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Clinical features, Pathogenesis and Treatment of Female Pattern Hair Loss

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ABSTRACT— Female pattern hair loss (FPHL) presented with diffuse thinning over the entire scalp particularly on the crown. It is nonscarring hair loss characterized by gradual conversion of terminal hair to vellous with follicular miniaturization in a special distribution. It is very common and also increasing with age. The most common age is from 20 to 40years, some women don't experience noticeable thinning until their forty. It affects quality of life and has psychosocial effects. The pathogenesis may be multifactorial related to genetic, hormonal such as the androgen may play a role in FPHL, as women polycystic ovary syndrome had features of early-onset FPHL. On the other hand, the majority of these women have normal androgen levels, which may indicate that the androgen hormones aren't the only factors. Female pattern hair loss is characterized by diffuse thinning of the central and parietal region with preservation of the frontal hair line. This review describes the clinical features, diagnosis, and also, treatment of FPHL.

KEYWORDS: Female pattern hair loss, Trichogram, Androgenic alopecia, Ludwig scale, Dermoscopy

1. INTRODUCTION

Pattern hair loss is the most common type of hair loss in women. It is characterized by follicular miniaturization, the terminal hair is converted to villous in a characteristic distribution that typically affects the central scalp in women. Early recognition and treatment can control its progression. The process can begin after puberty, and the hair loss negatively affects quality of life and self-steem [1- 3]. It affects about 6% to 38% of women. Twelve percent of women may develop FPHL at age 29 years, 25% by 49 years and 41% by 69 years. Pattern hair loss is commonly diagnosed by a careful history, physical examination of the scalp, and nails [3], [4]. In addition to the hair-pull test, dermoscopy, and laboratory tests are also required. In patients with signs of hyperandrogenism, search for ovarian or adrenal disorders should be done. The objective of treatment is to reverse or even stabilize the process of follicullar miniaturization [4- 6].

- Pathophysiology

A- Genetic

Increased frequency of balding in first-degree male relatives of the women with FPHL can suggest that at least some genetic commonality between female and male androgenic alopecia exist [6], [7]. There are an eighteen case-control gene association studies have demonstrated an association between the *AR/EDA2* locus and early-onset FPHL. There is a weak association with the gene for estrogen receptor 2 (*ESR2*), suggesting the involvement of estrogenic pathways in FPHL [8].

2. Hormonal

1) Androgens

It was thought that androgen was responsible for FPHL, as women with androgenic disorders such as polycystic ovary syndrome had features of early-onset FPHL. But, the majority of these women have normal androgen levels, which may indicate that the androgen hormones aren't the only factors [9], [10].

Although the role of androgens in the pathogenesis of male hair loss has been clearly established, the role of androgens in FPHL is less clear. In fact, FPHL may develop even in the absence of androgens (Activation of the Wnt/β-catenin signaling pathway is an essential factor for hair morphogenesis, and maintenance of dermal papillae required for the growth of hair shaft. In FPHL, androgens can inhibit Wnt signaling and thus interfere with hair follicle stem cell differentiation [11], [12].

2) Estrogens

It was reported that estrogens influence hair follicle growth and cycling by binding to estrogen receptors (ERs). In human, there are two types of ER: ERα, which is an activator of transcription but poorly expressed in hair follicles, while ERβ, is expressed in many parts of the hair follicle and suppresses the cellular functions [5- 7]. Moreover, it modifies the androgen metabolism in the pilosebaceous unit, Therefore, the hair follicle is a target and source for estrogen. Moreover, the estrogens have stimulating effects on the hair shaft, keratinocytes of the hair matrix and prolong the anagen phase in hair follicles [10-12].

2) Role of Oxidative Stress

Reactive oxygen species (ROS) can be increased by extrinsic factors such as smoke inhalation, inflammatory processes or by drugs such as chemotherapeutics and accumulate in the hair follicle (HF). They induce DNA damage, impair tissue remodeling with release of pro-inflammatory cytokines from HF and keratinocytes, that may lead to hair loss. The oxidative stress induces damage to cellular macromolecules and cell death [3- 6].

3. Classification

Female pattern hair loss is characterized by diffuse thinning of the central and parietal region with preservation of the frontal hair line (Christmas tree) and bitemporal thinning is also common. There are 2 scales describing this pattern: the 3-point Ludwig scale is presented in (Fig. 1)(Table1)(12) and Sinclair scale are 5 grades (Fig. 2)(Table2)(1).

- Clinical Diagnosis

FPHL is a clinical diagnosis, based on patient history and clinical evaluation, further diagnostics are often necessary. Patient and family history (H) of the first manifestation of hair loss and course of hair loss should be documented [3- 6]. FPHL is usually longstanding disease of slowly progressive reduction of hair density. Patients describe hair thinning associated with an accentuation of the frontal, parietal, and vertex region [7], [8]. The initial signs of FPHL may be pruritus or trichodynia. The family H is often positive, gynecologic history especially in those with peripheral signs of hyperandrogenism; menstrual cycle disturbances and intake of hormonal contraception. Detailed history is a must to exclude other causes of the hair loss such as drug history (chemotherapeutic agents, antithyroid, intake of anabolic steroids) or systemic diseases (infections, thyroid function disorders, or surgical procedures) that occurred within 6 months before appearance of the first signs of hair loss. Nutritional behavior, lifestyle procedures, and environmental factors like smoking and ultraviolet radiation exposure all these should be considered (Table 1) [13].

- Physical examination

Clinical examination should involve the scalp skin and hair, facial and body hair, and the nails. A complete skin evaluation should be conducted, including the face, scalp, and nails. In women, the vertex and midfrontal scalp are commonly affected, as described above. Hair loss can be assessed by comparing the hair part of the central scalp with that of the occipital scalp, which is generally spared. Hair miniaturization can be seen better using

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Scalp examination

The scalp skin usually appears normal in FPHL, but often associated with seborrhea and or seborrheic dermatitis, alopecia areata, lichen planopilaris or frontal fibrosing alopecia should be considered [11], [12].

-Hair examination

-Scalp hair

Hair should be parted to assess scalp hair density, comparison between the frontal, occipital, and temporal regions should be done to examine the distribution (Ludwig scale). Trichoscopy may be helpful in assessment of follicular openings to exclude scarring alopecia and to identify the fine miniaturized hairs [13], [14].

-The hair pull test

Fifty to 60 hairs are gently grasped between the thumb, index, and middle fingers from the base of the hairs tugged away from the scalp. In case of Positive pull test more than 10% of the grasped hairs are pulled away from the scalp, this confirms active hair shedding. The hair pull test may be positive in the frontal region, and is typically negative in the occipital region [2- 4].

4. Diagnostic Tools

1) Dermoscopy

It is a noninvasive technique can be used to examine the scalp skin and hair shafts. The dermoscopic features in FPHL include hair diameter diversity (HDD) has been reported in 22% of patients as an early sign (Fig. 3) [14]. Peripilar signs are peripilar brown depressions. They are commonly seen in early disease, due to a superficial perifollicular lymphocytic infiltrate. The mean percentage of single-hair pilosebaceous units in FPHL is higher in the frontal area. There are three major and three minor criteria that can give a 98% specificity of FPHL [15].

Major Criteria:

1) More than 4 yellow dots in 4 images at 70-fold magnification in the frontal area.
2) Lower average hair thickness in the frontal area in comparison to the occipital area (calculated from not less than 50 hairs from each area).
3) More than 10% of thin hairs (below 0.03 mm) present in the frontal area [15].

Minor Criteria:

1) Ratio of single-hair units percentage in frontal area to occiput >2:1
2) Ratio of number of vellus hairs, frontal area to occiput >1.5:1
3) Ratio of hair follicles with perifollicular discoloration, frontal area to occiput >3:1.

Fulfillment of 2 major criteria or 1 major and 2 minor criteria are needed for diagnose FPHL [15].

5. Photography

Global photographs are helpful tools for the objective evaluation of the course of hair growth, hair volume, and hair density in clinical studies, and for long-term follow up in daily practice [10], [13].

Trichogram

The trichogram is a semi-invasive microscopic method for evaluating hair cycle and hair root assessment at different growth phases. It may be used to rule out other differential diagnoses. With a rubber-armed forceps, 60 to 80 hairs are plucked at two specific scalp locations depending on the hair disorder. Hairs are removed with one, quick, forceful pull perpendicular to the scalp and always along the direction of hair

growth. Hair bulbs are immediately embedded with their roots on a glass slide and evaluated under a magnifying lens or low-power microscope to determine the number of hairs in the different phases of the hair cycle. The results are given as a percentage of the total number of plucked hairs [16], [17].

2) Biopsy

In general, the biopsy may not be essential but it can be useful when the clinical picture is unclear or when other scalp conditions are suspected such as diffuse alopecia areata or cicatricial alopecia. Three to 4mm punch biopsies are obtained. The histologic characteristics of FPHL include hair follicle miniaturization (hair shaft diameter ≤ 0.03 mm), increased number and percentage of telogen hairs (15%–20%), ratio of terminal to vellus is declined or (1.5:1 in women). Both vertical and horizontal sectioning should be used. Mild perifollicular lymphohistiocytic infiltration, may be present and perifollicular fibrosis, in advanced cases [5- 9].

6. Laboratory testing

If the history or clinical examination point to androgen excess, multiple approaches including endocrinologists, gynecologists and dermatologists is recommended to exclude the different causes such as polycystic ovary syndrome, congenital adrenal hyperplasia or androgen-secreting tumors. The free androgen level, sex hormone-binding globulin, follicle-stimulating hormone, estradiol, or thyroid-stimulating hormone also should be considered. Assessment of serum ferritin, serum iron, as well as total iron binding capacity, zinc, and vitamin D levels can be useful in FPHL. In patients with irregular menses, and acanthosis nigricans, a laboratory workup should be done for hyperandrogenism and serum prolactin [13- 16].

- Differential Diagnosis

Multiple hair or scalp disorders may be presented with clinical features similar to FPHL. Telogen efflufium, postpartum hair loss, cicatricial alopecia in pattern distribution, and diffuse alopecia all of these are a differential diagnosis of FPHL [11], [15].

1) Telegon effluvium

Telogen effluvium (TE) is an acute or chronic diffuse hair loss with increased shedding of telogen hairs. TE that is difficult to be distinguished from FPHL. Carful history taken is very important, as there are many inciting triggers such as psychological stress, weight loss, childbirth, or medications. TE and FPHL can coexist in the same patient. TE is usually associated with a precipitating event, like a severe illness or psychological trauma, crash diet or certain medications, and the results of the hair pull test are diffusely positive. Dermoscopy shows numerous short regrowing hairs of normal thickness (>0.03 mm) with absence of hair diameter variability [1], [5], [16].

2) Diffuse alopecia areata

Usually it does not follow a patterned distribution. The presence of a personal or family history of alopecia areata, the detection of patchy or total hair loss, hair loss in other body areas, and abnormalities of the nails can support the diagnosis. A biopsy is useful to confirm the diagnosis. Dermoscopic examination reveals presence of yellow dots, black dots, exclamation mark hairs (Fig. 9)

3) Central centrifugal cicatricial alopecia

Central centrifugal cicatricial alopecia is a type of scarring alopecia of the vertex region. It affects most commonly women of African descent. Dermoscopic examination reveals loss of follicular ostia and also, biopsy can be useful to confirm the diagnosis.

4)Frontal fibrosing alopecia

It is characterized by frontotemporal recession associated with loss of eyebrows, perifollicular erythema and keratotis papules. Histological examination demonstrates signs consistent with a lymphocytic scarring alopecia.

3) Traction alopecia

It occurs as a result of chronic tension on the hair shaft. The hair loss is reversible but later on may become permanent if tension on the hair follicles continues.

4) Trichotillomania

It is a psychiatric condition in which the patients often repeatedly pull the hair. Hair loss can occur at different lengths as a result of variations in breakage point along the hair shaft within the same episode. Hair loss takes bizarre patterns. (Figure 3).

- Treatment of FPHL

The main goal of treatment of FPHL is to promote hair regrowth and to prevent further hair thinning and loss. The first-line treatment for FPHL is topical minoxidil in addition to treatment of androgen excess and nutritional deficiencies. Mild-to-moderate FPHL can be treated with oral antiandrogen therapies (cyproterone acetate and spironolactone) which can arrest the progression of the disease and also reverse miniaturization. In patients with severe FPHL, hair surgery may be considered for selected cases [4], [16].

A-Medications:

1. Minoxidil:

Minoxidil can enhance hair growth, hair density and hair thickness by elongation of the anagen and shortening telogen. Minoxidil is approved for treatment of both male and FPHL. It is available in 2% and 5% solutions or foam and recently 10% concentration. Patients should apply 1 mL of 5% solution or half a cap of 5% foam once a day to the affected areas of the scalp. female patients older than 18 years of age (2% solution; 1 mL twice daily or half a cap of 5% foam once daily) [22], [23]. Evaluation of the response should be performed at 6 months. At first, the patients should be informed that transient increase in telogen hair shedding, often occurs during the first 8 weeks of treatment initiation. The side effect of topical minoxidil is hypertrichosis which results from either local spreading or excessive continuous application. The patient should be informed to apply it 2 hours before sleep to avoid contamination of the pillow. Another side effects is irritant or allergic contact dermatitis may occur which may be the higher content of propylene glycol [2].

2. Spironolactone (Antiandrogens drug)

In women with FPHL with clinical and or biochemical evidence of hyper androgenism, the use of oral anti androgens can be considered. Spironolactone inhibits the androgen receptor and ovarian production of androgens. The usual dose is 100 to 200 mg per day has a good safety profile. menstrual irregularity and hyperkalemia are the main side effects. It was found that 200 mg daily dose can improve the hair regrowth in about 44% of patients [16], [15].

3. Cyproterone acetate

Cyproterone acetate is (a progesterone derivative) prevents dihydroxytestosterone from binding to the androgenic receptor and also inhibits the release of follicle-stimulating hormone and luteinizing hormone. Therefore, it reduces the testosterone level. It is available in combination with ethynyl estradiol as an oral contraceptive (1,4,5).

7. Intervension

- Surgery:

In AGA, thinning or hairless areas can be cosmetically covered using hair restoration surgery. It includes

hair transplantation, scalp reduction surgery, or a combination of both. Hair transplantation is less invasive than scalp reduction surgery; follicular units of 1 to 4 hairs are transplanted in high densities and large numbers. Hair surgery, especially follicular unit transplantation, can be considered to improve AGA in patients with sufficient donor hair supply and stabilized AGA particularly in the frontoparietal area (14,19,21).

- Non permanent hair replacement measures:

It includes wigs, various hair-binding techniques and hair extension (14).

- Low-Level Laser Therapy:

Low-level laser therapy (LLLT) can be used for treatment of FPHL. It means exposure of the scalp to low levels of visible light. Its mechanism of action in improving hair loss is unclear; it can stimulate follicular stem cells, increase blood flow, promote mitosis and also have anti-inflammatory effects [24], [25]. It can be used at home by a Laser Comb or by wearing a helmet LaserCap device is a flexible firmly sealed dome-shaped membrane (650 nm at 5 mW) that fits in almost any hat to treat the whole scalp, powered by a rechargeable battery. Handheld laser devices in helmet type can be placed over the affected area to allow more homogeneous absorption of light in the scalp. It was demonstrated that LLLT increased hair density after 24 weeks of therapy [26].

- Platelet Rich Plasma:

Platelet-rich plasma (PRP) is defined as an autologous concentration of platelets in a small volume of plasma. PRP contains many growth factors which stimulate cellular proliferation, differentiation, and promote hair growth [26- 28]. Once the platelets are activated, the growth factors are released either by calcium chloride, thrombin or fibrinogen. All seem similarly effective in activating the platelets ex vivo Platelet-rich plasma is an autologous preparation of plasma with platelets, growth factors, and cytokines. It was initially used during hair transplantation procedures, with mixed results. Recently its use by itself has been explored to treat pattern hair loss. Preliminary evidence suggests that platelet-rich plasma may be advantageous in hair regrowth.39 Side effects include redness and pain at injection site and pinpoint bleeding. Adverse effects are minimal in all the clinical studies that evaluated its effect on hair growth. Mostly it may causes headaches, skin pain and burning sensation, pruritus, erythema, acne, and mild paresthesia [29], [30].

- Microneedling:

Using of microneedling has been investigated as a therapeutic option for the treatment of hair disorders owing to its capacity to enhance growth factor production, facilitating hair follicle development, stimulating collagen and elastin production. Moreover, microneedling produces microchannels that allow transdermal delivery of drugs via the stratum corneum. A randomized controlled trial revealed successful results with microneedling as an adjuvant to drug therapy for FPHL [31], [32].

8. References

[1] Fabbrocini G, Cantelli M, Masarà A , Annunziata AC, Marasca C, Cacciapuoti S. Female pattern hair loss: A clinical, pathophysiologic, and therapeutic review. International Journal of Women's Dermatology 4 (2018) 203–211.

[2] Kanti V, Messenger A, Dobos G, et al. Evidence-based (S3) guideline for the treatment of androgenetic alopecia in women and in men–short version. J EurAcadDermatolVenereol. 2018;32(1):11-22.

[3] Olsen EA, Messenger AG, Shapiro J, et al. Evaluation and treatment of male and female pattern

hair loss. J Am Acad Dermatol 2005;52(2):301–311. doi:10.1016/j.jaad.2004.04.008.

[4] Cousen P, Messenger A. Female pattern hair loss in complete androgen insensitivity syndrome. Br J Dermatol 2010; 162(5):1135–1137.doi:10.1111/j.1365-2133.2010.09661.x

[5] Futterweit W, Dunaif A, Yeh HC, Kingsley P. The prevalence of hyperandrogenism in 109 consecutive female patients with diffuse alopecia. J Am Acad Dermatol 1988; 19(5 pt 1):831–836. doi:10.1016/s0190-9622(88)70241-8.

[6] Birch MP, Lalla SC, Messenger AG. Female pattern hair loss. Clin Exp Dermatol 2002;27:383–8.

[7] Blumeyer A, Tosti A,Messenger A, Reygagne P, DelMarmol V, Spuls PI, et al. Evidencebased (S3) guideline for the treatment of androgenetic alopecia in women and in men. J Dtsch Dermatol Ges 2011(Suppl. 6):S1–57.

[8] Olsen EA. The midline part: an important physical clue to the clinical diagnosis of androgenetic alopecia in women. J Am Acad Dermatol 1999; 40(1):106–109. doi:10.1016/s0190-9622(99)70539-6.

[9] Ludwig E. Classification of the types of androgenetic alopecia (common baldness) occurring in the female sex. Br J Dermatol 1977;97(3):247–254. doi:10.1111/j.1365-2133.1977.tb15179.x.

[10] Strazzulla LC, Wang EHC, Avila L, et al. Alopecia areata: disease characteristics, clinical evaluation, and new perspectives on pathogenesis. J Am Acad Dermatol 2018; 78(1):1–12.doi:10.1016/j.jaad.2017.04.1141.

[11] Carmina E, Lobo RA. Treatment of hyperandrogenic alopecia in women. Fertil Steril2003;79:91–5.

[12] Dawber RP, Sonnex T, Ralfs I. Oral antiandrogen treatment of common baldness in women. Br J Dermatol 1982;107:20–1.

[13] Rodney DS. Female pattern hair loss: A pilot study investigating combination therapy with low-dose oral minoxidil and spironolactone. International Journal of Dermatology2017 57(Suppl 65): DOI: 10.1111/ijd.13838.

[14] Blume-Peytavi U, Blumeyer A, Tosti A, et al. S1 guideline for diagnostic evaluation in androgenetic alopecia in men, women and adolescents. Br J Dermatol. 2011;164(1):5-15.

[15] Rakowska A, Slowinska M, Kowalska-Oledzka E, Olszewska M, Rudnicka L. Dermoscopy in Female Androgenic Alopecia: Method Standardization and Diagnostic Criteria Int J Trichology. 2009 Jul-Dec; 1(2): 123–130.doi: 10.4103/0974-7753.58555

[16] Thamer M , Lidia R , Malgorzata O , Jerry S. Evaluation and diagnosis of the hair loss patient: part II. Trichoscopic and laboratory evaluations. J Am Acad Dermatol 2014 Sep;71(3):431.e1-431.e11.doi: 10.1016/j.jaad.2014.05.008.

[17] Özlem K, Tülin G. Clinical evaluation of alopecias using a handheld dermatoscope. Journal of the American Academy of Dermatology, 2012;5: 206-214.

[18] Miteva M, Tosti A. Hair and scalp dermatoscopy. J Am Acad Dermatol 2012; 67(5):1040–1048. doi:10.1016/j.jaad.2012.02.013.

[19] Asz-Sigall D, González-de-Cossio-Hernández AC, Rodríguez-Lobato E, Ortega-Springall MF, Vega-Memije ME, GuzmánSkin RA. Differential diagnosis of female-pattern hair loss. Skin Appendage Disord 2016;2:18–21.

[20] Atanaskova Mesinkovska N, Bergfeld WF. Hair: What is new in diagnosis and management? Female pattern hair loss update: diagnosis and treatment. Dermatol Clin 2013;31:119–27.

[21] El Sayed MH, Abdallah MA, Aly DG, Khater NH. Association of metabolic syndrome with female pattern hair loss in women: A case-control study. Int J Dermatol2016;55:1131–7.

[22] Birch MP, Messenger JF, Messenger AG. Hair density, hair diameter and the prevalence of female pattern hair loss. Br J Dermatol 2001;144:297–304.

[23] Blume-Peytavi U, Hillmann K, Dietz E, Canfield D, Garcia Bartels N. A randomized, single-blind trial of 5% minoxidil foam once daily versus 2% minoxidil solution twice daily in the treatment of androgenic alopecia in women. J Am Acad Dermatol 2011;65:1126–34.

[24] Avci P, Gupta G, Clark J, Wikonkal N, Hamblin M. Low-level laser (light) therapy (LLLT) for treatment of hair loss. Lasers Surg Med. 2014; 46(2): 144–151.

[25] Ghanaat M. Type of hair loss and treatment option, including the novel low-level light therapy and its proposed mechanism. South med J .2010;103(9):917-921.

[26] Delaney SW, Zhang P. Systematic review of low-level laser therapy for adult androgenic alopecia. J Cosmet Laser Ther 2018;20:229–36.

[27] Cervantes J, Perper M, Wong LL, Eber AE, Villasante Fricke AC, Wikramanayake TC, et al. Effectiveness of platelet-rich plasma for androgenetic alopecia: A review of the literature. Skin Appendage Disord 2018;4:1–11.

[28] Alves R, Grimalt R. Randomized placebo-controlled, double-blind, half-head study to assess the efficacy of platelet-rich plasma on the treatment of androgenetic alopecia. Dermatol Surg 2016;42(4):491–7.

[29] Gentile P, Garcovich S, Bielli A, et al. The effect of platelet-rich plasma in hair regrowth: a randomized placebo-controlled trial. Stem Cells Transl Med. 2015;4:1317-1323.

[30] Garg S. Outcome of intra-operative injected platelet-rich plasma therapy during follicular unit extraction hair transplant: a prospective randomized study in forty patients. J Cutan Aesthet Surg. 2016;9:157-164.

[31] Dhurat R, Mathapati S. Response to microneedling treatment in men with androgenetic alopecia who failed to respond to conventional therapy. Indian J Dermatol. 2015;60(3):260.

ISSN: 1343-4292
Volume 140, Issue 01, April, 2022

[32] Kim YS, Jeong KH, Kim JE, et al. Repeated microneedle stimulation induces enhanced hair growth in a murine model. Ann Dermatol 2016;28:586–92.