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PRACTICAL DERMATOLOGY

Management of Androgenetic Alopecia in Postmenopausal Women

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Abstract. Female androgenetic alopecia or female-pattern alopecia is one of the most common causes of hair loss, affecting 50 % of women over their lifetime. The appearance of this condition is the cause of significant stress and psychological problems, making appropriate management important. Cases exist in which it is associated with hyperandrogenism. Here, we review the different clinical forms (diffuse, male-pattern, and Christmas-tree pattern), discuss the most appropriate laboratory tests (complete blood count, thyroid stimulating hormone, ferritin, prolactin, free and/or total testosterone, and dehydroepiandrosterone sulfate), and the different treatments, including finasteride.

Key words: female androgenetic alopecia, female-pattern alopecia, finasteride.

MANEJO DE LA ALOPECIA ANDROGENÉTICA EN MUJERES POSMENOPÁUSICAS

Resumen. La alopecia androgenética femenina, o alopecia de patrón femenino, es una de las causas más frecuentes de caída de pelo, afectando al 50 % de las féminas a lo largo de su vida. Su aparición origina importante estrés y problemas psicológicos, de ahí la relevancia de un manejo adecuado. Hay casos que se asocian a hiperandrogenismo. En este trabajo revisamos las distintas formas clínicas –difusa, similar a la masculina y en árbol de Navidad–, discutimos las pruebas de laboratorio más indicadas (hemograma, tirotropina [TSH], ferritina, prolactina, testoterona libre y/o total y dehidroepiandrosterona sulfato) y los distintos tratamientos, entre ellos la finasterida.

Palabras clave: alopecia androgenética femenina, alopecia de patrón femenino, finasterida.

Introduction

Although loss of scalp hair is a problem that has a psychological effect on individuals of both sexes, the impact is greater in women, even when the degree of alopecia is small, as shown by studies from North America[1] and Spain.[2,3]

The term *female-pattern alopecia* (FPA) is more appropriate than *female androgenetic alopecia* as its dependence on androgens and the hereditary character of the process are not clear in all cases. Female pattern alopecia is the most common form of hair loss, affecting more than 50% of women throughout their lifetime,[4] and its prevalence and severity increase with age.[5] Similar to male androgenetic alopecia, it is characterized by the progressive miniaturization of the hair follicles and a reduction of the percentage of hair in anagen in the affected areas due to this phase becoming shorter and the telogen phase becoming longer.[6]

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Clinical Characteristics

Three clinical forms of FPA have been described (Figure): (1) a diffuse form (Ludwig pattern[7]), where there is a general reduction of frontoparietal hair density, with a preserved frontal hairline and no crown alopecia; (2) a form with a similar distribution to that of male pattern alopecia (Hamilton pattern[8]), with recession of the frontal hairline and crown alopecia to varying degrees—this form has been observed in 37% of post-menopausal women[9]; and (3) an alopecia described by Olsen[10] as having a Christmas-tree pattern, with increased hair loss at the scalp midline, gradually increasing toward the frontal area. This third form is the most common, appearing in 70% of a series of 163 women with mild androgenetic alopecia.[10]

The age at onset varies considerably; there are 2 peaks at 30 years and 50 years. If the onset of puberty is early,

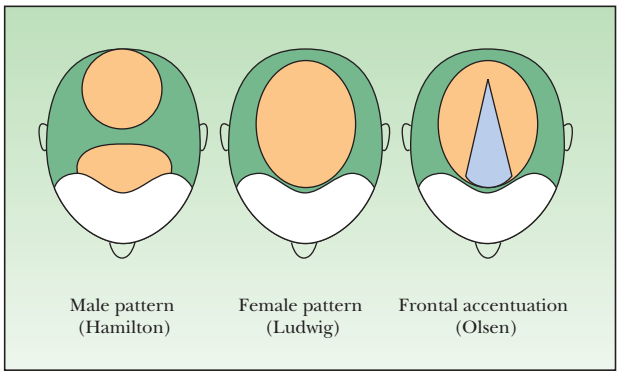

Figure 1. Phenotypic patterns of female alopecia.

Table 1. Assessment of Female Androgenetic Alopecia

Complete blood count (hemoglobin)
General biochemistry
ESR
Serum ferritin (acute-phase reactant) (<40 ng/mL increase in telogen phase)
TSH
If there are clinical signs of hyperandrogenism (hirsutism, acne, nigricans acanthosis, menstrual dysfunctions, and galactorrhea), the following should be assessed: – Total and free testosterone – DHEAS – If testosterone is ≥2.5 times reference values or >200 ng/dL or DHEAS is >2 times reference or >700 µg/dL in premenopausal women or 400 µg/dL in postmenopausal women, a tumor can be ruled out – If galactorrhea is present or ↑ testosterone request prolactin test – If testosterone or DHEAS are ↑ rule out congenital adrenal hyperplasia by a 17-OH progesterone blood test – PSA (>0.02 ng/mL)

Abbreviations: DHEAS, dehydroepiandrosterone sulfate; ESR, erythrocyte sedimentation rate; PSA, prostate-specific antigen; TSH, thyroid stimulating hormone.

FPA can appear before these ages and the degree of alopecia can increase if left untreated.[11] The hair-pull test is usually negative, unless effluvium is also present. The patients frequently experience high levels of anxiety, and if these processes are not treated they can progress rapidly. Some women with FPA (less than 40%) have hyperandrogenism,[12] along with other clinical signs such as hirsutism, treatment-resistant acne, galactorrhea, infertility, or menstrual dysfunction, although most women with FPA do not have clinical or analytical signs of excess androgens. Family history of FPA is less clear than in men with androgenetic alopecia.

Pathophysiology

The pathophysiology of FPA is thought to be similar to that of androgenetic alopecia in men,[13] where the enzyme 5α reductase (5αR) plays a key role in the peripheral conversion of testosterone to dihydrotestosterone (DHT). Two isoenzymes encoded by 2 different genes have been described: 5αR-I, which is widely distributed throughout the body, and 5αR-II, which is expressed in androgen-dependent tissues such as the prostate gland and hair follicles. The different clinical patterns in women compared to men are due to the differences in the levels and distribution of 5αR, aromatase, and androgen receptors in the hair follicles.[14]

Laboratory Tests

Diagnosis of FPA is more difficult than in men, because there is usually less hair loss in women and other factors with which loss can be easily confused must be excluded. Such factors include alopecia areata, telogen effluvium, loose anagen hair syndrome, trichotillomania, and scarring alopecia. A general examination is required to eliminate other causes of hair loss. Laboratory tests should include complete blood count, thyroid stimulating hormone, and serum ferritin, as well as prolactin, free and total testosterone, and dehydroepiandrosterone sulfate (DHEAS). The last 2 should be especially assessed in women with other presentations of excess androgens (hirsutism, treatment-resistant adult acne, nigricans acanthosis, menstrual dysfunction, and galactorrhea). If an increase in DHEAS is observed, a 17-OH progesterone blood test can be performed to rule out congenital adrenal hyperplasia during the follicular phase of the menstrual cycle[15] (Table 1).

Treatment

After appropriate examination, all postmenopausal women consulting for hair loss should be advised to adopt a suitable diet in terms of number of calories. Hair loss due to the following drugs should be ruled out: retinoids, cytotoxic or anticoagulant agents, and those used to treat other scalp problems such as seborrheic dermatitis or psoriasis and that can interfere with the action of specific topical treatment. This is usually based on minoxidil, an effective treatment but one which is not always tolerated by patients. A 1-mL solution of 2% or 5% minoxidil (the only drug approved by the US Food and Drug Administration for the treatment of FPA) applied once in the morning and night for 12 months produces peak hair growth at 16 weeks. It can lead to telogen effluvium at 2 to 8 weeks after beginning treatment. More than 5% of patients describe local irritation, with allergic contact dermatitis being less common.

Hypertrichosis may also appear, usually going into remission 4 months after stopping treatment.

Good results are obtained with oral antiandrogens such as cyproterone acetate that have central and peripheral antiandrogenic activity, especially in patients with hyperandrogenism. Spironolactone and flutamide are useful, although their side effects, which are sometimes serious, prevent them from being used in all cases. Cyproterone acetate prevents DHT from binding to its receptor and suppresses the secretion of follicle stimulating hormone and luteinizing hormone. A dose of 50 mg/d is administered on an ongoing basis to postmenopausal women. Spironolactone at a dose of 100-200 mg/d should be administered for a minimum of 6 months. Blood potassium levels should be monitored at baseline and every month, due to the risk of hyperkalemia, and oral rehydration therapy is recommended. Flutamide at minimum doses of 62.5-125 mg/d is more effective for hirsutism than alopecia. A quarterly blood test is recommended due to the moderate risk of liver toxicity. Birth-control methods should be employed as all the treatments mentioned may cause feminization of the male fetus.

Finasteride is a peripheral nonsteroidal antiandrogen that acts by inhibiting 5αR-II, thus blocking the conversion of free testosterone to DHT. Finasteride at a dose of 1 mg/d has proven efficacy in treating alopecia in men; however, its efficacy in women is less clear. An anovulatory drug should also be given if finasteride is administered to premenopausal women, as it can cause feminization of the male fetus, similar to other antiandrogens. Table 2 shows the results of the most relevant studies on the use of oral finasteride in women. Price et al[16] conducted a double-blind, randomized, multicenter study that compared finasteride at 1 mg/d with placebo. That study included the greatest number of patients (n = 137), all of whom were postmenopausal and had normal androgen levels, and no differences in efficacy were found at 12 months. The authors pointed out that the advanced age of some of the women may have contributed to this lack of response, as hair thinning in these patients no longer depends as much on 5αR or DHT. The other studies shown in Table 2 were case series or isolated cases. Shum et al[17] treated 4 postmenopausal women with hyperandrogenism using finasteride at a dose of 1.25 mg/d for 2.5 years, finding improvements in hair loss and increased hair growth. The authors explained this difference on the basis of the long treatment period (2 of the 4 patients noted no increase in hair until 2 years of treatment had elapsed), and the higher dose, although they recognized that the increase in dose was so small that it may have played no significant role. Finally, all the women had hyperandrogenism, suggesting that this type of female alopecia could have the same pathophysiology as male androgenetic alopecia, unlike other FPA. Thai and Sinclair[18] described the case of a postmenopausal woman with normal androgen levels who displayed increased hair density after 12 months of treatment with finasteride at 5 mg/d; previous treatment with spironolactone and cyproterone acetate failed to achieve this response. Trüeb and the Swiss Trichology Study Group[19] studied 5 postmenopausal women with normal androgen levels (3 with Ludwig pattern FPA, 1 with Hamilton pattern FPA, and 1 with Olsen pattern FPA). Four were treated with finasteride at 2.5 mg/d and 1 with 5 mg/d for 12 months; all the women improved 6 months after beginning treatment. The most recent study was by Iorizzo et al[20] and included 37 premenopausal women without signs of hyperandrogenism treated with finasteride at 2.5 mg/d and an anovulatory drug (drospirenone 3 mg and ethinyl estradiol 30 µg [Yasmin, Schering, Berlin, Germany]) for 12 months; 23 improved (mild improvement in 12, moderate in 8, and marked improvement in 3),

Table 2. Studies of Oral Finasteride in Women

Reference	*Women, No.*	*Age, y*	*Hyperandrogenism*	*Finasteride dose*	*Duration of Treatment*	*Results*
Price et al[16]	137 (67 with finasteride and 70 with placebo)	41-60	–	1 mg/d	12 mo	No difference between finasteride and placebo
Shum et al17	4	36-66	+	1.25 mg/d	>2.5 y	Improvement
Thai and Sinclair[18]	1	67	–	5 mg/wk	12 mo	Improvement
Trüeb et al[19]	5	52-69	–	2.5 or 5 mg/d	>18 mo	Improvement
Iorizzo et al[20]	37	19-50	–	2.5 mg/d and drospirenone + ethinyl estradiola	12 mo	Improvement in [27]
Camacho[21]	41		+ (SAHA)	2.5 mg/d	2 y	Improvement 75

Abbreviation: SAHA, seborrhea, acne, hirsutism, and alopecia.
[a]Yasmin, Schering, Berlin, Germany.

Table 3. Key Points in the Treatment of Female Pattern Alopecia With Finasteride

Finasteride seems to be an effective treatment of alopecia in women
A better response is obtained in women with early-onset alopecia and hyperandrogenism
Efficacy is lower if the alopecia onset occurs later
A higher dose than that given to men should be administered to women for at least 2 years to achieve improvement
It is also effective in premenopausal women, but suitable birth-control methods must be employed due to the risk of feminization of the male fetus

13 did not note any improvement, and 1 patient worsened despite treatment. Camacho[21] also successfully treated alopecia in 41 women with SAHA (seborrhea, acne, hirsutism, and alopecia) using finasteride at 2.5 mg/d. Camacho and Tosti[22] described their personal experience in treating alopecia with finasteride at doses between 2.5 mg/d and 5 mg/d. They studied 65 postmenopausal women with stage I-III female androgenetic alopecia or stage I-II male pattern androgenetic alopecia with increased concentrations of androgens, hypophysial hormones, or with prostate-specific antigen (PSA) above 0.02 ng/mL (PSA should be absent in women). Finasteride was used in combination with a 5% minoxidil solution twice a day and a promoter of vascular endothelial growth factor production (0.1% α-tocopherol nicotinate) twice a week. The patients noted that hair loss stopped at 3 months; regrowth began at 6 months, especially in the frontal and vertex region, becoming more evident between 12 and 18 months. No regrowth was observed in the frontotemporal regions (as in the case of male-pattern alopecia). They also used this treatment successfully in postmenopausal women with normal androgen levels. All the authors who have used finasteride in women highlight that it is well tolerated and that there are no side effects.

In summary, finasteride seems to be an effective treatment for alopecia in postmenopausal women (Table 3), although not in all cases.[23] Women with early-onset alopecia and hyperandrogenism respond better, although positive results have been obtained in women with alopecia who show no signs of hyperandrogenism. Almost all authors accept that the later the onset of alopecia the worse the response, as in these cases hair thinning depends less on the effect of androgens. In any case, double-blind, placebo-controlled trials, similar to those performed in men,[16] are needed to obtain definitive results in women, although the approach should involve higher doses than those used in men and treatment should last for at least 2 years.

Conflicts of Interest
The authors declare no conflicts of interest.

References

1. 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.
2. Camacho F. Aspectos psicológicos de la alopecia androgenética. Monogr Dermatol. 1998;11:335-42.
3. Camacho F, García-Hernández MJ. Psychological features of androgenetic alopecia. J Eur Acad Dermatol Venereol. 2002;16:467-80.
4. Price VH. Androgenetic alopecia in women. J Investig Dermatol Symp Proc. 2003;8:24-7.
5. 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.
6. Courtois M, Loussouarn G, Hourseau C, Grollier JF. Ageing and hair cycles. Br J Dermatol. 1995;132:86-93.
7. Ludwig E. Classification of the types of androgenetic alopecia (common baldness) occurring in female sex. Br J Dermatol. 1977;97:247-54.
8. Hamilton JB. Patterned loss of hair in man: types and incidence. Ann N Y Acad Sci. 1951;53:708-28.
9. Venning VA, Dawber RP. Patterned alopecia in women. J Am Acad Dermatol. 1988;18:1073-7.
10. Olsen EA. The midline part: an important physical clue to the clinical diagnosis of androgenetic alopecia in women. J Am Acad Dermatol. 1999;40:106-9.
11. Olsen EA. Female pattern hair loss. J Am Acad Dermatol. 2001;45:S70-80.
12. Futterweit W, Dunaif A, Yeh H-C, Kingsley P. The prevalence of hyperandrogenism in 109 consecutive female patients with diffuse alopecia. J Am Acad Dermatol. 1988;19:831-6.
13. Frieden IJ, Price VH. Androgenetic alopecia. In: Thiers BH, Dobson RL, editors. Pathogenesis of skin disease. New York: Churchill Livingstone; 1986. p. 41-55.
14. Sawaya ME, Price VH. Different levels of 5-reductase type I and II, aromatase and androgen receptor in hair follicles of women and men with androgenetic alopecia. J Invest Dermatol. 1997;109:296-300.
15. Olsen EA, Messenger AG, Shapiro J, Bergfeld WF, Hordinsky MK, Roberts JL, et al. Evaluation and treatment of male and female pattern hair loss. J Am Acad Dermatol. 2005;52:301-11.
16. Price VH, Roberts JL, Hordinsky M, Olsen EA, Savin R, Bergfeld W, et al. Lack of efficacy of finasteride in postmenopausal women with androgenetic alopecia. J Am Acad Dermatol. 2000;43:768-76.
17. Shum KW, Cullen DR, Messenger AG. Hair loss in women with hyperandrogenism: four cases responding to finasteride. J Am Acad Dermatol. 2002;47:733-9.
18. Thai KE, Sinclair RD. Finasteride for female androgenetic alopecia. Br J Dermatol. 2002;147:812-3.
19. Trüeb RM; Swiss Trichology Study Group. Finasteride treatment of patterned hair loss in normoandrogenic postmenopausal women. Dermatology. 2004;209:202-7.

20. Iorizzo M, Vincenzi C, Voudouris S, Piraccini BM, Tosti A. Finasteride treatment of female pattern hair loss. Arch Dermatol. 2006;142:298-302.
21. Camacho F. Hirsutismo. Enfoque clínico-terapéutico (2.ª parte). Act Terap Dermatol. 2001;24:190-206.
22. Camacho F, Tosti A. Tratamiento médico de las alopecias femeninas. Monogr Dermatol. 2005;18:92-117.
23. Rivera R, Guerra-Tapia A. ¿Sirve la finasterida en la alopecia de la mujer? Mas Dermatol. 2007;1:21-4.