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A REVIEW ARTICLE ON THE PATHOGENESIS AND DIAGNOSIS OF ANDROGENETIC ALOPECIA

Dermatology

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KEYWORDS

INTRODUCTION

Male pattern baldness, also referred to as androgenetic alopecia (AGA), is a prevalent type of progressive alopecia, and it is caused by a hereditary disorder of the androgen receptors in hair follicles. AGA is a multigenic disorder that can present in a range of severities, at different ages, and at various locations on the scalp. Hair loss in men, on the other hand, tends to occur in the temporal and vertex regions while sparing the occipital region, and therefore produces the classic "horseshoe"pattern.(1)

The development of AGA was also described by Hamilton in 1951 as the result of a "mutual interplay of androgens, genetic and age variables". Hamilton's studies on castrated men have shown that both androgens are necessary for common baldness, and that AGA may be initiated in castrated male with injections of testosterone(.2)

These changes are still poorly understood, limiting the current treatments.

Genetic predisposition to AGA is crucial. More than 80% of monozygotic twins have the same genes, according to twin studies. The risk of AGA is greater in males whose fathers were bald, but the risk is decreased in men whose fathers had no balding. Nonetheless, women having a positive genetic history of AGA also have a greater risk of getting it. Through multiple generations, this transmission implies the involvement of a single main gene.(1)

PATHOGENESIS

Androgenetic Alopecia (AGA) is defined by a progressive shrinkage of the hair follicle as a result of a change in hair growth physiology that leads to vellus change of the end hair follicle. The active development phase (anagen) of the regular hair physiology can last anywhere from two to seven years. After then, there is a small period of regression (catagen) that lasts 1 or 2 weeks, followed by a resting stage (telogen) that lasts anywhere from 5 or 6 weeks to roughly hundred days. A spurge of cell death happens in most of follicular keratinocytes during the catagen phase, coinciding with the cessation of pigment production as well as the condensation of dermal papillae. Dermal papillae shift upward as a result of this. The hair body grows as a club (vellus) hair during the telogen phase. As a effect of combing as well as washing, the hair eventually falls out, and the anagen stage starts again.(3)

The time of the anagen stage diminishes as AGA progresses, but the telogen phase lengthens. The highest length of the newer anagen hair gets smaller than that of before hair as the time of the anagen stage dictates hair length, leading to shrinkage and finally baldness.(3)

Mesenchyme-derived skin papillae have been shown in the last two decades to play a key role in hair growth, with multipotent dermal stem cells at the tip stimulating both expansion and differentiation. Other autocrine and paracrine proteins and signalling pathways affect this bridge between papillary dermis and follicular stem cells.(3)

There are a lot of tissues in the skin that break down testosterone, as well as lesser androgens like dehydroepiandrosterone as well as androstenedione. DHT is produced in the cytoplasm by the enzyme 5a reductase, which converts testosterone to dihydrotestosterone (DHT). Upon binding DHT to the androgen receptor (AR), it is transported to the nucleus via AR coactivators, where it activates gene expression. Target gene transcription and translation result in the production of genes with biological activity. (Fig.1).(3)

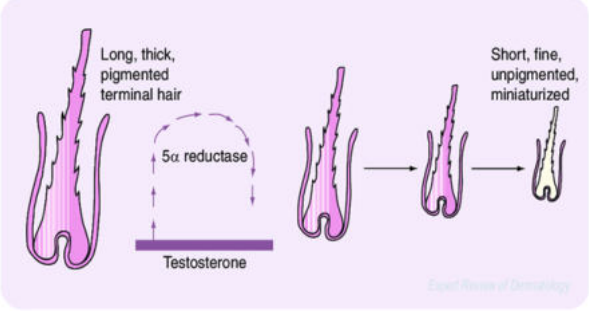

Figure1. Pathogenesis of Androgenetic alopecia.(4)

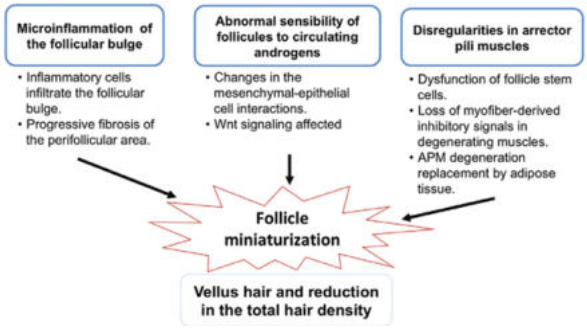

Figure2. Factors involved in pathogenesis.(5)

Dermal papillae release a variety of chemicals, resulting in bridge among the papillae as well as hair follicular cells when androgens are present. These have an autocrine effect on the dermal papillae and a paracrine effect on the hair follicle epithelial cells. There are several growth factors, including insulin-like growth component 1 (IGF-1), basic fibroblast growth component (bFGF), and vascular endothelial growth component (VEGF), as well as cytokines, including transforming growth factor beta 1 (TGF-1), interleukin 1 alpha (IL-1), as well as tumour necrosis factor alpha (TNF-A).(6)

Genes in Androgenetic alopecia

AGA occurs as a result of high frequency and a wide variety of phenotypes. Individual Vulnerability to disease may be affected by genetic variants, microsatellite repeating patterns,insertion alterations, deletion mutations, and variations in copy number.(7) The AR/EDA2R region on chromosome 20 and the PAX1/FOX A2 region on X chromosome are indeed the two most important genetic risk factors. A novel susceptibility locus, HAD C9, has been found on chromosome 7, according to recent investigations.(7)

The gene encoding the androgen receptor

Androgen receptors are what govern how cells respond to androgens. In humans, theAR gene determines how much androgen the hair follicles can take in. One of the many known AR gene variations is the Stu 1 polymorphism, which has the strongest connection to the onset of AGA.33 5-reductase, aromatase, the estrogen receptor delta, and insulin like growth factor-2are among the several genes for which no clear link could be established. An in-depth investigation of the genome's Y chromosome is needed.(8)

Environmental variables and hair follicle inflammation

Several investigations have proven that follicular inflammation implies a correlation.Contrary to the inflammatory as well as annihilative process of traditional scarring alopecia,the method is sluggish, subtle, and indolent. Several microbe-related toxins could be implicated in the production of an inflammatory response.

Another possibility is that keratinocytes are stimulated by chemicals in grooming products, contaminants, and other UVdamage by creating reactive oxygen species and nitric oxide.(9)

Diagnosis

History

To eliminate other potential causes of hair loss, a correct history typically proves useful. The most common history of hair loss is of persistent shedding with thinning occurring most frequently in the frontal, side, or central areas. The subject may also report scratchy and painful hair follicles. The history of systemic disorders, as well as new prescriptions from the preceding year, should be considered. There is a positive association between family history and AGA. Another essential component of history is diet, which is used to rule out nutrition-related effluvium. People can inquire about how certain lifestyles, such smoking and UV exposure, affect problems with the AGA. Doctors must look out for any linked hormonal abnormalities in female patients.(10)

Examination of scalp and hair

In AGA, the scalp is normally unaffected, however variables such seborrheic dermatitis and photo-damage might cause irritation. An important purpose of clinical assessment is to find out if the hair loss is patterned.

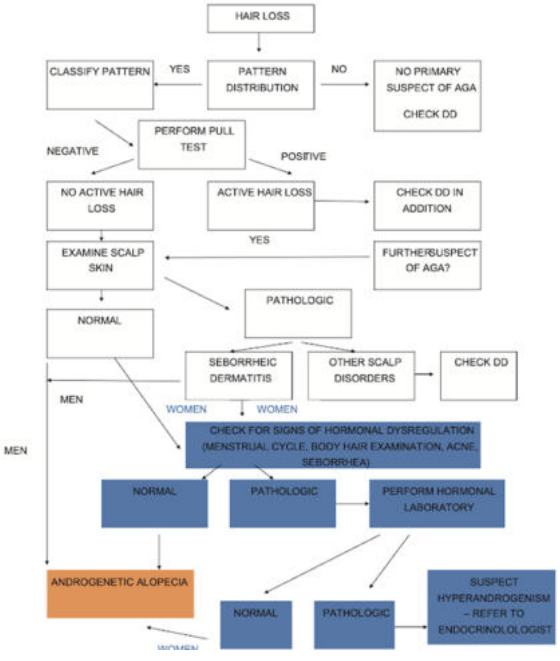

Figure3. Diagnosis of androgenetic alopecia.(11)

Pull test

A basic hair loss assessment method is the "pull test." The thumb and index and middle fingers each clasp about 60 hairs. The hairs are then plucked with a gentle yet forceful hand. If the test shows six or fewer hairs (less than 10 percent of the total hairs obtained), then the shedding is normal. However, if more than six hairs (10 percent of the total hairs obtained) are present, then means the shedding is definitely active. Patients with AGA normally show a negative test result, except when the condition is active, when only the affected areas, such the front of the scalp, display a positive result. The probability of telogen effluvium (or other disorders) is suggested by a diffusely positive pull test.(11)

Trichoscopy

Androgenetic alopecia can be diagnosed with trichoscopy, which has been established to be a valuable diagnostic tool. It's important to take note of the perifollicular colouration / peripilar mark (the most common variation seen in Oriental) and the yellow dot in AGA trichoscopy, which show a hair diameter diversity of over 20%. The term 'anisotrichosis' has been proposed to describe the HDD that occurs early in the course of AGA and is found in some patients. Telogen effluvium and pattern hair loss can be distinguished in females, according to Rakowska et al.(12)

Major criteria

1. Female AGA with telogen effluvium had a ratio of over four yellow spots in 4 pictures in the frontal area.
2. AGA women have thinner hair in the frontal region than in the back region, and
3. Over 10% of female AGA's frontal hairs are thin (less than 0.03 mm).

Minor criteria

1) One -hair pilosebaceous group,
2) vellus hairs,
3) colour change around follicle.

AGA in females requires the presence of two major or one major plus two minor diagnostic criteria to be definitively diagnosed. Trichoscopy has an accuracy rate of 98 percent.(12)

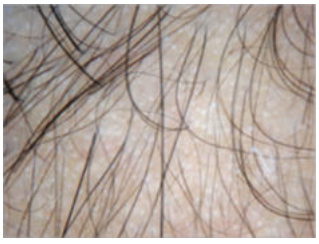

Figure 4. Trichoscopy shows a substantial rise in HDD, characterised by prominent vellus hair follicle alteration, perifollicular pigmentation, as well as yellow spots in patients with AGA.(11)

Trichogram or photo-trichogram

Trichograms are able to distinguish different kinds of alopecia, but are less useful for patients with AGA. Five days after the patient's hair is washed, the 60-80 hairs to be plucked out are extracted with forceps which has rubber in its ends. The examination of the hair begins as soon as it is plucked.(13)

Unit – area trichogram

In an area measuring about 30 cm2, a small number of hairs are plucked and studied to determine the hair follicle density, percentage of anagen fibres, as well as hair shaft diameter.(14)

Phototrichogram (PTG)

A non-invasive procedure, Phototrichogram (PTG) employs the creation of a series of close-up images to evaluate follicular volume, rate of increase in length of hair, and hair shaft diameter. The contrast enhanced PTG as well as the automated PTG are two variations of this technology (Trichoscan).(15)

Hair wash examination

There is an assay called the hair wash test that was developed by Rebora et al. to determine whether or not the patient has AGA or TE by counting how many vellus hairs as well as ending telogen hairs were washed away five days after washing and shampooing. They offer the data on the number of telogen and the proportion of vellus hairs in telegenic phase. Nevertheless, there are disadvantages to this method: It may lead to broken hair causing double counts, it is useless for people with curly hair, and it is a very lengthy process.(16)

Laboratory investigations

AGA doesn't require comprehensive lab testing, especially in men. Some experts recommend prostate specific antigen (PSA) testing for men older than 45 prior to beginning treatment with finasteride. Laboratory tests in women try to identify any hormonal problems, such as polycystic ovarian disease. Androgen index test, DHEAS, and prolactin are the recommended assessments. Additional testing might be needed to rule out less common disorders including congenital adrenal hyperplasia. Even though numerous research have shown conflicting results on the importance of assessing serum ferritin levels in AGA, the actual value of doing so is still not known.(17)

Biopsy of the scalp

Because of its invasiveness, scalp biopsy is not advised for patients with AGA.Biopsies are obtained from the most inflamed regions. Biopsies from the bitemporal area should be avoided since miniaturised hairs tend to be present in this area even when AGA is absent. For horizontal as well as vertical sectioning, a 4-mm drill is recommended. The Follicular density, concentration, and form can all be seen on the horizontal plane. While inAGA, the proportion of ending to vellus strands can be as low as 3:1, healthy hair can have aratio as high as 7:1. In addition to an increase in follicular steleae, a higher proportion oftelogen over anagen hair follicles, and a small<lymphohistiocytic infiltrate around the folliclewhich may have<substantial scarring in<the higher follicle, other important findings may be identified in AGA.(18)

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