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Female Androgenetic (?) Alopecia

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It is nearly 100 years since the publication of Dorothy Osborn's paper on the inheritance of common balding.[1] From a study of 22 families, she concluded that balding is due to a single gene and is inherited as an autosomal dominant trait in men and autosomal recessive in women. Two twin studies, one in young men and the other in elderly men, have confirmed the importance of genetics in male balding showing heritability in the region of 80-95%,[2,3] although the single gene idea has now been supplanted by a polygenic model. Initial case control studies found an association between male AGA and polymorphisms within the androgen receptor gene on the X chromosome.[4] The presence of a major AGA locus within the androgen receptor/ectodysplasin A2 receptor region has been confirmed in subsequent genome wide association studies (GWAS)5 and these studies have gone on to identify a further 11 loci scattered across the genome that also show association with male AGA.[6-8] The functional significance of these loci is not yet known but may include the regulation of androgen responses and participation in WNT signaling.

Ectodysplasin A2 Receptor: This is an isoform of ectodysplasin encoded by the ectodermal dysplasia gene. It is an integral component in epidermal and embryonic development and cell differentiation. Variants in EDA2R have been linked to the AR receptor role in androgenetic alopecia.

GWAS: Genome-wide association study is an examination of many common genetic variants in different individuals to see if any variant is associated with a trait.

WNT: WNT protein is a family of signaling molecules that regulate cell to cell interactions during embryogenesis. Abnormalities in these pathways have been linked to a number of clinical conditions.

What about female AGA? The application of the term "androgenetic" to female hair loss has implied an identity with male AGA, but it has also colored our thinking—because we have given it the same name it must be the same condition. Is this really true? There are certainly similarities; like male AGA the female form is common and increases in prevalence and severity in the population with advancing age, and the histopathology of male and female AGA is essentially indistinguishable. Androgens are clearly required for the expression of male AGA and there is little doubt that hyperandrogenism in women, particularly when severe, is associated with scalp hair loss. Hamilton refers to reports of such cases in his seminal publication on the role of testosterone in causing male AGA.[9] On the other hand, many women with AGA have no other clinical or biochemical signs of hyperandrogenism and female AGA has been reported in the absence of circulating androgens and in androgen insensitivity syndrome.[10,11] A recent questionnaire study in women being treated with testosterone implants for androgen deficiency actually reported an improvement in hair growth in those complaining of hair thinning prior to treatment.[12] Antiandrogens have been widely used to treat female AGA but the quality of evidence for efficacy is poor. Of the better studies, a randomized clinical trial (RCT) of finasteride 1mg daily in postmenopausal women with AGA failed to show any benefit after a year of treatment.[13] A 1-year trial comparing topical minoxidil with cyproterone acetate (CPA) reported improvement in the minoxidil group but overall deterioration in those receiving CPA.[14] Sub-group analysis did show a small improvement in women with menstrual irregularities taking CPA, possibly suggesting that antiandrogen treatment may work in women with hyperandrogenism. Opinions amongst clinicians treating female AGA do differ and there are those who strongly believe that antiandrogens are effective, but until we get proper RCTs, the controversy is likely to live on. Unfortunately, there is no commercial interest in the field, which makes funding such trials difficult.

Further differences emerge when we explore the genetics of female AGA. The few early studies, such as that of Osborn, assumed male and female AGA share the same genes and provided some evidence that this is the case. However, a twin study in women, although showing evidence for a significant genetic contribution to fronto-temporal recession and to hair graying, found none to hair thinning over the rest of the scalp, implying that hair thinning was non-genetic in origin and presumably had an environmental cause.[15] This study was conducted

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