Male pattern androgenetic alopecia

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Untreated hair loss progresses at a rate of 5 to 10% per year, but the onset of hair loss and the rate of progression vary from person to person. Reduced self-esteem, loss of confidence, anxiety and depression may occur in affected men.

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Male pattern androgenetic alopecia, or common baldness as it is also known, affects about 50% of Caucasian males by the age of 50 years. By the age of 80 years, over 95% of Caucasian males are affected to some degree.[1] Often considered a secondary sexual characteristic, hair loss can have significant psychosocial manifestations, especially when the hair loss is severe and premature. Reduced self-esteem, loss of confidence, anxiety and depression may occur in affected men.[2]

AETIOLOGY

Androgenetic alopecia is familial, with heredity accounting for about 80% of the predisposition to baldness.[3] Diet, lifestyle, stress and other environmental factors are relatively unimportant. An inherited susceptibility is a prerequisite and androgens initiate and perpetuate the hair loss.

Genetics

The inheritance of androgenetic alopecia is polygenic. Up to five separate genes are likely to influence susceptibility, age of onset, rate of progression and dominant pattern of hair loss. The first gene association identified is a polymorphism of the androgenic receptor gene on the X chromosome. The X chromosomal location of the androgenic receptor gene indicates that the maternal line is the major inheritance of androgenetic alopecia in men. However, family studies have shown resemblance of hair loss between fathers and sons, which cannot be explained by androgenic receptor gene mutations.

Additional autosomal gene associations that also contribute to the phenotype have now been identified. Unconfirmed associations of several other gene loci with male androgenetic alopecia have been reported with the 5α-reductase type II gene (SRD5A2)[4] and the ectodysplasin A2 receptor gene (EDA2R).[5] One study reported linkage mapped to chromosome 3q26 in a genome-wide scan,[6] and two independent genome-wide association studies reported a susceptibility locus for male androgenetic alopecia at chromosome 20p11, which contains two nonfunctional polymorphisms within a gene-poor region.[7,8] Causative genes responsible for the linkage reported in these genome-wide studies have not been identified and therefore the implications of these findings are yet unknown. Selected single nucleotide polymorphisms of the human hairless (HR), 5α-reductase type I

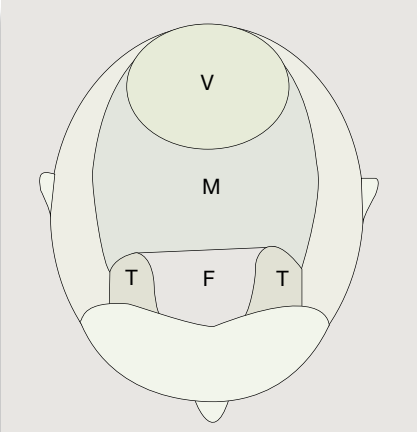

Figure 1. Areas of the scalp. F = frontal; M = midfrontal; T = temple; V = vertex.

(SRD5A1), aromatase (CYP19A1), oestrogen receptor-α (ESR1), insulin-like growth factor-2 (IGF-2) and insulin genes, as well as the nonrecombinant region of the Y chromosome, have also been examined but no apparent association with male androgenetic alopecia was found.[9-11]

The role of androgens

The role of androgens in male-pattern hair loss is well established. Castrated males do not develop androgenetic alopecia unless treated with testosterone.[12] In most body sites, hair growth is mediated by 5α-dihydrotestosterone, a potent metabolite of testosterone that has a several-fold higher avidity for the androgen receptor. The conversion of testosterone to dihydrotestosterone is catalysed by 5α-reductase. Higher concentrations of 5α-reductase activity have been observed in men with bald scalps. The importance of 5α-reductase activity is supported by the absence of temporal regression and baldness in cases of 5α-reductase deficiency caused by mutations in the 5α-reductase gene.[13] Moreover, 5α-reductase inhibitors can halt the progression of hair loss.

CLINICAL FEATURES

The hallmark of androgenetic alopecia is hair miniaturisation in a characteristic distribution over the scalp. In male pattern androgenetic alopecia, large terminal hairs are replaced by small vellus hairs. This miniaturisation is only partially reversible.[14] Early treatment is associated with superior regrowth.[15]

The three most commonly affected areas are the temples, vertex scalp and midfrontal scalp (Figure 1). The occipital hair is usually preserved (Figure 2). The hair loss progresses in an orderly fashion as described by Hamilton and Norwood.[14,16] Untreated hair loss progresses at a rate of 5 to 10% per year; however, the onset of hair loss and the rate of progression vary from person to person.

TREATMENT

There are a number of medical treatments currently available for androgenetic alopecia that will arrest progression and stimulate partial regrowth. Maintenance therapy is required. Regrowth is more likely when the treatment is initiated early. When the hair loss is advanced, hair transplantation surgery may be combined with medical therapy to repopulate the bald vertex and frontal scalp with hair from the occipital scalp.

Medical treatment

Minoxidil

Oral minoxidil was first used to treat hypertension in the 1960s.[17] Hypertrichosis was said to occur in 100% of people taking oral minoxidil.[18-20] This observation led to the development of topical minoxidil as a treatment for hair loss.[21]

The exact mechanism of action of minoxidil on hair growth is unknown. Original postulates of an increase in cutaneous blood flow[22] and effect on the cell cycle to initiate the onset of anagen[23] have now been discounted and the current theory centres around a direct effect on potassium channels within hair matrix cells.[23,24]

Currently, the 5% minoxidil solution is available in Australia and twice daily use is recommended. Scalp irritation is a frequent side effect; however, allergic contact dermatitis is uncommon.[25,26]

The 5% minoxidil foam was released in Australia in November 2010. In clinical trials it demonstrated equivalent efficacy to the solution but was less irritating and easier to apply. A five-year follow-up study with topical minoxidil has shown a sustained effect.[27] It is not uncommon for patients to observe increased hair shedding a few weeks after starting therapy; this resolves spontaneously within a few weeks with continued treatment. Cessation of treatment results in loss of all new hairs. Hypertrichosis on the temples and face is another common side effect and can be managed by reducing the quantity of minoxidil applied to the scalp or the dosing frequency to once daily use.

Finasteride

Finasteride is a type II 5α-reductase inhibitor that reduces the synthesis of dihydrotestosterone.[28] The optimal dose of finasteride in the treatment of androgenetic alopecia is 1 mg a day. Placebo-controlled studies have shown that finasteride significantly increases hair count after one and two years of therapy and the effect is sustained after five years of therapy.[15,29-31] In comparative studies, treatment with oral finasteride resulted in more hair growth than topical minoxidil.[32] Good quality serial photographs (pre- and post-treatment) help both the patient and clinician to objectively assess the response to finasteride.

Decreased libido, erectile dysfunction and ejaculatory problems have been reported in about 1 to 3% of men taking finasteride, but these effects are fully reversible on discontinuation of treatment.[33] Painful gynaecomastia occurs in approximately one in 10,000 men and is also reversible on discontinuation.[34] Rare case reports of exfoliative dermatitis, testicular pain and depressive mood changes are of uncertain significance.[35,36]

Ketoconazole

Ketoconazole is an imidazole antifungal and a weak androgen receptor antagonist. When topical ketoconazole is used

off-label for androgenetic alopecia in conjunction with oral finasteride, it may help achieve more complete reduction of dihydrotestosterone.[37,38] One small, open-label study of minoxodil 2% and ketoconazole 2% shampoo for androgenic alopecia in men showed comparable hair growth in both groups, with both achieving better growth than unmedicated shampoo alone.[39] However, larger, controlled studies are needed before ketoconazole can be recommended to patients.

Surgical treatment with hair transplantation

Hair transplantation involves removal of hair from the occipital scalp and re-implantation into the bald vertex and frontal scalp. Prerequisites are stabilisation of the hair loss with medical treatment and a good donor hair population on the occipital hair.

Follicular unit hair transplant is the preferred technique.[40] Donor hair is harvested either by 1 mm punch biopsies or by removing a strip of occipital scalp that is then microdissected into follicular units under a dissecting microscope. Each unit is then individually reinserted into the bald scalp using a microblade. Experienced operators achieve graft survival in excess of 90% with this technique.

Complications are rare with this procedure. Early postoperative problems include periorbital swelling from tumescence of the frontal scalp approximately two to three days' postprocedure, which usually improves with use of postoperative prednisone. A folliculitis can occur in follicles that have been buried too deeply; this usually resolves spontaneously or can be treated with deroofing using a hypodermic needle.

Widened donor site scars can occur with excessive donor wound tension and local tissue trauma, including follicular transaction. Careful surgical technique is required to not injure the donor site follicles. Limiting the width of the harvested strip to 1 to 2 cm reduces wound tension.

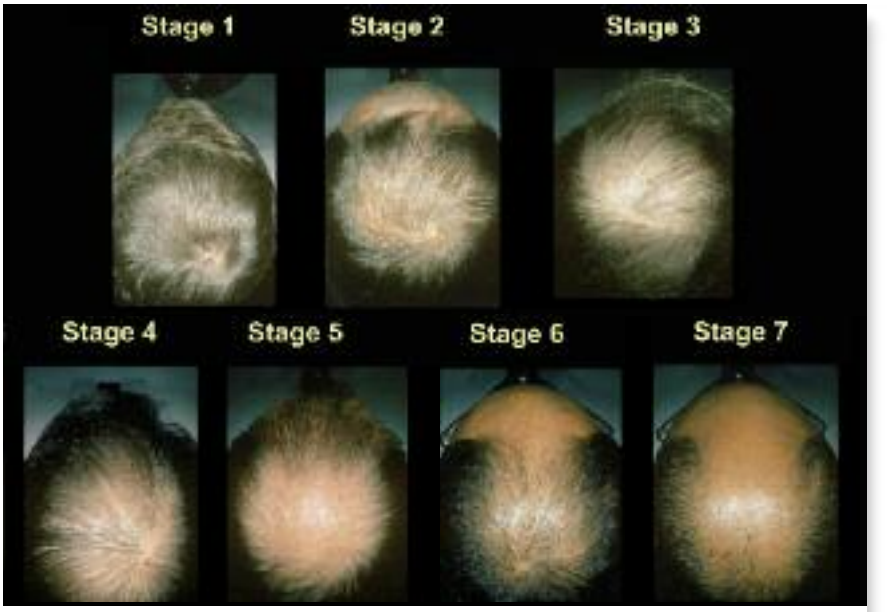

Figure 2. Progressive hair loss in the crown in advancing stages, with relative sparing of the occipital hair.

Combination of medical and surgical therapy

Combination of medical and surgical therapy enhances efficacy in men with androgenetic alopecia. An open, randomised, parallel-group study comparing the efficacy of available medications as monotherapy or as combined therapy showed that oral finasteride in combination with either topical minoxidil or ketoconazole had significantly better hair regrowth than oral finasteride monotherapy, and no difference in the incidence of side effects.[41] Topical minoxidil and oral finasteride are important adjuncts to hair transplant surgery. The use of topical minoxidil pre-hair transplant surgery has the advantage of stabilising the hair loss, increasing the number of hairs in anagen and decreasing postsurgical telogen effluvium.[42] Minoxidil should be stopped two to three days before surgery to minimise skin irritation and reduce the theoretical risk of intraoperative bleeding caused by vasodilation. Therapy should be restarted again after one to two weeks.

Follow-up treatment with oral finasteride protects the hairs surrounding the transplant from further recession, reducing the need for second and third transplants five to 10 years after the initial procedure.

CONCLUSION

Androgenetic alopecia is a common and progressive condition. Current treatments with topical minoxidil and oral finasteride are effective in arresting hair loss progression, and stimulate partial regrowth of hair. For patients who present with early hair loss, medical treatment usually suffices, whereas patients who present with more advanced hair loss may require a combination of medical and surgical treatment to achieve the best result. MT

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A list of references is available on request to the editorial office.

COMPETING INTERESTS: Professor Sinclair was convener of the World Congress of Hair Research in 2010. Johnson and Johnson (the makers of minoxidil) and Merck Sharp and Dohme, (the makers of finasteride) and Bosley hair transplantation group were all conference sponsors. Dr Asgari: None.

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