



# Small Pheochromocytomas: Clinical, Diagnostic and Perioperative Issues of Disease



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## Abstract

### Small Pheochromocytomas: Clinical, Diagnostic and Perioperative Issues of Disease

**Introduction:** Pheochromocytoma (P) is considered as relatively rare adrenal tumor with clinical manifestation after reaching the size of 4-6cm. Meanwhile, it's supposing that small P can be not rare found within different diagnostic imagination. Some of these, being clinically silent, can cause serious cardio-vascular risk undergoing unrelated medical procedures. We compared clinical course, peculiarities of diagnostics and treatment of small P (less than 3cm) and bigger P on the basement of own clinical experience among patients underwent adrenalectomy on proven or suspected P.

**Material and methods:** Group of small P was comprised by 14 patients aged from 21 to 62 years with mean size of tumor 23mm (range: 4-29mm). Control group consisted of 35 patients corresponded on age (23-75 years) with mean P diameter of 56mm (range: 30-127mm). Small P comprised 8% of all 175 patients with P operated on during the last 19 years in endocrine surgery hospital from the whole group of 967 adrenalectomies. Prevalence of women and right side lesions characterized both groups.

**Discussion:** Principal differences between groups were less prominent clinical activity (any symptoms were detected in half of small P) with less level of catecholamines and metanefrines in lab examination of serum and urea of small P patients. Computed tomography was often the first but not targeted diagnostic step. Silent clinical course was the main reason that small P have been discovered predominantly incidentally with no blockage of alpha-adrenergic receptors before surgery in 6 of 14 patients. Most of them had a critical elevation of blood pressure during operation (43% against 9% in control group;  $p < 0.05$ ). Despite small size and mild catecholamine excess in small P group, 4 from 14 patients (29%) experienced episodes of potentially harmful hypertensive crisis during unrelated medical procedures in the past. All small P were treated successfully by laparoscopic adrenalectomy. Most of patients became free from hypertension.

**Conclusion:** Small P may carry actual risk of unexpected hypertensive crisis during any unrelated medical procedures. The clinical course of small P is hidden in half of patients and laboratory investigations are interfered with mild elevation of biochemical markers. Laparoscopic adrenalectomy is safe mode of treatment of small P in case of adequate preparation.

**Keywords:** Pheochromocytoma; Small size; Diagnostics; Peculiarities; Laparoscopic adrenalectomy

## Introduction

Pheochromocytoma (P) is considered as relatively rare adrenal tumor which typically demonstrates clinical manifestation after reaching the size of 4-6cm. The rate of P among adrenal incidentalomas is about 5 %, and on autopsy among died from all causes 1:1000 [1]. Meanwhile, it's supposing that small P can be not rare found within different diagnostic imagination. Some of these, being clinically silent, can cause serious cardio-vascular risk undergoing unrelated medical procedures [2].

Half of P are discovered only at autopsy despite most of them demonstrated bright clinical symptoms [2,3]. From this point of view the case of 34<sup>th</sup> USA President Dwight David Eisenhower, whose diagnosis of small P was revealed only postmortem, is

a very illustrative example. He suffered from poor controlled arterial hypertension for a long time and sustained 4 myocardial infarction [4].

## Purpose

To compare clinical course, peculiarities of diagnostics and treatment of small P (less than 3cm) and bigger P on the basement of own clinical experience among patients underwent adrenalectomy due proven or suspected diagnosis.

## Material and Methods

There was a retrospective study with randomized historical control group. All together during 1.01.1997-1.08.2016 years

in Department of Endocrine Surgery of Ukrainian Research Center for Endocrine Surgery of Public Health Ministry 967 adrenalectomies have been performed. Tumors arisen from adrenal medulla comprised 18.1% (175 cases). Patients were aged from 8 to 75 years with female prevalence (74.3%). Size of P mostly exceeds 30mm ranged from 3.8mm to 127mm (mean 47.99±2.93mm). Adrenalectomy was performed initially through open conventional lumbotomy, but during last decade predominantly by laparoscopic methodic (71.4% among all cases).

The group of small P was comprised by 14 patients aged from 21 to 62 years with mean size of tumor 23 mm (range: 4-29mm). Control group consisted of 35 patients corresponded on age (23-75 years) with mean tumor diameter of 56mm (range: 30-127mm). Small P comprised 8% of all 175 patients with P operated on during the last 19 years in endocrine surgery hospital from the whole group of 967 adrenalectomies. Prevalence of women and right side lesions characterized both

groups. We excluded from both groups all cases of malignant P, family forms, bilateral P, children and pregnant.

After laboratory confirmation of diagnosis patients were prepared by alpha-adrenoblockers till stable normalization of BP. Computed tomography was the main method of visualization (in most cases – on «Toshiba Aquilion 64» CT). Laparoscopic adrenalectomy was performed by well known traditional methodic of M. Gagner [7] with authors modification [8]. Statistics for compared groups of study based on paired “t” test. Difference considered significant if P was less than 0.05.

Results and Discussion

Typical presentation of P in group of small P was the incidentally discovered on CT adrenal tumor of high native attenuation (mean - +31.06±3.52HU) – Figure 1. Macroscopically small P looks like homogenous solid tumor of grey or grey-cherry color defined by thin capsule (Figure 2). Clinical and laboratory data of studied groups are presented in Table 1.

Table 1: Main clinical and laboratory features of studied groups of P.

Compared features:	Small Pheo (n=14)	Bigger Pheo (n=35)	p	
Size; mm	< 30	≥30	<0.05	
	Mean Ø - 22.96±1.30	Mean Ø - 56.03±3.22		
	(3.8-29.9)	(30-127)		
Age: mean (range); years	42.12±3.53	44.91±1.26	>0.05	
	(21-62)	(23-75)		
Sex: female/male; %	71.43/28.57	68.57/31.43	>0.05	
Clinical diagnosis established: before operation/after operation (n)	6 (42.9%)/	34 (97.1%)/	<0.05	
	8 (57.1%)	1 (2.9%)		
Tumor visualization: incidentally/ based on clinical suspicion (n)	10 (71.4%)/	7 (20.0%)/	<0.05	
	4 (28.6%)	28 (80.0%)		
Arterial hypertension: Yes/No (n)	8 (57.1%)/	34 (97.1%)/	<0.05	
	6 (42.9%)	1 (2.9%)		
Previous cardio-vascular complications: Yes/No (n)	2 (14.3%)/	12 (34.3%)/	>0.05	
	12 (85.7%)	23 (65.7%)		
Presented with clinical symptoms (n):	6 (42.9%)	33 (94.3%)	>0.05	
	- tachycardia	3 (21.4%)		28 (80.0%)
	- palpitations	5 (35.7%)		32 (91.4%)
	- headache	0 (0%)		18 (51.4%)
	- face hyperemia	0 (0%)		16 (45.7%)
	- sweetening	0 (0%)		31 (88.6%)
	- fatigue, dizziness syncope			
Hypertensive crisis during unrelated medical procedures: Yes/No (n)	4 (28.6%)/	21 (60.0%)/	>0.05	
	10 (71.4%)	14 (40.0%)		
Predominantly elevated: metanefrines/normetanefrines/ other (n)	7 (50.0%)/	29 (82.9%)/	>0.05	
	2 (14.3%)/	2 (5.7%)/		
	1 (7.1%)	1 (2.9%)		

Grade of hormonal elevation: normal / 1,5-2 times / 2-4 times / >4 times	4 (28.6%)/	3 (8.6%)/	>0.05
	5 (35.7%)/	10 (28.6%)/	>0.05
	4 (28.6%)/	14 (40.0%)/	>0.05
	0 (0%)	8 (22.8%)	<0.05
Signs of Pheo on imagination: suspicion / apparent / adenoma- like	5 (35.7%)/	2 (5.7%)/	>0.05
	6 (42.9%)/	33 (94.3%)/	>0.05
	3 (21.4%)	0 (0%)	>0.05
Alpha-adreno blockage before operation (n)	8 (57.1%)	34 (97.1%)	<0.05
Hemodynamic disturbance during operation, episodes of BP>180mm Hg.: Yes/No (n)	6 (42.9%)/	3 (8.6%)/	<0.05
	8 (57.1%)	32 (91.4%)	<0.05
Term of postoperative follow-up, mean (diapason); years	2.23 (1-13)	4.89 (1-13)	>0.05
Withdraw of antihypertensive drugs after operation: Yes/No (n)	2-Jun	28/6	>0.05
Normalization of BP after operation: Yes/No (n)	2-Jun	25/9	>0.05

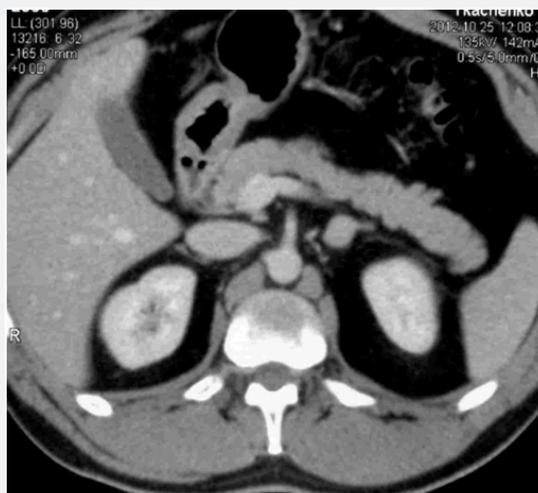


Figure 1: Small P (14mm) of left adrenal gland on non-contrast CT.



Figure 2: Macroscopic view of removed small P within left adrenal gland.

The less prominent clinical activity (any symptoms were detected in half of small P) with less level of catecholamines and metanefrines in lab examination of serum and urea of small P patients represented the principal difference between groups. Computed tomography was often the first but not targeted diagnostic step. Silent clinical course was the main reason that small P have been discovered predominantly incidentally with no blockage of alpha-adrenergic receptors before surgery in 6 of 14 patients. Most of them had a critical elevation of blood pressure during operation (43% against 9% in control group).

Despite small size and mild catecholamine excess in group of small P, 4 from 14 patients (29%) experienced some episodes of potentially harmful hypertensive crisis during unrelated medical procedures in the past. All small P were treated with successful laparoscopic adrenalectomy. Most of patients became free from arterial hypertension.

### Discussion

Our study confirmed opinion of some authors that even small P can bring significant risk for patients in case of stressful situation or unrelated medical procedures [5,6]. Despite existing information about significant rate of "hidden" P in population [1,9], targeted screening of P among patients with elevated BP or sympathetic crisis is not recommended routinely. Yu R et al. [5] supposed that small P could carry the 17% cardio-vascular risk in case of unrelated surgical or dentistry manipulation, that is equal to P of regular size. We found two fold differences in such risk for small and bigger P (29% against 69%), but it even more than found previous authors and allow us strongly recommend surgical operation for all such patients, as it sounds from other investigators [5,6]. Some authors recommend adrenal venous sampling with glucagon stimulation test in patients with negative visualization but clinical suspicion to catecholamine producing tumor, that prove presence of P in 36 from 41 patients[6]. More than half of those patients became normotensive after operation. We also observed normalization of BP in  $\frac{3}{4}$  of operated patients within first months after adrenalectomy. Laparoscopic method of adrenalectomy for patients with P is well recognized type of surgery all around the world [1,7,8], all the more for small tumors, and we confirm it one more time on our clinical series [9].

### Conclusion

Pheochromocytomas of size less than 3cm is not exclusive catecholamine producing tumors and comprise 8 % of operated

on P in large clinical series. Small P may carry actual risk of unexpected hypertensive crisis during any unrelated medical procedures. The clinical course of small P is hidden in half of patients and laboratory investigations are interfered with mild elevation of biochemical markers. Laparoscopic adrenalectomy is reliable and safe mode of treatment of small P in case of adequate preparation with alpha-blockers.

### Notice

This study was presented on 7<sup>th</sup> Symposium of European Society of Endocrine Surgeons, 6-8 April, 2017, Oxford, UK.

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