A Clinical Study of Androgenetic Alopecia(III)

Joo Hyun Shim, M.D., Sung Wook Ro, M.D., Byung In Ro, M.D.

Department of Dermatology, College of Medicine, Chung-Ang University, Seoul, Korea

Background : Androgenetic alopecia is considered to be a genetically determined disorder influenced by age and androgen. The proportion of patients with androgenetic alopecia among the total number of patients with alopecia seems to be gradually increasing.

Objective : The purpose of this study is to evaluate the family history, clinical and endocrine status of the patients with androgenetic alopecia.

Method : 1113 patients with androgenetic alopecia who had visited the Department of Dermatology, Yongsan Hospital, College of Medicine, Chung-Ang University during the 3 years (1995.1-1998.12) have been examined.

Results : The results are summarized as follows

1) The incidence of androgenetic alopecia among the total number of alopecia patients was 64.5%, showing recent increment.

2) There were 855 male and 258 female patients being most prevalent in the third decade in both sexes and the patients younger than 30 years old with premature androgenetic alopecia, made up 70.3% of the male patients and 48.8% of the female patients with androgenetic alopecia.

3) While Norwood's type IIa was the most common and following type II, III vertex, and IV in the male AGA, Ludwig's type II was the most common in female AGA

4) There was a family history of baldness in 53.5% of first degree relatives in male patients and 51.6% in female patients.

5) Associated diseases were observed in 565(66.8%) of the male patients and 219 (84.8%) of the female patients: diseases associated with androgen such as seborrheic dermatitis and acne vulgaris occupied 39.1%.

Conclusion : Based on our findings, those who want to treat androgenetic alopecia at the earlier ages are gradually increasing and it seems to be reasonable to believe that the age, genetic factors, localized effects of androgens on the scalp and the density and/or functional activity of androgen receptors may influence the pathogenesis of androgenetic alopecia.

(Ann Dermatol 14(1) 11-17, 2002).

Key Words : Androgenetic alopecia, Testosterone

Received August 20, 2001
Accepted for publication August 20, 2001
Reprint request to : Joo Hyun Shim, Department of Dermatology, Yongsan Hospital, College of Medicine, Chung-Ang University,
65-207, Hangangro-3-ka, Yongsan-ku 140-757, Seoul, Korea.
Tel. (02)748-9573, Fax. (02)6359-9573
*This article was presented at the 51st Annual Meeting of the Korean Dermatological Association on April 22, 1998

Androgenetic alopecia, the most common type of alopecia after puberty, is characterized by progressing change of hairs into fine vellus form on the frontal and parietal scalp progressively, shortening in length and miniaturization of both the papillae and matrices, as well as the resulting hair shaft1.

In our department, Han et al2 and Lim et al3, already reported the clinical aspects of androgenetic alopecia. Hence this report is in the continuation of the previous study and consecutive analysis of clinical aspects of

Annals of Dermatology
Vol. 14, No. 1, January 2002

androgenetic alopecia has been performed since then. We studied 829 patients with androgenetic alopecia who visited our Department for 3 years, and compared the results with those previously reported.

PATIENTS AND METHODS

Patients

Of 1725 patients with alopecia who had visited the Department of Dermatology, Yongsan Hospital, College of Medicine, Chung-Ang University from January 1995 to December 1998, 1113 patients (male:855, female:258) with androgenetic alopecia who had vellus hairs with decreased hair density were examined.

Methods

Prospective examinations concerning the following clinical parameters were conducted through chart review, and the results were analyzed.

1) Frequency of occurrence

2) Age and sex distribution

3) Clinical classification : We analyzed the pattern of androgenetic alopecia male patients by Norwood's classification and female patients by Ludwig's classification.

4) Family history : Familial androgenetic alopecia was examined by history taking of the first degree relatives of the patient.

5) Associated disease : By inspection and physical examination, seborrhea, acne, hirsutism, and hyperandrogenicity had been evaluated. And we also checked up for other possibilities of underlying systemic disorders. The population who manifested erythema, exudate, crusts, scale were diagnosed as a "seborrhea" and people who had oily skin type especially on the scalp, face, postauricle, thorax, and abdomen were catagorized as "seborrhea" too.

6) Serum testosteron level using radioimmunoassay method.

RESULTS

Incidence of alopecia

Of the 1725 patients with alopecia, 1113 patients were androgenetic alopecia, accounting for 64.5% of cases. The other causes included alopecia areata, which accounted for 524 cases of the patients(30.4%), 37 cases of alopecia totalis(2.1%), 39 case of alopecia universalis(2.3%) and 12 cases of cicatricial alopecia (0.7%)(Fig. 1).

Age and sex distribution

Male accounted for 3.3 times greater distribution of patients, with 855 patients, while there were 258 female patients. On the hand, female showed higher age distribution with a mean age of 31.4 years, while male showed 27.5 years. Most patients were in their third decades, embracing 562 of the male patients(65.7%) and 110 of the female patients(42.6%). 602 of the male patients(70.5%) and 126 of the female(48.8%) had premature androgenetic alopecia before 30 years of age(Fig. 2,3,4).

Clinical classification

We analyzed the pattern of androgenetic alopecia in 855 male patients by Norwood's classification4 and 258 female patients by Ludwig's classification5. Most male patients were type II(17.5%) and IIa(21.9%) showing bitemporal recession, and type IIIv(16.1%) and IV(13.5%) showing vertex hair loss(Fig. 5,6). In women, type II of the Ludwig's classification-where the frontal hair line is preserved with loss of hair in vertex only-showed the highest frequency, accounting for 129 patients(50.0%) with type I and type following in order of frequency, with 124 of the patient(48.4%) and 5 of the patients(2%) respectively(Fig. 7).

Family history

457 out of 855 male patients(54%) and 133 out of 258 female patients(52%) had positive family history, showing similar familial tendency. Among these patients, 45% of male and 29% of female had first degree male relatives with androgenetic alopecia(Fig. 8).

Associated diseases

Associated diseases were observed in 398

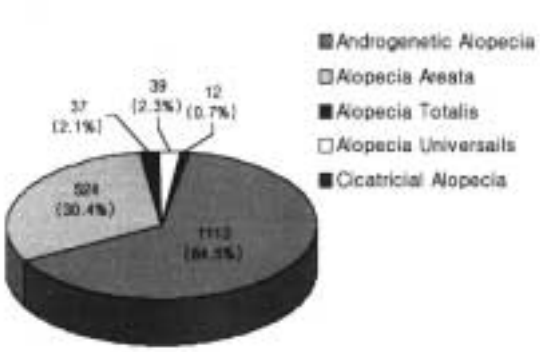

Fig. 1. Incidence of AGA among Total Alopecia Patients ('95-'98, III).

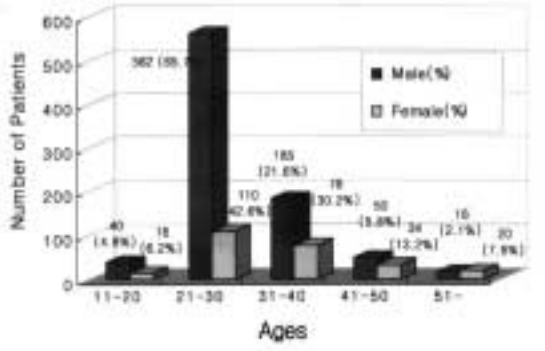

Fig. 2. Age and Sex Distribution of AGA ('95-'98, III).

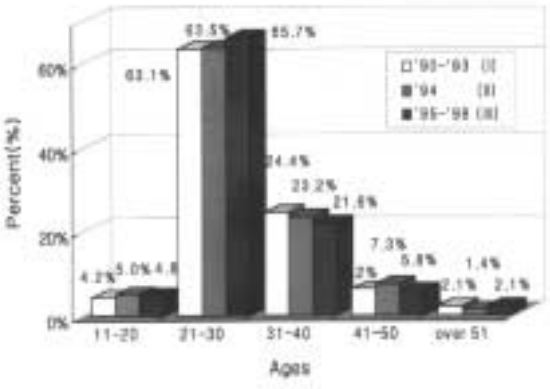

Fig. 3. Comparison of the Age Distribution of AGA in Male.
(Permitted from Han ES, KIM MN, Hong CK, Ro BI: A clinical study of androgenetic alopecia. Kor J Dermatol 33:44-51,1995 and Lim HS, Lee CK, Ro BI: A clinical study of androgenetic alopecia(1994). Kor J Invest Dermatol 4:27-34,1997).

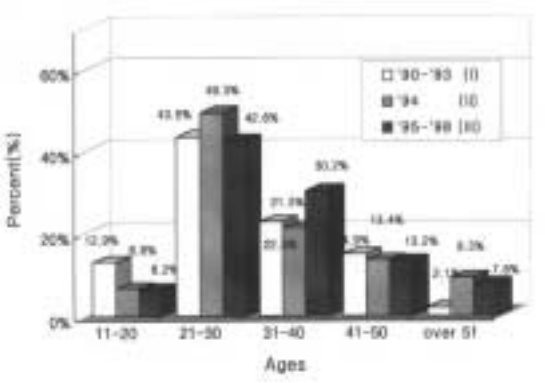

Fig. 4. Comparison of the Age Distribution of in AGA in Female.
(Permitted from Han ES, KIM MN, Hong CK, Ro BI: A clinical study of androgenetic alopecia. Kor J Dermatol 33:44-51,1995 and Lim HS, Lee CK, Ro BI: A clinical study of androgenetic alopecia(1994). Kor J Invest Dermatol 4:27-34,1997).

male patients and 118 female patients. Seborrheic dermatitis was the most common, followed by acne vulgaris, atopic dermatitis in order of frequency. In women, anemia and thyroid disease were also observed(Table 1).

Serum testosterone level

In male patients, serum testosterone level was from 1.5 ng/ml to 19.7 ng/ml(normal range; 3 - 10 ng/ml), with a mean value of 8.5 ng/ml. The hormone level was increased

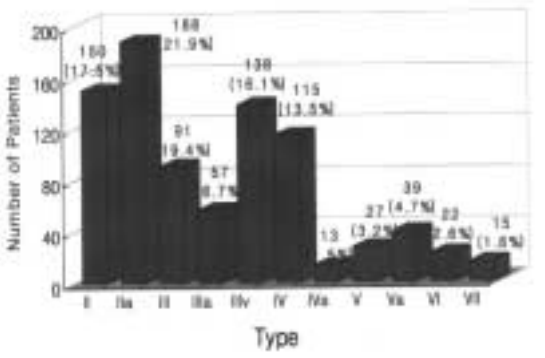

Fig. 5. Clinical Type of AGA in Male Patients by Norwood's Classification ('95-'98, III).

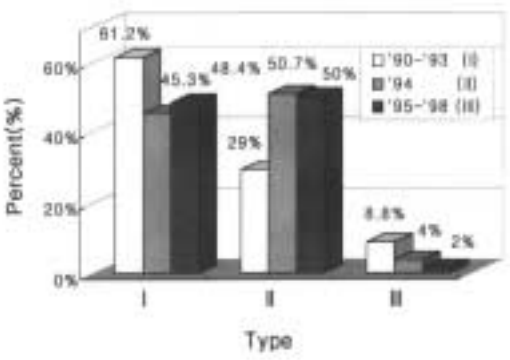

Fig. 7. Comparison of Clinical Type in Female AGA Patients by Ludwig's Classification.
(Permitted from Han ES, KIM MN, Hong CK, Ro BI: A clinical study of androgenetic alopecia. Kor J Dermatol 33:44-51,1995 and Lim HS, Lee CK, Ro BI: A clinical study of androgenetic alopecia(1994). Kor J Invest Dermatol 4:27-34,1997).

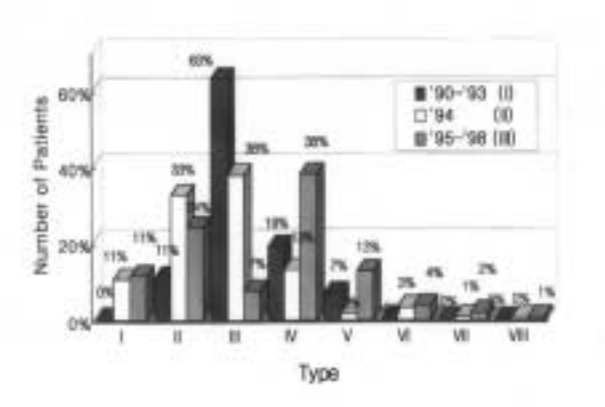

Fig. 6. Clinical Type of AGA in Male Patients by Hamilton's Classification.
(Permitted from Han ES, KIM MN, Hong CK, Ro BI: A clinical study of androgenetic alopecia. Kor J Dermatol 33:44-51,1995 and Lim HS, Lee CK, Ro BI: A clinical study of androgenetic alopecia(1994). Kor J Invest Dermatol 4:27-34,1997).

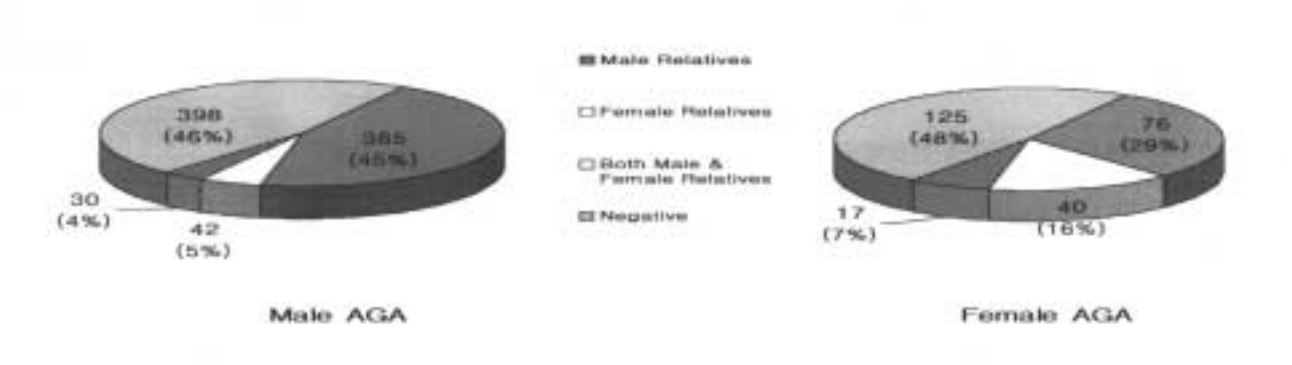

Fig. 8. Family history of baldness in male and female patients with AGA.
Male AGA Female AGA.

only in 43 patients (5.0%). In female patients, serum testosterone level was from 0.01 ng/ml to 4.8 ng/ml(normal range; 0.2 - 0.8 ng/ml. The hormone level was increased in 33 patients(12.8%)(Table 2).

DISCUSSION

Androgenetic alopecia is considered as a pathologic state by most physicians and affected subjects, but as a normal variant of aging process by others. Certainly it is a common problem, affecting a half of male patients, and perhaps as many women, over the age of 401. There is a genetically determined predisposition in androgenetic alopecia, but expression is quite variable. Although women and men have much different clinical presentations of androgenetic alopecia as well as potential systemic influence, the underlying mechanisms are presumably the same.

Age, genetic factor and androgen are suspected as causative factors of androgenetic alopecia and among them, androgenic effect is thought to be the most essential one. For example, androgenetic alopecia does not occur in

Table 1. Associated Diseases in Patients with AGA.

Associated Diseases	Male(%) (n=855)	Female(%) (n=258)	Total(%) (n=1113)
Seborrheic dermatitis	398 (46.5%)	118 (45.7%)	516 (46.4%)
Acne vulgaris	26 (3.0%)	11 (4.1%)	37 (3.3%)
Dysmenorrhea	0 (0%)	16 (6.2%)	16 (1.4%)
Atopic dermatitis	12 (1.4%)	4 (1.6%)	16 (1.4%)
Anemia	0 (0%)	15 (7.6%)	15 (1.3%)
Urticaria	9 (1.0%)	4 (1.2%)	13(1.2%)
Thyroid disease	3 (0.3%)	10 (3.9%)	12(1.2%)

Table 2. Serum testosterone level in patients with androgenetic alopecia.

Sex	Increase	Normal*	Decrease
	Number(%)	Number(%)	Number(%)
Male (n=855)	43 (5.0%)	768 (89.8%)	44 (5.1%)
Female(n=258)	33 (12.8%)	215 (83.3%)	10 (3.9%)
Total (n=1113)	76 (6.8%)	983 (88.3%)	54 (7.9%)

*Normal Range : male ; 3-10 ng/ml
female ; 0.2-0.8 ng/ml

people who castrated testis or had hypogonadism in spite of genetic predisposition of androgenetic alopecia. But when androgen is commenced, alopecia occur and when androgen is stopped, does not progress6. Androgenetic alopecia is also seen in athletes who use excessive androgen hormones for the purpose of having powerful muscles7, and in patients with endocrinologic disorders such as ovarian or adrenocortical disease in which blood androgen level is increased8,9. The results on prevalence of androgenetic alopecia in general population by Yoo et al10, is that 4.7% occur in twenties, 15.8% in thirties, 27.9% in forties, 36.8% in fifties, 50.7% in sixties and 66.7% in seventies. The prevalence of androgenetic alopecia is proportionate to the increase of age. Among the patients who visited our clinic, 65.7% of male patients, and 42.6% of female patients were in the third decade of life. The result is coincidental with the reports of Han et al2 (63.1% of male, 43.5% of female) and Lim et al3 (63.5% of male, 49.3% of female). Early androgenetic alopecia which occurs before the age of thirty is 70.3% in male and 49.0% in female among the patients who visited our clinic(Fig. 2). The result indicates that the incidence of early androgenetic alopecia is increased compared with the previous report of Lim et al3 (Fig. 3, 4). The reasons are essentially unclear on why the prevalence and age of androgenetic alopecia are different between general population and the patients who visit our clinic. But it is thought that several factors may play some role; that is, the increased stress by the complexity of society, exaggeration of seborrheic dermatitis which can trigger hair loss and indirect effect of social activities such as marriage and occupation.

Androgenetic alopecia can be diagnosed clinically when the hair gradually thins on the frontal and parietal scalp showing diffuse alopecia. Histologically, the diagnosis can be confirmed when the specimen from the alopecia scalp shows the shortening of length of individual follicle, majority of follicles are in the stage of telogen phase and the number of anagen follicle is decreased in

the serial vertical section and folliculogram11,12,13.

There are some differences in the clinical manifestations of male and female androgenetic alopecia. In men, hair loss begins from the frontal hair line which results in bitemporal recession and progression into parietal baldness6. Women, on the other hand, rarely present baldness. Instead, frontal hair line is spared with only diffuse hair loss on the frontal and parietal scalp. The process of miniaturization in women assumes more of a mosaic pattern in affected area, with an exaggerated wide range in hair diameter in affected areas compared with normal.

In this study, by different way of Lim's reports3, Norwood's classification which eliminated Hamilton's type III and IV and emphasized the progressive loss in hair over the midscalp4, we classified the type of hair loss. That is to say, Norwood type IIa includes 188 men(21.9%) and Ludwig type II includes 129 women(50%) which is the most common type in man and woman respectively.

There is no question about the fact that androgenetic alopecia is caused by genetic factors, but the way of inheritance remain unclear and some mysteries still remain. Osborn[14] said that androgenetic alopecia is caused by single gene with dominant inheritance in man, so heterogeneous gene may result in alopecia. But in woman, the way of inheritance is autosomaly recessive, so only homologous gene can cause alopecia. It is reported that the inheritance of androgenetic alopecia is autosomal dominant with incomplete penetration, androgenetic alopecia is mediated by multiple gene defect, and the threshold of alopecia is much higher in woman than in man[15]. The authors stated that there is family history of 54.0% in men and 52.0% in women among the family members. In this study the presence of family history is equal in both sexes and slightly lower than that the previous report by Lee et al,[16] where the presence was 60%.

There is a tendency of seborrheic dermatitis, acne, dysmenorrhea and atherosclerosis to be accompanied with androgenetic alopecia9,13,17. It is known that seborrheic dermatitis, acne, hypertrichosis are related to the elevated production of 5α- dihydrotestosterone(DHT) in the lesional area18. The aggravating disease of androgenetic alopecia includes chronic disease, metabolic disease, endocrinologic disease, stress, emotional change, operation and medication19. In the consideration of female patients with androgenetic alopecia, it is recognized to be associated with anemia. Low serum ferritin levels and hemoglobin levels had been detected in a significant number of female patients with androgenetic alopecia20. In the postmenopausal woman, decreased estrogen level can affect the loss of hair21. In this study, androgenetic alopecia associated diseases were found in 546 men(63.8%) and 219 women(84.8%). Among them, testosterone-related diseases such as seborrheic dermatitis, acne and dysmenorrhea accounted for 51.1%(49.5% in men and 56.0% in women).

To investigate androgen excess in androgenetic alopecia, testosterone, dihydro - testosterone(DHT), androstenedione, dihydroepiandrosterone sulfate (DHEAS), sex hormone binding globulin(SHRG) can be examined22,23,24. Pitts et al24, reported that DHEA in blood is significantly elevated among the 18 patients with androgenetic alopecia than in normal control. De Villes et al25 and Georgala et al22, reported that blood testosterone, DHEAS and DHT among the female androgenetic alopecia are not significantly different from normal control, but SHRG is significantly diminished. On the other hand, Futterweit et al9 reported that hyperandrogenism was found in 38.5% of female with diffuse alopecia and testosterone level among the group is significantly higher than androgenetic alopecia without hyperandrogenism and normal control. We studied testosterone level in patients with androgenetic alopecia. The result was similar to the report of Lim et al3, namely, most patients(89.7% in men, 79.7% in women) reveal normal range and only a small portion shows elevated level (4.2% in man, 14.7% in woman). The result comes from the fact that androgenetic alopecia is not related with blood testosterone, but related with the DHT, enzyme and protein that act fo-

cally. In this study, we cannot find the endocrinologic disorders in patients with elevated blood testosterone, but Takashima et al26 reported that hyperandrogenism can be accompanied with endocrinologic disorders in androgenetic alopecia patients.

On the basis of findings in this study, those who want to treat androgenetic alopecia at earlier ages are gradually increasing and it seems to be reasonable to believe that the age, genetic factors, localized effects of androgens on the scalp and the density and/or functional activity of androgen receptors may influence the pathogenesis of androgenetic alopecia.

REFERENCES

1. Olsen EA. Androgenetic alopecia. In: Olsen EA, editors. Disorders of hair growth diagnosis and treatment. 1st ed. McGraw-Hill, 257-284. 1994.
2. ES Han, MN Kim, CK Hong, BI Ro. A clinical study of androgenetic alopecia. Kor J Dermatol 33:44-51, 1995.
3. HS Lim, CK Lee, BI Ro. A clinical study of androgenetic alopecia(1994). Kor J Invest Dermatol 4:27-34, 1997.
4. Olsen EA, EA, Weiner MS, DeLong ER, Pinnel S. Topical minoxidil in early male pattern baldness. J Am Acad Dermatol 13:185-192, 1985.
5. Ludwig E. Classification of the types of androgenetic alopecia(common baldness) occuring in the female sex. Br J Dermatol 97:247-253, 1977.
6. Hamilton JB. Male hormone stimulation is prerequisite and an incitant in common baldness. Am J Anat 71:451-80, 1942.
7. Scott MJ 3rd, Scott AM. Effects of anabolic-androgenic steroids on the pilosebaceous unit. Cutis 50:113-6, 1992.
8. Ludwig E. The role of sexual hormones in pattern alopecia. In : Biopathology of pattern alopecia. New York, Karger, 50-60, 1968.
9. Futterweit W, Dunaif A, Yeh HC, et al. The prevalence of hyperandrogenism in 109 consecutive female patients with diffuse alopecia. J Am Acad Dermatol 19:831-836, 1988.
10. JH Yoo, KJ Kim, HC Eun. Prevalence and clinical classification of androgenetic alopecia in Korean. (abstract) 117, 1994.
11. Uno H, Kurata S. Chemical agents and peptides affect hair growth. J Invest Dermatol 101:143-147, 1993.
12. Uno H. Quantitative models for the study of hair growth in vivo. In : Stenn KS, Messenger AG, Boden HP, eds. Molecularand Structural biology of hair. NY Acad Sci, 107-124, 1991.
13. Brigham PA, Cappas A, Uno H. The stump-tailed macaque as a model for androgenetic alopecia: effects of topical minoxidil analized by use of folliculogram. Clin Dermatol 6:177-187, 1988.
14. Osborn D. Inhertance of baldness. J Hered 7:347-355, 1916.
15. Kuster W, Happle M. The inheritance of common baldness : Two B or not two B? J Am Acad Dermatol 11:921-926, 1984.
16. MK Lee, MS Yoon, JB Lee, BI Ro, KO Kim, et al. A Clinical Study of Topical Minoxidil Therapy in Alopecia : Multicenter Trials. Kor J Dermatol 24:181-189, 1986.
17. Lesko SM, Rosenberg L, Shapiro S. A case-control study of baldness in relation to myocardial infarction in men. JAMA 269:998-1003, 1993.
18. De Villez RL, Dunn J. Female androgenetic alopecia. Arch Dermatol 122:1011-1015, 1986
19. Bergfeld WF. Diffuse hair loss in woman. Cutis 22:190-195, 1987.
20. IS Lee, CW Ihm. Clinical study on 25 cases of female pattern baldness before the age of 25. Kor J Dermatol 36:827-835, 1998.
21. Bergfeld WF, Redmond GP. Androgenetic alopecia. Dermatologic Clinics 5:491-500, 1987.
22. Georgala S, Gourgiotou K, Kassouli S, et al. Hormonal status in post menopausal androgenetic alopecia. Int J Dermatol 31:858-859, 1992.
23. Fauze M, Drapier-Fraure E. Hormonal assessment in a woman with acne and alopecia. Revue Francaise de Gynecologie et de Obstetrique(Abstract) 87:331-334, 1992.
24. Pitts RL. Serum elevation of dehydroepiandrosterone sulfate associated with male pattern baldness in young men. J Am Acad Dermatol 16:571-573, 1987.
25. De Villez RL, Dunn J. Female androgenetic alopecia. Arch Dermatol 122:1011-1015, 1986
26. Takashima I and Montagna W. Studies of common baldness of the stump-tailed macaque(Macaca speciosa)VI. The effect of testosterone on common baldness. Arch Dermatol 103:527-534, 1971.