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ORIGINAL ARTICLE

Male Androgenetic Alopecia and Cardiovascular Risk Factors: A Case-Control Study☆

S. Arias-Santiago,[a,*] M.T. Gutiérrez-Salmerón,[a] L. Castellote-Caballero,[b] A. Buendía-Eisman,[c] and R. Naranjo-Sintes[a]

[a]*Servicio de Dermatología, Hospital Clínico San Cecilio, Granada, Spain*
[b]*Servicio de Radiología, Hospital Clínico San Cecilio, Granada, Spain*
[c]*Departamento de Dermatología, Facultad de Medicina, Granada, Spain*

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Intima-media thickness;
Insulin;
Aldosterone

Abstract

Background and objectives: The relationship between androgenetic alopecia and cardiovascular disease has been studied by some authors in the past, although the results of epidemiological studies have been variable. The objective of this study was to determine the prevalence of metabolic syndrome and carotid arteriosclerosis in patients with early-onset androgenetic alopecia.

Patients and methods: Seventy men were studied, 35 with diagnosis of early-onset (before 35 years of age) androgenetic alopecia and 35 control subjects who consulted for other skin conditions. In both groups, the criteria for metabolic syndrome according to the Adult Treatment Panel-III were studied (obesity, triglycerides, high-density lipoprotein cholesterol, systolic and diastolic blood pressure, and blood glucose), presence of atheromatous plaques, and carotid intima-media thickness using Doppler ultrasonography. Other cardiovascular risk factors, hormones, and acute-phase reactants were also analyzed.

Results: Criteria for metabolic syndrome were met by 57.1% of the patients with androgenetic alopecia compared to 14.3% of the controls ($P<.0001$). Thirty-four percent of the patients with androgenetic alopecia had atheromatous plaques compared to 8.6% of the controls ($P=.018$). In an independent correlation analysis, abdominal obesity, systolic blood pressure, triglycerides, and blood glucose levels were significantly greater among patients with androgenetic alopecia. Testosterone and sex hormone binding globulin levels were similar in the 2 groups whereas insulin and aldosterone levels were higher in patients with androgenetic alopecia ($P<.05$).

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*Corresponding author.
E-mail address: salvadorarias@hotmail.es (S. Arias-Santiago).

Conclusions: The high frequency of metabolic syndrome and carotid atheromatous plaques in patients with androgenetic alopecia suggests cardiovascular screening should be done to enable early detection of individuals at risk and initiation of preventive treatment before cardiovascular disease becomes established

PALABRAS CLAVE
Alopecia androgénica masculina;
Síndrome metabólico;
Placa de ateroma carotídea;
Grosor íntima-media;
Insulina;
Aldosterona

Alopecia androgénica masculina y factores de riesgo cardiovascular: estudio de casos y controles

Resumen

Introducción y objetivos: La relación entre la alopecia androgénica (AAG) y la enfermedad cardiovascular ha sido objeto de estudio por parte de algunos autores en las últimas décadas, y se han obtenido diferentes resultados en los distintos estudios epidemiológicos. El objetivo de este trabajo es conocer la prevalencia del síndrome metabólico y de la arteriosclerosis carotídea en los pacientes con AAG de inicio precoz.

Pacientes y métodos: Se han estudiado 70 pacientes varones, 35 diagnosticados de AAG de inicio precoz (antes de los 35 años) y 35 controles atendidos por otras enfermedades dermatológicas. En ambos grupos se estudiaron los criterios de síndrome metabólico que propone la ATP-III (obesidad, trigliceridemia, cHDL, presión arterial sistólica, presión arterial diastólica y glucemia), la presencia de placa de ateroma y el grosor íntima-media carotídeo mediante ecografía Doppler. También se analizaron otros factores de riesgo cardiovascular, un estudio hormonal y de reactantes de fase aguda.

Resultados: El 57,1% de los pacientes con AAG cumple criterios de síndrome metabólico frente al 14,3% del grupo control ($p < 0,0001$). El 34% de los pacientes con AAG presentó placa de ateroma frente al 8,6% de los controles ($p = 0,018$). Los valores de obesidad abdominal, presión arterial sistólica, trigliceridemia y glucemia analizados de forma independiente fueron estadísticamente superiores en el grupo de pacientes con AAG. Los niveles de testosterona y de la proteína transportadora de hormonas esteroideas fueron similares en ambos grupos; sin embargo, los niveles de insulina y aldosterona resultaron ser mayores en el grupo de pacientes con AAG ($p < 0,05$).

Conclusiones: La elevada frecuencia con la que se presenta el síndrome metabólico y la ateromatosis carotídea en los pacientes con AAG hace necesario un cribado cardiovascular para detectar precozmente a aquellos individuos en riesgo e iniciar tratamiento preventivo antes de que se establezca la enfermedad cardiovascular.

Introduction

Male androgenetic alopecia is the most prevalent form of alopecia and is determined by 2 basic factors: heredity and the peripheral action of androgens. Epidemiological studies of the association between androgenetic alopecia and cardiovascular disease have produced varying results. While some have shown an increase in cardiovascular risk,[1,2] especially in early-onset alopecia, others have failed to confirm this observation.[3] In their case-control study, Lesko et al[4] showed that vertex alopecia was associated with myocardial infarction. In addition, Lotufo et al[5] showed an association between the severity of alopecia and coronary artery disease. Most of these studies, however, examined the risk of myocardial infarction or death due to heart disease without independently analyzing cardiovascular risk.

Cardiovascular disease has a major impact on morbidity and mortality. Thus, an understanding of the relationship between male androgenetic alopecia and cardiovascular disease may be important in improving primary prevention. We therefore undertook a case-control study to determine the prevalence of metabolic syndrome—according to Adult Treatment Panel III (ATP-III) criteria[6]—and of carotid atherosclerosis (atheromatous plaque and carotid intima-media thickness) in male patients with androgenetic alopecia.

Patients and Methods

Ours was a case-control study comprising 70 male patients: 35 with male androgenetic alopecia and 35 controls. All patients were diagnosed at the dermatology department of Hospital San Cecilio in Granada, Spain (days and visits selected at random). Diagnosis of androgenetic alopecia was based on clinical findings, such as early-onset alopecia, reduced diameter and density of hair in the frontal area or vertex with greater density in the occipital area, and the presence of miniaturized hairs of different diameters as observed using dermoscopy. The inclusion criteria were age 35 to 55 years, early-onset androgenetic alopecia (before age 35 years), at least

type III according to the Ebling classification, and patient agreement to participate. The exclusion criteria were as follows: other types of alopecia; hormone replacement therapy with testosterone or corticosteroids; presence of hyperaldosteronism, psoriasis, cutaneous lymphoma, or other neoplasms (except nonmelanoma skin cancer); and patient refusal to participate. The inclusion criteria for controls were age 35 to 55 years and agreement to participate in the study. The exclusion criteria for the controls were the same as for the cases, as well as the presence of androgenetic alopecia.

We collected the following data: age, family history of androgenetic alopecia, current or previous treatment for alopecia, smoking habit, family history of early-onset cardiovascular disease (before 55 years in men and before 65 years in women), personal history of cardiovascular disease, and drug treatments (oral antidiabetic agents, lipid-lowering agents, and antihypertensive drugs). Weight and height were recorded to calculate the body mass index (BMI). In addition, we recorded waist circumference, blood pressure (average of 2 readings taken 10 minutes apart), and the degree of alopecia according to the Ebling classification.

We determined erythrocyte sedimentation rate (ESR) along with serum levels of glucose, triglycerides, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), total cholesterol, sex hormone–binding globulin (SHBG), aldosterone, insulin, C-reactive protein (CRP), fibrinogen, and D-dimer (DD) between 8 AM and 9 AM after a 10-hour fast. Carotid ultrasound scans were performed using the Acuson Antares system (Siemens); a 10-5 MHz transducer enabling visualization of the supra-aortic vessels was used to study the presence of atheromatous plaques (defined as an intima-media thickness greater than 1.5 mm) and the intima-media thickness of the common carotid arteries, carotid bulb, and internal carotid arteries. The value recorded was the mean of 5 measurements in both the right and left carotid arteries. Doppler ultrasound was used to determine abnormalities in carotid flow.

Qualitative differences between the study variables were analyzed using contingency tables with the Pearson χ^2 test. The Fisher exact test was applied when the conditions for the Pearson χ^2 were not met. The means of quantitative variables were compared using the *t* test; the Shapiro-Wilk test was used to confirm that the variables were normally distributed and the Levene test was used to assess the equality of variances. The correlation between variables was studied using the Pearson correlation coefficient and exponential regression techniques. A *P* value ≤.05 was considered statistically significant. Statistical analyses were performed using SPSS version 15.0.

Results

General

We studied 35 white men with male androgenetic alopecia (31.4% with type III, 45.7% with type IV, and 22.9% with type V alopecia according to the Ebling classification). The control group comprised 35 men with other common dermatologic diseases. The mean (SD) age for both groups was similar, namely, 43 (8.8) years in the controls and 45.71 (10.6) years in the cases (*P*=.25). The mean time since onset of alopecia was 18.03 (8.1) years. There was a family history of alopecia in 85.7% of the cases compared with 17.1% of the controls (*P*<.0001; odds ratio [OR], 29; 95% confidence interval [CI], 7.9-105.5). Alopecia was treated using 5% minoxidil in 14.3% of patients, and only 2.9% took finasteride 1 mg. There were no significant differences in blood pressure values for patients using minoxidil. Table 1 shows the mean values for weight, height, BMI, drug treatments (antihypertensive agents, antidiabetic agents,

Table 1 Mean Values for Weight, Height, Body Mass Index, Drug Treatments (Antihypertensive Agents, Antidiabetic Agents, Lipid-Lowering Agents), Personal and Family History of Cardiovascular Disease, Sedentary Lifestyle, and Smoking in Cases and Controls

	Cases	Controls	*P* Value
Weight, kg, mean (SD)	82.06 (13.8)	83 (11.6)	.25
BMI, kg/m^2, mean (SD)	27.41 (3.6)	27.15 (3.6)	.76
Height (SD), cm	172.7 (8.4)	174.9 (8.2)	.27
Antihypertensive agents, %	17.1	11.4	.24
Oral antidiabetic agents, %	8.5	2.8	.60
Lipid-lowering agents, %	0	0	–
Personal history of coronary disease, %	0	0	–
Family history of heart disease, %			
Paternal	11.4	5.7	.21 (OR, 2.6, 95% CI, 0.7-9.7)
Maternal	8.5	2.8	
Both	5.7	2.8	
Sedentary lifestyle, %	48.5	40	.63
Smoking habit, %	28.5	25.7	.88

Abbreviation: BMI, body mass index.

lipid-lowering agents), personal and family history of cardiovascular disease, sedentary lifestyle, and smoking. Neither the *t* test (comparison of means for quantitative samples) nor the Pearson χ^2 test (qualitative variables) revealed statistically significant differences; therefore, the distribution of the variable was assumed to be similar between the groups.

Metabolic Syndrome

The prevalence of metabolic syndrome was established according to ATP-III criteria[6] (Table 2): 57.1% of patients with androgenetic alopecia fulfilled 3 or more of the criteria for metabolic syndrome compared with 14.3% of the controls (*P*<.0001; OR, 8; 95% CI, 2.5-24.6). Table 3 shows the differences between cases and controls for all the parameters that make up the metabolic syndrome. The *t* test for equality of means revealed statistically significant differences in mean values of waist circumference, hypertriglyceridemia, systolic blood pressure, and fasting glucose concentration. However, the mean diastolic blood pressure and HDL-C were similar in both groups (*P*>.05). No significant differences were observed in the mean values of LDL-C (120.6 mg/dL vs 107.0 mg/dL; *P*=.096) or in total cholesterol (198.7 mg/dL vs 184.2 mg/dL; *P*=.1) for cases and controls, respectively. All variables in the metabolic syndrome were independent of age, weight, height, and time since onset of alopecia, except for abdominal obesity, which correlated positively with weight (*r*=0.75; *P*<.0001) and time since onset of alopecia (*r*=.24; *P*=.037), and negatively with HDL-C (*r*=-0.31; *P*=.007). Systolic blood pressure correlated with central obesity (*r*=0.36; *P*=.02).

Table 2 Adult Treatment Panel III Criteria for Metabolic Syndrome in Men

Abdominal obesity	> 102 cm
Triglycerides	> 150 mg/dL
Systolic blood pressure	> 130 mm Hg or treatment
Diastolic blood pressure	> 85 mm Hg
HDL cholesterol	< 40 mg/dL
Blood sugar	> 110 mm Hg or treatment

A diagnosis of metabolic syndrome requires the presence of 3 or more criteria.
Abbreviation: HDL, high-density lipoprotein.

Carotid Atherosclerosis and Flow Studies

Atheromatous plaque was unilateral in 20% of cases (Figure) and bilateral in 14.3%. Unilateral atheromatous plaque was present in 8.6% of controls (OR, 5.5; 95% CI, 1.4-21.9; *P*=.018). Except for 8.5% of patients in whom abnormal blood flow was detected (moderate to severe stenosis) and magnetic resonance angiography was performed, atheromatous plaques did not lead to significant hemodynamic abnormalities (no stenosis). In the

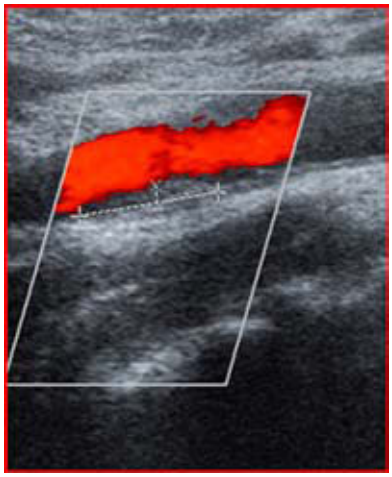

Figure Carotid atheromatous plaque in a patient with androgenetic alopecia.

Table 3 Differences Between Cases and Controls for All the Parameters That Make Up the Metabolic Syndrome

	Presence of Androgenetic Alopecia	N	Mean	SD	*P* Value
Abdominal obesity, cm	Yes	35	103	8.5	.039
	No	35	98.6	8.7	
Hypertriglyceridemia, mg/dL	Yes	35	164.9	106.2	.05
	No	35	123.4	69.1	
HDL cholesterol, mg/dL	Yes	35	48.1	14	.49
	No	35	50.6	16.3	
Systolic blood pressure, mm Hg	Yes	35	135.5	16	.049
	No	35	125.9	23.3	
Diastolic blood pressure, mm Hg	Yes	35	83.7	9.3	.71
	No	35	82.5	15.8	
Fasting blood glucose, mg/dL	Yes	35	105.7	42.9	.04
	No	35	89.8	16.6	

Abbreviation: HDL, high-density lipoprotein.

cases, 46.5% of the plaques were described as fibroadipose (hyperechoic-hypoechoic) and the remainder as calcified (hyperechoic). Right and left carotid intima-media thickness was statistically greater in cases than in controls (0.70 mm vs 0.55 mm [*P*<.001] for the left side; 0.69 mm vs 0.60 mm [*P*=.022] for the right side). The correlation between right and left carotid intima-media thickness was very strong (*r*=0.76; *P*<.0001). Metabolic syndrome was present in 60% of patients with atheromatous plaque (OR, 3.65; 95% CI, 1.1-11.9; *P*=.027). Patients with atheromatous plaque had significantly greater abdominal obesity (104.9 cm vs 99.8 cm; *P*=.04), hypertriglyceridemia (190.5 mg/dL vs 130.8 mg/dL; *P*=.024), diastolic blood pressure (89.3 mm Hg vs 81.8 mm Hg; *P*=.047), and blood sugar (120.0 mg/dL vs 89.5 mg/dL; *P*=.001).

Markers of Chronic Inflammation

The mean values for fibrinogen, DD, and ESR were significantly higher in the cases (Table 4); however, there were no significant differences in mean CRP values. Patients with metabolic syndrome had significantly higher fibrinogen values (347.0 mg/dL vs 301.2 mg/dL; *P*=.042) and ESR (12.6 mm/h vs 7.2 mm/h; *P*=.03), and patients with atheromatous plaque had significantly higher values for DD (159.5 ng/mL vs 104.8 ng/mL; *P*=.043) and ESR (13.9 mm/h vs 6.4 mm/h; *P*=.027). The mean values for DD correlated positively with abdominal obesity (*r*=0.27; *P*=.022) and the ESR values correlated positively with hypertriglyceridemia (*r*=0.46; *P*<.0001).

Hormone Study

Mean levels of aldosterone and insulin were significantly higher in the cases (Table 5). However, there were no differences in the mean values for testosterone or SHBG. Mean values for insulin were significantly higher in patients with metabolic syndrome (12.3 µU/mL vs 9.0 µU/mL; *P*=.020), and there were no differences between the groups for the remaining hormone parameters. The group of patients with atheromatous plaque also had higher basal insulin levels (13.3 µU/mL vs 8.9 µ/mL; *P*=.007), with no differences in the remaining parameters. Insulin values correlated positively with fasting glucose levels (*r*=0.54; *P*<.0001). Hypertensive cases had higher aldosterone values than nonhypertensive cases. However, aldosterone values in the controls were similar, irrespective of blood pressure, and they were lower than in the cases.

Discussion

The results of this study confirm that male androgenetic alopecia is associated with a greater prevalence of cardiovascular risk factors included in the metabolic syndrome and with an increase in carotid atherosclerosis.

Table 4 Comparative Study of Acute Phase Reactants in Cases and Controls

	Presence of Androgenetic Alopecia	N	Mean	SD	*P* Value
CRP, mg/dL	Yes	35	0.39	0.57	.83
	No	35	0.36	0.65	
Fibrinogen, mg/dL	Yes	35	337.74	61.3	.037
	No	35	290.51	116.2	
DD, ng/mL	Yes	35	157.2	108.3	.046
	No	35	109.4	87.4	
ESR, mm/h	Yes	35	13.5	14.2	.05
	No	35	8.3	6.4	

Abbreviations: CRP, C-reactive protein; DD, D dimer; ESR, erythrocyte sedimentation rate.

Table 5 Comparative Study of Hormone Parameters in Cases and Controls

	Presence of Androgenetic Alopecia	N	Mean	SD	*P* Value
Testosterone, ng/mL	Yes	35	5.25	1.8	.16
	No	35	4.69	1.5	
Aldosterone, pg/mL	Yes	35	199.24	110.8	.041
	No	35	152.28	74.4	
Insulin, µU/mL	Yes	35	11.7	6.5	.004
	No	35	7.9	3.8	
SHBG, nmol/L	Yes	35	29.5	34.3	.97
	No	35	29.3	21.7	

Abbreviations: SHBG, sex hormone–binding globulin.

The association between androgenetic alopecia and cardiovascular disease was first posited by Cotton et al[1] in 1972. Since then, although several epidemiology studies have investigated this association, the results have been inconsistent. Most have focused on the analysis of coronary disease (acute myocardial infarction or cardiac death), and few authors have analyzed the association with cardiovascular risk factors, such as criteria for metabolic syndrome or the presence of carotid atheroma.

Both our groups were very homogeneous in terms of anthropometric data (weight, height, and BMI), and they were similar in terms of other confounders, such as smoking habit, sedentary lifestyle, personal or family history of heart disease, and drug treatment.

Metabolic Syndrome

A comparison of the frequency of metabolic syndrome revealed considerable differences between the groups. More than half of the cases met 3 or more of the criteria for metabolic syndrome, an essential criterion being the presence of abdominal obesity, according to the latest recommendations of the International Diabetes Foundation. Metabolic syndrome was diagnosed in only 14.3% of the control group.

The association between cardiovascular disease and metabolic syndrome is well documented. Recent studies show that people who meet ATP-III criteria are 2.59 to 3.5 times more likely to have a cardiovascular event during the next 10 years.[7,8] Furthermore, the authors of those studies state that the ATP-III criteria correlate better with cardiovascular disease than other criteria used to define the metabolic syndrome.

No published studies analyze the prevalence of metabolic syndrome according to ATP-III criteria in individuals with androgenetic alopecia. However, the prevalence of metabolic syndrome reported for the general population ranges from 11.7%[9]—similar to the value found in our study—to 30% in the population of Brazil,[10] with a mean value of 20% in some studies published in Spain.[11,12]

In our study, abdominal obesity was significantly higher among the cases; however, there were no significant differences between the groups in terms of weight or BMI, indicating that, among the cases, there is a redistribution of abdominal fat. This is an important cardiovascular risk factor associated with insulin resistance in many studies. Our study showed that the cases presented higher mean insulin values, thus indicating peripheral insulin resistance and a compensatory attempt by the pancreas to maintain its action. Similarly, we found that patients with metabolic syndrome have hyperinsulinemia (insulin levels greater than 10 μU/mL), confirming that insulin resistance is a key element in the pathogenesis of this syndrome.

Matilainen et al[13] established the association between early-onset androgenetic alopecia and insulin resistance, although the mechanism by which insulin resistance affects alopecia is not clear. Excess circulating insulin could lead to vasoconstriction and nutritional deficiency in the follicles of the scalp, thus favoring the effect of dihydrotestosterone (DHT) on follicular miniaturization. Consistent with this possibility, Klemp et al[14] reported that reduced blood flow in the scalp could be associated with early-onset androgenetic alopecia. There has also been a report of microvascular insufficiency in areas of alopecia.[15]

Mean systolic blood pressure values were significantly higher in our cases, although there were no differences in diastolic blood pressure values. The slightly larger proportion of patients receiving antihypertensive medication in the group with alopecia may have reduced the differences in diastolic blood pressure between the groups.

A recently published study analyzing the association between androgenetic alopecia and hypertension showed that 82% of patients with hypertension (>140/90 mm Hg) had alopecia, compared with 56% of those with normal blood pressure levels (P<.001), and confirmed that this association was independent of age.[16] The authors offered 2 explanations for this association: first, the androgens involved in the pathogenesis of androgenetic alopecia bind to vascular receptors and favor the increase in blood pressure; and second, hyperaldosteronism, which is an underlying condition in most cases of hypertension, plays a direct role in the development of alopecia, according to the results of a study in which transgenic mice overexpressing mineralocorticoids developed alopecia.[17] However, the authors did not determine aldosterone values.

The aldosterone values in our cases were significantly higher than in the controls (199.0 pg/mL vs 152 pg/mL; P<.05), thus supporting the hypothesis presented above. However, we did not find significant differences in testosterone values. In these cases, the use of aldosterone antagonists could have a doubly beneficial effect, namely, control of blood pressure and a halt to the progression of alopecia. The new selective aldosterone receptor antagonists could prove useful in the treatment of male androgenetic alopecia and prevent the adverse effects of spironolactone antiandrogenic agents.[18]

Hirsso et al[19] also found higher blood pressure values in patients with androgenetic alopecia than in a control group (65% vs 45%), as well as a greater frequency of diabetes and hyperinsulinemia. However, a study published in 2007 did not find statistically significant differences for systolic or diastolic blood pressure levels in patients aged less than 35 years.[2]

Mean HDL-C values, while somewhat lower in the case of patients with alopecia, were quite similar. Their plasma levels were strongly associated with physical exercise; the high rates of sedentary lifestyle we found in both groups explain the low HDL-C values and the absence of differences. However, mean triglyceride values were higher in cases than in controls (164.0 mg/dL vs 123.0 mg/dL; P<.05). Matilainen et al[20] found similar results when triglyceride levels in men with alopecia who had undergone revascularization due to heart disease were compared with those in a control group. Sharrett et al[21] studied both HDL-C and triglycerides in the general population and confirmed that the association with the presence of atheromatous plaque was not very strong; however, both were associated with coronary disease. Thus, the authors showed that high triglyceride values and low HDL-C values

were associated with the transition from atheroma to atherothrombosis and that, therefore, control of both these cardiovascular risk factors is essential in patients with subclinical disease.

Blood sugar values were significantly higher in the cases (105.0 mg/dL vs 89 mg/dL; *P*=.04). Abnormal fasting glucose levels were present in 19% of the cases; however, in the control group, each patient had glucose levels lower than 110 mg/dL. One of the most notable observations in the study by Hirsso et al[2] was that 21% of patients with androgenetic alopecia and 12% of the control group had diabetes. Hyperglycemia in patients with higher insulin values is explained by peripheral resistance to the action of insulin.

Carotid Atherosclerosis and Flow Studies

The second key area analyzed here is the presence of carotid atheromatous plaques, as studied by Doppler ultrasound. Many studies assume that pathogenesis is similar for coronary atherosclerosis and carotid atherosclerosis and, therefore, that the presence of carotid atheroma also predicts coronary disease.[21] Atheromatous plaque was present in 34% of cases, and 3 of these patients had hemodynamic abnormalities with altered carotid flow. In contrast, only 8.6% of patients in the control group had unilateral atheroma. In addition, carotid intima-media thickness was greater in cases.

Most studies on this topic do not analyze the presence of carotid atherosclerosis as a predisposing factor for cardiovascular disease. Instead, they directly analyze cardiovascular events, generally myocardial infarction, although they restrict their analysis to patients who have survived coronary disease; therefore, they miss data on patients who die and do not take into account asymptomatic individuals with coronary disease.

Despite revealing an OR of 1.43 (95% CI, 1.05-1.86) for patients with moderate alopecia on the vertex, the new study by Shahar et al[22] on alopecia and myocardial infarction concluded that male pattern baldness is not an important risk factor for myocardial infarction or asymptomatic atherosclerosis. The authors performed a very interesting analysis involving measurement of carotid intima-media thickness in patients who did not have cardiovascular disease and compared the results according to the degree of alopecia. They did not find statistically significant differences in carotid intima-media thickness according to the degree of alopecia, despite studying a large number of patients. However, they did not determine whether the presence of atheromatous plaque differed between the groups, and we must bear in mind that, for some authors, this parameter correlates better with myocardial infarction than carotid intima-media thickness.[23] Dogramaci et al,[24] on the other hand, found an association between severe androgenetic alopecia and a higher carotid intima-media thickness, although they did not analyze the prevalence of atheromatous plaque either.

No published studies have analyzed the prevalence of atheromatous plaque in patients with androgenetic alopecia. Junyent et al[25] examined the frequency of atheromatous plaque in the general population and observed figures that were similar to those recorded in our control group for similar age groups. Our study analyzed the prevalence of atheromatous plaque and carotid intima-media thickness in patients with androgenetic alopecia. Atheromatous plaque is an easier parameter to measure than carotid intima-media thickness and is very useful when evaluating overall cardiovascular risk in our patients. The approach is noninvasive, reliable, reproducible, and inexpensive; therefore, it is the technique of choice for the detection of subclinical atherosclerosis, and makes it possible to establish a classification that goes beyond common risk factors.

Markers of Chronic Inflammation

We also measured acute phase reactants in both groups. These included DD, fibrinogen, ESR, and CRP. Mean values were significantly higher for all reactants except CRP in the cases. Patients with metabolic syndrome had higher values for fibrinogen and ESR (*P*<.05). There was also a statistically significant association between the presence of atheromatous plaque and increased ESR and DD. However, Hirsso et al[2] reported high-sensitivity CRP values that increased with the waist-to-hip ratio in patients aged less than 35 years who had moderate or severe alopecia.

Chronic inflammation has been shown to play a key role in the presence of insulin resistance, endothelial dysfunction, and cardiovascular disease.[26] The proinflammatory stress underlying androgenetic alopecia that manifests with the presence of increased mean values for acute phase reactants could favor the increase in proinflammatory cytokine levels found in the arterial wall and hair follicles. Microinflammation in hair follicles related to the pathogenesis of alopecia may be a local manifestation of a systemic inflammation that is associated with a higher frequency of metabolic syndrome and cardiovascular disease in individuals with alopecia.[2]

Hormone Study

The hormone study we performed in our patients did not reveal significant differences in levels of testosterone or SHBG in either of the groups. This was to be expected, as patients with androgenetic alopecia do not have higher testosterone levels, but greater peripheral sensitivity to androgens. Testosterone is converted by 5α-reductase into DHT. This then acts to miniaturize the hair follicles.

There have also been reports of the presence of 5α-reductase in the muscle layer of blood vessels and the heart.[27] This leads to the conversion of testosterone into DHT, which stimulates smooth muscle proliferation in the blood vessels. Therefore, the association between androgenetic alopecia and the presence of atheromatous plaque could be explained by a greater sensitivity of androgens in the scalp and in vascular smooth muscle, thus favoring miniaturization of the hair follicles in one case and the presence of atheromatous plaque in the other.

Pathogenic Mechanisms Underlying Increased Cardiovascular Risk in Patients With Androgenetic Alopecia

1. Hyperinsulinemia caused by increased resistance to the peripheral action of insulin has been posited to explain the association between androgenetic alopecia and cardiovascular disease. Elevated insulin levels are the main cause of metabolic syndrome and favor intolerance to carbohydrates and central obesity. Insulin has also been shown to favor vasoconstriction and nutritional deficiency in the follicles of the scalp, and it enhances the effect of DHT on follicular miniaturization. Our study revealed higher insulin levels in patients with metabolic syndrome. This was clearly expected. In addition, the values for this hormone were significantly higher in the cases, thus supporting this theory.
2. Overexpression and stimulation of mineralocorticoid receptors in transgenic mice has been shown to cause alopecia.[17] This seems to be a suitable explanation for the association between hypertension and androgenetic alopecia reported by some authors.[16] Hyperaldosteronism has been posited as a cause of essential hypertension; therefore, aldosterone would stimulate these skin receptors, thus favoring progression of alopecia. We also found higher levels of aldosterone in the cases, and the difference was statistically significant. In addition, we observed that aldosterone values were higher only among hypertensive cases, and that they were lower in hypertensive controls.
3. Androgenetic alopecia is caused by greater peripheral sensitivity to androgens. Thus, free testosterone is converted into DHT by 5α-reductase and this leads to follicular miniaturization. Similarly, 5α-reductase has been detected in blood vessels and the heart, as have DHT receptors, which are involved in smooth muscle proliferation in blood vessels, a key phenomenon in arteriosclerosis, together with lipid deposition. One of the mechanisms responsible for the increased occurrence of atheromatous plaques in our cases could be increased sensitivity to androgens both at the level of the scalp—thus favoring follicular miniaturization—and at the vascular level—thus promoting development of atheromatous plaque.
4. The association between alopecia and cardiovascular disease may have a genetic origin. Family history plays an important role in the development of alopecia, just as it does in cardiovascular disease. We found a very significant association between the presence of androgenetic alopecia and family history of this condition. Family history of heart disease was also more important in our cases (OR, 2.6; 95% CI, 0.7-9.7).
5. Chronic inflammation, which is more prevalent in patients with androgenetic alopecia, has served to explain the association with cardiovascular disease. The possible proinflammatory stress underlying androgenetic alopecia that manifests with the presence of increased mean values for acute phase reactants in individuals with alopecia could favor the increased proinflammatory cytokine levels observed in the arterial wall and hair follicles. We found higher values for DD, ESR, and fibrinogen in patients with androgenetic alopecia in the control group, thus supporting this explanation.

A larger sample would enable us to analyze how these cardiovascular risk factors behave according to the Ebling classification. It would also be interesting to study these same parameters in women with androgenetic alopecia and make a comparative analysis with men. Although case-control studies are susceptible to selection bias, the distribution of confounders in the present study was homogeneous in both groups.

We have established that androgenetic alopecia is associated with the cardiovascular risk factors included in the metabolic syndrome and with carotid atheromatosis. This association can be explained by different mechanisms that are not exclusive but complementary. In our opinion, cardiovascular screening by the dermatologist in patients with androgenetic alopecia could prove useful for detection of at-risk individuals and for initiation of preventive therapy before cardiovascular disease develops.

Conflicts of Interest

The authors declare no conflicts of interest.

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