The balding woman

Premature or extensive hair loss in a woman can cause considerable distress. An important part of management involves patient counselling regarding pathogenesis and treatment options, so that realistic outcomes can be achieved.

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As evidenced by the amount of time and money spent at hairdressing salons and on hair care products, a full, healthy head of hair is crucial to most women's feelings of attractiveness, their sexuality and even gender identity. As a result, androgenetic alopecia (hair thinning), which is a normal physiological occurrence, can lead to a great deal of anxiety and distress if it is premature or extensive. This can have a significant impact on a woman's self-esteem and psychological wellbeing. Most women tend to present for treatment if hair loss occurs prematurely or is exaggerated.

Androgenetic alopecia is as common in women as it is in men. The pattern of inheritance is polygenic. It appears it can be inherited from either parent. This genetic predisposition plus sufficient circulating androgens are prerequisites for the progressive miniaturisation of scalp follicles that characterises this condition. Thinning of the hair usually begins between the ages of 12 and 40 years in both sexes.

The diagnosis of female androgenetic alopecia is essentially a clinical one, after exclusion of other causes of nonscarring diffuse hair loss. Appropriate treatment can be offered based on an understanding of the pathogenesis of this condition.

The hair cycle

To understand the terminology used in describing hair disorders it is necessary to have a basic understanding of the hair growth cycle. In scalp hairs, the phase of active growth, called anagen, lasts two to five years. This is followed by a transition phase of a couple of weeks, where the hair spontaneously stops growing. This phase is known as catagen. The hair then goes into a three-month resting phase known as telogen. The telogen, or club hair, is retained in the follicle with its white bulb until the new anagen phase starts. The new growing hair then pushes the old hair out, and the old hair is shed. It is normal to lose 100 telogen hairs each day.

Pathogenesis

The cause of androgenetic alopecia in women is the same as in men (Figure 1). In genetically predisposed areas of the scalp, terminal hairs are progressively replaced by finer, shorter and ultimately nonpigmented hairs over successive growth cycles. This progressive minaturisation and shortening of the duration of the anagen growth phase is a consequence of the action of circulating androgens, particularly dihydrotestosterone (DHT).

IN SUMMARY

- **Androgenetic alopecia affects the majority of women progressively as they age.**
- **Approximately 50% of women will experience significant hair loss by the age of 60. This is a normal physiological occurrence, but it is usually well disguised by hair styling in women so its frequency is underestimated in the general community.**
- **The pattern of hair loss in women is commonly diffuse, but it tends to be most marked over the crown with retention of the frontal hairline.**
- **Endocrine function is normal in most women with androgenetic alopecia.**
- **The realistic aim of currently available treatments is to prevent or delay further hair loss; however, some improvement may be seen in up to 50% of patients after six to 12 months of therapy.**

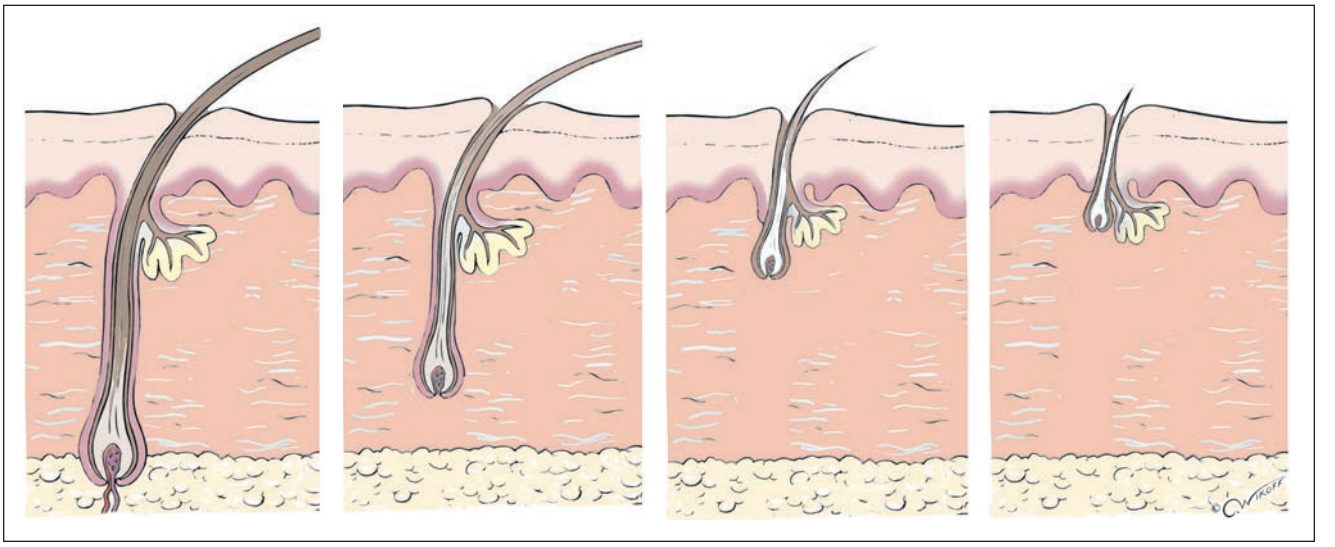

Figure 1. Dihydrotestosterone acts on receptors in the dermal papilla cells to progressively shorten the duration of each anagen growth cycle and miniaturise genetically predisposed scalp follicles.

The enzyme 5α-reductase is found in the dermal papilla cells and converts testosterone to the more active DHT. These cells also possess receptors for DHT. The highest levels of both DHT receptors and 5α-reductase are found in those regions of the scalp in which androgenetic alopecia develops.

In men, all follicles that are genetically predisposed to undergo this process will do so because there is sufficient circulating testosterone to act as substrate for conversion to DHT. In premenopausal women, however, normal levels of circulating androgen will only induce balding in those who have a strong genetic predisposition. If there is no strong genetic susceptibility, baldness develops in women when androgen production is increased or drugs with androgen-like activity are taken. In most cases, women presenting with androgenetic alopecia will have normal endocrine function, shown by conventional testing of plasma androgens.

Clinical features

The pattern of hair loss in women tends to be different from that in men. In the 1970s, Ludwig described three grades of female androgenetic alopecia (Figure 2). The age of onset is genetically determined and can begin at any age after puberty. The loss tends to occur in fits and bursts over a period of years. It is common for people to go through periods of accelerated hair loss lasting three to six months followed by periods of stability lasting six to 18 months.

The usual presentation is diffuse hair loss that is more marked over the crown with an intact frontal hair line (Figures 3 to 5). However, some degree of frontal and frontoparietal recession may also be seen in women.

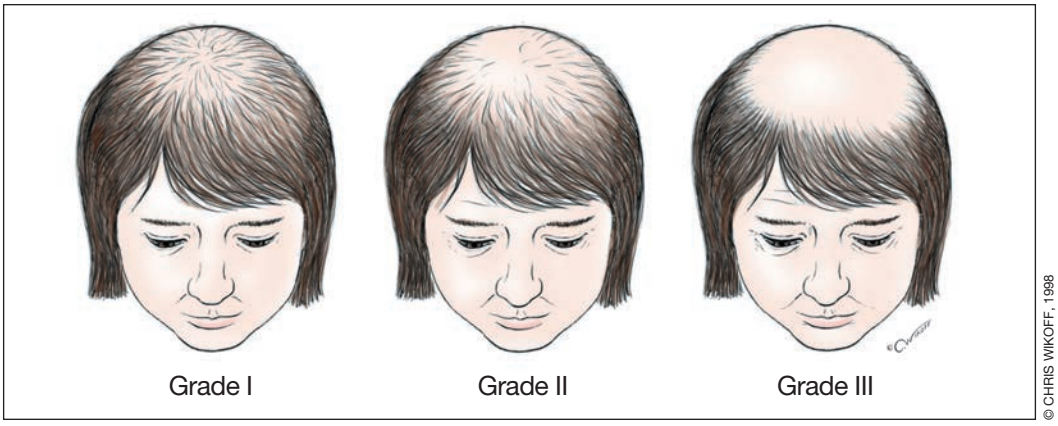

Figure 2. Ludwig classification of female androgenetic alopecia.

Figure 3. Androgenetic alopecia – Ludwig grade I.

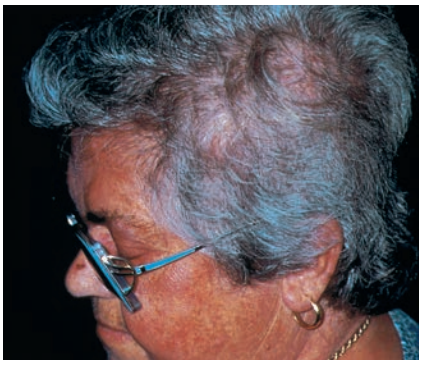

Figure 4. Androgenetic alopecia – Ludwig grade II.

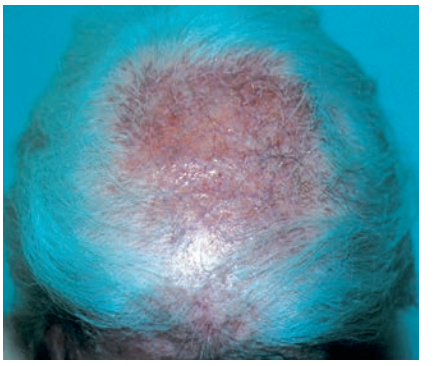

Figure 5. Androgenetic alopecia – Ludwig grade III.

Table 1. Drug causes of diffuse telogen hair loss

Drugs with proandrogen action
Oral contraceptive pill
Testosterone
Danazol
Anabolic steroids
Drugs with antithyroid action
Carbimazole
Propylthiouracil
Amiodarone
Lithium
Drugs with prothyroid action
Thyroxine
Hypolipidaemic agents
Clofibrate
Drugs causing telogen effluvium
Beta blockers (propranolol, metoprolol)
ACE inhibitors (captopril, enalapril)
Anticoagulants (heparin, warfarin)
Oral retinoids (acitretin, isotretinoin)
Allopurinol
Colchicine
Glibenclamide
Cimetidine
Bromocryptine
Levodopa
Sulfasalazine
Penicillamine
Gold
Interferon
Amphetamines

It has been postulated that the decline in oestrogen levels after the menopause, allowing unopposed androgen stimulation, may account for the increased frequency of frontoparietal recession (the so-called male pattern hair loss) seen with increasing age in women. This sign, therefore, is not necessarily a marker for hyperandrogenism; however, significant frontoparietal recession should raise suspicion. Hyperandrogenism should be suspected if the alopecia is of rapid onset (over months to a year as opposed to slowly over many years) or if there is associated menstrual irregularity, hirsutism or acne. An underlying endocrine abnormality is less likely if there is a strongly positive family history of androgenetic alopecia.

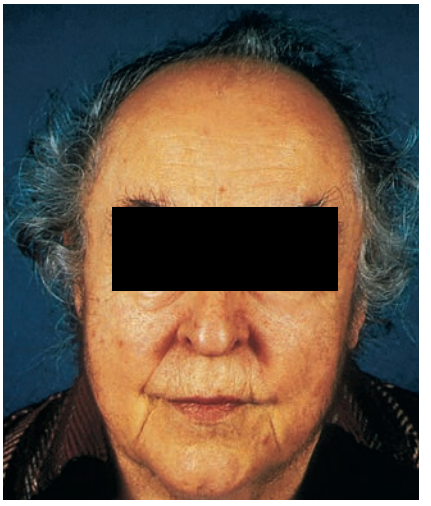

Figure 6. Diffuse hair loss secondary to hypothyroidism.

Differential diagnosis

In men, the diagnosis of androgenetic alopecia is usually straightforward. In women, however, early androgenetic alopecia may present with a diffuse pattern of loss, making it more a diagnosis of exclusion. The box on page 63 lists other causes of diffuse telogen hair loss that need to be considered. Drugs should always be excluded as a possible cause of diffuse hair loss (Table 1). It is important to recognise that other factors, such as iron deficiency, may coexist and aggravate or even unmask an underlying tendency to androgenetic alopecia. Because hair loss may precede other clinical manifestations of thyroid disease (Figure 6), it is always important to perform screening blood tests.

Zinc is important for healthy hair growth. Hereditary zinc deficiency, known as acrodermatitis enteropathica, is due to impaired zinc absorption from the gastrointestinal tract. It manifests in infancy and early childhood and is characterised by the clinical triad of alopecia, an acral dermatitis and diarrhoea. In adults with diffuse hair loss, zinc deficiency should be considered in the setting of prolonged parenteral feeding, malabsorption or diarrhoea, or if there is

other evidence of nutritional disease, such as a high mean corpuscular volume to indicate folate deficiency.

Chronic telogen effluvium is a more recently described cause of diffuse hair loss in women that persists beyond six months. It may follow an acute telogen effluvium, but often no trigger is found. The cause is not known, but it may be due to a change in the dynamics of the hair cycle with shortening of the anagen phase. Patients may give a history of being able to grow their hair very long in childhood, suggesting a long anagen phase. Chronic telogen effluvium is not androgen dependent, does not progress to baldness and does not respond to oral antiandrogen therapy. It tends to follow a fluctuating course over several years before resolving spontaneously.

Investigations

Apart from a directed history and examination, most women do not require investigation for virilisation. It is more important to direct investigations toward excluding other causes of diffuse hair loss, especially in cases of early androgenetic alopecia when the patten of hair loss is not readily apparent. Table 2 outlines an approach to women with diffuse hair loss.

Differential diagnosis of diffuse hair loss

Androgenetic alopecia

History

Gradual onset. May be cyclic increases in hair shedding. If rapid, consider virilisation.

Examination

Widening of the central parting. Preservation of the frontal hair line. Thinning over the crown. Male pattern can occur in postmenopausal women.

Telogen effluvium

History

Dramatic hair loss, about two to three months after a triggering event, such as physical or emotional stress. Self-limiting over three to six months.

Examination

No widening of the central parting. Bitemporal recession can occur. Thinning not usually marked, but if present it occurs all over the scalp. Positive hair pull test equally over the vertex and occiput.

Iron deficiency

History

Iron deficiency may be an aggravating rather than causative factor, especially in androgenetic alopecia.

Examination

Iron deficiency can occur in the absence of anaemia in about 20% of cases. If serum ferritin >60 mg/L and hair loss persists, consider another cause.

Drug-induced hair loss

History

Hair loss tends to begin six to 12 weeks after starting drug treatment. Progressive while the drug is continued.

Examination

Usually diffuse loss. Thinning may be profound. Oral retinoids may induce straight hair to curl.

Thyroid disease

History

Both hyper- and hypothyroidism. Antithyroid medications.

Examination

Hair loss may precede other clinical manifestations. Gradual diffuse loss seen with both hyper- and hypothyroidism. Loss of the outer third of the eyebrows seen in hypothyroidism.

Chronic telogen effluvium

History

Hair loss tends to be distinctive. In women aged between 30 and 50 years. Patients complain of abrupt-onset shedding and hair thinning. Hair blocks shower drain after washing.

Examination

Patients often have a thick head of hair; significant thinning unusual. Bitemporal recession. No widening of the central parting. Positive hair pull test equally over the vertex and occiput. Usually resolves spontaneously over three to four years.

Systemic lupus erythematosus

History

Hair loss occurs especially in the active phase of the disease.

Examination

Diffuse shedding with scalp erythema. Hair is dry, fragile and easily broken. Short unruly 'lupus' hairs may be seen at the frontal margin.

Diffuse alopecia areata

History

Chronic diffuse loss is very rare. There may be a positive past history or family history of this disease.

Examination

May find exclamation mark hairs. Would need supportive histology to distinguish alopecia areata from other causes.

Secondary syphilis

Comments

Secondary syphilis is rare.

Examination

Classically causes the so-called moth-eaten appearance with patchy loss.

Traction alopecia

Comments

Traction alopecia is rare. Due to tight hairstyles.

Examination

May be worse at scalp margins. Short broken hairs and mild circumscribed scarring may be seen.

Clinical features associated with hair loss that necessitate androgen investigations are:

- alopecia of rapid onset
- menstrual irregularity
- hirsutism
- acne.

Table 2. An approach to women with diffuse telogen hair loss

Initial investigations

- Full blood examination
- Iron studies including serum ferritin
- Thyroid function tests
- Urea, electrolytes and liver function tests

Consider if clinically indicated

- Serum zinc
- Antinuclear antibody
- Androgen screen (serum testosterone, serum dihydroxyepiandrosterone sulfate, serum sex hormone binding globulin, free androgen index, LH:FSH ratio)
- Syphilis serology

Scalp biopsy is recommended but not mandatory

Table 3. Contraindications to the use of cyproterone acetate

- Pregnancy or lactation
- A history of jaundice or persistent itch during a previous pregnancy
- Hepatic diseases
- A history of, or existing, hepatic tumours
- Severe chronic depression
- Previous, or existing, thromboembolic processes
- Severe diabetes with vascular changes
- Sickle cell anaemia

The hair pull test

The hair pull test is a simple clinical test that allows you to determine if abnormal hair loss is occurring and its distribution. With the thumb and forefinger, a clump of hairs is grasped near the scalp. Firm traction is applied as the hand slides along the hair from the base to the tip. This is repeated at a number of sites over the scalp. Normally, after five or six passes only two to five hairs should have come out. In a telogen effluvium, up to 30 hairs may come out. Telogen hairs can be recognised by the small white bulb at the root.

Treatment

Conservative management

For mild androgenetic alopecia, camouflage alone may suffice. A good hairdresser can provide advice about cutting and styling techniques to minimise the thinned area over the crown. To give the illusion of thicker hair, camouflage treatments that dye the scalp can be used. Pressurised sprays containing dyes mixed with a holding hair spray can be sprayed onto the base of the hair after it has been dried and styled.

In cases of extensive alopecia, a wig should be considered. These can be made from synthetic acrylic fibre or natural fibre (most commonly human hair). A good wig can look very natural and can be styled and washed. The Alopecia Areata Support Association (PO Box 89, Camberwell VIC 3124; phone 03 9513 8580) can give excellent advice on wigs and wigmakers. Hair transplantation can also be an option in women.

Medical management

Pharmacological treatment options for women include topical minoxidil and oral antiandrogens (spironolactone and cyproterone acetate). When you are prescribing these treatments it is important to counsel patients realistically: overall the aim is to reduce hair shedding, any significant regrowth being a bonus. The effects are generally not noted for four to six months and tend to continue for only as long as the treatment is used. My practice is to suggest that oral antiandrogen therapy be continued for at least 12 to 24 months and then tapered off over a further 12 months. Both antiandrogens tend to be well tolerated, and few patients have to cease treatment because of side effects.

Although finasteride has revolutionised the treatment of balding in men, unfortunately it has not proven so useful in women. It is contraindicated in women who are or may become pregnant, because 5α-reductase inhibitors may cause abnormalities of the external genitalia of male fetuses. A recent large clinical trial found that finasteride did not work in postmenopausal women.

Minoxidil

Minoxidil (Regaine Topical) is a vasodilator originally developed to treat hypertension but found to induce hypertrichosis. It comes as a 2% and a 5% solution. A more rapid initial response may be seen with the 5% concentration; however, whether this provides any additional benefit in the longer term remains controversial. Retinoic acid has

been added, theoretically to try to aid penetration, but the benefits are minimal and it tends to increase irritation. Minoxidil can be used alone or as an adjunct to systemic antiandrogen therapy.

One millilitre of minoxidil should be applied to the thinning area and gently massaged into the scalp twice daily. The scalp should be dry when it is applied and kept dry for one hour after the application. This can be a drawback for many women because it can make their hair harder to style.

It is useful to warn people that they may notice increased shedding initially as resting telogen hairs are stimulated to re-enter anagen. If this does occur, it is usually a sign that the patient's hair will respond. Good responses are also more likely early in the course of the alopecia.

Hair regrowth can usually be detected at four to eight months but sometimes not until 12 months, so it is worth persisting this long. Generally, no further regrowth is seen after about 12 to 18 months. Hair loss will stabilise in about 50% of users; significant regrowth can be seen in an additional 10%. If the treatment is stopped, the new hairs will fall out, with regression to the pretreatment state in about six months. For this reason, if the patient feels she has benefited from minoxidil, it needs to be continued indefinitely to maintain this response.

Pruritus, irritant contact dermatitis and occasionally allergic contact dermatitis may develop with minoxidil use. Contraindications include any known hypersensitivity to minoxidil, propylene glycol or ethanol. Because there is minimal systemic absorption, hypotension is not a problem. Women are more likely than men to develop hypertrichosis on the face (in 3 to 5% of cases with the 2% solution and higher with the 5% solution). The hypertrichosis tends to diminish or disappear after about one year, even with continued use, and it resolves within one to six months after the drug is stopped. The reason for this is not clear.

Spironolactone

Spironolactone (Aldactone, Spiractin) is a weak competitive inhibitor of androgen binding. It also decreases androgen production and secretion from the ovaries and adrenals. The oral dose is 100 to 200 mg per day. The therapeutic benefit tends to plateau at about 12 to 18 months, after which it is worth trying to slowly titrate to the lowest efficacious dose.

There have been few trials of this drug in androgenetic alopecia, but clinical experience suggests it tends to slow progression of balding without significantly reversing the process. Hair loss is retarded in around 60 to 70% of women; regrowth occurs in only 10 to 20%.

As menstrual irregularity can be a side effect, concurrent administration of the oral contraceptive pill (preferably one with minimal androgenic effects, such as those containing desogestrel,

norethisterone or cyproterone acetate) can help control this. Women of childbearing age should be warned against becoming pregnant while on spironolactone because of the risks of feminising a male child. Because this drug inhibits aldosterone-related potassium excretion by the kidney, patients should be advised to avoid potassium supplements and excessive intake of beverages that can act as diuretics (e.g. tea and coffee). Renal function should be checked at baseline and at six-monthly intervals. Other side effects can include breast tenderness, lethargy and mild postural dizziness, but these tend to subside after one to two months of treatment.

Cyproterone acetate

Cyproterone acetate (Androcur, Cyprone, Procur) is a systemic antiandrogen that inhibits gonadotrophin secretion. The response rates are similar to those seen with spironolactone and, again, trial data with this drug in the treatment of androgenetic alopecia are lacking.

In premenopausal women, to prevent pregnancy and control menstrual irregularity, cyproterone acetate should be combined with a low dose oral contraceptive and given in a dose of 50 to 100 mg on days 5 to 15 of the menstrual cycle. Doses lower than 100 mg per day tend not to work as effectively. In postmenopausal women or women who have had a hysterectomy, it may be given continuously or as the progestogen in a hormone replacement therapy regimen in older women.

The full blood count, electrolytes and liver function should be checked before treatment and at least three monthly during treatment. In patients with diabetes, carbohydrate metabolism should be monitored carefully. Side effects can include weight gain, fluid retention, decreased libido and tiredness. Contraindications to the use of cyproterone acetate are listed in Table 3.

Conclusion

Androgenetic alopecia will affect most women as they age. If it is premature or extensive, it can cause considerable distress and loss of self-esteem. The diagnosis is generally a clinical one, after excluding other causes of diffuse hair loss. An important part of management involves patient counselling regarding pathogenesis and treatment options. MT

Suggested reading

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