REVIEW ARTICLE

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Hair loss in women: medical and cosmetic approaches to increase scalp hair fullness

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Summary

Androgenetic alopecia affects both men and women. In men it produces male pattern hair loss with bitemporal recession and vertex baldness. In women it produces female pattern hair loss (FPHL) with diffuse alopecia over the mid-frontal scalp. FPHL occurs as a result of nonuniform hair follicle miniaturization within follicular units. Diffuse alopecia is produced by a reduction in the number of terminal fibres per follicular unit. Baldness occurs only when all hairs within the follicular units are miniaturized and is a relatively late event in women. The concepts of follicular units and primary and secondary hair follicles within follicular units are well established in comparative mammalian studies, particularly in sheep. However, discovery of these structures in the human scalp hair and investigation of the changes in follicular unit anatomy during the development of androgenetic alopecia have provided a clearer understanding of the early stages of androgenetic alopecia and how the male and female patterns of hair loss are related. FPHL is the most common cause of alopecia in women and approximately one-third of adult caucasian women experience hair loss. The impact of FPHL is predominantly psychological. While men anticipate age-related hair loss, hair loss in women is usually unexpected and unwelcome at any age. Treatment options to arrest hair loss progression and stimulate partial hair regrowth for FPHL include the androgen receptor antagonists spironolactone and cyproterone acetate, the 5α-reductase inhibitor finasteride and the androgen-independent hair growth stimulator minoxidil. These treatments appear to work best when initiated early. Hair transplantation should be considered in advanced FPHL that is resistant to medical treatments. Hair transplantation requires well-preserved hair growth over the occipital donor area. The psychological impact of FPHL may also be reduced by cosmetic products that improve the appearance of the hair. These agents work to minimize hair fibre breakage, improve hair volume or conceal visible bald scalp.

Androgenetic alopecia (AGA) is the most common cause of hair loss in both men and women. The pattern of hair loss in women (female pattern hair loss, FPHL) was defined by Ludwig in 1977[1] and later modified by Sinclair *et al.*[2] in 2004. FPHL presents with diffuse thinning (loss of hair volume) over the mid-frontal scalp with minimal or no bitemporal recession. Vertex baldness is rare. Ludwig illustrated the stages of progression of FPHL into three grades (Ludwig grades I, II, III). The Sinclair scale identified five visually distinct stages that can be used to monitor clinical severity and treatment response (Figs 1 and 2).

Female pattern hair loss is generally less severe than male pattern hair loss (MPHL), occurs later, and the response to antiandrogen therapy is more variable.[3] The pattern of hair loss in women is less easily recognized, but FPHL can still be diagnosed clinically.

The purpose of this paper is to provide current information on the prevalence, pathophysiology, diagnosis and management of this condition. In particular the medical and cosmetic approaches to increase volume and fullness will be explored. A new hypothesis on the mechanism of balding is presented.

Epidemiology

An Australian epidemiological study indicated that in caucasian adult females over the age of 20 years, the prevalence (age adjusted) of FPHL (as defined by Sinclair stage 2 or greater

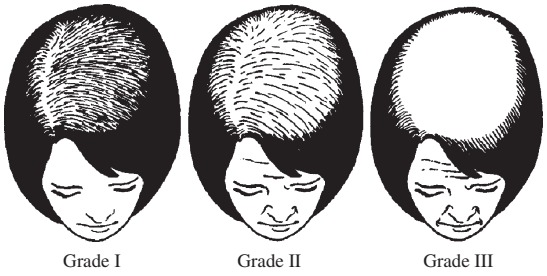

Fig 1. Ludwig scale.

hair loss) is 32·2% of whom 10·5% (95% confidence interval 8·2–12·7%) have moderate to severe hair loss (Sinclair stage 3 or greater).[4] FPHL among Chinese women is reported as 6%,[5] and lower prevalence rates have also been reported in African[6] and Korean women.[7]

Psychological morbidity

Hair is an essential part of a woman's appearance, attractiveness and identity. For many women, how attractive they feel will correlate closely with their self esteem[8] and this is reflected in the predominantly psychological morbidity that can be associated with female AGA. A study exploring the psychological impact of FPHL in Australian females revealed that women with AGA experience poorer health-related quality of life than women without hair loss.[9]

Pathogenesis and pathology

In FPHL, there is alteration in the hair cycle dynamics with shortening of the anagen phase and elongation of the latent part of the telogen phase. This leads to a decrease in anagen to telogen hair ratio from about 12 : 1 to < 8 : 1. With each successive hair cycle, the length of anagen is progressively reduced whereas the length of telogen remains constant.[10] This affects hair fibre length and leads to shortening of the terminal hair. In addition, progressive reduction of the hair diameter also occurs by miniaturization of the entire follicle.[11] Combined, the decrease in fibre length and reduction in fibre diameter leads to progressive replacement of long terminal hairs by short fine vellus hairs.[12]

In humans, scalp hair follicles exist within follicular units. A follicular unit typically consists of a larger, central primary follicle surrounded by smaller secondary follicles. A single arrector pili muscle is predominantly attached to the primary follicle with variable attachment to secondary follicles.[13] Yazdabadi *et al.*[14] demonstrated that the diffuse hair loss pattern seen in FPHL is due to reduction in the number of terminal hairs per follicular unit rather than miniaturization of entire follicular units. They hypothesized a hierarchy of androgen sensitivity within follicular units that resulted in secondary follicles having an increased susceptibility to androgen-sensitive miniaturization into vellus hairs. Miniaturization of secondary follicles leads to loss of hair volume. The appearance of bald scalp only occurs when the entire follicular unit is miniaturized (Fig. 3). This diffuse thinning that precedes baldness is also observed in men with MPHL, and can be readily identified on close examination of the scalp. Females present earlier, complaining of reduction of the volume of the ponytail while men often delay presentation until the appearance of a bald spot on the scalp.

Role of androgens

The role of androgens in the development of AGA has been clearly established in MPHL but not in FPHL.[15] FPHL is known to occur in women with hyperandrogenism where other signs of virilization may also be present such as hirsutism, acne and/or menstrual disturbance. These clinical signs do not always correlate with increased levels of serum androgens but may reflect a hypersensitivity to physiological concentration of androgens.[16] Most women with FPHL have androgen levels within normal limits.[17]

Genetics and female pattern hair loss

AGA is a complex polygenic condition both in men and in women.

Clinical features and diagnosis

Female pattern hair loss is the most common cause of diffuse hair loss in women. The onset of FPHL may be any time after menarche; however, many women develop the first signs of FPHL after the age of 50 years.[18] Patients with FPHL may present less severe hair loss than their male counterparts and may describe intermittent or continuous hair shedding, either alone or together with loss of hair volume (thinning)

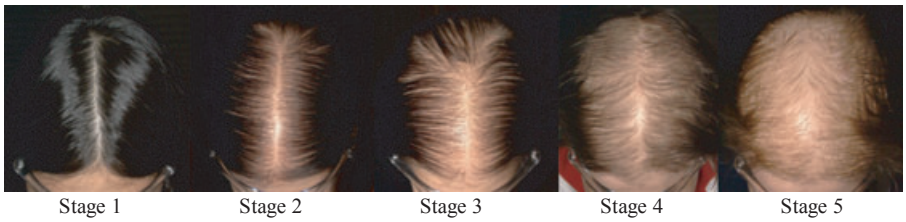

Fig 2. Sinclair scale.

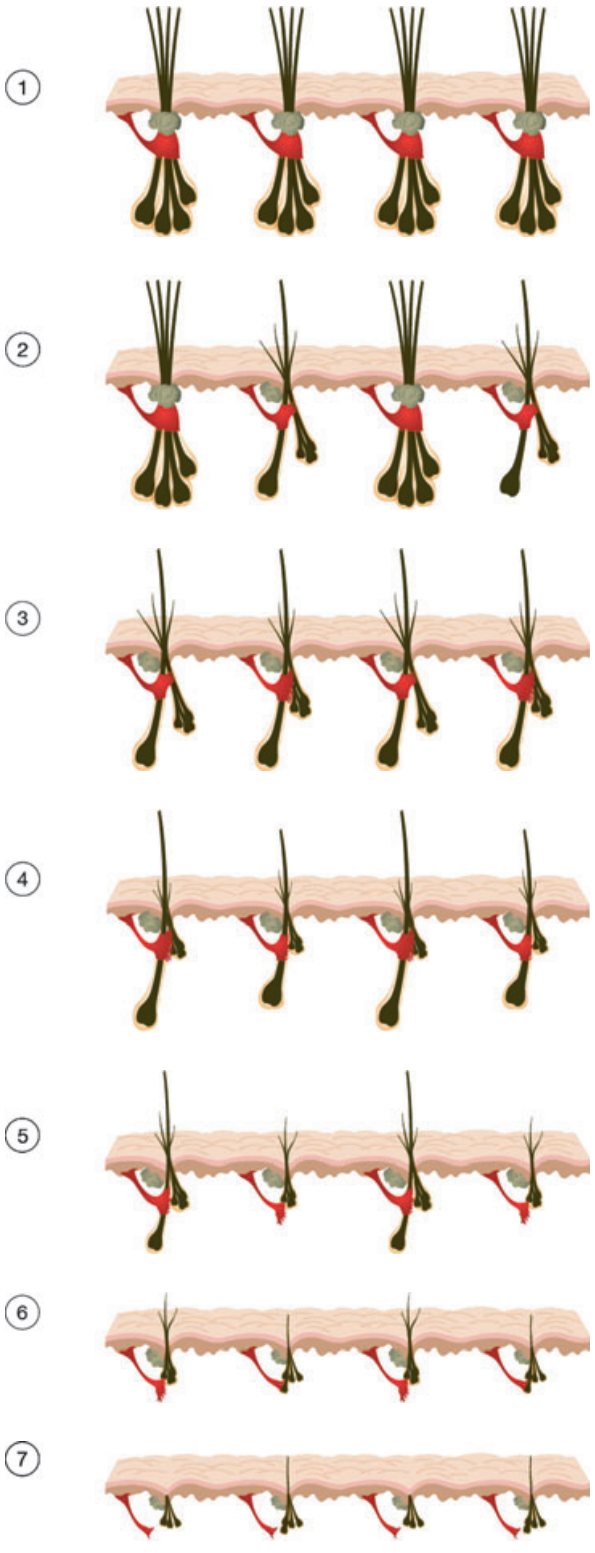

Fig 3. Progressive miniaturization within follicular units. Initially multiple compound follicular units are found across the scalp comprising a primary follicle and multiple secondary follicles. Miniaturization occurs initially in the secondary follicles, leading to a reduction in hair density but no visible baldness. Baldness occurs when the entire follicular unit is miniaturized.

confined to the frontal scalp.[11] Frontal hair thinning leads to widening of the midline part in a Christmas tree pattern. The Christmas tree distribution of hair loss facilitates the diagnosis of FPHL. Involvement of parietal and occipital scalp in FPHL is also significant in some women and this can also be demonstrated histologically[19] and by phototrichogram[20] studies.[21,22]

Diagnostic techniques

The hair pull test, hand-held epiluminescent microscopy and global photography are valuable in the diagnosis and management of this condition. The hair pull test is an examination technique that crudely assesses active hair shedding. It involves grasping 50–60 strands of hairs by thumb, index and middle fingers and gently sliding the fingers along the hair shafts. If more than 10% of grasped hairs are pulled out then the test is positive. A positive test indicates increased telogen hairs which may be the case in a recently active phase of either AGA or chronic telogen effluvium.[23]

Epiluminescent microscopy demonstrates the nonscarring nature of this process as well as the hair diameter variety and presence of vellus hairs reflecting ongoing miniaturization, the hallmark of AGA (Fig. 4). A reduction in the average number of terminal hairs per follicular unit is seen over the mid-frontal scalp when compared with the occipital scalp.

Phototrichograms performed using a TrichoScan (Tricholog GmbH, Freiburg, Germany) combine epiluminescence microscopy and automatic digital image analysis providing information on hair calibre, density and growth rate. This technique is noninvasive and in future with improved sensitivity it may reduce the need for a diagnostic scalp biopsy in some patients.[24]

Extensive metabolic and endocrinological work-up is not routinely necessary. A history of menstrual disturbance, impaired fertility and signs of hyperandrogenism should be investigated further to exclude polycystic ovary syndrome.[23]

Fig 4. Follicular miniaturization.

In women, some disorders causing diffuse hair loss may have similar features to those seen in FPHL and so it may initially be difficult to distinguish FPHL from these.[3,25] Furthermore, aggravating and associated factors such as a superimposed acute telogen effluvium may need to be excluded. Causes of acute telogen effluvium include childbirth, metabolic or endocrinological factors as well as drug-induced hair loss including introduction or withdrawal of contraceptive methods or hormone replacement therapy.[11] Some progesterone-based preparations, including those containing levonorgestrel, norgestrel, norethisterone as well as tibolone may precipitate hair loss while drosperinone, desogestrel, norgestimate and dihydro- and medroxyprogesterone have a more favourable effect on hair.[26]

Oral contraceptive pills containing oestradiol and cyproterone acetate may have a beneficial effect in women with FPHL.[27] Although patients with FPHL experience intermittent shedding, a positive hair pull throughout the scalp indicates that the differential diagnosis to consider in early FPHL is chronic telogen effluvium. Chronic telogen effluvium is an idiopathic disease entity characterized by chronic and fluctuating increase in telogen hair shedding without any loss of hair density.[28] Women may present with increased telogen hair shedding of more than 6 months duration but with no visible reduction in hair density over the crown. Scalp biopsy may be warranted to differentiate these two conditions.[4]

Scalp biopsy

A horizontally sectioned 4 mm scalp biopsy is the most reliable method for diagnosing FPHL. Histologically, the follicular changes seen in FPHL appear to be identical to those seen in male pattern baldness.[11] The ratio of terminal to vellus hairs on a horizontal scalp biopsy is used to differentiate FPHL from chronic telogen effluvium. A ratio of $< 4 : 1$ is diagnostic of FPHL whereas a ratio of $> 8 : 1$ is indicative of chronic telogen effluvium. Ratios in between these values are usually indeterminate.[29,30] Other findings that may be seen on biopsy in FPHL are an increased number of telogen hairs, a decrease in total terminal hair follicles in subcutaneous fat and presence of fibrous streamers.[30] Chronic telogen effluvium can often be excluded on a clinical basis alone in patients with Sinclair grades of 3, 4 or 5 and a scalp biopsy is not required. When a biopsy is required, it is recommended that a triple-biopsy procedure be performed on the vertex rather than a single horizontal biopsy as a likelihood of reaching an accurate diagnosis is greater with such a method.[4]

Another potential differential diagnosis, albeit rare, includes the so-called alopecia areata incognita. Alopecia areata incognita is a type of alopecia areata affecting mostly women. It is characterized by diffuse shedding of telogen hairs leading to severe hair thinning over a few months in the absence of typical patches of alopecia areata. Scalp biopsy reveals a peribulbar lymphocytic infiltrate around anagen follicles at middermis level, differentiating it from AGA and chronic telogen effluvium.[31]

Pharmacological treatment of female pattern hair loss

Minoxidil

Minoxidil was first introduced in the early 1970s as a treatment for hypertension. Its mode of action is not fully understood but it is thought to act mainly by increasing anagen duration, with the added effect of increasing hair diameter. Minoxidil also stimulates regrowth by inducing early anagen in follicles that are in the latent part of telogen.[32] Its mode of action is androgen independent and so it is effective in women with FPHL both with and without hyperandrogenism and in women who are both pre- and postmenopausal.[11]

Topical minoxidil is available as 2% and 5% strength but only the 2% topical minoxidil is currently approved by the U.S. Food and Drug Administration for the treatment of pattern hair loss in women. Treatment with topical minoxidil should be continued for at least 12 months before any decision on the efficacy of it can be made.[3,11] In women with FPHL, 5% minoxidil has not been shown to be statistically more advantageous than 2%.[33]

Antiandrogens

Women with FPHL in the presence of other signs of androgen excess may respond to antiandrogen therapy with agents such as spironolactone or cyproterone acetate. Spironolactone and cyproterone acetate are antiandrogen medications that compete with androgens for androgen receptors. All antiandrogen medications have the potential to feminize a male fetus and so pregnancy should be avoided while on any of these. Many clinicians would also recommend concurrent oral contraceptives throughout the course of treatment.[11,18,28] These agents provide more secure contraception, may increase therapeutic effect and minimize menstrual irregularities due to antiandrogen therapy.

Spironolactone is an aldosterone antagonist that competitively blocks androgen receptors. It is also a weak inhibitor of androgen synthesis.[21] Spironolactone at a dose of 200 mg daily has been shown to be safe and effective both in at least preventing further hair loss and/or in inducing hair growth in women with FPHL (Fig. 5).

Cyproterone acetate also blocks androgen receptors and inhibits gonadotropin releasing hormone.[28] It should be given at a dose of 100 mg daily for 10 days per month (or first 10 days of active pill) in premenopausal women[27,28] or at 50 mg daily in postmenopausal women.[21]

Combination therapy in patients using two agents with different mode of action has also been reported. A 53-year-old woman with FPHL was successfully treated with spironolactone 200 mg daily and 5% minoxidil solution with an additive effect on hair regrowth.[34] This case highlights the benefit of using combination therapy to treat FPHL with more than one agent with varied mode of action. The first controlled study of 66 women with FPHL, comparing treatment with topical

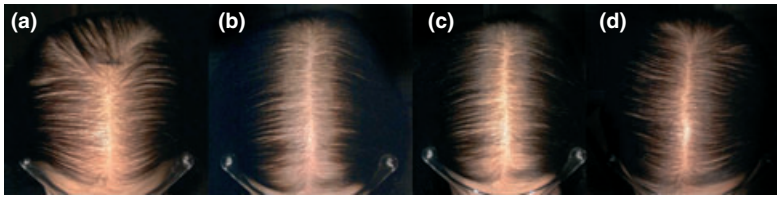

Fig 5. Response to spironolactone over 24 months.

minoxidil 2% and cyproterone acetate, showed that cyproterone was more effective in women who had signs of hyperandrogenism (particularly hyperseborrhoea) and minoxidil 2% was more effective in those without evidence of hyperandrogenism.[35]

Finasteride

Finasteride is a specific inhibitor of type 2 5α-reductase which functions to catalyse the peripheral conversion of testosterone to a more active steroid dihydrotestosterone. Like the antiandrogen medications, finasteride may also cause abnormalities in the male fetus and therefore is contraindicated in pregnant women.

A 1-year, double-blind, placebo-controlled, randomized study investigating treatment of FPHL with finasteride 1 mg daily in 137 postmenopausal women did not show any benefit in slowing disease progression and/or in hair regrowth.[36] However, one of the authors (R.S.) reported successfully treating a 67-year-old postmenopausal woman with FPHL with finasteride 5 mg weekly given for 12 months. Finasteride was effective in reversing the progress of pattern hair loss in this patient (Fig. 6).

Hair transplantation

Hair transplants should be considered for those women with FPHL who have had little success with pharmacological treatments. The surgical option for the management of FPHL is not widely appreciated even though many women today are suitable candidates for hair transplant. It is possible in some females to achieve outcomes comparable with that in men with male pattern baldness undergoing hair transplant surgery. Patient selection is important to avoid disappointment with the end results.[37] The ideal female patient is one who has dense hair in the donor site over the occipital scalp and extensive thinning or hair loss over the frontal scalp.[27]

Cosmetic products

Various nonmedical treatment modalities exist which may be used alone or as adjuvant therapy. These cosmetic products are designed to cover exposed scalp where there is visible hair loss. Commonly used products are hair building fibres, tinted hair sprays and lotions, hair pieces, wigs and hair extension. Most women are able to find one that is suitable to their skin type and budget.[3,11]

Additional strategies centre on minimizing hair breakage. Fibre diameter is reduced in AGA, increasing susceptibility to weathering and fracture. External protective lubrication to minimize friction along with agents that provide temporary, external 'gluing' to prevent damage to uplifted cuticles help reduce hair breakage.

Shampoos and other topical agents can deposit particles to add bulk to the fibre surface and create space between fibres. These can also be used to lift and hold the hair by tethering neighbouring fibres and thus help to mask visible scalp.

Conclusion

Female pattern hair loss is the most common cause of alopecia in women. It differs from male pattern baldness in epidemiology, clinical presentation and management. The impact of FPHL is predominantly psychological. Several medications, including topical minoxidil, oral finasteride, spironolactone

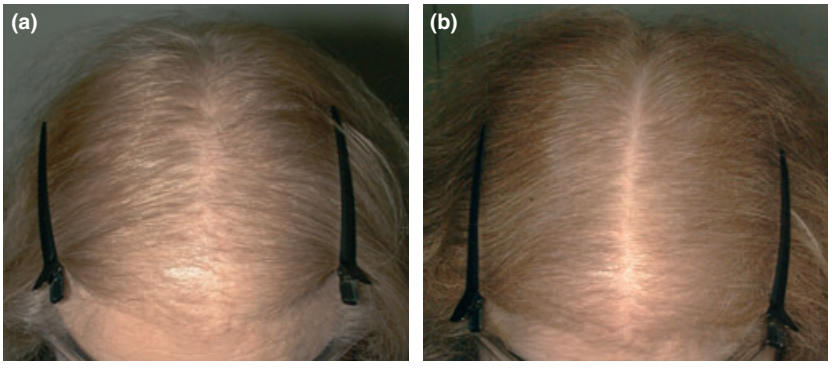

Fig 6. Response to finasteride at 12 months.

and cyproterone acetate, are widely used in the treatment of this condition. Although not as commonly performed as in male pattern baldness, hair transplantation should be considered in advanced FPHL resistant to medical treatments.

The psychological impact of FPHL can also be reduced by cosmetic products that improve the appearance of the hair. These agents work to minimize hair fibre breakage, improve hair volume or conceal visible bald scalp.

The concept of follicular units and primary and secondary follicles is well established in comparative mammal studies, particularly in sheep.[38] However, it is also applicable to human scalp hair and provides us with a clearer understanding of the pathogenesis of this disease. A hierarchy in androgen sensitivity, with secondary follicles more prone to initial miniaturization, has been postulated to explain the diffuse hair loss seen in FPHL.[14]

What's already known about this topic?

- Androgenetic alopecia is a complex polygenic condition that produces diffuse hair loss over the mid-frontal scalp in women.
- Mammalian hair follicles generally exist in follicular units of between one and five follicles, serviced by a single arrector pili muscle.
- In androgenetic alopecia hair follicle miniaturization does not affect all follicles within a follicular unit equally.
- In most mammals there is a clearly discernable difference between primary and secondary follicles within a follicular unit.

What does this study add?

- Diffuse hair loss in women can be modelled on the concept of preferential loss of secondary follicles within scalp follicular units with relative sparing of primary follicles.
- The psychological morbidity associated with androgenetic alopecia may be reduced by both medical and surgical treatments as well as by cosmetic products that improve the appearance of the hair.

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