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THE ADRENAL MASSES AND THEIR ASSOCIATION WITH ARTERIAL HYPERTENSION

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ABSTRACT

The work was initiated to study peculiarities of arterial hypertension (AH) in patients with adrenal masses. Data on 282 patients, 169 women (59.9%) and 113 (40.1%) men among them, with adrenal masses were analyzed. All patients underwent general clinical, biochemical, hormonal and instrumental tests. Arterial hypertension was the main clinical manifestation with various intensities registered in 218 patients (77.3%). Mean systolic and diastolic arterial pressures were significantly higher in the index group (p=0.0001). In this group, the proportion of persons with III-degree AH was significantly higher than in the controls (26.6% versus 10.3%; χ^2=4.09; p=0.04), while in the control group the proportion of persons with II-degree AH was higher than in the index one ((38.5% versus 17.4%; χ^2=8.27; p=0.004). Arterial hypertension in patients with adrenal masses can be continuous (29.2%) or regular (20.2%) or with sharp rises of blood pressure.

KEY WORDS: adrenal masses, arterial hypertension, cardiovascular disease.

INTRODUCTION

Among disorders with concurrent arterial pressure (AP) increase, the proportion of the secondary arterial hypertensions (AH) is estimated 25-35%; arterial hypertensions of adrenal genesis account for 15-25% of them.[1,2,3,4] For the last years, their proportion rises steadily. Adrenal AH can be suspected in patients with short medical history of the disorder, with sever and/or rapidly progressing AH, resistant to a drug therapy and in young patients with AH resistant to the combined antihypertensive therapy.[5]

The tumors in the adrenal cortex (aldosteroma, corticosteroma) and medulla (pheochromocytoma) resulting in respective overproduction of aldosterone, cortisol, adrenalin and noradrenalin are the most frequent endocrine causes of symptomatic AH. Clinical syndromes, including primary hyperaldosteronism, endogenous hypercortisolism and hypercathecholaminemia, are characterized primarily with severe and hardly manageable AH in the symptomatic period and irreversible complications, such as acute myocardial infarction, hypertensive crisis and acute cerebrovascular disease.[6,7,8,9] Effective diagnosis of various systolic arterial hypertensions allows selecting specific pathogenetic therapies for them. It is of particular significance for patients with various hormonally active adrenal masses, as well as upon their incident detection aiming at their timely surgery.[5] As soon as the adrenal AH is diagnosed, the chance appears to use a pathogenetic therapy; in some cases, it facilitates recovery or makes unnecessary surgery. That is why, the well-timed diagnosis and adequate treatment of adrenal disorders is an urgent problem of current clinical medicine having high social-economic value.[10,11,12,13,14,15]

The work was initiated to study peculiarities of arterial hypertension in patients with adrenal masses.

MATERIALS AND METHODS

We recruited 282 patients with adrenal masses, referred to the Center for the Scientific and Clinical Study of Endocrinology, Uzbekistan Public Health Ministry, within the period from 2000 to 2018. There were 169 (59.9%) women and 113 (40.1%) men among the patients. As to medical conditions, there were 44 corticosteromas (15.6%), 51 pheochromocytomas (18.1%), 16 aldosterone-producing adenomas (5.6%), 9 verilizing tumors (3.2%), 5 adrenocortical carcinomas (1.8%), 11 cases of metastases to the adrenals (3.9%) and 146 incidentalomas (51.8%).

All patients with adrenal masses underwent general clinical, biochemical, hormonal and instrumental tests. The medical histories were thoroughly examined for cardiovascular disorders, such as arterial hypertension, ishaemic heart disease, cardiac rhythm disorders, chronic cardiac

insufficiency, acute cerebrovascular disease, as well as signs of kidney disease; the findings from ophthalmoscopy were studied too. In addition, to evaluate familial susceptibility to AH and cardiovascular disorders, data on the cardiovascular diseases in the relatives, that is, in men under 55 years and under 65 years in women were analyzed. Special attention was focused on information on the family background, AH duration, as well as on the hypotensive drugs received at the moment of inclusion in the study. The anthropometric parameters, such as height and body mass were measured to calculate body mass index (BMI). Arterial pressure was measured thrice with 2-minute intervals after 5-minute rest in the sitting position on one and the same arm; mean of the three measurements was registered.

Biochemical analysis of blood included measurement of serum potassium, sodium, calcium, lipid profile, fasting glycemia, 2-h glycemia, glycated hemoglobin, creatinine and urea; in some cases the oral glucose tolerance test was performed. Concentrations of plasma aldosterone and plasma renin activity in the standing position were evaluated; aldosterone-renin ratio ≥ 30 allowed suspecting autonomous overproduction of aldosterone requiring additional testing of high specificity in diagnosing primary hyperaldosteronism. Among other hormones, concentrations of ACTH, cortisol, plasma metanephrines, normetanephrines, estradiol, testosterone, dehydroepiandrosterone sulfate and 17-OH-progesterone were evaluated; in some cases daily rhythm of cortisol secretion was assessed and high dose dexamethasone test was performed. Multislice spiral computed tomography of the adrenals was performed as a special visualization method. ECG and ophthalmoscopy were mandatory.

According to the WHO age classification 2017, age under 45 years is considered young. In this context, we divided our patients into two age groups to compare clinical parameters. The first group consisted of 178 patients younger than 45 years of age, 104 patients older than 45 were included into the second one. 39 patients with arterial hypertension without adrenal pathology matching by age and sex were included into the control group. The patients' age for the first referral to the clinic ranged from 4 months to 74 years (mean 39.8±15.7 years). Mean age for men and women was 37.4 ± 16.7 and 41.4 ± 14.9 years, respectively.

RESULTS AND DISCUSSION

For the purpose of the study, we preliminary made up electronic data base containing information about age, sex, arterial hypertension, arterial pressure (AP) rise, AH course, character of hypertensive crisis (self-limitation of the crises, their association with food products, drugs, repeated crises in association with psycho-emotional hypertension and physical loads), age of a patient at the first AP rise, duration of AH, duration of underlying disease before referral for medical care, signs of the disease, complaints, association of the disease with anything, personal and family medical history, including risk factors, clinical and laboratory characteristics of hormonal activity and disturbance of target organs, such as the heart, the eyes, the kidneys.

Arterial hypertension was the main clinical manifestation in patients with the adrenal masses; it was found in 218 (77.3%) patients and had various intensities in accordance with classification of arterial hypertension by the new "2018 European Society of Cardiology (ESC) and European Society of Hypertension (ESH) Guidelines for the management of arterial hypertension" (Table 1).

The groups of patients with AH were comparable by age and AH duration. AH duration in the index group ranged from 6 months to 38 years (mean duration 4.2 ± 5.5 years), in the control group it ranged from 6 months to 18 years (mean duration 3.9 ± 3.7 years).

Among the index group patients, AH was diagnosed in 32 (11.3%) within the period less than 1 year , that is, starting from the moment the increased AP values were measured. AH duration from 1 to 5 years was registered in 120 (42.6%), from 5 to 10 years in 36 (12.8%) and more than 10 years in 30 (10.6%) patients.

Mean systolic and diastolic arterial pressure were higher in the index group patients (p=0.0001). Hereditary burden by AH was found in the controls more frequently than in the index group patients (82.1% versus 45.0%; χ^2=17.3; p=0.0001). Proportion of patients with the III degree AH in the index group was significantly higher than among the controls (26.6% versus 10.3%, χ^2=4.09; p=0.04), while there were more controls with the II degree AH than the patients in the index group (38.5% versus 17.4%, χ^2=8.27; p=0.004). The AP rise was not registered in 64 (22.7%) patients.

The AP rise in patients with the adrenal masses was not found to depend on age, but in the group with the adrenal masses younger than 45 men prevailed (42.7%), while in the group ≥ 45 years women predominated (Table 2). Mean age at the moment of AP rise in the above groups was 28.2 ± 8.5 and 50.0 ± 9.4 years, respectively. Mean systolic/diastolic pressures in the above two groups were 179.4±38.6/188.4±38.5 and 108.0±17.0/109.3±15.9 mm Hg, respectively. The hypertensive crises took place in 56 (19.6%), those with AP rise> 200 mm Hg were seen in 60 (21.3%), continuous in 84 (29.8%), regular in 57 (20.2%) and continuous malignant in 21 (7.4%). The self-limited hypertensive crises were observed in 8 (2.8%) patients, the repeated hypertensive crises could be seen in 25 (9%).

Table 1: Clinical characteristics of patients with adrenal masses.

Parameters	Groups				P value
	Control (n=38)		Index (n=282)		
Age, years	37.2±11,7		39.8±15.7		0.32
AH duration, years	3.9±3,7		4.2±5.5		0.74
Mean systolic AP, mm Hg	152.3±16,1		182.8±38.7		**0.0001**
Mean diastolic AP, mm Hg	97.9±12,6		108.5±16.6		**0.0001**
	N	%	n	%	χ^2 ; p
AH heritability	32	82.1	127	45.0	**17.3; 0.0001**
Without AH rise	-	-	64	22.7	
Normal arterial pressure	2	5.1	2	0.7	2.44; 0.12
High limit normal AP	7	17.9	41	14.5	0.10; 0.75
I degree AH	11	28.2	51	18.1	1.65; 0.20
II degree AH	15	38.5	49	26.6	**8.27; 0.004**
III degree AH	4	10.3	75	26.6	**4.09; 0.04**

Table 2: Characterization of AH by age.

Parameters	Under 45 years (n=178)		≥ 45 years (n=104)		χ^2 ; p
	N	%	n	%	
Men	76	42.7	37	35.6	1.11;0.29
Women	102	57.3	67	64.4	
High arterial pressure	136	76.4	82	78.8	0,11;0,75
Hypertensive crises	30	16.9	26	25	2.25;0.13
Regular crises	32	18.0	25	24	1.14;0.29
Continuous crises	63	35.4	21	29.2	**6.54;0.01**
Continuous crises, malignant	11	6.2	10	9.6	9.68;0.29
Crises with AP higher than 200 mm Hg	35	19.7	25	24	0.51; 0.47
Self-limited hypertensive crises	5	2.8	3	2.9	0.11;0.74
Crises-food association	3	1.7	2	1.9	0.10;0.75
Crises-drug association	-	-	1	1.9	
Repeated hypertensive crises	18	10.7	7	6.7	0.56;0.46
In association with psycho-emotional hypertension	3	1.7	1	1.0	0.001;0.98
In association with physical loads	5	2.8	3	2.9	0.11;0.74
Duration of AH					
No AH	42	23.6	22	21.2	0.11;0.75
Less than 1 year	27	15.2	5	4.8	**6.01;0.01**
1-5 years	80	44.9	40	20.2	0.88;0.35
5-10 years	15	8.4	21	20.2	**7.14;0.008**
More than 10 years	14	7.9	16	15.4	3.15;0.08

Our findings demonstrate that continuous AH course in patients younger than 45 years was found more frequently (35.4% versus 20.2% in patients older than 45; χ^2=6.54; p=0.01); by other characteristics the groups were found comparable.

As to AH duration, its duration of less than 1 year was registered more frequently (15.2% versus 4.8% of patients older than 45; χ^2=6.01; p=0.01), while in patients older than 45 the proportion of subjects with AH duration from 5 to 10 years was higher (20.2% versus 8.4% in patients younger than 45 years; χ^2=7.14; p=0.008).

Thus, our findings demonstrate that AH of various degrees was diagnosed in the majority (77.3%) of 282 patients; it was continuous in the most cases, the crises and regular character were found in a number of cases.

CONCLUSIONS

The AP rise in patients with the adrenal masses was not found to depend on age, but in the group with the adrenal masses younger than 45 men prevailed (42.7%), while in the group ≥ 45 years women predominated. Mean age at the moment of AP rise in the above groups was 28.2 ± 8.5 and 50.0 ± 9.4 years, respectively. Mean systolic/diastolic pressures were significantly higher in the index group (p=0.0001). The hypertensive crises took place in 56 (19.6%), those with AP rise> 200 mm Hg were seen in 60 (21.3%), continuous in 84 (29.8%), regular in 57 (20.2%) and continuous malignant in 21 (7.4%). The self-limited hypertensive crises were observed in 8 (2.8%) patients, the repeated hypertensive

crises could be seen in 25 (9%). Hereditary burden by AH was found in the controls more frequently than in the index group patients (82.1% versus 45.0%; χ^2=17.3; p=0.0001). Proportion of patients with the III degree AH in the index group was significantly higher than among the controls (26.6% versus 10.3%, χ^2=4.09; p=0.04), while there were more controls with the II degree AH than the patients in the index group (38.5% versus 17.4%, χ^2=8.27; p=0.004). Continuous AH was registered more frequently among patients younger than 45 years (35.4% versus 20.2% in patients older than 45; χ^2=6.54; p=0.01). As to AH duration, its duration of less than 1 year was registered more frequently (15.2% versus 4.8% of patients older than 45; χ^2=6.01; p=0.01), while in patients older than 45 the proportion of subjects with AH duration from 5 to 10 years was higher (20.2% versus 8.4% in patients younger than 45 years; χ^2=7.14; p=0.008).

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