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CLINICAL STUDY

The association of urolithiasis and androgenetic alopecia

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Abstract

Objectives: The objective of this study is to investigate whether patients with androgenetic alopecia were at risk in terms of urinary system stone disease. *Patients and methods*: Patients with no baldness (Hamilton–Norwood Scala [HNS] stage I) were categorized as Group I, those with hair loss in the frontal region (HNS stages II, III, IIIa, and IVa) as Group II, those with hair loss in the vertex region (HNS stage III-vertex, V) as Group III and those with hair loss in both vertex and frontal regions (HNS stages IV, Va, VI, and VII) as Group IV. Patients in all groups were compared in terms of presence of stone, and the presence of any association between alopecia and urolithiasis, with common etiological risk factors, was investigated. *Results*: Three hundred and two male patients were included in the study. The presence of urolithiasis was detected in 28.9% of patients in Group I; 26.5% of Group II; 36.9% of Group III; and 44.4% of Group IV ($p = 0.085$). Among patients aged under 60, urinary stone disease was detected in 30.8% of patients in Group I; 26.4% of Group II; 41.2% of Group III; and 53.8% of Group IV ($p = 0.001$). In patients aged over 60, urolithiasis was detected in 12.5% of patients in Group I; 26.9% of Group II; 32.2% of Group III; and 37.8% of Group IV ($p = 0.371$). *Conclusions*: We determined a significant correlation between vertex pattern and total alopecia with urolithiasis in patients younger than 60 years old.

Keywords

Androgenetic alopecia, ultrasound, urolithiasis

History

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Introduction

Although the lifetime prevalence of urinary system stone disease varies depending on elements such as age, sex, race, and genetic factors, it is estimated at between 1% and 15% worldwide.[1] Epidemiological studies have shown that it is 2–3 times more common in males than females.[2–4] Although the reason for the difference in incidence between the sexes is unclear, apart from stone disease being multifactorial and having a complex pathogenesis, both clinical and experimental studies have reported that the main cause stems from testosterone inducing stone formation.[1–6] These studies have sought to explain the mechanism by which androgens lead to stone formation in terms of increasing endogenous oxalate synthesis, suppressing expression of osteopontin from the kidneys, reducing citrate excretion in urine, and leading to oxidative cell damage.[2–7]

Androgenetic alopecia (AGA), otherwise known as male pattern baldness, is a disorder characterized by follicular miniaturization resulting from increased sensitivity at the follicular level to dihydrotestosterone, a metabolite of testosterone.[8,9] Patients typically present with progressive hair thinning in the area affected, followed by hair loss.[10] The disorder affects nearly 50% of men in their lifetimes, and is more common in men with specific polymorphisms in their androgen receptor genes.[9,11] Association with diseases proposed as being involved in the etiology of AGA, such as benign prostatic hyperplasia, prostate cancer, atherosclerosis, acne vulgaris, and testicular germ cell tumor, has been investigated in various studies, and it has been reported that AGA may be an early marker of these diseases.[9,10,12–14]

However, whether or not there is a correlation between AGA and urinary system stone disease, in whose etiology androgens have been shown to be involved, has not been investigated to date. In this study, we investigated whether patients with AGA were at risk in terms of urinary system stone disease.

Patients and methods

Study population

Three hundred two patients aged over 18 who underwent urinary system ultrasonography (US) due to abdominal or flank pain and meet study conditions were included in the study following approval of its design by the Çanakkale

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Onsekiz Mart University Faculty of Medicine Ethical Committee. Subjects with renal malformation that might create predisposing factors for urolithiasis, such as horseshoe kidney, polycystic renal disease, malrotated or ectopic kidney or ureteropelvic junction obstruction, or with glomerular or tubular renal disease were excluded. Patients with a history of stone surgery or stone formation but without urinary stone disease on the basis of imaging results were not included. Non-contrast computed tomography was obtained for patients with suspect hydronephrosis and urolithiasis. Patients were divided into two groups on the basis of imaging results, with or without urinary system stone disease. Demographic data such as participants' age, occupation, body mass index (BMI), presence of chronic diseases such as hypertension (HT) and diabetes mellitus (DM), and baldness pattern were recorded.[15] All these variables were investigated in terms of whether or not they constituted a risk factor for the presence of stone in the urinary system.

Balding pattern

Classification of baldness was performed using the Hamilton–Norwood Scale, and patients were then divided into four categories as described by Severi et al.[15,16] Patients with no baldness (Hamilton–Norwood Scala [HNS] stage I) were categorized as Group I, those with hair loss in the frontal region (HNS stages II, III, IIIa, and IVa) as Group II, those with hair loss in the vertex region (HNS stage III-vertex, V) as Group III and those with hair loss in both vertex and frontal regions (HNS stages IV, Va, VI, and VII) as Group IV (Figure 1). Patients in all groups were compared in terms of the presence of stone, and the presence of any association between alopecia and urolithiasis, with common etiological risk factors, was investigated.

Ultrasound measurements

All examinations were performed by radiologists experienced in the field of ultrasound. Sonographic examinations were performed with gray scale ultrasound machines (Toshiba Aplio XG and General Electric Logiq 9, Toshiba, Tokyo, Japan) using two convex transducers at frequencies of 3.5 MHz and 4.0 MHz. The presence of stone was defined as an echogenic image with or without posterior acoustic shadowing, clearly located within the urinary tract.

Statistical analysis

All statistical analyses were performed using SPSS, version 20.0 (SPSS Inc., Chicago, IL). All values are shown as mean ± standard deviation. Comparisons were performed using the Chi-square test. Differences between groups were considered statistically significant at $p < 0.05$.

Results

Three hundred two male patients were included in the study. Stone was detected in the urinary system through US examination in 100 (33.1%), while no presence of stone was encountered in 202 (66.9%). Mean age of the patients with urolithiasis was 53.03 ± 19.3 years (18–86), compared with 51.6 ± 18.6 (18–88) for those with no stone ($p = 0.337$). BMI values in patients with and without stone were 27.1 ± 4.38 (19–38) and 24.5 ± 4.41 kg/m^2 (12–42), respectively ($p = 0.008$). No difference was determined between the groups in terms of DM (18% versus 15.3%), while the presence of HT was greater in patients with stone detected in the urinary system (35% versus 16.3%; $p < 0.001$). At multivariate regression analysis involving risk factors that might be correlated with the presence of urolithiasis; increased BMI and the presence HT emerged as being significantly associated with urolithiasis. Age and the presence of DM were not risk factors for development of stone. Patients' demographic data are given in Table 1.

In terms of baldness patterns, no baldness was observed in 76 (25.1%) patients (HNS stage I; Group I), hair loss in the frontal region was observed in 98 (32.4%) (HNS stages II, III, IIIa, and IVa; Group II), in the vertex region in 65 (21.5%)

Table 1. Patient demographics.

	Urolithiasis		
Variable	Yes	No	*p*-Value
No. patients	100 (33.1%)	202 (66.9%)	
Mean age ± SD (years)	53.03 ± 19.3	51.6 ± 18.6	0.337
Profession (%)			
Student	4%	6.9%	
Retired/unemployed	51%	50.9%	
Officer	15%	10.9%	
Worker	23%	26.2%	
Tradesman	7%	2.9%	
Body mass index (mean)	27.1 kg/m^2	24.5 kg/m^2	0.008*
Underweight (< 18.5)	0%	1.5%	
Normal weight (18.5–24.9)	22%	38.1%	
Overweight (25–29.9)	56%	52.4%	
Obesity (30–34.9)	22%	7.4%	
Severely obese (≥ 35)	0%	0.5%	
Diabetes mellitus (%)	18%	15.3%	0.086
Hypertension (%)	35%	16.3%	$p < 0.001$*

*Statistically significant at $p < 0.05$.

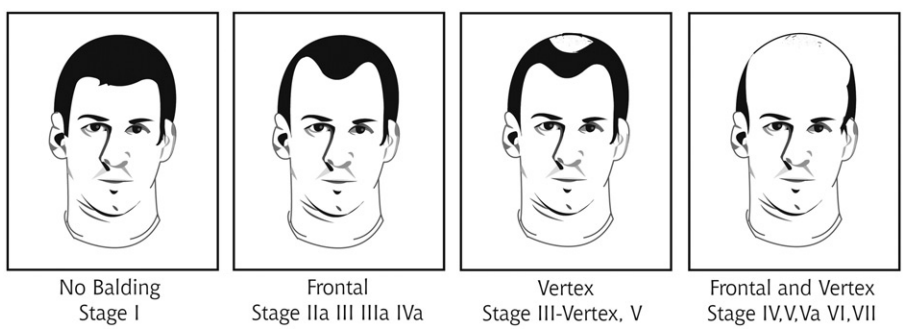

Figure 1. Classification of baldness pattern using the Hamilton–Norwood Scala.

(HNS stage III-vertex, V; Group III), and in both the frontal and vertex regions in 63 (20.8%) (HNS stages IV, Va, VI, and VII; Group IV). The presence of stone in the urinary system was detected in 28.9% of patients in Group I; 26.5% of Group II; 36.9% of Group III, and 44.4% of Group IV. Although there was a high incidence of urolithiasis in patients with total and vertex alopecia than frontal alopecia and no baldness, statistically significant difference was not determined between the groups ($p = 0.085$).

However, when age was used as a categorical variable (<60 years and ≥ 60 years), there was a significant association between the baldness pattern and the presence of urolithiasis in patients aged under 60 years. Among patients aged under 60, the presence of stone in the urinary system was detected in 30.8% of patients in Group I; 26.4% of Group II; 41.2% of Group III, and 53.8% of Group IV ($p = 0.001$). We determined that risk of urolithiasis increased 1.5-fold in patients with vertex pattern alopecia and two-fold in patients with total alopecia compared with those with no hair loss (Table 2). Among patients aged over 60, the presence of stone in the urinary system was detected in 12.5% of patients in Group I; 26.9% of Group II; 32.2% of Group III, and 37.8% of Group IV. In this age group of patients, there was no association between the baldness patterns and the presence of urolithiasis ($p = 0.371$).

We also analyzed the association between baldness pattern and other risk variables in each groups. No difference was determined between the groups in terms of HT ($p = 0.174$) and BMI values ($p = 0.077$), while the presence of DM was greater in patients with severe alopecia (6.5%, 14.2%, 20%, and 26.9% in Groups I, II, III, and IV, respectively; $p = 0.009$). Mean age of the patients was 41.1 years in Group I; 51.3 years in Group II; 58.4 years in Group III; and 60.3 years in Group IV ($p = 0.001$).

Discussion

This study determined that risk of urolithiasis increased in patients younger than 60 years old that 1.5-fold with vertex pattern alopecia and three-fold in patients with total alopecia compared to those with no hair loss. These results are important in terms of precautionary measures being taken through the early identification of groups at risk of urinary stone and the development of treatment strategies by fully revealing the mechanisms involved in the etiopathology. To the best of our knowledge, this study is the first publication investigating the relationship between alopecia and urinary system stone disease.

Several previous clinical and experimental studies have revealed that androgens play a role in the etiopathology of urolithiasis, for which reason stone disease is more common in men than in women.[1–7] These studies have proposed various theories regarding the role of androgens in stone formation. In one of these theories, Yoshioka et al.[4] showed that sex hormones in a rat model increased endogenous oxalate synthesis by affecting two major hepatic peroxisomal enzymes, and that testosterone increased crystal deposition by causing oxidative stress injury. Yagisawa et al., however, in a study of male and female rats, determined that testosterone increased oxalate secretion in urine by suppressing release of osteopontin in the kidneys.[3] The results of both studies support and explain the results of Lee et al.'s 1992 study showing greater release of oxalate in urine in male rats compared with females and castrated male rats.[17]

In another study, Li et al. investigated the relationship of urolithiasis with plasma testosterone and androgen receptor up-regulation in the kidneys.[18] From their immunohistochemical investigation, the authors determined up-regulation in androgen receptors in the kidneys of patients with urolithiasis and suggested that this increased androgen signal transmission might be a reason for the difference in incidence of renal stone between the sexes. In addition, although some authors have maintained that estrogen plays a protective role against urinary system stone disease and that urolithiasis is less common in women for that reason, this theory has not been confirmed by studies.[19,20] Mattix et al.[21] corroborated this by showing that the use of estrogen in the postmenopausal period has no protective effect against stone formation.

AGA, or male pattern baldness, is a widely seen androgen-dependent skin problem, the causes of which are not fully understood.[22] The active androgen dihydrotestosterone (DHT) is thought to play the basic role in the disorder, and increased sensitivity to this hormone at the hair follicle level is believed to cause hair loss by leading to follicular miniaturization.[8,9] AGA not being observed in males with 5α-reductase

Table 2. Association of urolithiasis and hair loss pattern of patients.

	Urolithiasis rate (%)			
	Total	<60 years	≥60 years	
Balding pattern				
Group I	28.9%	30.8%	12.5%	
Group II	26.5%	26.4%	26.9%	
Group III	36.9%	41.2%	32.2%	
Group IV	44.4%	53.8%	37.8%	
	Balding pattern rate (%)			
	Group I	Group II	Group III	Group IV
Urolithiasis				
Yes	22%	26%	24%	28%
No	26.7%	35.6%	20.3%	17.3%

deficiency, an autosomal recessive genetic disorder, proves that DHT is the androgen metabolite actively involved in the development of male pattern hair loss.[22]

Following the demonstration of the role played by androgens in the etiology of alopecia, various studies investigated AGA in combination with other diseases in which androgens are known to be involved and examined whether or not AGA is an early marker of these diseases.[9,10,12–14] Oh et al.[12] showed that males with benign prostatic hyperplasia (BPH) had more severe alopecia compared with an age-matched control group and that there was a powerful relation between BPH and AGA. The authors stated that although they did not evaluate DHT levels in prostate tissue and hair follicles, this powerful relation was associated with increased 5α-reductase activity and androgen receptor levels in prostate tissue and hair follicles in patients with BPH compared with the control group.

Like BPH, prostate cancer is a disease in which androgens are involved in whose etiology and which has similar risk factors to AGA. In 2013, Amoretti et al. evaluated seven studies in a meta-analysis and showed that vertex pattern baldness is correlated with prostate cancer.[9] No risk in terms of prostate cancer was determined in patients with frontal or total AGA. Signorella et al.[23] investigated the association between various growth factors and hormones and male pattern baldness and reported that high testosterone insulin-like growth factor-1 (IGF-1) levels were correlated with vertex pattern baldness. Elevated testosterone and IGF-1 levels also being associated with an increased risk of prostate cancer explains the association between vertex pattern baldness and prostate cancer in Amoretti et al.'s meta-analysis.

In addition to prostate diseases, various studies have also investigated the association between AGA and coronary heart diseases and atherosclerosis. One rat study performed in order to explain this association reported that serum androgens accelerated atherosclerosis by stimulating vascular smooth muscle cell proliferation.[24] Dogramaci et al.[10] showed a greater common carotid artery intima media thickness and an increased risk of subclinical atherosclerosis in patients with vertex pattern AGA compared to those with other baldness patterns or no baldness. In another study, Santiago et al.[25] reported a higher level of metabolic syndrome and atheromatous plaque in patients with AGA compared with the control group and lower serum insulin, aldosterone and fibrinogen levels in patients with AGA compared with the control group.

AGA is thus associated with several diseases (e.g., prostate diseases, atherosclerosis, metabolic syndrome) in whose etiology androgens are involved and may perhaps serve as an early marker in terms of these diseases. In our study, too, we investigated whether there is a correlation between urinary system stone disease, in whose etiology androgens have a proven role, and male pattern baldness, and determined a significant correlation between both vertex pattern and total alopecia with urolithiasis in patients younger than 60 years old. We think that decreased endogenous testosterone levels during the late adulthood period may be a reason for the decreased correlation between alopecia and urinary stone disease. Furthermore, higher rate of alopecia in elderly patients may be another factor for the decreased correlation between alopecia and urolithiasis.

Although there are some limitations to our study, it is still the first to investigate the relation between alopecia and urinary system stone disease. The results are important in terms of protective measures being taken through the early identification of risk groups in terms of urinary system stone disease and in terms of the development of new treatment strategies by revealing the mechanisms involved in the pathogenesis.

Declaration of interest

The authors report that they have no conflicts of interest.

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