Female pattern hair loss

M. P. Birch, S. C. Lalla and A. G. Messenger

Department of Dermatology, Royal Hallamshire Hospital, Sheffield, UK

Summary

Female pattern hair loss is a common condition characterized by a diffuse reduction in hair density over the crown and frontal scalp with retention of the frontal hairline. The prevalence increases with advancing age. It has been widely thought to be the female counterpart of male balding and is often referred to as female androgenetic alopecia. However, the role of androgens is not fully established. Scalp hair loss is undoubtedly a feature of hyperandrogenism in women but many women with female pattern hair loss have no other clinical or biochemical evidence of androgen excess. Female pattern hair loss is probably a multifactorial genetically determined trait and it is possible that both androgen-dependent and androgen-independent mechanisms contribute to the phenotype. In managing patients with female pattern hair loss the physician should be aware that the adverse effects on quality of life can be quite severe and do not necessarily correlate with the objective degree of hair loss. The treatment options are currently limited but modest improvements in hair density are achievable in some women.

Introduction

In a short but influential paper, published as recently as 1977, Ludwig described the distinctive features of female pattern hair loss and classified it into three grades of severity, often referred to as Ludwig I, II and III.[1] Although Ludwig is rightly credited with delineating the clinical presentation of female pattern hair loss, it was well known to previous generations that women commonly develop an age-dependent form of scalp hair loss. In 1935 Snyder and Yingling[2] examined 1883 women over 35 years of age and found that 8% were balding, and Hamilton reported that 15–30% of women aged over 30 showed temporal recession. Ludwig used the term 'androgenetic alopecia' to describe female hair loss in the belief that it is the same entity as male balding. However, the role of androgens in women with hair loss is far from clear-cut and in this article we use the less committal term 'female pattern hair loss'.

Correspondence: A. Messenger, Department of Dermatology, Royal Hallamshire Hospital, Sheffield S10 2JF, UK.
Tel.: +44 114 2712188. Fax: +44 114 2713763.
E-mail: A.G.Messenger@Sheffield.ac.uk

Clinical features

Most women present with a history of gradual thinning of scalp hair, often over a period of several years. The hair loss can start at any time between early teens and late middle age. There is frequently a history of excessive hair shedding, but unlike telogen effluvium, hair thinning is usually noticed from the outset. Examination of the scalp shows a widening of the central parting with a diffuse reduction in hair density affecting mainly the frontal scalp and crown. In some women the hair loss may affect a quite small area of the frontal scalp whereas in others the entire scalp is involved, including the parietal and occipital regions. The frontal hairline is typically retained although many women develop a minor degree of postpubertal recession at the temples (equivalent to a Norwood–Hamilton II frontal hairline), whether or not they have diffuse hair loss. Some women have more pronounced temporal recession although in our experience this usually manifests as thinning rather than the complete loss of temporal hair seen in men. Venning and Dawber reported that 13% of premenopausal women had fronto-temporal recession increasing

to 37% in postmenopausal women.[3] In advanced female pattern hair loss (Ludwig III) the hair becomes very sparse over the top of the scalp but a rim of hair is retained along the frontal margin. The vertex balding seen in men is rare in women. On the other hand a 'female' pattern of balding is not uncommon in men. We found that 20 out of 331 balding men (6%) showed a female pattern of hair loss (unpublished observations) and in Asian men the frequency is much higher.[4]

The diagnosis is usually straightforward but other causes of diffuse hair loss may need to be excluded, particularly when the hair loss progresses rapidly. In the presence of overt hair loss a positive tug test should raise the possibility of diffuse alopecia areata. Occasionally, systemic lupus erythematosus can also present in this way. In alopecia areata there may be hair loss in other sites, and other symptoms, such as joint pain, may be present in those suffering from lupus. In difficult cases a biopsy should clarify the diagnosis. The hair loss seen in thyroid deficiency closely resembles female pattern hair loss and may indeed be identical.[5,6] Thyroid deficiency also causes a reversible increase in hair shedding.[7] Rapidly progressive hair loss with oligo- or amenorrhoea and other signs of virilization should prompt measurement of serum testosterone to rule out the rare cases of androgen-secreting tumour. The most difficult differential diagnosis is from telogen effluvium, particularly the chronic form.[8] In some women with female pattern hair loss excessive shedding may be present for months or even years before there is an obvious reduction in hair density and occasionally it develops following typical acute telogen effluvium, suggesting that the shedding episode has revealed a pre-existing trait. A biopsy can be helpful in doubtful cases but needs a pathologist experienced in the interpretation of hair pathology.

Prevalence

Three recent studies from the USA,[9] Korea[4] and the UK[10] have reported on the prevalence of female pattern hair loss. All show an age-related increase in the prevalence (Fig. 1). In the UK study, but not in the other two, this increase became more pronounced in women aged over 50 years. The UK and USA studies show similar frequencies, increasing from 3% to 6% in women aged under 30 years to 29–42% in women aged 70 and over. The frequencies in the Korean study were lower; this study also found a lower frequency of balding in Korean men compared to reported frequencies in European racial groups.

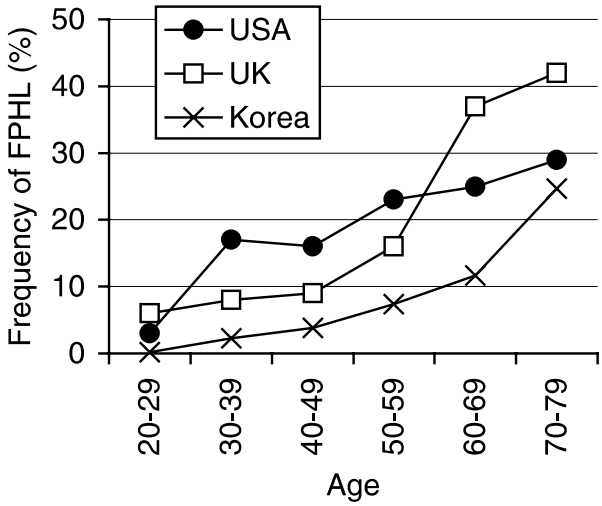

Figure 1 Age related prevalence of female pattern hair loss (FPHL) in the USA, UK and Korea.

Hair density in female pattern hair loss

Using a macrophotographic method in an unselected population sample of 377 women we found that mean hair density on the frontal scalp became progressively lower with increasing age after the age of about 40 years (Fig. 2).[10] Within each age group hair density was normally distributed in the sample and there was substantial overlap in hair densities between those women classified clinically as having hair loss and those without hair loss, an observation that can also be

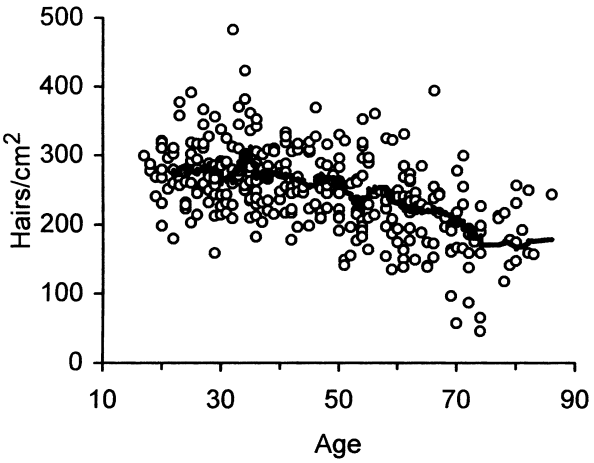

Figure 2 The distribution of hair density by age in an unselected sample of 377 women. Individual hair densities are shown as open circles. The moving average is shown as a solid line. From Birch *et al.*[10]

gleaned from other studies.[11] Low hair density was the major factor in determining whether hair loss was evident but it is apparent that other factors relating to 'hair quality' contribute to the subjective assessment of hair status. This effect is well illustrated by the observation that average hair density is lower in Korean women than in European women,[12] yet the frequency of clinical hair loss in this racial group is apparently much lower.[4] This discrepancy is presumably due to racial differences in other characteristics of the hair which affect its overall appearance. The high frequency of female hair loss reported by Venning and Dawber (87% in premenopausal women) may have been due to their method of wetting and combing the hair, thus minimizing hair 'body', before classifying hair status.[3] Hair diameter is one factor which contributes to the clinical assessment,[10] but there may be others such as curl and hair fibre stiffness.

Genetics

Genetic factors are assumed to predispose to balding in men although their nature and the mode of inheritance are uncertain. Osborn proposed that balding in men and in women is due to a single gene with two alleles, *B* (balding) and *b* (nonbalding).[13] She suggested that balding occurs in homozygous (*BB*) and heterozygous (*Bb*) men but only in homozygous women. Smith and Wells found that first-degree male relatives of women with hair loss showed an increased frequency of balding compared with the male relatives of nonbalding women but they concluded that balding is unlikely to be due to a single gene.[14] This idea was supported by Kuster and Happle in a critique of the published data.[15] They argued that the predisposition to balding is a polygenic trait in which clinical expression represents a threshold effect. As the less frequently affected sex women should require more or stronger balding genes than men. Balding in the male relatives of women with hair loss should therefore be more common than in male relatives of balding men. This idea, which assumes that male and female patterns of balding are the same condition, has yet to be tested, although the normal distribution of hair density in the female population strongly supports the idea that hair density is determined as a multifactorial trait.

Histopathology

Male balding involves a change in the hair cycle and a change in the size of hair follicles. The mean duration of anagen falls so that hairs become shorter. In some men there is also a prolongation of the latent period of the hair cycle (the period between shedding of the club hair and onset of the next anagen) giving rise to an increase in the number 'empty' follicles.[16] The fall in anagen duration predominates so that the overall effect is a shortening of the hair cycle. Terminal hair follicles on the scalp also become miniaturized, a change generally thought to occur gradually over the course of several hair cycles. These changes are reflected histologically by an increase in the proportion of follicles in telogen and an increase in the vellus : terminal ratio. The more limited information available on female pattern hair loss indicates that the histological features are similar, if not identical, to those of male balding.[17] Mean hair diameters are lower in women with hair loss than in those with normal hair density.[6,11] This observation is generally taken to indicate a progressive reduction in the diameter of individual hairs with falling hair density. However, this interpretation may be incorrect. Low hair density in women is associated with a smaller number of terminal hairs of all diameters but with a proportionately greater reduction in the number of large diameter hairs.[10] We suggested that the fall in mean hair diameter with increasing hair loss may be due to preferential loss of large diameter hairs rather than a reduction in the size of hairs produced by individual follicles. The number of 'vellus' hairs is the same or only slightly increased in women with low hair density. Thus, if miniaturization does occur in female pattern hair loss it may be a relatively rapid process, possibly occurring within the space of a single hair cycle.

Is female pattern hair loss androgen-dependent?

Hamilton showed that testosterone is necessary for the development of male balding.[18] His inspired ideas arose at least partly from case reports of balding in women with virilizing ovarian tumours.[19,20] Although there are no systematic studies, clinical experience suggests that balding is common in women with hyperandrogenism, where it is often associated with other features of androgen excess such as hirsutes and oligo- or amenorrhoea. Balding can occur rapidly if the cause is an androgen-secreting tumour. The anecdotal view is that hyperandrogenism is more commonly associated with a male pattern of balding, i.e. frontal recession and vertex balding. However, many hyperandrogenic women show a female pattern of hair loss and those with a male pattern do not always have androgen excess.

Several groups have examined circulating androgen levels in women with scalp hair loss. A reduced level of

sex hormone-binding globulin (SHBG) compared to control values, leading to elevated levels of free androgens has been the most consistent finding.[11,21–23] Vexiau and colleagues found that SHBG levels correlated inversely with the severity of the alopecia.[23] Two studies found significant elevations of the androgen metabolites 5α-androstane-3α,17β-diol glucuronide (3α-AdiolG), 5-androstene-3β,17β-diol sulphate and 5α-androstane-3α,17β-diol sulphate.[23,24] 3α-AdiolG levels correlated with the severity of alopecia. Not all women with hair loss show biochemical evidence of hyperandrogenism. In Vexiau's study 23% of women with alopecia alone and 16% of women with both alopecia and hirsutism had normal hormonal profiles.[23] In the earlier study by Futterweit and colleagues 67 out of 109 women with hair loss (61%) had normal androgen levels.[22] Elevated androgen levels were seen in 79% of women with hirsutism or menstrual disturbance as well as hair loss but in only 16% of those with hair loss alone. Schmidt and colleagues found no significant elevation of circulating androgens in 46 women with hair loss although they did detect elevated levels of thyroid stimulating hormone in this group.[25] Other observations have further questioned the role of androgens in female pattern hair loss. Norwood described families where female pattern hair loss appeared to be inherited independently of male balding,[26] and in a single case report female pattern hair loss occurred in a young woman who lacked circulating androgens or other signs of postpubertal androgenization.[27] The 5α-reductase inhibitor finasteride is effective in the treatment of male balding but, in a randomized controlled trial, failed to prevent the progression of hair loss in postmenopausal women with female pattern hair loss and normal androgen levels.[28] Taken together these observations suggest that androgens play a role in female pattern hair loss but that androgen-independent mechanisms are also involved in some women.

Management

Female pattern hair loss may be considered a biologically normal ageing process. In contrast with the prevailing attitude to male balding, however, society generally regards it as abnormal for women to lose their hair. Consequently the adverse effect of balding on quality of life tends be more severe in women than in men. As a group, women seeking medical advice for their hair loss experience more negative body-image feelings, more social anxiety, poorer self-esteem and psychosocial well-being than control subjects with nonvisible skin disease, as well as dissatisfaction with their hair. In quality of life studies, individual responses were more related to self-perception of hair loss than to objective or clinical ratings and those women most distressed by hair loss were more poorly adjusted and had a greater investment in their appearance.[29,30] The physician managing patients with female pattern hair loss needs to be alert and sensitive to these issues and needs counselling and psychotherapeutic skills which go beyond merely prescribing treatment.

Nevertheless, some women are content to be reassured that their hair loss is not a manifestation of a serious disease and that it is very unlikely that they will go bald. For those who are keen to be treated there are two medical options: anti-androgens and minoxidil lotion. In both cases it should be stressed that treatment will, at best, produce only a modest increase in hair density and that it is not possible to fully reverse hair loss. Furthermore, in those who respond, treatment probably has to be continued indefinitely to maintain the response.

Anti-androgens

The androgen receptor blocker cyproterone acetate has been widely used in Europe to treat female pattern hair loss, usually in a cyclical regimen in combination with Dianette™, but its effectiveness has not been studied in a randomized blinded trial. In a trial of cyclical treatment with cyproterone acetate in women with serum ferritin levels above and below 40 μg/L (10 subjects in each group) hair densities increased by about 15% in the high ferritin group after 1 year of treatment whereas the low ferritin group failed to respond.[31] Hair densities in an untreated control group fell by about 7% after 1 year. In a trial of the anti-androgen, spironolactone, women receiving spironolactone showed less hair loss than an untreated control group after 1 year but did not have more hair than at baseline.[32] Anti-androgen treatment is not without problems. Dose-related side-effects of cyproterone acetate, including weight gain, fatigue, loss of libido, mastodynia, nausea, headaches and depression, are common. Cyproterone acetate is potentially hepatotoxic and liver function tests should be performed periodically. The main side-effects of spironolactone are breast soreness and menstrual irregularities.

Minoxidil

Minoxidil was introduced in the early 1970s as a systemic treatment for hypertension. A high proportion of patients taking oral minoxidil develop hypertrichosis

which is not confined to androgen-dependent sites. This led to the use of a topical formulation, initially for the treatment of male balding. A 2% formulation of minoxidil lotion is now licensed for the treatment of hair loss in women in most European countries. Trials in female pattern hair loss using hair counts as a primary endpoint have shown a mean increase in hair growth of 15–33% in the minoxidil-treated groups compared with 9–14% in the vehicle control groups.[33–35] One small study using hair weight as the endpoint found an increase of 42.5% in hair weights in the minoxidil group compared to 1.9% in the controls.[36] In the investigator and subject assessments minoxidil was superior to the vehicle but about 40% of subjects appeared not to respond to minoxidil.[34,35] None of the trials has been extended beyond 32 weeks and the long-term results of minoxidil treatment are uncertain. In men the beneficial effects on hair growth are lost rapidly on cessation of treatment and it is likely that the same is true in women. The increase in hair counts following treatment with minoxidil lotion is noticeable within 8 weeks and has peaked after 16 weeks. It is unlikely that this rapid increase in terminal hair counts can be explained by reversal of follicular miniaturization; a more plausible explanation is that minoxidil triggers follicles in a latent phase of the hair cycle into anagen.

Minoxidil is a safe treatment. Some patients complain that it leaves unsightly deposits on the hair. Occasionally it causes scalp irritation which may be severe enough to cause a temporary increase in hair shedding and patients should be warned about this. Hypertrichosis on the face and on more remote sites has been reported, particularly when higher concentrations of minoxidil are used.[37] This resolves if treatment is stopped.

In the authors' experience minoxidil lotion is more reliably effective and better tolerated than anti-androgen treatment. The gains are modest and it is helpful to have an objective measure, such as serial standardized clinical photographs, to convince the patient (and the physician) of the response.

Hair surgery

Hair transplantation is a well-established treatment for male balding. It is increasingly being used in female hair loss although the expense and trauma mean that only a small minority of women pursue this avenue of treatment. Surgery is most suited to those women in whom hair loss is limited in extent and who fail medical treatment. A skilled surgeon is essential for good results.

Finally, we should be aware that the distress caused by female pattern hair loss means that some women are prepared to go to great lengths in search of effective treatment (the same is true of male balding), making them vulnerable to exploitation by the unscrupulous. The physician has an important role in explaining the reality of what can be achieved by treatment and dissuading the sufferer from indulging in illusory and expensive 'cures'.

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References

1 Ludwig E. Classification of the types of androgenetic alopecia (common baldness) occurring in the female sex. *Br J Dermatol* 1977; **97**: 247–54.
2 Snyder LH, Yingling HC. Studies in human inheritance XII. The application of the gene-frequency method of analysis to sex-influenced factors, with especial reference to baldness. *Hum Biol* 1935; **7**: 608–15.
3 Venning VA, Dawber RP. Patterned androgenic alopecia in women. *J Am Acad Dermatol* 1988; **18**: 1073–7.
4 Paik JH, Yoon JB, Sim WY *et al.* The prevalence and types of androgenetic alopecia in Korean men and women. *Br J Dermatol* 2001; **145**: 95–9.
5 Saito R, Hori Y, Kuribayashi T. Alopecia in hypothyroidism. In: Kobori T, Montagna, W, eds. *Biology and Disease of the Hair*. Baltimore: University Park Press, 1976: 279–85.
6 Jackson D, Church RE, Ebling FJ. Hair diameter in female baldness. *Br J Dermatol* 1972; **87**: 361–7.
7 Freinkel RK, Freinkel N. Hair growth and alopecia in hypothyroidism. *Arch Dermatol* 1972; **106**: 349–52.
8 Whiting DA. Chronic telogen effluvium: increased scalp hair shedding in middle-aged women. *J Am Acad Dermatol* 1996; **35**: 899–906.
9 Norwood OT. Incidence of female androgenetic alopecia (female pattern alopecia). *Dermatol Surg* 2001; **27**: 53–4.
10 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.
11 Rushton DH, Ramsay ID, James KC *et al.* Biochemical and trichological characterization of diffuse alopecia in women. *Br J Dermatol* 1990; **123**: 187–97.
12 Lee HJ, Ha SJ, Lee JH *et al.* Hair counts from scalp biopsy specimens in Asians. *J Am Acad Dermatol* 2002; **46**: 218–21.
13 Osborn D. Inheritance of baldness. *J Hered* 1916; **7**: 347–55.
14 Smith MA, Wells RS. Male-type alopecia, alopecia areata, and normal hair in women. *Arch Dermatol* 1964; **89**: 155–8.

15 Küster W, Happle R. The inheritance of common baldness: two B or not two B? *J Am Acad Dermatol* 1984; **11**: 921–6.
16 Courtois M, Loussouarn G, Hourseau C *et al.* Ageing and hair cycles. *Br J Dermatol* 1995; **132**: 86–93.
17 Whiting DA, Waldstreicher J, Sanchez M *et al.* Measuring reversal of hair miniaturization in androgenetic alopecia by follicular counts in horizontal sections of serial scalp biopsies: results of finasteride 1 mg treatment of men and postmenopausal women. *J Invest Dermatol Symp Proc* 1999; **4**: 282–4.
18 Hamilton JB. Male hormone is pre-requisite and an incitant in common baldness. *Am J Anat* 1942; **71**: 451–80.
19 Baldwin LG, Gafford JA. Arrhenoblastoma case report. *Endocrinology* 1936; **20**: 373–82.
20 Kantner AE, Ragins AB. Arrhenoblastoma of the ovary. *Am J Obst Gyn* 1941; **42**: 1061–6.
21 Miller JA, Darley CR, Karkavitsas K *et al.* Low sex-hormone binding globulin levels in young women with diffuse hair loss. *Br J Dermatol* 1982; **106**: 331–6.
22 Futterweit W, Dunaif A, Yeh HC *et al.* The prevalence of hyperandrogenism in 109 consecutive female patients with diffuse alopecia. *J Am Acad Dermatol* 1988; **19**: 831–6.
23 Vexiau P, Chaspoux C, Boudou P *et al.* Role of androgens in female-pattern androgenetic alopecia, either alone or associated with other symptoms of hyperandrogenism. *Arch Dermatol Res* 2000; **292**: 598–604.
24 Montalto J, Whorwood CB, Funder JW *et al.* Plasma C19 steroid sulphate levels and indices of androgen bioavailability in female pattern androgenic alopecia. *Clin Endocrinol (Oxf)* 1990; **32**: 1–12.
25 Schmidt JB, Lindmaier A, Trenz A *et al.* Hormone studies in females with androgenic hair loss. *Gynaecol Obstet Invest* 1991; **31**: 235–9.
26 Norwood OT, Lehr B. Female androgenetic alopecia: a separate entity. *Dermatol Surg* 2000; **26**: 679–82.
27 Orme S, Cullen DR, Messenger AG. Diffuse female hair loss: are androgens necessary? *Br J Dermatol* 1999; **141**: 521–3.
28 Price VH, Roberts JL, Hordinsky M *et al.* Lack of efficacy of finasteride in postmenopausal women with androgenetic alopecia. *J Am Acad Dermatol* 2000; **43**: 768–76.
29 van der Donk J, Passchier J, Knegt-Junk C *et al.* Psychological characteristics of women with androgenetic alopecia: a controlled study. *Br J Dermatol* 1991; **125**: 248–52.
30 Cash TF, Price VH, Savin RC. Psychological effects of androgenetic alopecia on women: comparisons with balding men and with female control subjects. *J Am Acad Dermatol* 1993; **29**: 568–75.
31 Rushton DH, Ramsay ID. The importance of adequate serum ferritin levels during oral cyproterone acetate and ethinyl oestradiol treatment of diffuse androgen-dependent alopecia in women. *Clin Endocrinol (Oxf)* 1992; **36**: 421–7.
32 Rushton DH, Futterweit W, Kingsley D *et al.* Quantitative assessment of spironolactone treatment in women with diffuse androgen-dependent alopecia. *J Soc Cosmet Chem* 1991; **42**: 317–25.
33 Olsen EA. Topical minoxidil in the treatment of androgenetic alopecia in women. *Cutis* 1991; **48**: 243–8.
34 Whiting DA, Jacobson C. Treatment of female androgenetic alopecia with minoxidil 2%. *Int J Dermatol* 1992; **31**: 800–4.
35 Jacobs JP, Szpunar CA, Warner ML. Use of topical minoxidil therapy for androgenetic alopecia in women. *Int J Dermatol* 1993; **32**: 758–62.
36 Price VH, Menefee E. Quantitative estimation of hair growth. I. androgenetic alopecia in women: effect of minoxidil. *J Invest Dermatol* 1990; **95**: 683–7.
37 Peluso AM, Misciali C, Vincenzi C *et al.* Diffuse hypertrichosis during treatment with 5% topical minoxidil. *Br J Dermatol* 1997; **136**: 118–20.