnese zu erheben.

Die Diagnose stützte sich auf die typischen klinischen Merkmale (Rückgang der fronto-temporalen Haarlinie mit oder ohne begleitenden Verlust der Augenbrauen, perifollikuläres Erythem oder Hyperkeratose, blasse Haut, Atrophie und einzeln stehende Haare).

Die Untersuchung wurde mithilfe eines polarisierten und eines nicht-polarisierten Dermatoskops durchgeführt, außerdem wurden die betroffenen Areale fotografiert.

Die Bilder wurden von zwei DermatologInnen, die sehr erfahren auf dem Gebiet der Dermatoskopie und der FFA sind, anhand der typischen dermatoskopischen Merkmale dieser Erkrankung evaluiert. Im Anschluss wurden die Ergebnisse statistisch ausgewertet.

Ergebnisse

Unser Kohorte setzte sich aus 29 Frauen (96.5%) und einem Mann (3.5%) zusammen. Das Alter lag zwischen 42 und 85 Jahren, wobei das Durchschnittsalter 62.3 Jahre betrug. Bei allen 30 PatientInnen (100%) fand man klinisch einen Rückgang der frontalen Haarlinie; bei 10% kam es zu keinem temporo-parietalen Rückgang. Acht PatientInnen (26.67%) wiesen einen Rückgang der occipitalen Haarlinie auf, während dieses Merkmal bei 22 ProbandInnen (73.33%) nicht nachgewiesen werden konnte. Insgesamt 19 (63.33%) PatientInnen zeigten einen Verlust der Augenbrauen und einer (3.33%) den Verlust der Wimpern. Bei 2 PatientInnen (6.67%) war eine Autoimmunerkrankung und bei 6 PatientInnen (20%) ein Lichen plano-pilaris bekannt, darüberhinaus bestand bei 3 PatientInnen (10%) eine Schilddrüsenerkrankung. Bei 12 PatientInnen (40%) schien sich die Erkrankung in einem aktiven Stadium zu befinden. Im Verlauf entwickelten 22 PatientInnen (73.33%) ein perifollikuläres Erythem und 18 PatientInnen (60%) eine perifollikuläre Hyperkeratose. Bei 12 PatientInnen (40%) fanden sich follikuläre rote Punkte, während bei 30 PatientInnen (100%) follikulären Öffnungen fehlten.

Zusammenfassung

Die Trichoskopie ist in der Diagnostik der meisten Erkrankungen des Haarapparates, insbesondere der FFA, ein zuverlässiges und hilfreiches Instrument. Darüberhinaus ist sie auch in der Abschätzung der Krankheitsaktivität und Schwere von großem Nutzen. Zusätzlich helfen Aufzeichnungen, Dokumentation und der Vergleich mit Bildern vor Behandlungsbeginn den therapeutischen Erfolg zu evaluieren.

English Abstract

Trichoscopic findings in Frontal Fibrosing Alopecia (FFA)

Background

Frontal fibrosing alopecia, (FFA), is a disease that belongs to primary cicatricial alopecias and described by Steven Kossard in 1994. During the last two decades many patients have been diagnosed with the disease worldwide and dermatologists worldwide think that we might face a kind of epidemy.

The aetiopathogenesis of FFA is not fully understood. The main clinical signs of the disease are the symmetric recession of the frontal and temporal hairline, the eyebrows loss as well as eyelash loss and body hair. The therapy is, in the majority of cases, difficult and sometimes disappointing, due to the unpredictable nature of the disease.

Trichoscopy is a valuable noninvasive and low-cost technique, to differentiate clinically frequent hair disorders. Furthermore, trichoscopy provides to the clinician the ability to have a better follow- up of the patient and additionally to identify the suitable site for a biopsy.

Material and method

The main aim of our present work was to research and document the trichoscopic findings of 30 patients with a diagnosis of FFA attending the Laboratory of Physiology and Diseases of the Hair at the "Andreas Syggros" hospital in Greece. All patients were examined during the period of September 2015 - December 2015.

The studying process included a questionnaire for collecting demographic data and information on the patient's personal medical record as well as information on their family's record.

The diagnosis was made by the typical clinical clues of the disease (recession of the hairline at frontal and temporal area, concomitant loss or not of the eyebrows, perifollicular erythema, perifollicular hyperkeratosis, pale skin, atrophy and the presence of lonely hairs).

The examination was carried out using a polarized and a non-polarized dermatoscope and pictures of the examined areas were taken as well. In each patient, several photos were taken and afterward checked and evaluated by the specialists based on the dermatoscopic features of FFA.

The findings were assessed by two dermatologists who specialized in dermoscopy and in FFA. Lastly, a statistical analysis of the findings was conducted and once completed the study's final conclusions were drawn.

Results

Among the patients, there were 29 women (96.5%) and only 1 man (3.5%). The ages ranged between 42-85 years. The average age was 62.3 years. For all 30 patients (100%) the clinical findings included recession of the frontal hairline. (10%) did not have a temporoparietal recession. 8 patients (26.67%) had occipital recession, compared to 22 patients (73.33%) who had not developed this type of hairline recession. In 12 patients (40%) the disease seemed to be active and 18 patients (60%) did not have activity signs. 22 patients (73.33%) had developed perifollicular erythema. 18 patients (60%) had perifollicular hyperkeratosis, compared to 12 patients (40%) who had not developed perifollicular hyperkeratosis. 12 of the patients, (40%), had follicular red dots and 18 of the patients (60%) had no follicular red dots. All 30 patients (100%) showed lack of follicular openings. 19 patients (63.33%) suffered from eyebrow alopecia and only 1 patient (3.33%) suffered from eyelash alopecia. 2 patients (6.67%) had a history of autoimmune diseases and 28 patients (93.33%) had no such history. Additionally, 3 patients (10%) suffered from thyroid diseases and 6 patients (20%) had a history of LPP.

Conclusions

Trichoscopy is a reliable and helpful method to diagnose the majority of hair diseases, especially FFA. It is essential for dermatologists because helps them to estimate the degree of severity and also the activity of FFA.

In addition easy record keeping, documentation and comparison with pre-treatment images help to evaluate therapeutic response.

Trichoscopic findings in frontal fibrosing alopecia

Introduction

Frontal fibrosing alopecia (FFA) is a disease that recognized lately. It was described, for the first time in 1994, by Steven Kossard and since that time many studies and case reports have been published. In the beginning, the disease was rather rare and was thought to affect only menopausal women. Because of this observation, the disease was named "postmenopausal frontal fibrosing alopecia". Later, with several reports including younger women, premenopausal women and in some cases even men among the patients, the scientists realized that the disease was not as rare as they initially believed and that it did not affect only women. Thus, they came up with the term "frontal fibrosing alopecia".

During the last years, many patients with the disease worldwide have been diagnosed and many dermatologists think that we might face a kind of epidemic of FFA. (2, 3)

Epidemiology

Nowadays we can't estimate the incidence of FFA. The dermatologists around the world believe that the number of patients has been increased the last years. (2-7) MacDonald and all described "a tenfold increase in the number of cases seen annually over the last decade" (5).

Additionally, according to the last published reports, a percentage of 85% of the patients were white women. FFA has also been described in Asian, Black and Hispanic female and male patients (2, 5, 8, 9, 10). Furthermore, according to numerous studies, it was observed a high incidence of FFA among women with early menopause, (17%), compared with the percentage of 6% in the general population (2, 3). In addition, according to other reports,

in a considerable number of women with FFA, menopause had been presented post-surgically (after hysterectomy) (2, 3). It has been observed that the disease remains unaffected when these women received hormone replacement therapy. (4, 11)

The time when FFA presents varies from 18 to 87 years of life. The highest incidence is often observed in the sixth decade of life. (2) The authors of another study showed that black women, at a percentage of 74%, diagnosed with FFA before menopause (12), while in another study it was shown that "the age of onset comparative to the age of Caucasians". (13) At the same time, there are several reports mentioning patients (8%) who had a family history of FFA. (3, 12, 14) So far, cases of FFA have been described concomitant with autoimmune diseases such as alopecia areata, vitiligo, polymyositis, psoriasis, atopia, lupus erythematosus, and rheumatoid arthritis. (3, 5, 10)

Additionally, about 9 to 23% of patients may present thyroid abnormalities. (3, 4) There are also reported cases of patients suffering from simultaneous lichen planus or former lichen planus with a frequency ranging from 2% to 17%. The overlapping among cutaneous or mucosal lichen planus and frontal fibrosing alopecia appears uncommon (4, 5, 10). More recent studies reported also that other diseases like hypothyroidism, hypertension, dyslipidemia, and osteoporosis can be associated with FFA. (3) Moreover, associations among non-steroidal anti-inflammatory drugs, beta-blockers have been reported. The possibility that angiotensin-converting enzyme might have a protective role has also been described.

Noteworthy, 0%-68% of the patients might also suffer from aging alopecia or female pattern hair loss (3, 5)

Incidences of FFA have been reported in patients after face lifting or after hair transplantation. (15) A large majority of 87% of FFA patients are non-smokers. Finally, laboratory tests of the patients (especially hormonal tests) have not yielded any pathological findings in studies. (18)

Pathogenesis

The pathogenesis of FFA is unknown. A very important clue might be "the destruction of the epithelial hair follicle stem cells located in the bulge region of the hair follicle. This is the region where the inflammatory cell infiltrate is primarily located in FFA" (21). This destruction of the stem cells results in permanent hair loss. Some other factors that seem to connect to this destruction might be "an ongoing inflammatory response triggered by proinflammatory cytokines, such as interferons, increased apoptotic response, and collapse of the relative immune privilege of the hair follicle". Moreover in latest studies observed "deficiency in Peroxisome proliferator-activated receptor gamma (PPAR- γ)-mediated" signaling in Lichen Planopilaris. With that last observation, the researchers showed "a defective lipid metabolism" in frontal fibrosing alopecia. (21)

Although the pathways resulting in FFA remain to be elucidated, several theories have been suggested to expound the aetiopathogenesis of the disease.

Those are:

- Hormonal influence
- Sebaceous gland dysfunction
- Inflammation and Autoimmunity
- Environmental triggers
- Epithelial-Mesenchymal Transition
- Loss of CD200 "no danger" signal
- Keratin mutations
- PPAR- γ deficiency
- Collapse of immune privilege
- Cytokine release

- Autoimmune response
- Neurogenic inflammation
- Bulge eHFSC damage
- Genetic factors
- Stearoyl-CoA desaturase-1 deficiency
- Impaired self-maintenance of hair follicle stem cells
- Abnormal apoptosis
- Programmed organ deletion

(Figure 1)

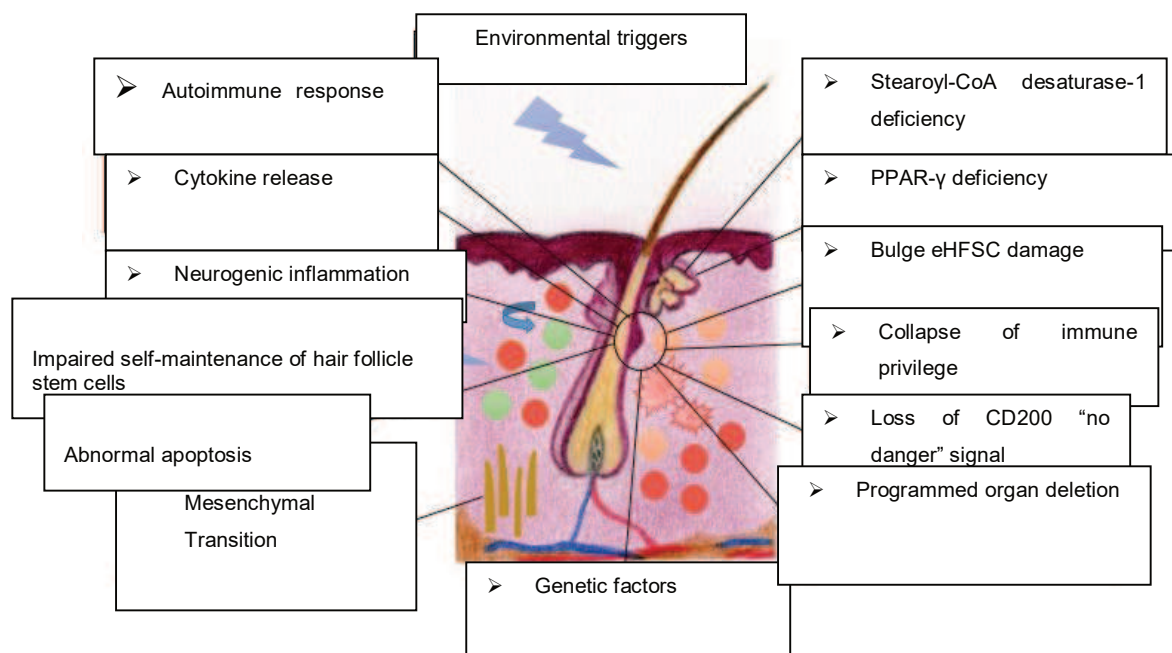


Figure 1(Adapted with permission)

V. Chasapi, Stratigos A., Antoniou Ch. Primary cicatricial alopecias Hellenic Dermato-Venereological Review. October - December 2015, Vol 26. No 4

Clinical presentation

Recession of the frontal and temporal hairline

Patients diagnosed with this condition, typically present a symmetric, at times irregular (moth eaten) band like pattern of "progressive recession of the frontal and parietal hairline" (Figure 2 and figure 3). This is a very common and also typical clinical sign of FFA. In most cases, the disease is diagnosed clinically. A histopathological study takes place only if the patient's clinical diagnosis is not conclusive. (19).



Figure 2



Figure 3

The recession may spread slowly or be rapidly progressive. Sometimes it can be self-limited. It is observed very often bilaterally and symmetrically (19). This recession leads to a band of alopecia 0.5 cm and 8 cm from the initial

hairline. However, in some cases of long-term evolution, the recession can result in a total hair loss from the frontoparietal area, giving the clinical picture of the "clown" pattern. (Figure 4, 5)



Figure 4



Figure 5

Sometimes the disease might be observed on other body sites like the temporal- parietal, or the retro-auricular and occipital areas.

FFA seems to progress slowly and often comes to an end spontaneously many years later. As a result of the slow progression of FFA, it is not easy sometimes to estimate the true time of onset. (20, 25)

Scarring Alopecia

At the alopecic area, the typical changes consist of atrophic, smooth, shiny and pale skin. The majority of published cases of patients with FFA describe the destruction of the follicular openings and atrophy. In FFA patients, the skin of the forehead has a different color from the hyperpigmented skin (caused by sun damage) of normal people. The demarcated line indicates the site of the initial hairline. (14) (Figure 6, 7)



Figure 6

Figure 7

Erythema, perifollicular inflammation and papules

At the site of alopecia, the clinician can observe some characteristic clues of FFA like Inflammatory papules, follicular or perifollicular erythema and follicular keratosis in "the line of progression of the alopecia". (31) The presence of these initial findings led to the hypothesis that FFA may represent a clinical subtype of lichen planopilaris. (31) (Figure 8)

Follicular hyperkeratosis

Many researchers observed the presence of follicular keratotic plugs or hyperkeratotic in FFA patients and should be differentiated from the similar findings that usually observed on the trunk and the limbs of patients with Graham-Little-Piccardi-Lassueur syndrome. (Figure 8)

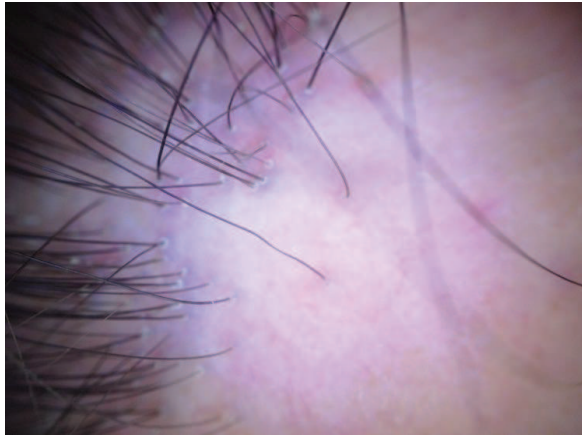


Figure 8

Alopecia of the eyebrows and eyelashes

The loss of the eyebrows, and rarely the eyelashes and the body hair loss are clinical signs that can be seen in FFA patients. The loss is observed at the lateral third of the eyebrows and in some cases affects the whole eyebrow. (Figure 9, 10)



Figure 9



Figure 10

Alopecia of the axillae

The hair loss can be also seen at other sites of the body as the axillae, the pubic area, and the limbs.

Frontal vein depression

On the forehead of patients with frontal fibrosing alopecia sometimes can be observed depressed veins. This observation seems to have no association with intralesional corticosteroids therapy. (Figure 11, 12).



Figure 11



Figure 12

"Lonely hair" sign

The presence of isolated terminal hairs, "lonely hair", is also an important clinical finding for the diagnosis of FFA, as described by Tosti and others. (26) The solitary hairs are 3 to 7 cm long and may be accompanied by perifollicular

erythema and scaling. Such hairs are located in the central or lateral aspect of the forehead (26), (Figure 13, 14).



Figure 13



Figure 14

Follicular red dots

The presence of follicular red dots is another important clinical clue for FFA. This clinical finding described initially by Tosti and others (27) as a sign of active discoid lupus erythematosus of the scalp. This trichoscopic clue, according to the authors, could prognose a better outcome of the disease, as it was associated with viable hair follicles. Follicular red dots sometimes can be seen also at the eyebrows of patients diagnosed with FFA. (29)

Pruritus and other symptoms

Very often patients complain about itching, hair pain (trichodynia), or burning sensations at the affected sites (especially at the active phase of the disease).

The severity of the disease ranges between moderate and severe and, as shown on the FFA severity scale below, it is based on the frontotemporal hairline recession.

FFA severity scale

Frontotemporal hairline recession	Severity scale
I: < 1 cm	Moderate
II: 1 - 2.99 cm	
III: 3 - 4.99 cm	Severe
IV: 5 - 6.99 cm	
V: > or = 7cm "clown" alopecia	

Differential Diagnosis

Many types of alopecia have to be included in the differential diagnosis.

These are:

- 1) Alopecia areata
- 2) Chronic telogen effluvium
- 3) Discoid lupus erythematosus (DLE)
- 4) Traction alopecia
- 5) Androgenetic alopecia
- 6) Lichen planopilaris (LPP)
- 7) Female pattern hair loss (FPHL)
- 8) Cicatricial marginal alopecia (CMA)
- 9) Graham- Little- Piccardi- Lassueur Syndrome

- 10) Genetic high hairline
- 11) Central centrifugal scarring alopecia
- 12) Pseudopelade of Brocq
- 13) Keratosis follicularis spinulosa decalvans (CCSA)
- 14) Alopecia mucinosa
- 15) Keratosis follicularis spinulosa decalvans (KFSD)

Histopathology

The North American Hair Research Society (NAHRS), in 2001 during a meeting at Dukes University, proposed a classification, of all known cicatricial alopecias, according to the cell type of scalp biopsies. (27) Thus, they divided the cicatricial alopecias into three major categories: the lymphocytic alopecias, the neutrophilic alopecias and "the mixed". Hence, as stated by NAHRS, FFA belongs to lymphocytic cicatricial alopecias.

In order to take a biopsy, from a patient with FFA, it is proposed by the experts to prefer a 4 mm punch biopsy from a site in active phase of the disease. A horizontal section seems to give more information compared with the vertical one. (34) Steven Kossard described for the first time the histopathological findings of the disease and the lately many authors confirmed them at their studies. (19) These histopathological findings are:

"1) Lichenoid lymphocytic infiltrate mainly localized to the isthmus and the infundibulum 2) Follicular interface dermatitis pattern, with sparing of the interfollicular epidermis 3) Reduced number of hair follicles, perifollicular lamellar fibrosis and replacement of hair follicles by fibrous tracts 4) Absent or only focally present sebaceous glands 5) Vacuolar degeneration of the basal layer and apoptosis of follicular keratinocytes in the external root sheaths 6) Absence of perivascular and periadnexal inflammation 7) Follicular triad sign" (1,37)

The follicular triad, recently described by Tosti and Miteva, (37) describes the "simultaneous involvement of hair follicles of different types" and additionally at different cycle phase of growth. This histopathological clue cannot be explained by the researchers so far.

The histopathology of FFA has many common features with the histopathology of LPP. The histopathologists observed, at the active stages of the disease, a lichenoid interface infiltrate, especially at the upper pilosebaceous unit, "with Civatte body formation, vacuolar changes, and pigmentary incontinence". This lymphocytic infiltrate is also combined with a perivascular component especially at the interfollicular areas but spares the lower third of the hair follicle. Also, immunofluorescence may present IgM or IgA staining of cytoid bodies. This staining is located along the basement membrane zone. And last but not least the pilosebaceous units are replaced by concentric lamellar fibrous tracts.

Therapy

The dermatological community believes that the treatment of FFA is difficult and sometimes disappointing, due to the unpredictable nature of the disease. It has been observed that although most of the cases FFA are self - limited, the severity of each case cannot be predicted before the condition becomes stable. As it is widely known, the disease leads to irreversible hair loss. Up to date, many topical and systemic therapeutic treatments have been proposed. However, most of the treatments are of limited benefit in halting the progressive course of the disease. (33) Treatment options for FFA include:

Topical corticosteroids

The large majority of patients are treated with topical corticosteroids of moderate or high potency. For many patients, this treatment with topical corticosteroids managed to reduce the inflammation, but in most cases, it did not stop the progression of alopecia. (33)

Systemic administration of corticosteroids

When patients present with the clinical image of the rapid progress of the disease, the administration of oral prednisone may help. Nonetheless, in the cases where the therapy with systemic corticosteroids was helpful, the disease continued to progress when the drug was discontinued (33)

Intralesional corticosteroids

Intralesional corticosteroids are preferred to be administrated in the early stages of the disease in order to offer better therapeutic results, especially to patients who present with prominent clinical and histological inflammation. (33) Nearly all researchers agree that is better to administer a lower concentration of corticosteroids in order to avoid the possibility of cutaneous atrophy. If alopecia is diagnosed to the fibrotic phase, intralesional corticosteroids should not be administrated by dermatologists because they could worsen the fibrosis and atrophy at this phase of the disease. (33)

Minoxidil

In many reports the treatment with topical minoxidil was combined with topical corticosteroids or 5-alpha reductase inhibitors. (19) This combination therapy was effective in many cases. Be that as it may, it is not clear if the results are related to the use of minoxidil or to the additional medication that had been provided. Moreover, it remains to be elucidated whether the improvement was due to the impact of frontal fibrosing alopecia or, on an overlapping hair loss of female pattern. (33)

Antimalarial drugs

Described protocols include the administration of hydroxychloroquine. The drug is usually provided in a dose of 200-400 mg per day for the duration of at least 6 months. (33) The administration is suspended if there is no evident clinical improvement after the 6th month. (33)

Tetracycline antibiotics

Oral antibiotics have been proposed as a treatment for FFA, in the following doses: Tetracycline at a dose 500 mg twice daily or minocycline given 100 mg twice daily. Tetracyclines, like some other anti-inflammatory treatments, caused a decrease in inflammation in some patients, but it is not sure if they are efficient enough at controlling the alopecia. (24, 33)

Alternative treatments

According to some reports some patients suffering from FFA were treated by some other therapies like isotretinoin, griseofulvin, pimecrolimus, tacrolimus, cyclosporine or Peroxisome proliferator-activated receptor (PPAR) γ agonists. These therapies seem that couldn't manage to stop the progression of alopecia in any of the patients. (33)

Conclusively, because FFA causes permanent hair loss, correct diagnosis is needed to explain the patients the course of the disease.

Trichoscopy in frontal fibrosing alopecia

Dermoscopy is believed to be an essential method for improving the diagnosis of skin tumors (benign or malignant) as well as inflammatory, infectious and parasitic dermatoses. (34)

Although dermoscopy is known by dermatologists for a long period it was in 1993 that Kossard and Zagarella reported the use of dermoscopy in the diagnosis of follicular fibrosis. (39)

Lacarrubba and others and Ross and others were the first who described dermoscopic findings at a variety of scalp abnormalities, like alopecia areata, androgenetic alopecia, lichen, lupus erythematosus (DLE), and seborrheic dermatitis. (35)

In 2006 Ross and colleagues (35) reported the videodermoscopic findings at a significant number of hair diseases. Rakowska and others, in 2007, reported that trichoscopy could help the clinician to evaluate the pulled hairs in the majority of genetic hair shaft abnormalities. (39) One year later A. Tosti published the first trichoscopy atlas.

Trichoscopy (scalp and hair dermoscopy) represents a valuable noninvasive and low-cost technique, still underutilized, to rapidly differentiate clinically frequent hair disorders. In their revision, Miteva and Tosti gave a comprehensive and thorough description of the usefulness of this technique not only for the diagnosis but also for the follow-up of the most common hair diseases, based on updated data from literature and their personal experience.

The use of trichoscopy helps the dermatologist to evaluate different types of alopecia and in addition improved the diagnostic capacity. (36)

Furthermore, provides a more precise follow-up and it can be used to identify an adequate biopsy site. (40)

Regarding the eyebrow area, trichoscopy shows regularly distributed red or gray dots throughout the course of the disease, with some tendency toward a loss of follicular openings in the advanced stages. (43)

Trichoscopic features of frontal fibrosing alopecia

The trichoscopic features of frontal fibrosing alopecia are: “Absence of follicular openings, minor perifollicular scaling, homogenous ivory-colored background, perifollicular erythema, follicular openings with only one hair at the hair-bearing margin, perifollicular brown or brown-violet areas (in dark-skinned patients), follicular hyperkeratosis, hair diameter diversity, yellow dots, multiple regularly distributed red dots (early phase of the disease) (Figure 24), multiple regularly distributed red or gray to gray-brown dots (advanced phase of the disease)”.



Figure 17: Absence of follicular openings

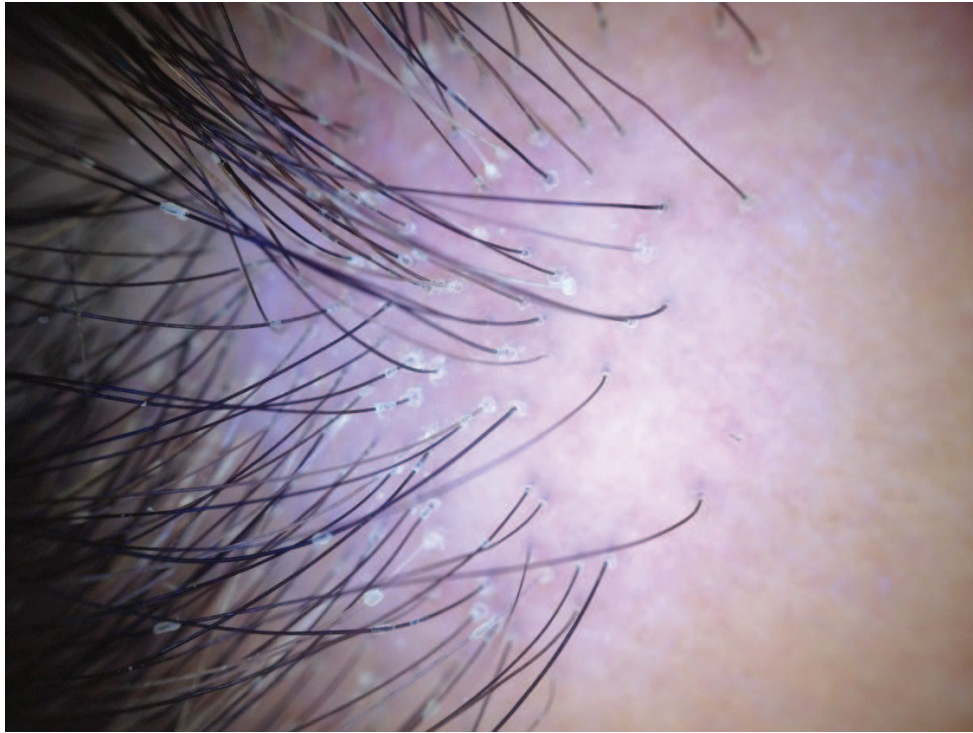


Figure 18: Follicular hyperkeratosis

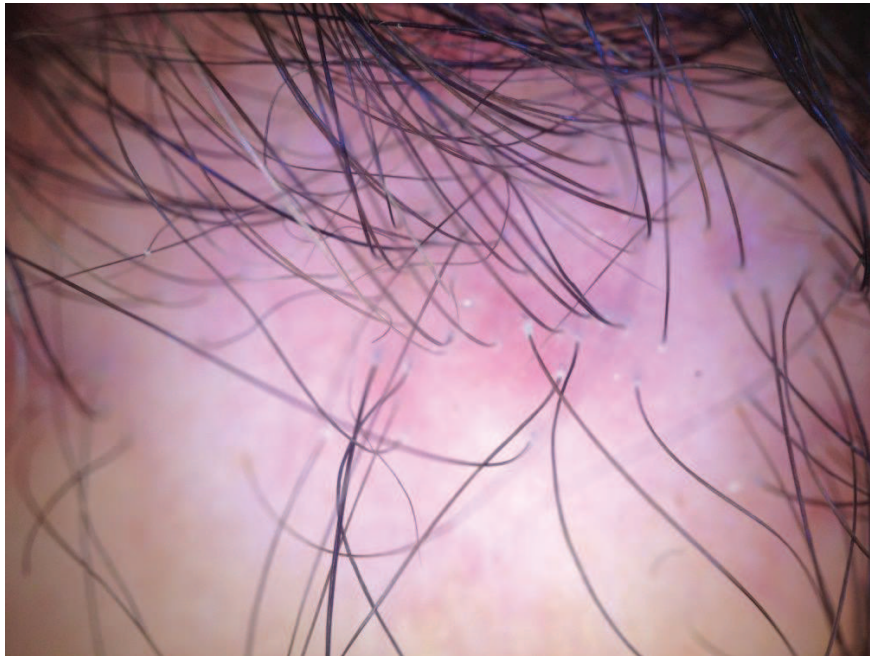


Figure 19: Perifollicular erythema



Figure 20: Presence of one hair at the follicular openings



Figure 21: Brown or brown-violet areas (perifollicular)



Figure 22: Hair diameter diversity

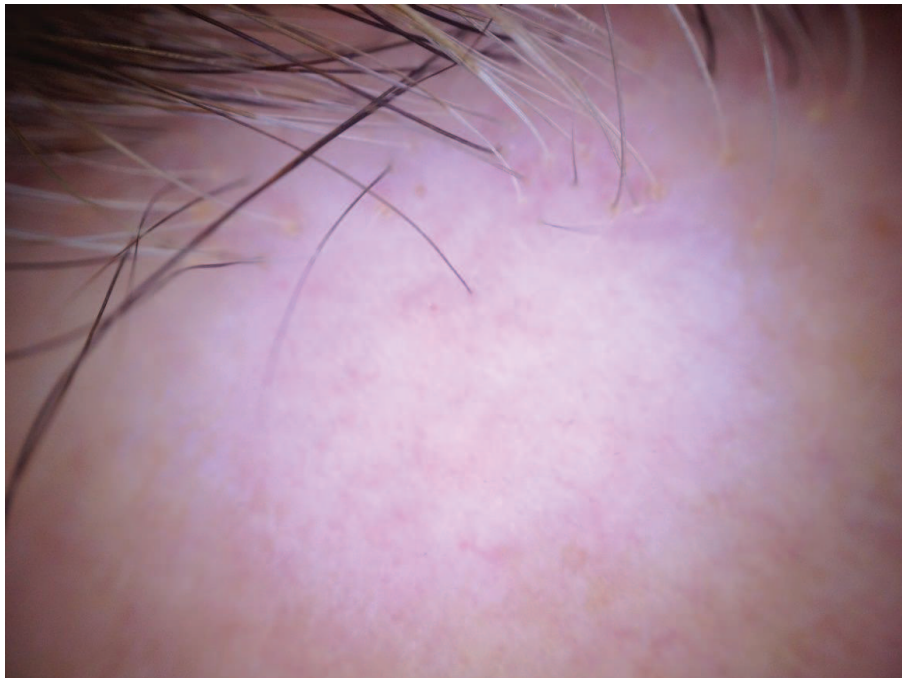


Figure 23: Cicatricial white patches



Figure 24: Multiple regularly distributed red dots

Aim of the study

The purpose of the present study is to research and document the trichoscopic findings of 30 patients diagnosed with FFA attending the Laboratory of Physiology and Diseases of the Hair at the "Andreas Syggros" hospital in Greece. All patients were examined during the period of September 2015 - December 2015 upon permission of the laboratory's Director, Ms. Vasiliki Chasapi.

Material and method of the study

The material for this study were patients diagnosed with FFA, chosen between cases examined in the Laboratory of Physiology and Diseases of the Hair in the hospital "Andreas Syggros", combined with information from the Laboratory's records.

The studying process included a questionnaire for collecting demographic data and information on the patient's personal medical record as well as information on their family's record.

The disease was diagnosed by the typical clinical findings (recession of the frontal and temporal hairline with the presence or the absence of eyebrows loss, perifollicular erythema, perifollicular hyperkeratosis, pale skin, atrophy and the presence of lonely hairs).

The examination was carried out using a polarized and a non-polarized dermatoscope and pictures of the examined areas were taken as well. In each patient several photos were taken and later evaluated by the experts (according to the dermatoscopic features of FFA).

The findings were assessed by two dermatologists who specialized in dermoscopy and in FFA (Ms. Vasiliki Chasapi and Ms. Sofia Papanikou).

Lastly, a statistical analysis of the findings was conducted and once completed the study's final conclusions were drawn.

Demographic features and clinical features of the patients are shown in tables 1-3.

Patient	Sex	Age	Recession of the frontal hairline	Temporo-parietal recession	Occipital recession	FFA severity scale	Activity of the disease	Follicular hyperkeratosis	Eye-brow Alopecia
1	F	46	+	-	-	I	-	-	-
2	F	57	+	+	-	IV	+	-	+
3	F	81	+	+	-	IV	+	+	+
4	F	59	+	+	-	II	+	+	+
5	F	52	+	+	-	II	-	-	-
6	F	60	+	+	-	II	-	-	-
7	F	63	+	+	-	II	-	-	-
8	M	49	+	-	-	I	+	+	-
9	F	84	+	+	-	II	-	-	+
10	F	63	+	+	+	III	+	+	+
11	F	85	+	+	+	IV	+	+	+
12	F	72	+	+	+	III	+	+	+
13	F	66	+	+	-	III	+	+	+
14	F	55	+	+	+	III	+	+	+
15	F	47	+	+	-	I	-	+	-
16	F	58	+	+	+	II	+	+	+
17	F	70	+	+	-	III	+	+	+
18	F	42	+	-	-	I	-	-	-
19	F	70	+	+	-	III	-	-	+
20	F	68	+	+	+	III	+	+	+
21	F	65	+	+	-	I	-	-	-
22	F	46	+	+	-	IV	+	+	+
23	F	80	+	+	+	IV	+	+	+
24	F	63	+	+	+	IV	+	+	+
25	F	58	+	+	-	III	+	+	+
26	F	65	+	+	-	III	-	-	+
27	F	66	+	+	-	II	-	-	-
28	F	65	+	+	-	II	+	+	+
29	F	51	+	+	-	III	-	-	-
30	F	65	+	+	-	I	+	+	-

Table 1

Patient	Eyebrow Dilution	Eyelash Alopecia	Eyelash Dilution	Lonely hair	Follicular red dots	Frontal Vein Depression	Pale skin	Atrophy	Pull Test	Lack of follicular openings
1	+	-	-	+	-	-	-	-	+	+
2		-	+	+	-	+	+	+	-	+
3		+		+	-	+	+	+	-	+
4		-	+	+	-	+	+	+	-	+
5	+	-	-	+	-	-	+	+	-	+
6	+	-	-	+	-	-	-	-	-	+
7	+	-	+	+	-	-	+	+	-	+
8	+	-	+	+	-	-	-	-	-	+
9		-	+	+	-	-	+	-	-	+
10		-	+	+	-	+	+	+	-	+
11		-	+	+	-	+	+	+	+	+
12		-	+	+	-	+	+	+	-	+
13		-	+	+	+	-	+	+	-	+
14		-	+	+	-	+	+	+	-	+
15	+	-	+	+	+	-	-	-	-	+
16		-	-	+	+	-	+	+	+	+
17		-	+	+	-	+	+	+	+	+
18		-	-	+	+	-	-	-	-	+
19		-	+	+	+	+	+	+	-	+
20		-	-	+	+	-	+	+	-	+
21		-	-	+	+	-	+	-	-	+
22		-	-	+	-	+	+	+	-	+
23		-	-	+	-	-	+	+	-	+
24		-	-	+	+	+	+	+	-	+
25		-	-	+	-	+	+	+	-	+
26		-	+	+	+	-	+	+	-	+
27		-	-	+	+	+	+	+	-	+
28		-	+	+	-	+	+	+	-	+
29	+	-	+	+	+	+	+	+	-	+
30	+	-	+	+	+	+	+	-	-	+

Table 2

Patient	Duration of the disease (years)	Autoimmune diseases	Thyroid diseases	Lichen plano pilaris	Topical Therapy	Systemic therapy	Combination Therapy
1	1	-	-	-	CORTOCOSTEROID-MINOXIDIL		+
2	8	-	-	-	CORTOCOSTEROID-MINOXIDIL	HYDROXYCHLORO QUINE	+
3	4	-	-	-	CORTOCOSTEROID-MINOXIDIL	HYDROXYCHLORO QUINE	+
4	2	-	-	-	CORTOCOSTEROID-MINOXIDIL		+
5	3	-	-	-	CORTOCOSTEROID-MINOXIDIL		+
6	2	-	-	+	CORTOCOSTEROID-MINOXIDIL		+
7	5	-	-	-	CORTOCOSTEROID-MINOXIDIL		+
8	7	-	-	-	CORTICOSTEROID		-
9	3	+	-	-	CORTOCOSTEROID-MINOXIDIL		+
10	6	-	-	+	CORTICOSTEROID	CORTICOSTEROID	+
11	4	-	-	+	CORTICOSTEROID		-
12	4	-	-	+	CORTOCOSTEROID-MINOXIDIL		+
13	5	+	+	+	CORTICOSTEROID		+
14	5	-	-	-	CORTICOSTEROID		-
15	2	+	+	-	CORTOCOSTEROID-MINOXIDIL	CORTCOSTEROID-HYDROXYCHLORO QUINE	+
16	4	-	-	-	CORTICOSTEROID		-
17	2	-	-	-	CORTOCOSTEROID-MINOXIDIL		+
18	6	-	-	-	CORTOCOSTEROID-MINOXIDIL		+
19	6	-	-	-	CORTOCOSTEROID-MINOXIDIL		+
20	6	-	-	-	CORTICOSTEROID		+
21	2	-	-	+	CORTICOSTEROID		-
22	10	-	-	-	CORTICOSTEROID	CORTCOSTEROID-HYDROXYCHLORO QUINE	+
23	5	-	-	-	CORTICOSTEROID		-
24	8	-	-	+	CORTOCOSTEROID-MINOXIDIL	HYDROXYCHLORO QUINE	+
25	6	-	-	-	CORTICOSTEROID		+
26	4	-	+	-	CORTICOSTEROID		-
27	4	-	-	-	CORTOCOSTEROID-MINOXIDIL		+
28	2	-	+	-	CORTICOSTEROID		-
29	2	-	-	-	CORTOCOSTEROID-MINOXIDIL		+
30	1	-	+	-	CORTICOSTEROID		-

Table 3

Results

Chart 1 shows that among the 30 patients who were examined there were 29 women and 1 man.

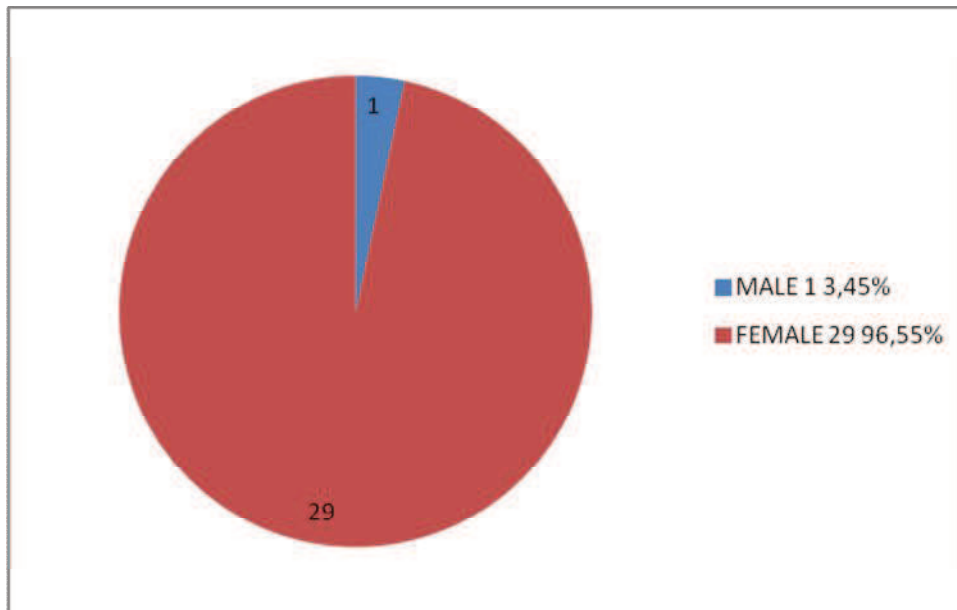


Chart 1

Column chart 2 shows the patients' age. The ages ranged between 42-85 years. The average age was 62.3 years.

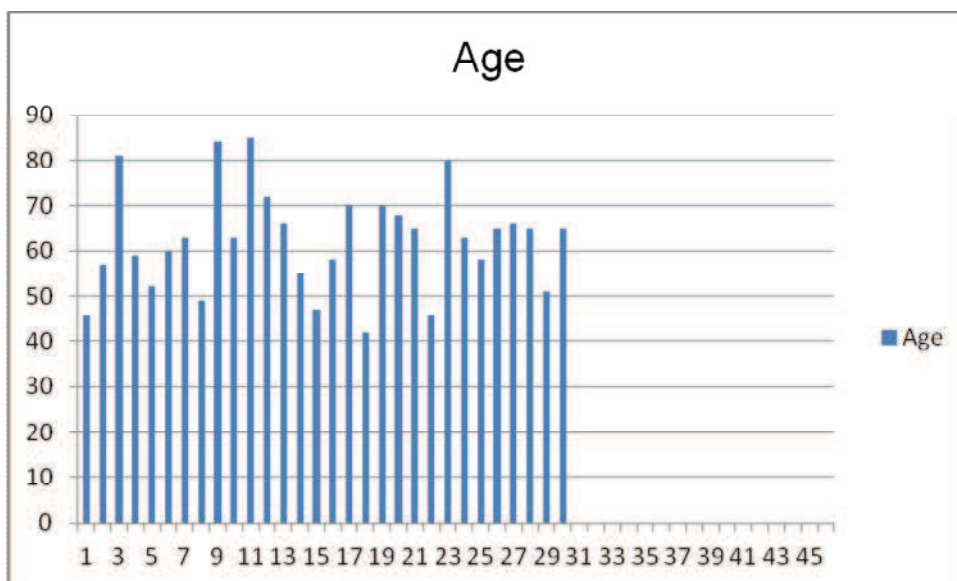


Chart 2

Chart 3 shows that for all 30 patients (100%) the clinical findings include frontal hairline recession.

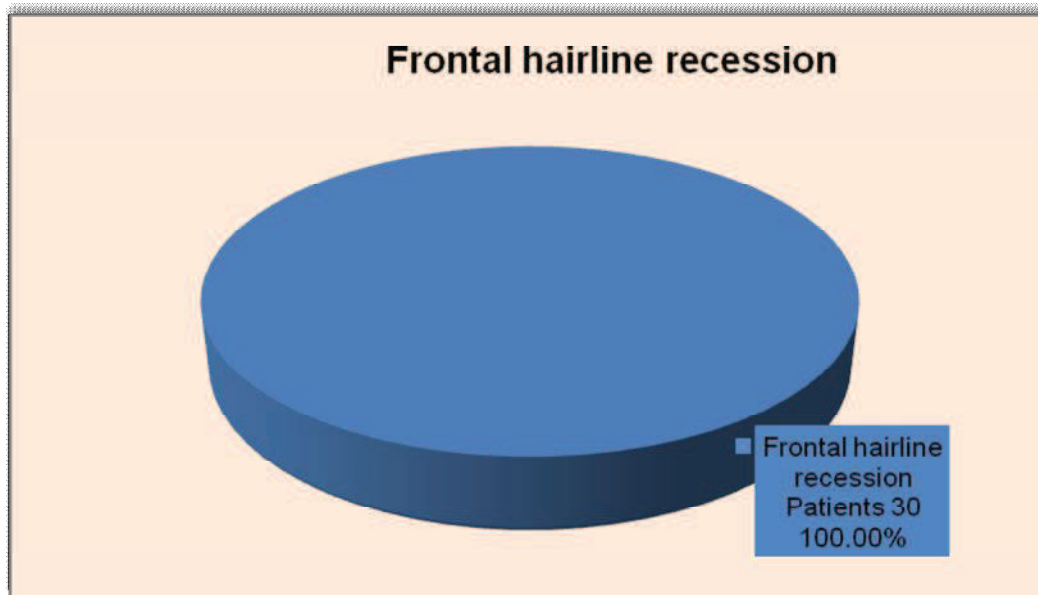


Chart 3

Chart 4 shows that only 3 from 30 patients (10%) did not have a temporoparietal recession. The rest of the patients, that is 27 patients (90%), had developed temporoparietal recession of the hairline.

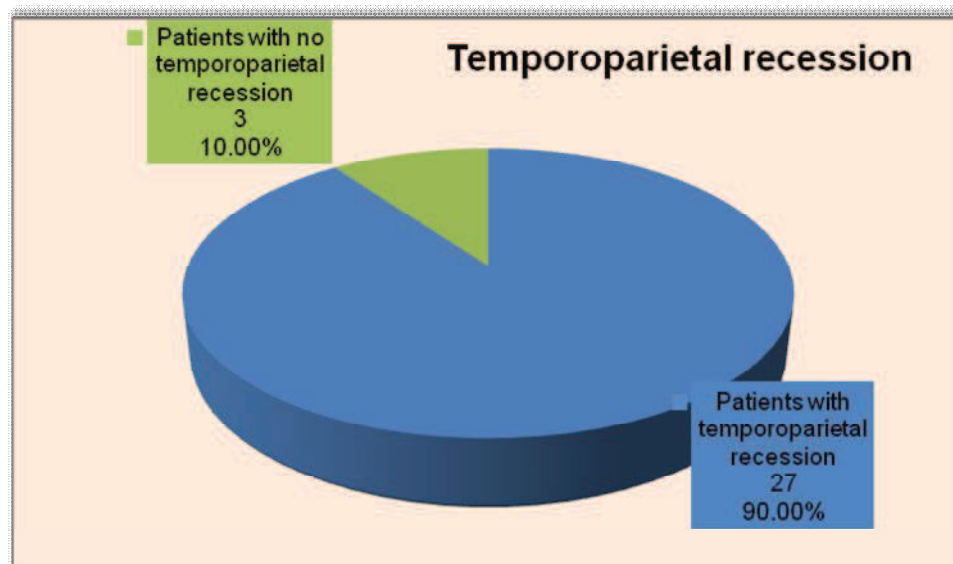


Chart 4

Chart 5 provides data on occipital recession findings: 8 patients (26.67%) had an occipital recession, compared to 22 patients (73.33%) who had not developed this type of hairline recession.

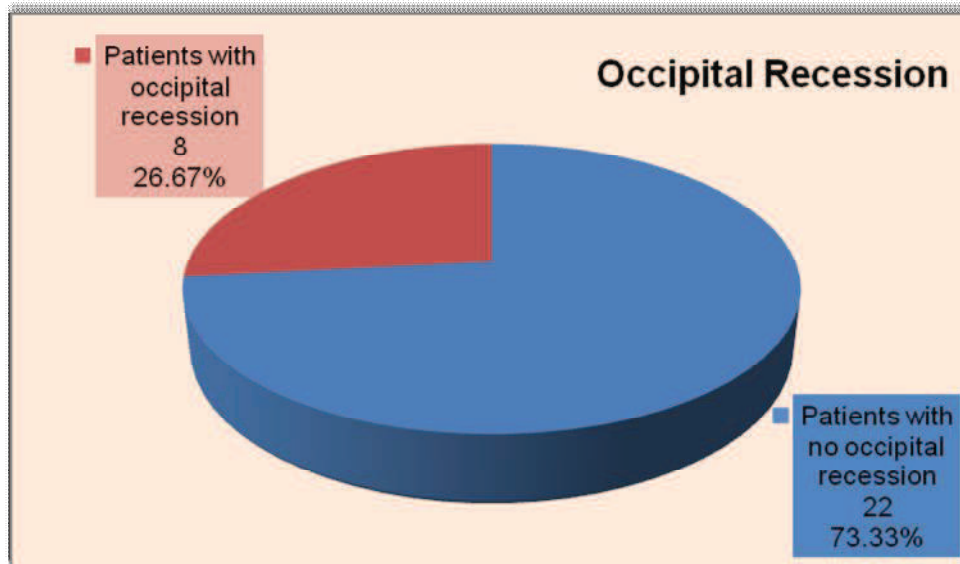


Chart 5

Chart 6 illustrates the degree of the disease's activity at the moment of the clinical examination: In 12 patients (40%) the disease seemed to be active and 18 patients (60%) did not have activity signs.

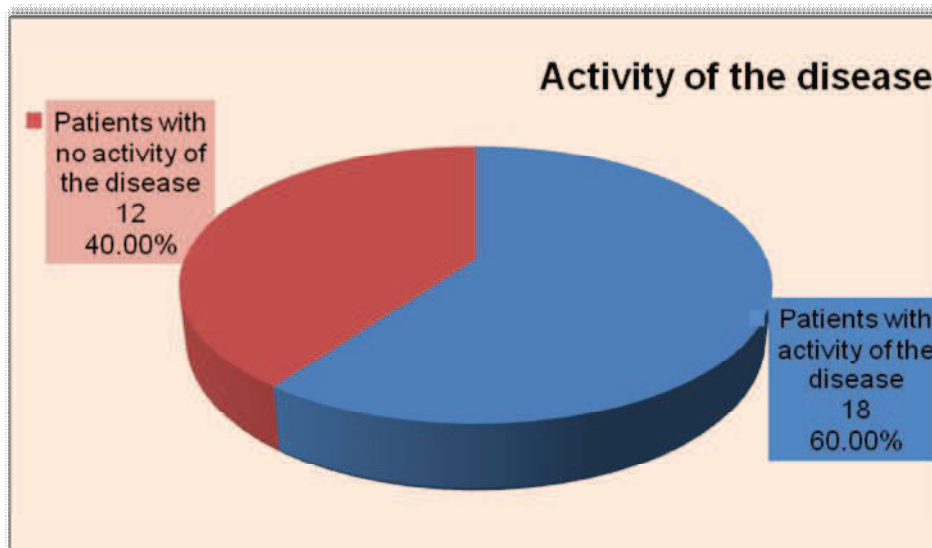


Chart 6

Chart 7 shows that 22 patients (73.33%) had developed perifollicular erythema and 8 (21.05%) had no erythema.

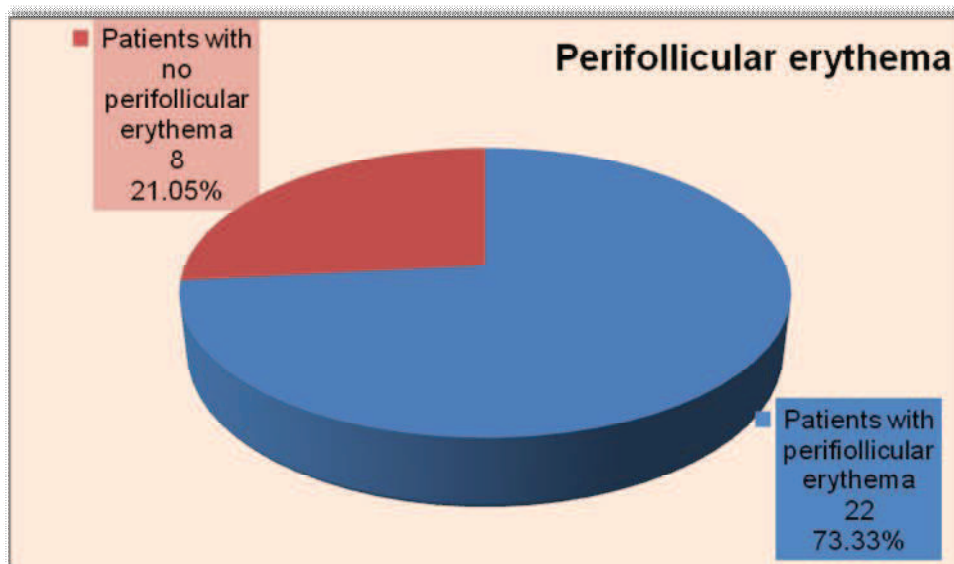


Chart 7

Chart 8 presents the results related to follicular hyperkeratosis: 18 patients (60%) had perifollicular hyperkeratosis, compared to 12 patients (40%) who had not developed perifollicular hyperkeratosis.

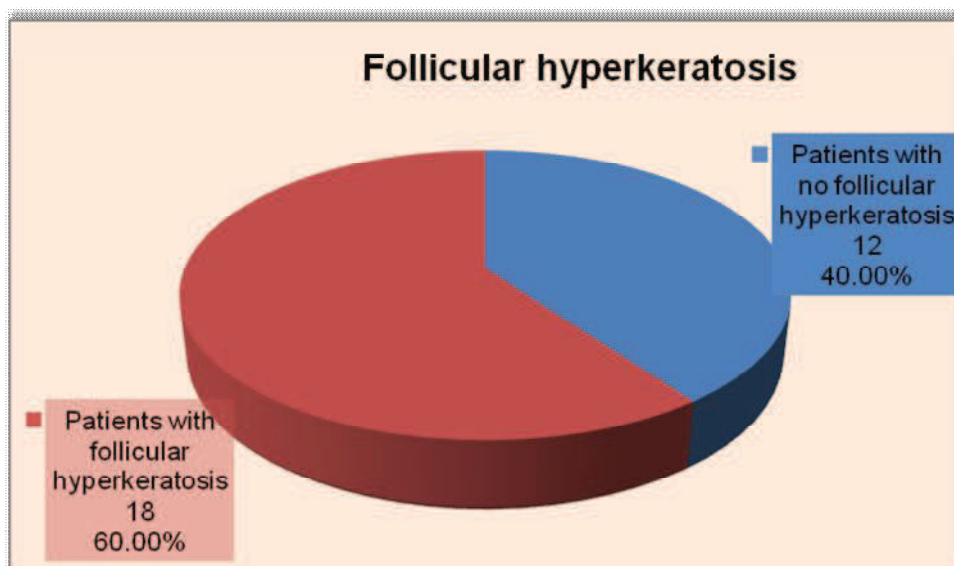


Chart 8

Chart 9 shows that 19 patients (63.33%) suffered from eyebrow alopecia, compared to 11 patients (36.67%) who did not suffer from this type of alopecia.

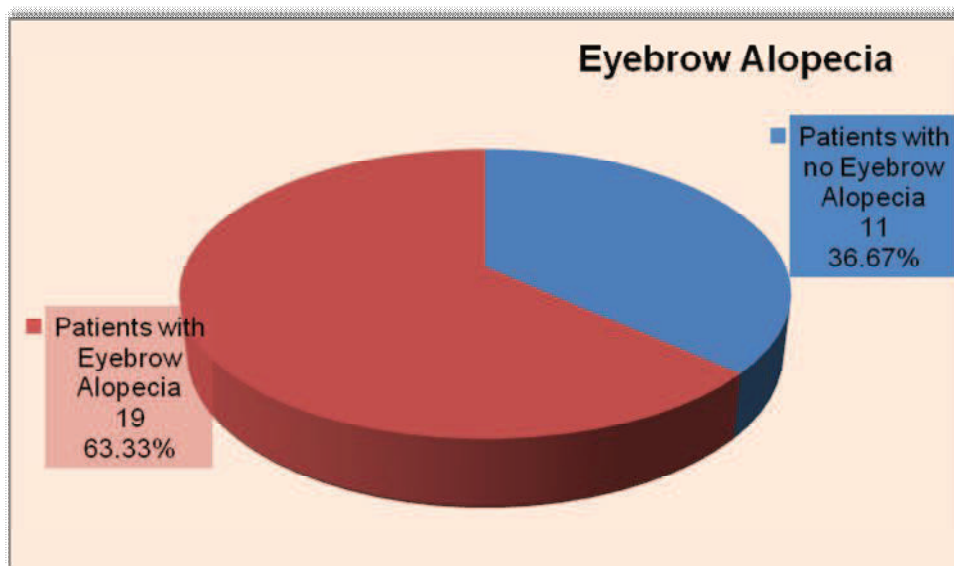


Chart 9

Chart 10 shows that 8 patients (26.67%) had eyebrow dilution and 22 patients (73.33%) had no eyebrow dilution.

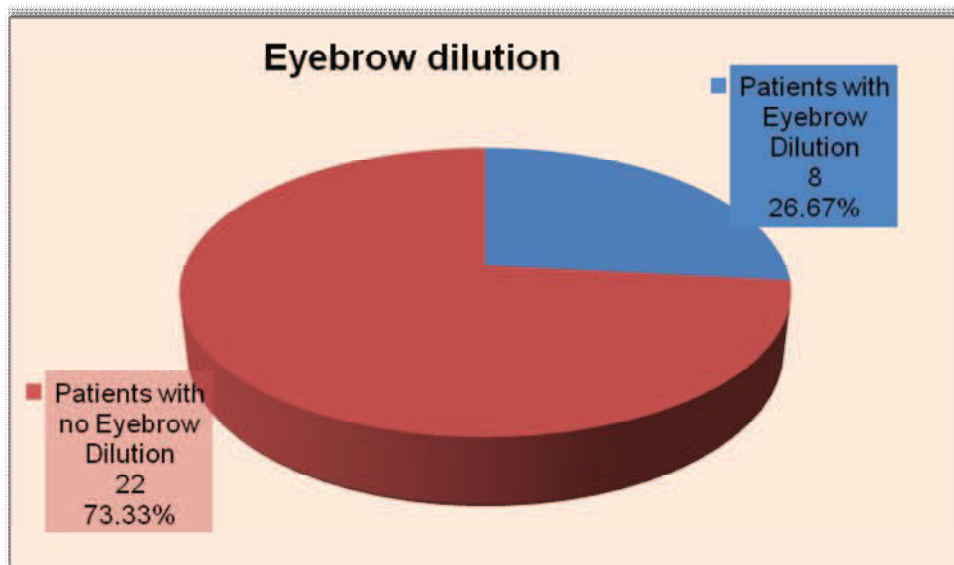


Chart 10

Chart 11 shows that only 1 patient (3.33%) suffered from eyelash alopecia and 29 patients (96.67%) had no eyelash alopecia.

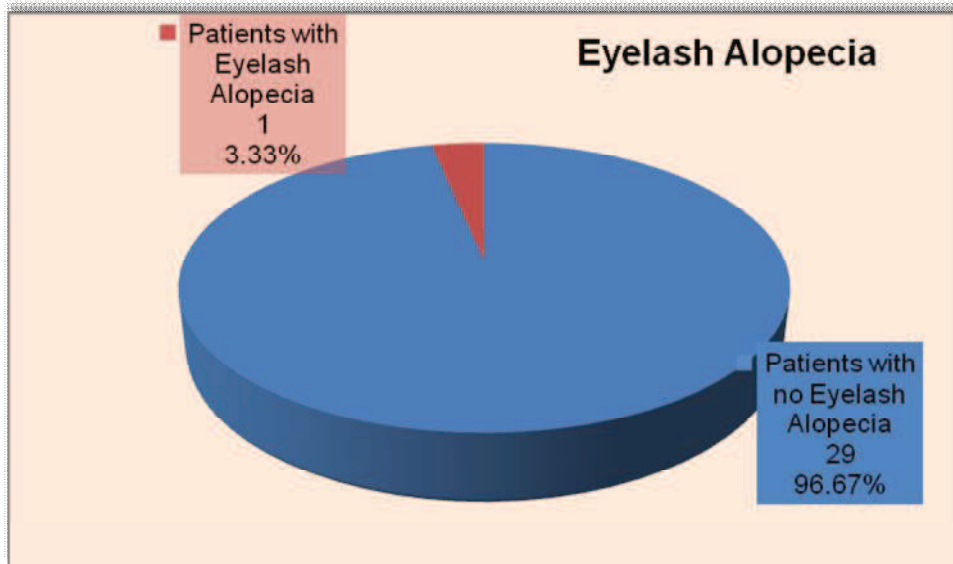


Chart 11

As it is illustrated from Chart 12, 17 patients (56.67%) had eyelash dilution when 13 patients (43.33%) did not have eyelash dilution.

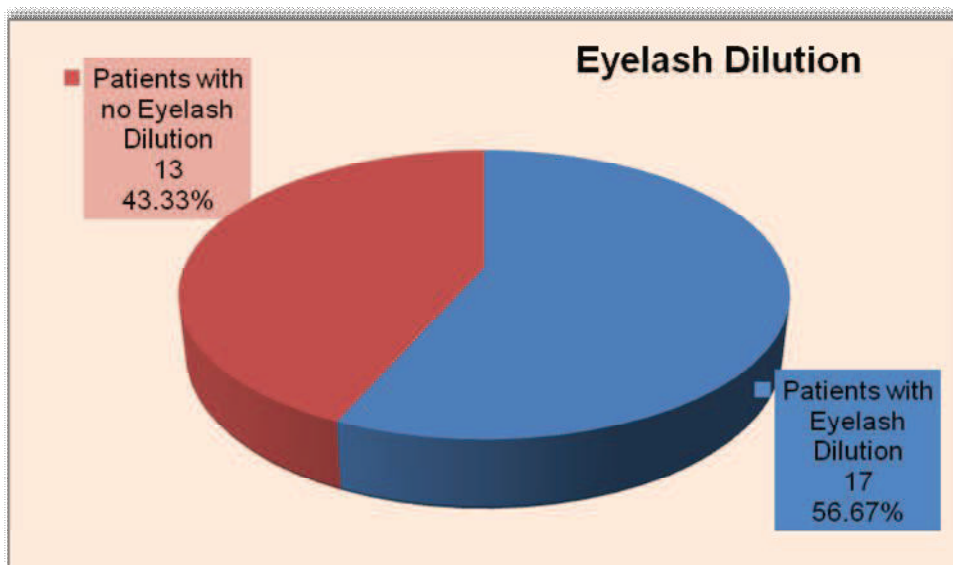


Chart 12

Chart 13 shows that all 30 patients (100%) had lonely hair.



Chart 13

Chart 14 shows that 6 patients (20%) were ranked in rank I on the severity scale, 8 patients (26.67%) were in rank II, 10 patients (33.33%) in rank III, 6 patients (20%) were included in rank IV and no patient suffered from severe alopecia, that is disease severity rank V.

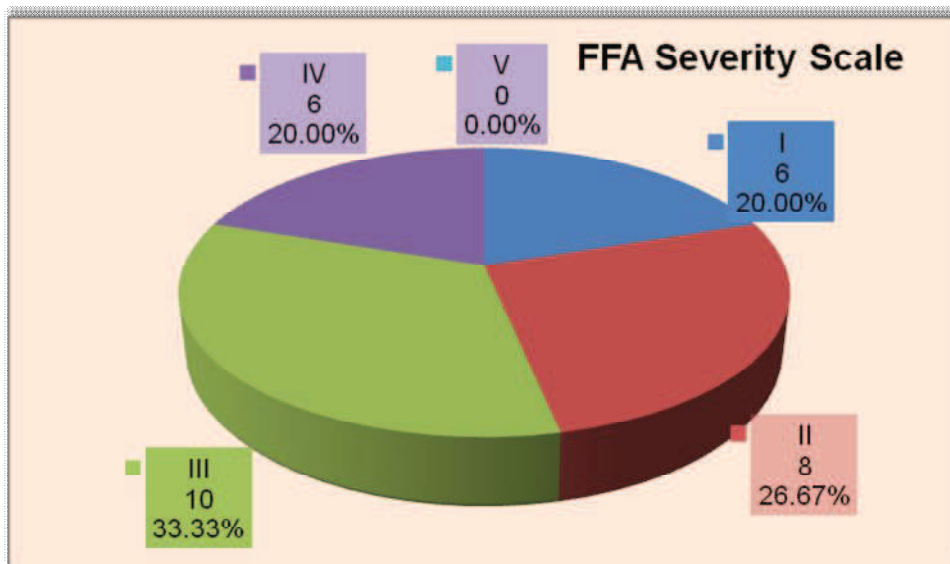


Chart 14

Chart 15 shows that half the patients, that is 15 patients (50%), had frontal vein depression and the other 15 patients (50%) had no frontal vein depression.

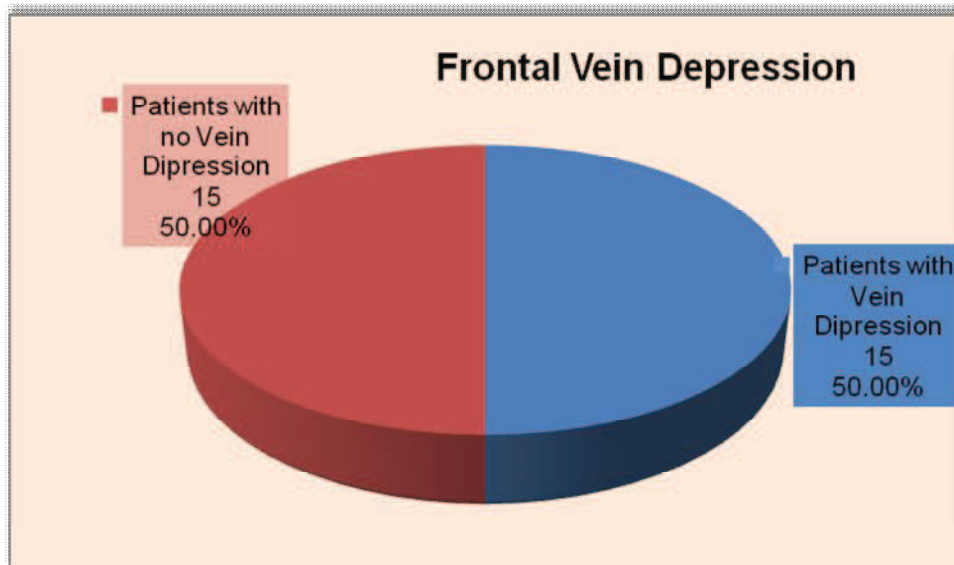


Chart 15

Chart 16 shows that 12 of the patients, (40 %), had follicular red dots and 18 of the patients (60%) had no follicular red dots.

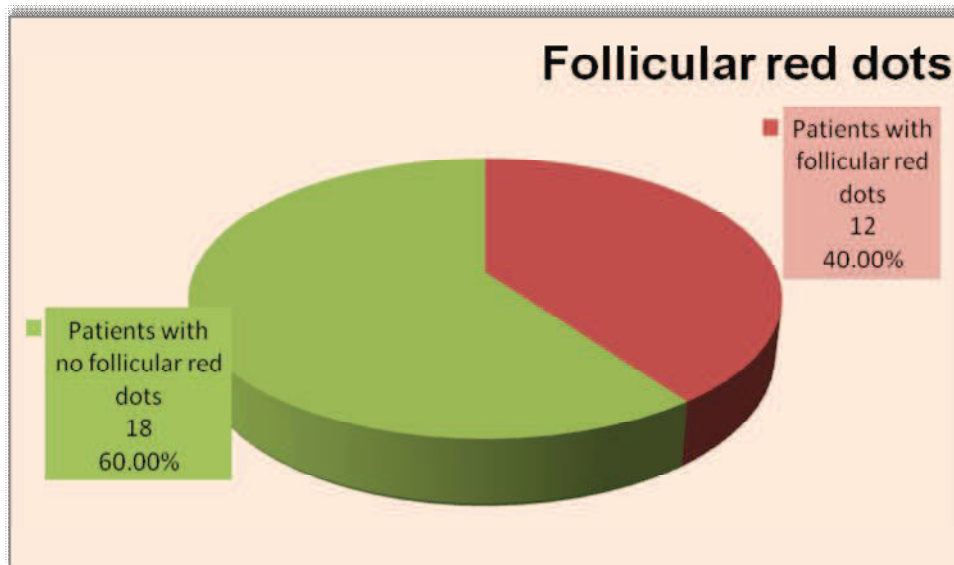


Chart 16

Chart 17 shows that 25 patients (83.33%) had pale skin and 5 patients (16.67%) did not have this sign.

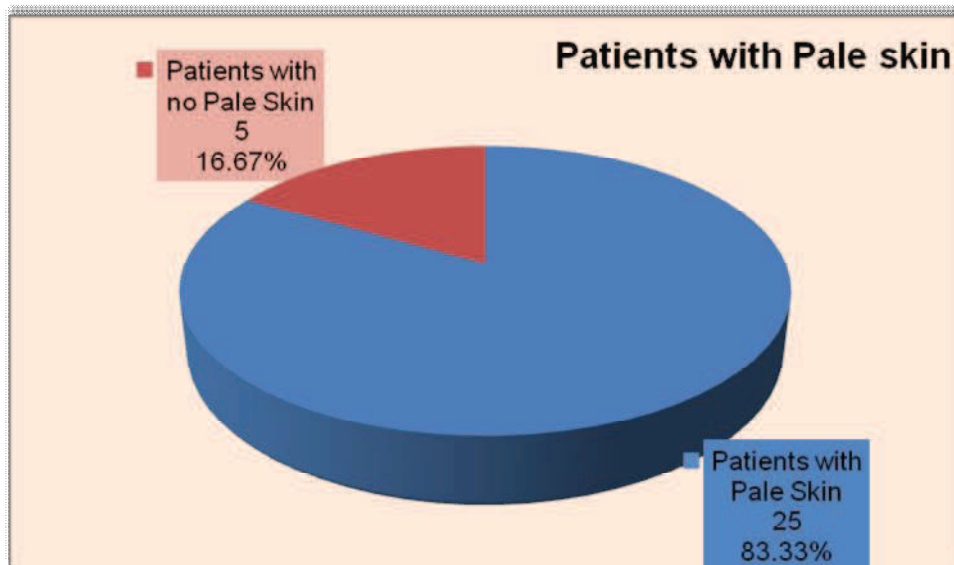


Chart 17

Chart 18 shows that 22 patients (73.33%) had developed atrophy and 8 (26.67%) had not developed atrophy.

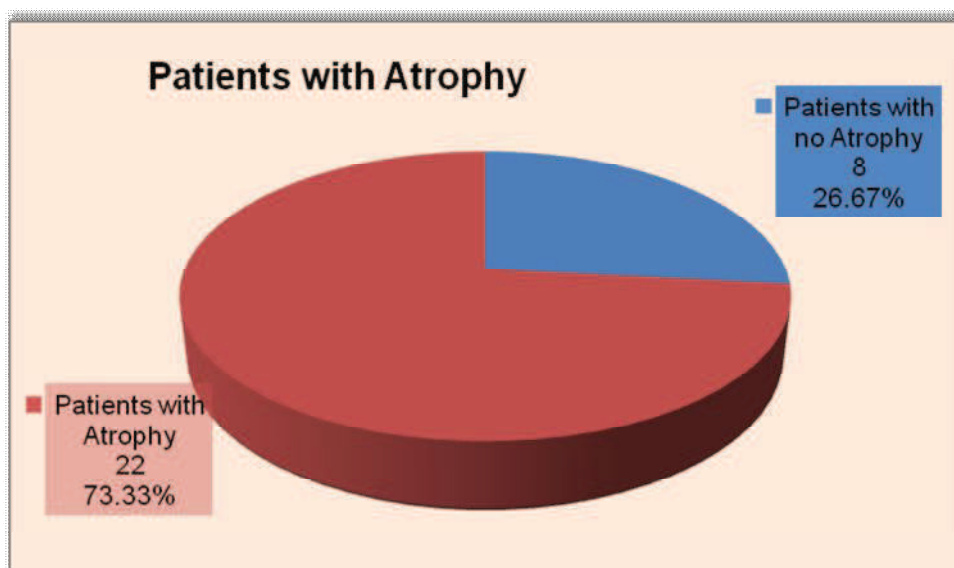


Chart 18

Chart 19 shows that 4 patients (13.33%) had a positive pull test and that the pull test of the rest 26 (86.67%) patients were not positive.

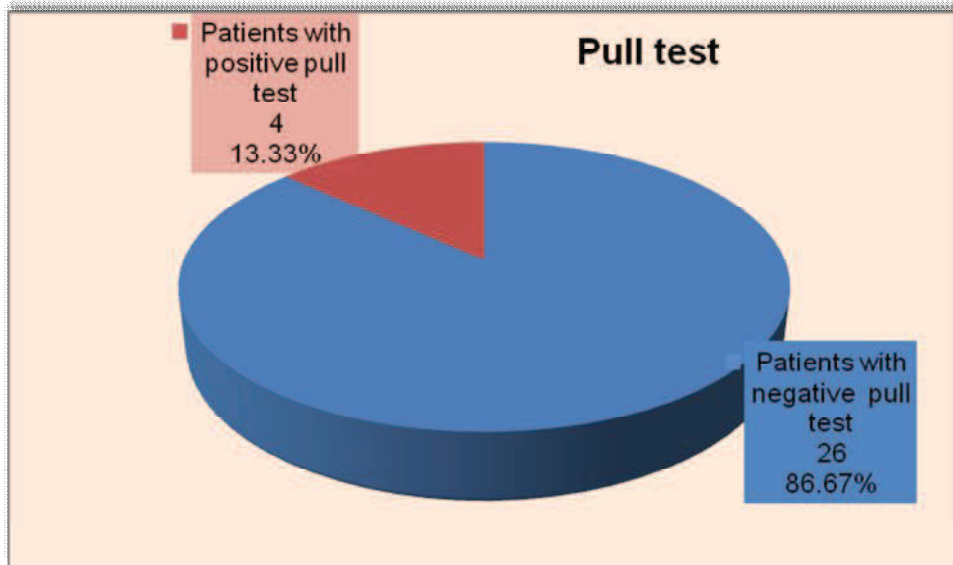


Chart 19

As it can be seen from Chart 20, all 30 patients (100%) show a lack of follicular openings.

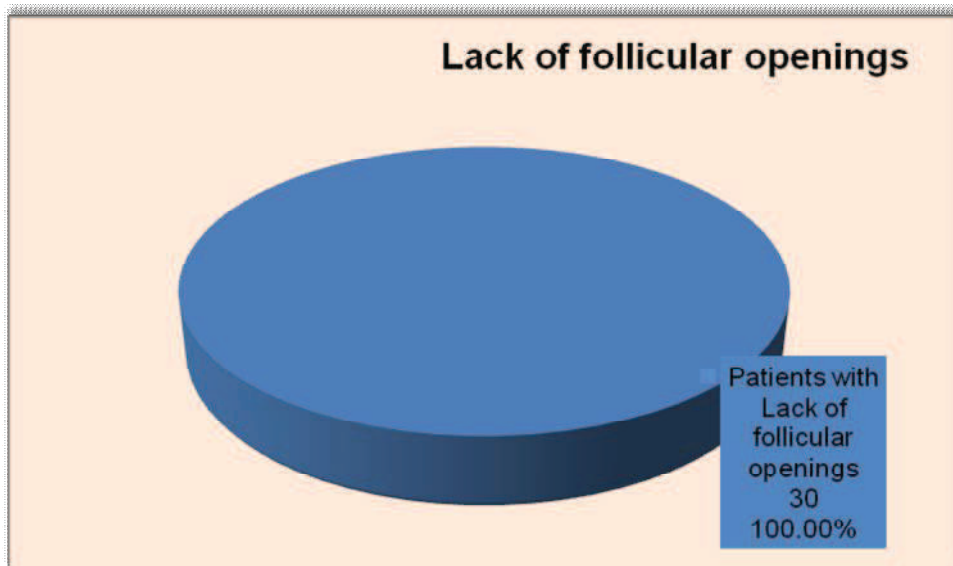


Chart 20

Chart 21 depicts the duration of the disease. It is seen that in 2 patients (6.67%) the disease occurred a year ago, in 7 patients (23.33%) it occurred two years ago, in 2 patients (6.67%) three years ago, in 6 patients (20%) four years ago, in 4 patients (13.33%) five years ago, in 5 patients (16.67%) six years ago, in 1 patient (3.33%) seven years ago, in 2 patients (6.67%) eight years ago and finally in 1 patient the disease occurred (3.33%) ten years ago.

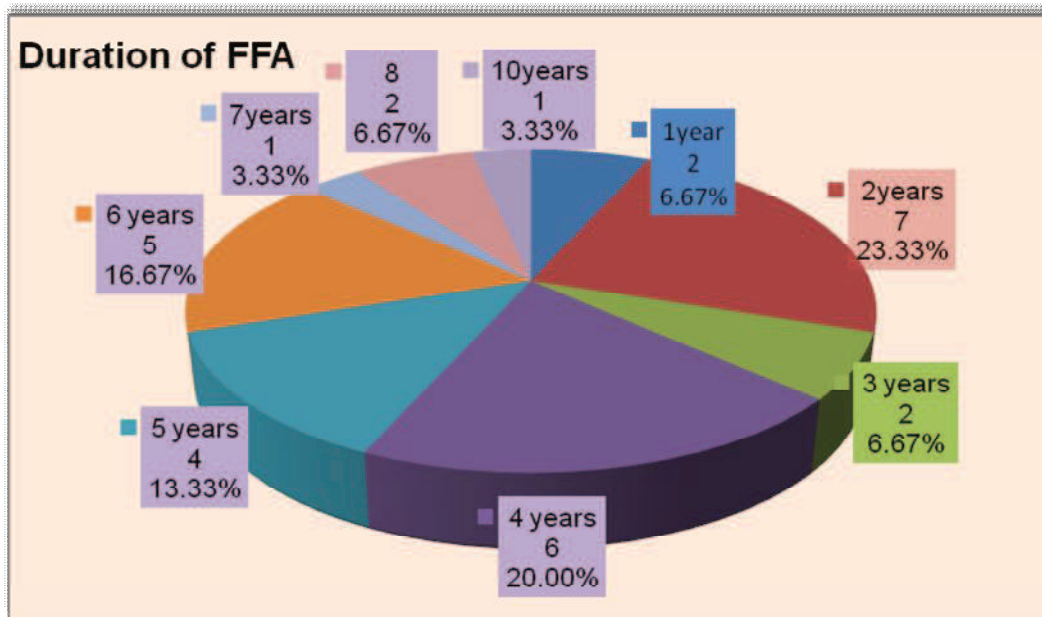


Chart 21

Chart 22 shows that 2 patients (6.67%) had a history of autoimmune diseases and 28 patients (93.33%) had no such history.

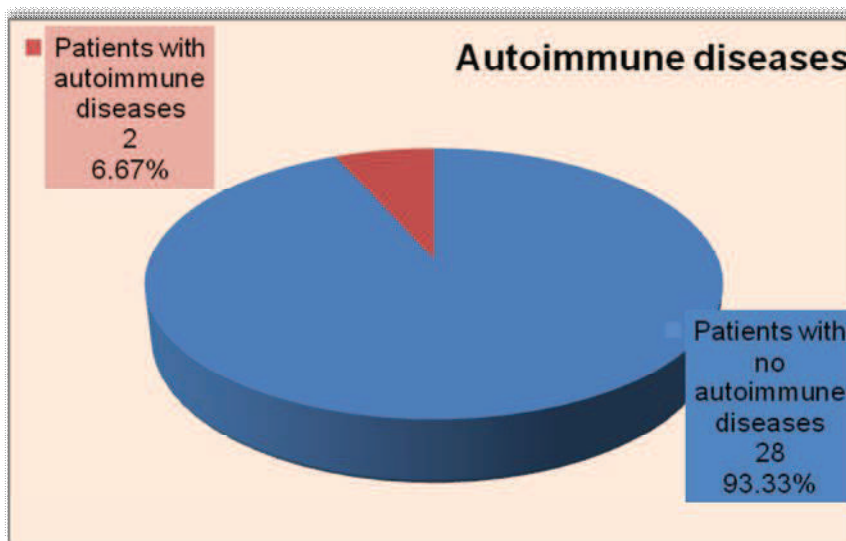


Chart 22

Chart 23 shows that 3 patients (10%) suffered from thyroid diseases, compared to 27 patients (90%) who did not have a thyroid disease.

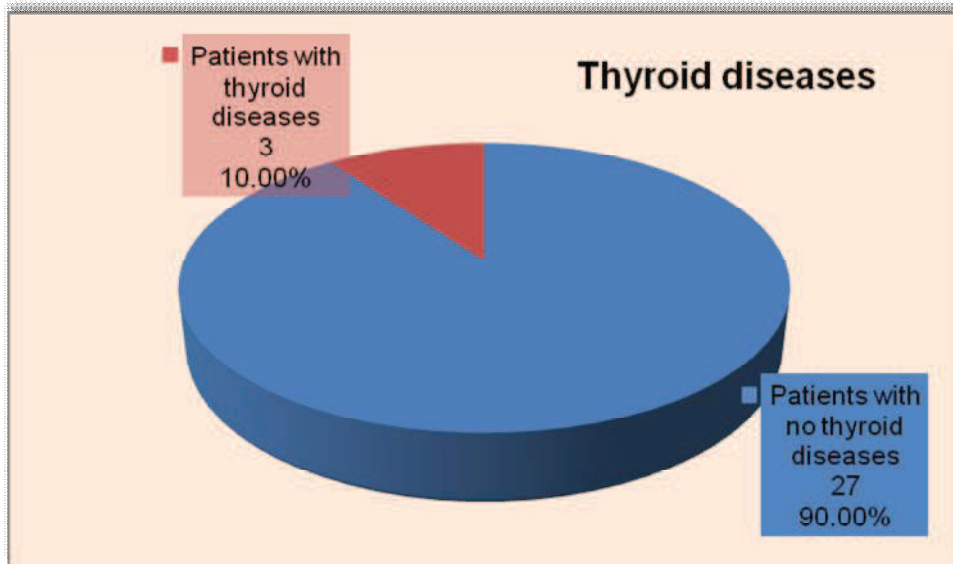


Chart 23

Chart 24 shows that 6 patients (20%) had a history of LPP and 24 patients (80%) had no such history.

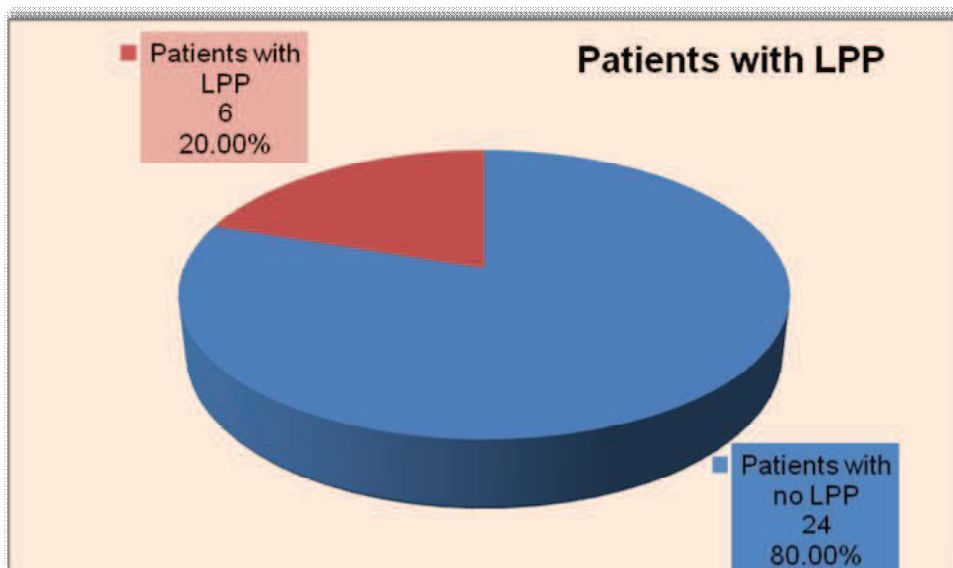


Chart 24

Chart 25 illustrates the results related to topical therapies. As it can be seen from this pie chart, 12 patients examined for this study (3.64%) were being treated with topical corticosteroids, 18 patients (60%) were under combination treatment with minoxidil and topical corticosteroids and no patient was being treated with minoxidil as a single agent.

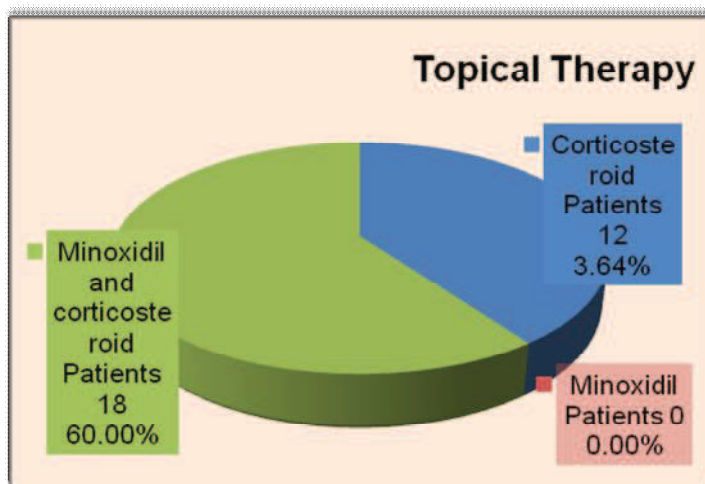


Chart 25

Chart 26 shows that among the 6 patients, who were under systemic therapy, 1 patient (16.67%) was treated with corticosteroids, 3 patients (50%) were treated with hydroxychloroquine and 2 patients (33.33%) were treated with a combination therapy of hydroxychloroquine and corticosteroids.

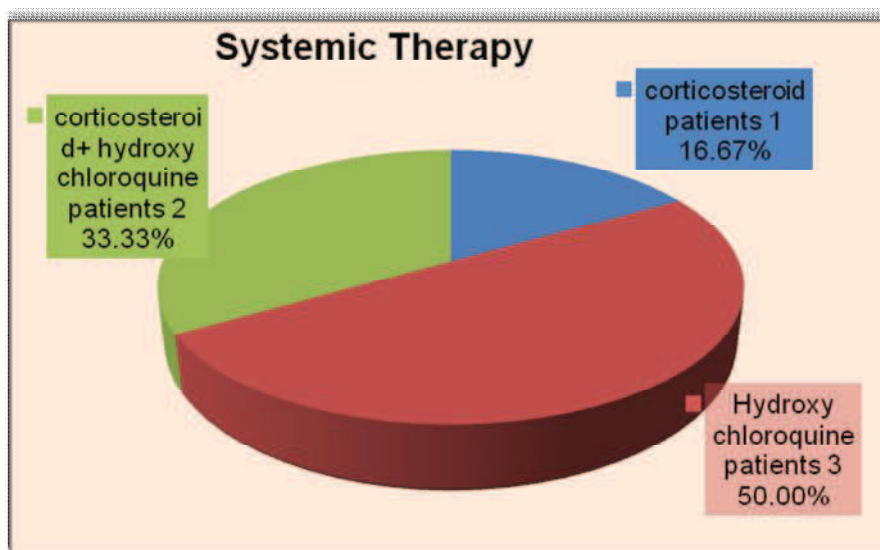


Chart 26

Chart 27 shows that 8 patients (26.67%) were under topical and systemic therapy, compared to 22 patients (73.33%) who were not under a combined regimen.

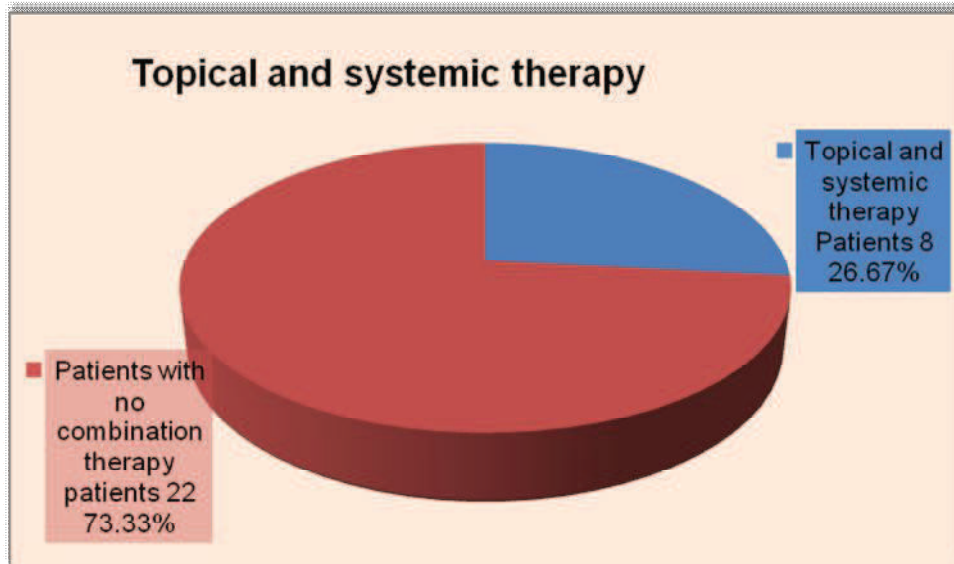


Chart 27

Discussion

Our study adds novel knowledge about the clinical and dermoscopic characteristics associated with FFA to the current literature.

In particular, we compared our findings with 3 large studies including 355 (4), 238 (40) and 79 (46) patients with FFA, which are summarized in table 4.

Similar to previous studies, we also observed a significant female predominance in our study cohort.

Among the 30 patients who were examined, there were 29 women (96.5%) and only 1 man (3.5%) This finding is similar to the reported gender-related frequency of FFA by Vañó-Galvan et al. (4) who reported on 343 (97%) women and 12 men (3%).

However, we also found some differences regarding the aforementioned study. As such, patients in our study were slightly older (62.3 years) compared to the mean age of their study cohort, which was 56.3 years. Moreover, we observed a higher frequency of occipital recession compared to the study of Vañó-Galvan et al. (26.7% vs. 15%, respectively) (4) whereas eyebrow alopecia was less common in our study than in their study (63.3% vs. 80%, respectively). We believe that the difference regarding the mean age of patients and the occipital recession can be explained by the fact that we examined a not so big group of patients in our study. Regarding the results we reported for the eyebrow alopecia in our study we had two parameters: total eyebrow alopecia and eyebrow dilation. So we think that the difference is due to that reason.

Convergent data currently exist with regard to the frequency of the lonely hair sign. While the study by Vañó-Galvan et al. (4) reported the frequency of this sign in 49% of their cohort, Fernández-Crehuet et al. (40) found approximately 90% of their patients revealing lonely hairs. Our data support the latter

findings, as we observed lonely hairs in all our patients. We also believe that the difference is due to the different number of patients.

Moreover, we observed similar frequencies with regard to perifollicular erythema, perifollicular hyperkeratosis, and lack of follicular openings as reported by Fernández-Crehuet P (40) and Toledo Pastrana and al (47).

	Current study	Vañó-Galvan study	Fernandez-Crehuet P study	Toledo Pastrana et al
Patients	30	355	238	79
Sex	29 women (96.5%) 1 man (3.45%)	343 women (97%) 12 men (3%)		
Age	42-85	23-86	n.d	n.d
Mean age of onset (in years)	62.3	56.3	n.d	n.d
Duration of FFA (in years)	1-10	0-41	n.d	n.d
Activity of the disease	12 (40%)	n.d	n.d	n.d
Severity scale	I 6 (20%) II 8 (26.67%) III 10 (33.33%) IV 6 (20%) V -	I 86 (24%) II 138 (39%) III 71 (20%) IV 45 (13%) V 15 (4%)	n.d	n.d
Recession of the frontal hairline	30 (100%)	n.d	n.d	n.d
Temporo-parietal recession	27 (90%)	nd	n.d	n.d
Occipital recession	8 (26.67%)	52 (15%)	n.d	n.d
Atrophy	22 (73.33%)	n.d	n.d	n.d
Pale skin	25 (83.33%)	n.d	n.d	n.d
Eyebrow Alopecia	19 (63.33%)	283 (80%)	n.d	n.d
Eyelash Alopecia	1 (3.33%)	50 (14%)	n.a.	n.a.
Perifollicular erythema	22 (73.33%)	n.d	(173/238 patients) 72.68%	66.3%
Perifollicular hyperkeratosis	18 (60%)	n.d	(213/238 patients) 89.49%	72.1%
Lonely hair	30 (100%)	176 (49%)	(212/238 patients) 89.07%	n.d
Follicular red dots	12 (40%)	n.d	n.d	n.d
Frontal Vein depression	15 (50%)	n.d	n.d	n.d
Lack of follicular openings	30 (100%)	n.d	n.d	100%
Autoimmune diseases	2 (6.67%)	n.d	n.d	n.d
Thyroid diseases	3 (10%)	52 (15%)	n.d	n.d
LPP	6 (20%)	n.d	n.d	n.d

n.d = no data

Table 4

Conclusion

Trichoscopy is a reliable and helpful tool that helps the dermatologist to diagnose the majority of hair diseases, (especially FFA) and also to estimate the degree of severity and activity of the disease.

In addition easy record keeping, documentation and comparison with pre-treatment images help to evaluate therapeutic response (45).

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