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Norepinephrine-secreting paraganglioma: a clinical case

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Abstract

Among the rare causes of secondary hypertension pheochromocytoma is traditionally considered. It represents a chromaffin tumor of the adrenal glands. Paraganglioma is an extra-adrenal chromaffinoma. High blood pressure due to the neurohormonal excess accelerates target organ damage. Variable manifestations of pheochromocytoma/paragangliomaclinical make more difficult timely diagnosis and dictate the need of multidisciplinary approach. We present a clinical case of norepinephrine-secreting retroperitoneal paraganglioma in a middle-aged female. An integrated approach to the diagnosis and the assessment of target organ damage is suggested. The features of renin status are highlighted. The case also demonstrates appropriate dynamics of the cardiovascular parameters, neurohormonal regulation of blood circulation, and carbohydrate metabolism after successful surgical treatment of chromaffin tumor.

Key words: pheochromocytoma, paraganglioma, hypertension, renin status, clinical case, follow-up

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Норадреналин-секретирующая параганглиома: описание клинического случая

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Резюме

Среди редко встречающихся причин вторичных артериальных гипертензий традиционно рассматривается феохромоцитома — опухоль из хромаффинных клеток надпочечников. Параганглиома — хромаффинома вненадпочечниковой локализации. Высокие показатели артериального давления в условиях нейрогормонального эксцесса оказывают ускоренное разрушительное воздействие на органы-мишени. Мозаичность клинической картины феохромоцитомы/параганглиомы создает трудности для своевременной диагностики и диктует необходимость применения междисциплинарного подхода. В статье приведено описание клинического случая норадреналин-секретирующей параганглиомы забрюшинного пространства у женщины среднего возраста. Показан комплексный подход к оценке диагноза и характера поражения органов-мишеней. Акцентировано внимание на особенностях ренинового статуса. Продемонстрирована закономерная динамика показателей состояния сердечно-сосудистой системы, нейрогормональной регуляции кровообращения, углеводного обмена после успешного хирургического лечения заболевания.

Ключевые слова: феохромоцитома, параганглиома, артериальная гипертензия, ренинoвый статус, клинический случай, наблюдение

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According to the definition of the WHO (2004), pheochromocytoma is a tumor originating from chromaffin cells of the adrenal glands, secreting one or more catecholamines: epinephrine, norepinephrine and dopamine. In rare cases, these tumors are hormonally inactive. A paraganglioma is considered to be a tumor originating from extraadrenal chromaffin tissue of the sympathetic paravertebral ganglia of thorax, abdomen and pelvis. Paragangliomas can also occur from parasympathetic ganglia (a non-chromaffin tissue, and, therefore, it does not secret catecholamines), located along the glossopharyngeal and vagus nerves in the neck and at the base of the skull and the main arteries [1]. The prevalence of all forms of arterial hypertension (HTN) in general population is 30–45 % [2]. Among patients with hypertension the detection rate of pheochromocytoma or paraganglioma ranges from 0.2 to 0.6 % [3]. The occurrence of chromaffinoma among patients with incidental adrenal tumor is 5 %. Approximately 80–85 % tumors of chromaf-

fin tissue (pheochromocytomas) are localized in the adrenal medulla, 15–20% are extraadrenal (paragangliomas) [4]. About 50–80% of the paraganglioma are Zuckerkandl tumors emanate from the para-aortic sympathetic ganglion at the site where the inferior mesenteric artery originates from the aorta [5]. In clinical practice, pheochromocytomas and paraganglioma may remain undiagnosed for a long time. One out of two chromaffin tumors is estimated to remain undiagnosed during the lifetime. One third of chromaffinomas is associated with hereditary mutations [6], 10–17% of chromaffin tumors are malignant [7]. The main clinical sign of pheochromocytoma/paraganglioma is severe HTN. A lack of awareness especially in out-patient medical care increases the ignificance of this problem. Consequently, a delayed initiation of appropriate treatment contributes to the occurrence of dangerous and often fatal cardiovascular complications [8]. We present a clinical case, illustrating the features of the diagnostic search and approaches to the treatment of paraganglioma occurring with severe HTN.

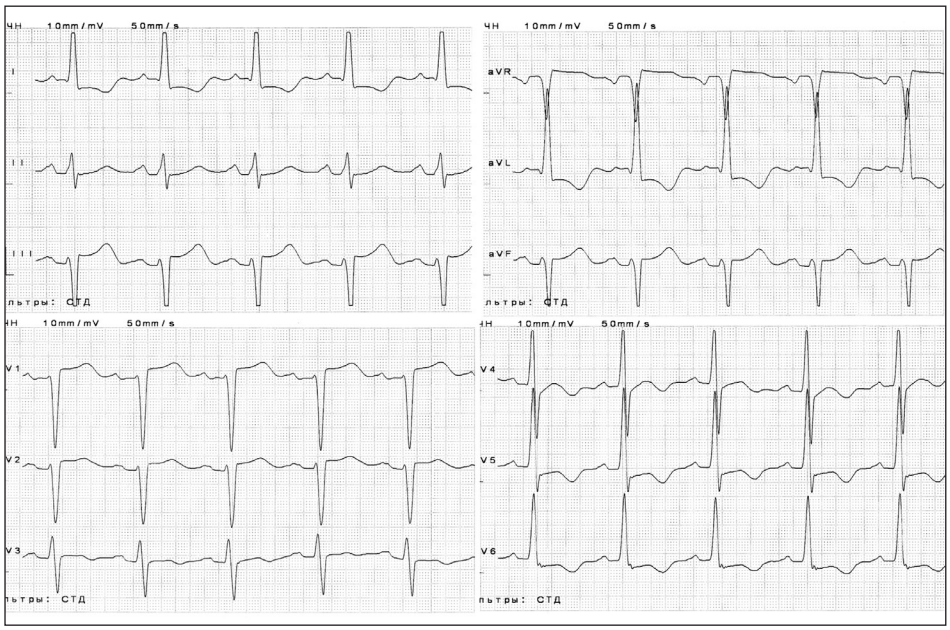
Patient Z., female, 53 years old, a primary school teacher (had not work for health reasons for two years preceding the survey), entered the Hospital Therapy Department of Military Medical Academy named after S. M. Kirov 30.10.2014 with complaints of occipital headache with the blood pressure (BP) increase up to 200–240/110–120 mm Hg, dizziness when moving from horizontal to vertical position, unsteadiness when walking, dyspnea (shortness of breath) and discomfort behind the breast bone that occurs at fast walking or climbing the stairs to the 3rd floor, lasting up to 5 minutes, stopping after the cessation of the exercise. In addition, she complained of dry mouth, gradual weight loss by 20 kg over the previous 8 years.

The episodes of BP elevations up to 160–180/90–100 mm Hg had occurred since she turned 42 years old. For five years the patient has not sought medical care. and in case of BP surge took on her own a variety of antihypertensive drugs (ACE inhibitors, beta blockers, centrally acting drugs) with poor effect. In January 2009 (at the age of 48 years) the patient was admitted to the Cardiology Department of one of St. Petersburg hospitals with complaints of dyspnea, pain in the heart and severe headache. So, ischemic heart disease, first onset angina pectoris, hypertension III stage and hypertensive crisis were diagnosed. Later she continued regular therapy with amlodipine 5 mg per day, enalapril 20 mg per day, hydrochlorothiazide 25 mg per day and metoprolol 100 mg per day. BP maintained within the range of 160–180/90–110 mm Hg. Exertional angina and chronic heart failure manifestations were assessed as corresponding to I–II functional classes. In January 2014, due to increasing signs of cerebrovascular disease and persistently high BP (headache, dizziness, unsteadiness when walking) she was admitted for a routine examination and treatment to a neurological hospital. Within one year prior to present hospitalization (2013–2014), the patient noticed frequent BP surges up to 200–240/100–120 mm Hg, as well as episodes of spontaneous decline to 120–140/90–100 mm Hg, accompanied by a sudden weakness.

In addition, the patient has compromised heredity (patient's mother suffered from stroke at the age of 51 years). The patient has a menopause (since the age of 48 years), reported no smoking or habitual alcohol consumption. Upon admission (17.12.2014.), the general condition was assessed as stable and corresponded to moderate severity due to the high BP. The patient was conscious and active. Her constitution was normosthenic, overweight (body mass index — 27.1 kg/m^2, waist circumference — 99 cm). No visible changes in musculoskeletal system were noticed. Skin and mucous membranes are of normal color and clean. No local hyper- and/or depigmentation, no peripheral edema were identified. Thyroid gland, peripheral lymph nodes were not enlarged. Pulse was 92 beats per minute, rhythmic, and intense. Vascular wall was not palpable outside of the pulse wave. BP in sitting position was 220/120 mm Hg on both hands. Left border of cardiac dullness was displaced to 2 cm outwards from the left medioclavicular line. A significant II tone accent over the aorta was determined. Respiratory rate was 17 per minute. Auscultation showed vesicular breathing without rattles. Tongue was moist and clean. At palpation the abdomen was painless. Effleurage on the lumbar region was painless on both sides.

Active orthostatic test showed transient hypertension. Systolic BP decline when moving to vertical position constituted 50 mm Hg, and decline of diastolic BP was 10 mm Hg (BP in supine position was 190/100 mm Hg, heart rate — 74 per minute; after 3 minutes in the orthostasis BP declined to 140/90 mm Hg, heart rate was 84 per minute). Blood tests showed hemoglobin of 124 g/l, leukocytes — 6,7×10^9/l, and erythrocyte sedimentation rate (ESR) — 25 mm/hour. Biochemistry test showed a slight decrease in potassium level to 3.6 mmol/l, an increase in fasting glycemia to 7,91 mmol/l, HbA1c — 7,97%, uric acid — 485,3 mcmol/l, fibrinogen — 4,98 g/l, C-reactive protein —

Figure 1. Surface electrocardiogram of the patient Z., 53 (November 2014)



Note: the signs of the left ventricular hypertrophy with its systolic overload are clearly defined.

16,53 mg/l, urea — 8,5 mmol/l, total cholesterol — 7,7 mmol/l, triglycerides — 2,97 mmol/L. Creatinine level was 80 mmol/L. GFR was 72,8 ml/min/1,73 m^2. When performing an oral glucose tolerance test fasting glycemia was 6,1 mmol/l, 2 hours after the glucose load — 13,7 mmol/L. Daily albumin urine excretion constituted 17,6 mg per day. Zimnitskiy's test showed a predominance of night diuresis over day diuresis (1050 and 790 ml, respectively), hyposthenuria (relative density of urine is 1003–1016). The chest x-ray (November 2014) showed an expansion of the heart shadow in diameter due to the left ventricle; aorta sealing and its reversal were detected. ECG (November 2014) demonstrated marked sinus tachycardia with heart rate 93 beats per minute, left ventricle myocardial hypertrophy and its systolic overload (Fig. 1). The index of Sokolow-Lyon was 53 mm, Cornell voltage index was 43 mm, Cornell product was 4300 mm×ms, Perugia University's sign of the left ventricle myocardial hypertrophy was positive (high values of the sum of (RaVL + SV3) and the typical violations of repolarization in the left chest leads).

Transthoracic echocardiography showed severe concentric left ventricular hypertrophy. The thickness of the interventricular septum and left ventricle posterior wall in diastole were 16.2 and 17.8 mm, respectively. Left ventricular myocardial mass index was 178 g/m^2. A very high degree of concentricity was found (relative LV thickness was 0,81). Systolic function of the left ventricle was normal (ejection fraction, EF = 72 %). Tissue Doppler signs identified rigid type of left ventricular diastolic dysfunction (E/A — 0,7, DT — 333мс, e' — 0,04 m/s, e/E' — 13). The volume index of the left atrium was 40 ml/m^2. We found mitral regurgitation 1 degree, and no changed in the myocardial kinetics.

The duplex scanning of common carotid arteries (November 2014) showed both-sided asymptomatic atherosclerotic plaques with a stenosis of the arterial lumen of 26 and 16 %, respectively. 24-hour ECG monitoring (November 2014) confirmed rigid circadian profile of heart rate (average heart rate — 77 beats per minute), ectopic activity presented by frequent single monomorphic ventricular ectopic beats (1983 episodes in total), repolarization signs of the left ventricular systolic overload. 24-hour BP monitoring (November 2014) showed a high systolic-diastolic hypertension throughout the study period (average daytime BP — 158/96 mm Hg, nighttime — 171/104 mm Hg); and nightpeaker daily profile. The variability of both daytime systolic and diastolic BP was increased. Episodes of hypotension were not registered. The velocity of morning SBP and DBP surges was increased.

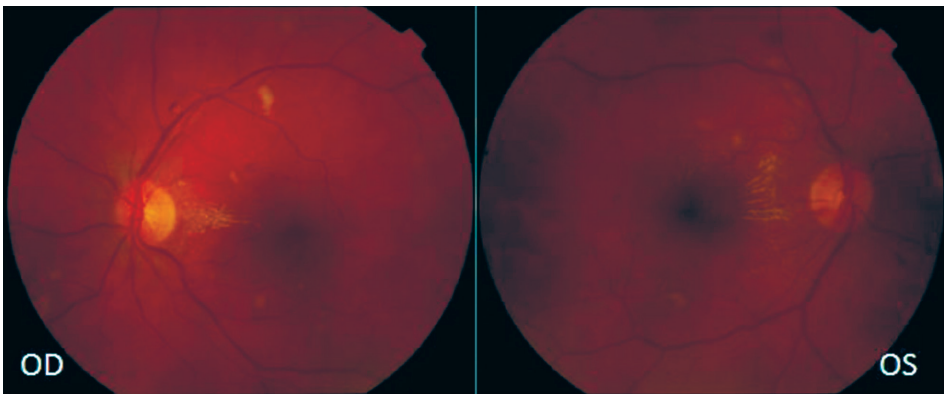
Symmetrical hypertensive angiopathy of the retina III stage was found at the examination of the eye fundus (December 2014) (Fig. 2). The optic disc was not changed, or prominent, there was an excavation of 0,1. The optical coherence tomography showed

radially located hard exudates, localized in the outer layers of the retina in the temporal side of the optic nerve disc. In the paramacular area outside the vascular arcades and nasal side of the optic disc, there were isolated soft exudates (areas of ischemia of the nerve fiber layer), rounded hemorrhage (in inner plexiform and nuclear layers) and dash-like (in nerve fiber layers) formations; arteriovenous crossing II. Macular edema was absent, and the retina thickness was normal.

The ultrasound examination of the abdomen showed the vascularized neoplasm of irregular shape between the liver and the pancreas (dimensions 32 × 36 × 47 mm). Kidneys were of normal size: right — 11.5 × 5.5 cm, homogeneous parenchyma, 15 mm; left — wavy boundary, 11.3 × 5.2 cm, homogeneous parenchyma, 18 mm. Calices-pelvis system of the kidney was not enlarged or hardened. The adrenal glands were not enlarged.

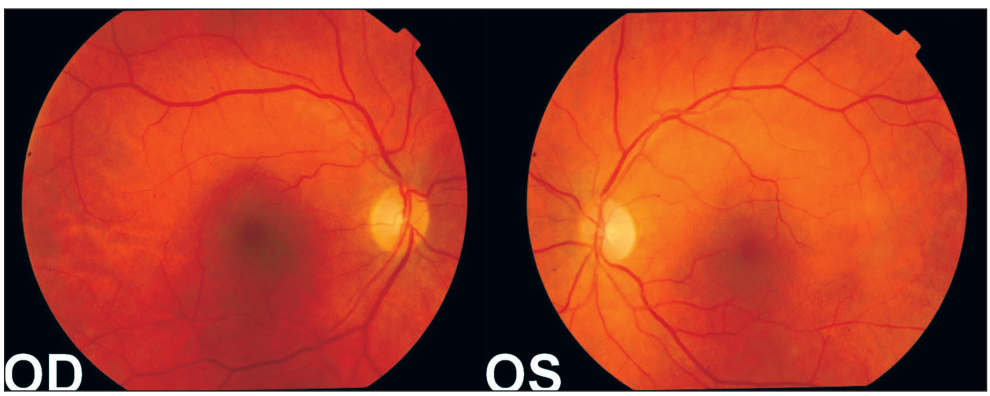
In December 2014, multidetector computed tomography (MCT) of abdominal cavity and retroperitoneal space with contrasting was performed (Figures 3 and 4), which visualized an extensive retroperitoneal formation with clear, uneven contours, of the irregular oval shape sizes 53 × 33 × 43 mm, with local vasculature, which intensively and inhomogeneously accumulated the contrast medium up to +80 and+100 HU, with preservation of lower density zones and the presence of a single hypervascular area (to +158 HU) at the right edge. The neoplasm was located between the liver on the right, the right adrenal gland and behind the right crus of diaphragm, in from of the pancreas and the stomach. It was connected with the diaphragm. Unmodified fatty tissue was found between the neoplasm and liver, right adrenal gland and the pancreas. The celiac trunk rounds it from the left, the common hepatic artery — in front, and the right renal artery — from the bottom. The formation

Figure 2. Fundoscopy of the patient Z., 53 years old (December 2014)



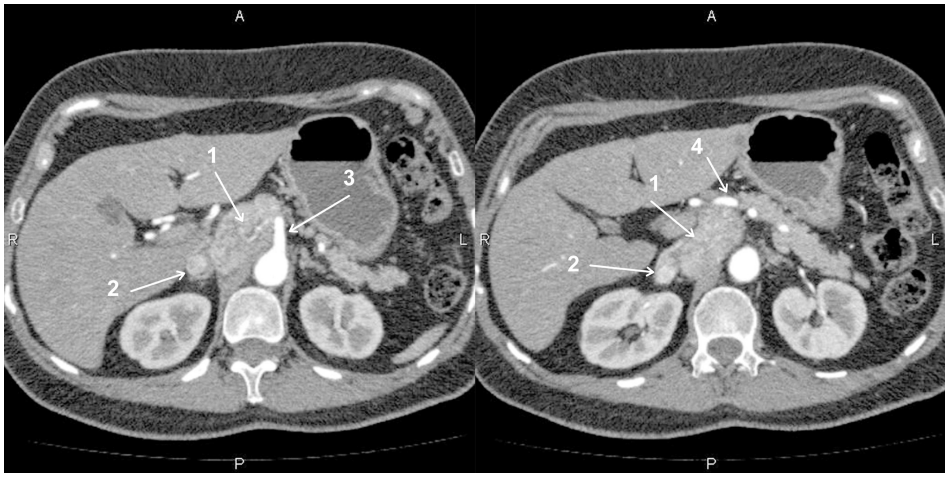
Note: on the right and left funduscopic signs of malignant hypertension are determined (the pattern of the fundus corresponds to the stage III of hypertensive angiopathy of the retina, according to the classification by Keith, Wagener & Barker, 1939).

Figure 3. Multi-layer spiral CT data of the abdomen and retroperitoneal space of the patient Z., 53 (December 2014)



Note: on the cut in the axial plane paraganglioma of size 53x33x43 mm is visualized. Retroperitoneal new formation (1) is located between the liver, right adrenal gland, right crus of diaphragm, the pancreas, the body of the stomach and is closely adjoint to the celiac trunk (3), common hepatic artery (4), the inferior cava vein (2).

Figure 4. Multi-layer spiral CT data of the abdomen and retroperitoneal space of the patient Z., 53



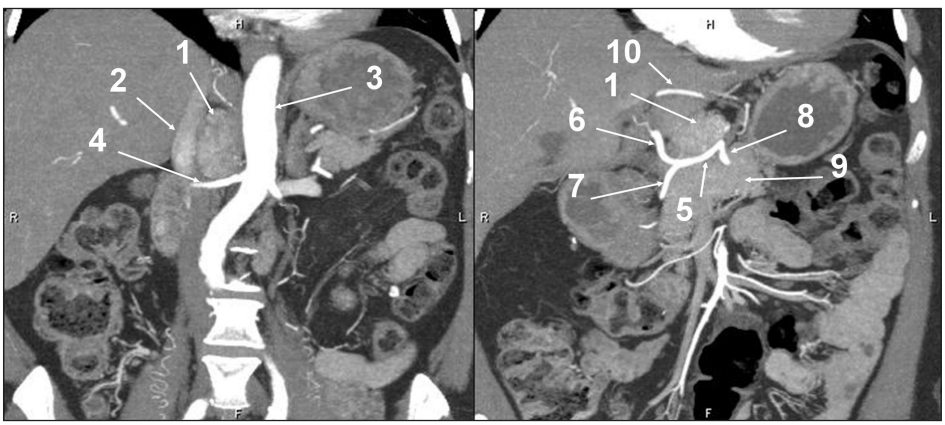
Note: the multiplanar reconstruction in the frontal plane into the arterial phase of contrast enhancement is represented. Designations: 1 — retroperitoneal extensive new formation, (paraganglioma), 2 — inferior cava vein, 3 — aorta 4 — right renal artery, 5 — common hepatic artery, 6 — right hepatic artery, 7 — gastroduodenal artery, 8 — splenic artery, 9 — pancreas 10 — the left hepatic artery.

displaced a lower cava renal vein behind and a right renal vein without evidence of invasion.

Due to the suspicion of pheochromocytoma / paraganglioma, catecholamines metabolites were assessed (November 2014). A significant increase in the blood concentration of normetanephrine — 2934 PG/ml (reference range: 0–180 PG/ml) was established, while metanephrine level was normal — 16.7 PG/ml (reference range: 0–90 PG/ml). Blood chromogranine level was also elevated up to 16 nmol/l (reference range: 0–3 nmol/l). These findings indicate the presence of a norepinephrine-secreting neuroendocrine tumor. We also studied the parameters of the renin-angiotensin system (November 2014): plasma concentration of the direct renin was increased up to 500 mcIU/ml (reference range: 2.8–39.9 mcIU/ml), aldosterone (164 PG/ml; reference range: 25–315 PG/ml) and cortisol (20.7 ng/DL; reference range: 6.7 to 22.6 ng/DL) levels were normal.

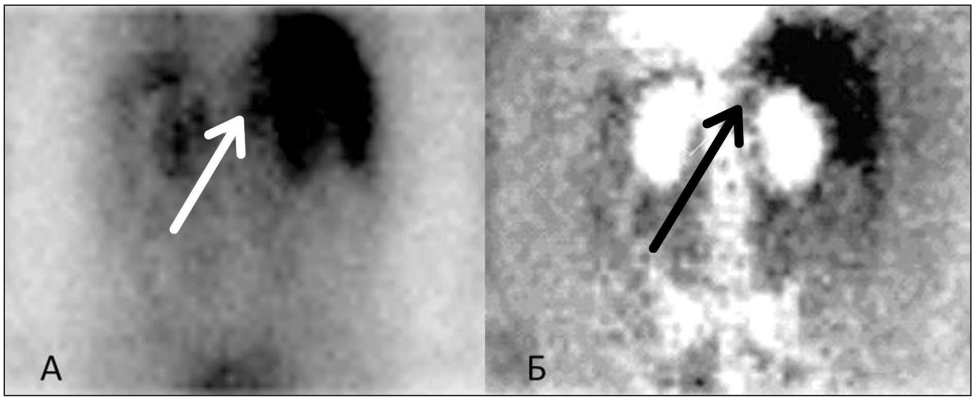
We performed body scintigraphy with metaiodinebenzylguanidine (MIBG) (which is isotropic to chromaffin tissue) to identify chromaffin extraadrenal tumors and to determine the neoplasm volume (to detect multiple tumors and metastases). Iodine-123 was used as a radioactive label. We visualized the radiopharmaceutical increased accumulation in the area above and medial to the right adrenal gland (MIBG) (Figure 5 A). For a better objective visualization of [123I] MIBG accumulation, we performed renal scintigraphy with 99Tc (which accumulates in the renal tissue) with subsequent overlay of two images. This allowed to distinguish the kidneys and the zone of [123I] MIBG accumulation (Fig. 5 B).

Figure. 5. A. The scintigraphy with [123I] MIBG



Note: Rear projection. The arrow indicates the area of increased accumulation of the drug. B. Thr scintigraphy's overlay on the image (with 99Tc). The arrow indicates the area of increased accumulation of [123I] MIBG.

Figure 6. Gross specimen of the patient Z.'s (53 years old) remote paraganglioma



Note: on the cut of the capsuled oval new formation of the size 5x4x3 cm there is a visible tissue of nodal structure with connective tissue inclusions. It is a grayish-pink colorored at the periphery with a yellowish tinge in the center.

Taking into consideration the extraadrenal localization of the chromaffinoma, noradrenaline secretion, we studied the most common mutation (single-nucleotide polymorphism at the position 598) of the gene VHL (von Hippel-Lindau) localized in the 3rd chromosome. As a result, the pathological alleles were not detected, the normal "wild type" homozygote was confirmed.

The diagnosis was the following: Noradrenalin-secreting paraganglioma of the retroperitoneal space. Secondary hypertension, malignant hypertensive syndrome. Hypertensive retinal angiopathy, stage III. Coronary heart disease. Exertional angina pectoris, I functional class. Atherosclerosis of the aorta and the coronary arteries. Congestive heart failure, stage I, II NYHA functional class. Type 2 diabetes mellitus (glycated hemoglobin < 7.0%).

The indications for a surgical intervention were defined and the surgical strategy was developed. Before the surgery, prolonged selective α1-adrenoblocker doxazosin (4 mg per day), α1-β1-β2-adrenoreceptor carvedilol (100 mg per day) were prescribed. The RAAS blocker losartan (150 mg per day), the antagonist of the mineralocorticoid receptor spironolactone (25 mg per day) and the long-term acting form of nifedipine (40 mg per day) were prescribed additionally. Biguanide metformin (1700 mg per day) and urea sulfonyl derivative glybenclamide (1.75 g per day) were prescribed to improve carbohydrate metabolism.

With the prescribed therapy, BP decreased. Heart rate stabilized within the normal range. No episodes of bradycardia or symptomatic hypotension were registered. Electrocardiography demonstrated an improvement in systolic left ventricular overload.

Afterwards, the patient was admitted to the 1st Surgical Department (postgraduate training) of Military Medical Academy named after S. M. Kirov, where on 02.02.2015 the retroperitoneal tumor was removed (surgeons: I. N. Pesikin, MD, PhD; A. V. Parkhomenko, MD; A. A. Bugaev, MD). Taking into consideration the extraadrenal localization and a close location of large vessels, the laparotomy via double subcostal access was applied. The neoplasm 5 × 4 cm was visualized in the retroperitoneal space. It was localized next to the pancreas, inferior cava vein, the celiac trunk, common hepatic and right hepatic arteries. Gradually, it was separated from all the vessels. A single branch of the celiac trunk, which provided blood supply, and the veins, which brought blood from the neoplasm into the inferior cava vein, were clipped and crossed. The tumor was removed with the adjoining fatty tissue and regional lymph nodes. Visually, the formation of 5 × 4 × 3 cm in size had an oval shape; when cut the tissue was grayish-pink and yellowish (Fig. 6).

At histology, the tumor appeared to be mostly formed by alveolar and trabecular structures. It consisted of large cells with light cytoplasm, pronounced cellular and nuclear polymorphism, not numerous mitoses, including atypical. It contained multinuclear giant cells with hyperchromatic nuclears without signs of invasion into the capsule (Fig. 7). The morphological pattern corresponded to a paraganglioma. Metastases to the lymph nodes of the hepatoduodenal ligament and the celiac trunk were not detected.

The immunohistochemistry demonstrated a paraganglioma-typical morphological pattern and immunophenotype of the tumor cells: neuron specific enolase (NSE), vimentin, synaptophysin, chromogranin, CD 56, S-100 (supporting cells) — positive reaction,

immunohistochemical reaction to the CMC, EMA, melan A, alpha-inhibin was negative (Fig. 8).

The reaction with monoclonal antibodies to Ki-67-protein of the proliferating cells nuclear showed the proliferation index of 1–2 % (Fig. 9). Thus, the low proliferative activity of the tumor was confirmed.

During the first 7 days after surgery BP was normalized, later BP increased up to 160–180/80–90 mm Hg, which required antihypertensive therapy (carvedilol 50 mg per day, losartan 100 mg per day). Two months after removal of paraganglioma, the patient noted significant improvement in general state (compared to the preoperative period), quality of life, a reduction of weakness/asthenia, a relative stabilization of BP within normotensive range without abrupt BP elevations and "reasonless" hypotension.

One month after surgery, metanephrine (26 PG/ml) and normetanephrine (90 PG/ml) serum levels were normal, and chromogranin A level decreased significantly from 16 to 3.5 nmol/l (normal: 0–3 nmol/l). The direct plasma renin level (20.8 mcIU/ml) and plasma aldosterone level (29 PG/ml) decreased to normal values. Hypercatecholaminemia was generated by a presence of a hormonally active tumor. Moreover, it could be intensified by the tumor-related mechanical compression of the right renal artery which caused the hyperrenin status at baseline. The blood glucose level also normalized, so the glucose-lowering drugs were withdrawn. Further, blood pressure was controlled by carvedilol 25 mg per day and losartan 50 mg per day. At 1.5-year follow-up in the Hospital Therapy Department of Military Medical Academy named after S. M. Kirov, persistent favourable changes in structural and functional indices of the cardiovascular system were found. Thus, a reduction of voltage ECG criteria of the left ventricular hypertrophy (the index of Sokolov-Lyon — 28 mm, Cornell product — 3700 mm × MS, Cornell index — 37 mm) was noted. Eighteen months after removal of paraganglioma (August 2016), a significant decrease in concentric left ventricular hypertrophy (LV myocardial mass index — 141 g/m^2), a degree of LV concentricity (a reduction of the left ventricular wall thickness — 0.57), an improvement in diastolic function (Table 1) were found by heart ultrasound.

The assessment of the sympathetic and adrenal activity (normetanephrine, metanephrine, blood chromogranin-a) indicated no relapse (Table 2).

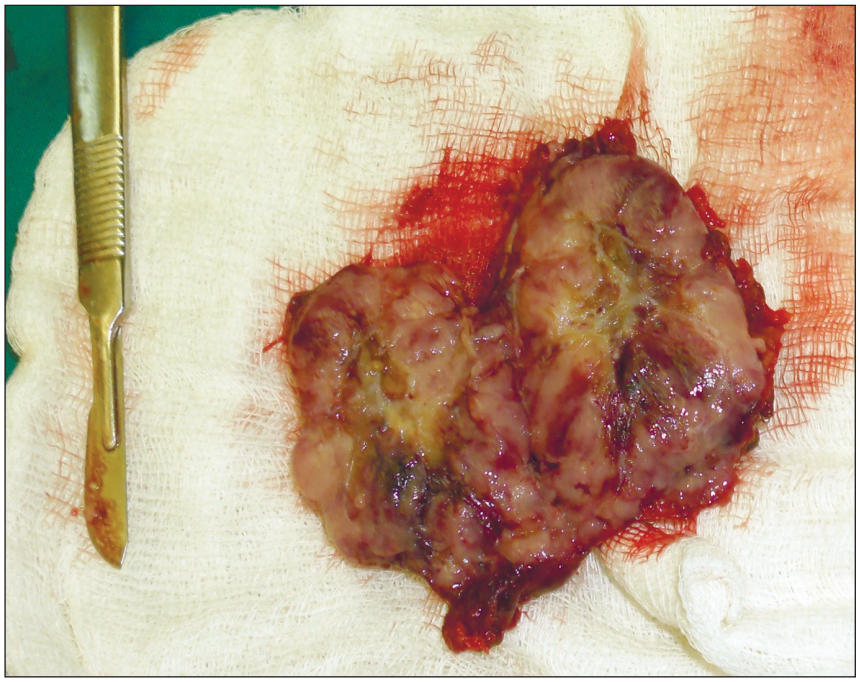
The biochemistry showed a sustained normalization of glucose, glycated hemoglobin, urea, uric acid and fibrinogen. The blood serum creatinine level decreased to the normal range, and glomerular filtration rate increased. The orthostatic hypotension, which had been identified earlier (before surgical treatment), did not occur during the follow-up. The data of Holter recording (August 2016) showed no significant ventricular or supraventricular ectopic activity. The ophthalmological evaluation showed significant favourable changes in the eye fundus (the interferential hemorrhages regressed) (Fig. 10).

Discussion

This clinical case demonstrates that a screening of neurohumoral regulation (in particular, renin-angiotensin-aldosterone and sympatho-adrenal systems) helped to understand the nature of the disease. The extraadrenal noradrenalin-secreting paraganglioma appeared to be associated with the high plasma renin level. However, in high systemic BP in chromaffinoma we would expect a decreased plasma renin level as a result of the pressure-sensitive mechanism of the afferent arteriole that reacts to a change in renal perfusion pressure. Some authors showed normal renin status in patients with adrenal pheochromocytoma [9]. We suggest that there are at least two mechanisms leading to hyperreninemia. First of all, the effect of catecholamines on the β1-adrenoceptor of the renal juxtaglomerular apparatus with subsequent release of renin and RAAS activation might be important. Secondly, in cases of extraadrenal paraganglioma the compression of the renal arteries should be considered (like in our patient). Additional (hyperreninemia-causing) mechanism leads to the more distinct manifestations of hypertension, and it partially explains the persistent form of BP elevation in chromaffin tumors.

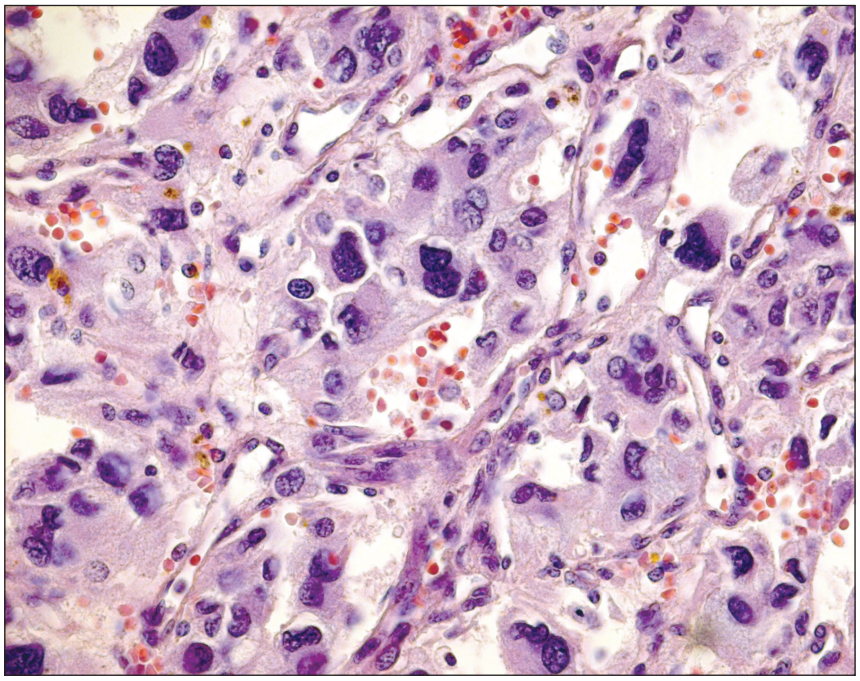
The initial disorders of carbohydrate metabolism significantly imporved after the tumor removal enabling the withdrawal of the glucose-lowering drugs. In fact, this confirms the role of contra-insular mechanisms of hypercatecholaminemia in the onset of diabetes mellitus in patients with chromaffinomas [10]. We would like to pay special attention to the favourable (reversed) changes in the structural and functional indices of the cardiovascular system after the surgical removal of the neoplasm. A reduction of the hypertension severity, a regression of the left ventricular hypertrophy, an improvement in diastolic function with the ongoing low(medium)-dose antihypertensive therapy should be considered as criteria for the prognosis improvement. The regression of cardiovascular remodeling after surgical treatment of chromaffinoma was also confirmed by other researchers [11].

Figure 7. Microslide of the patient Z.'s (53 years old) remote paraganglioma. Colouring with hematoxylin-eosin (zoom × 400)



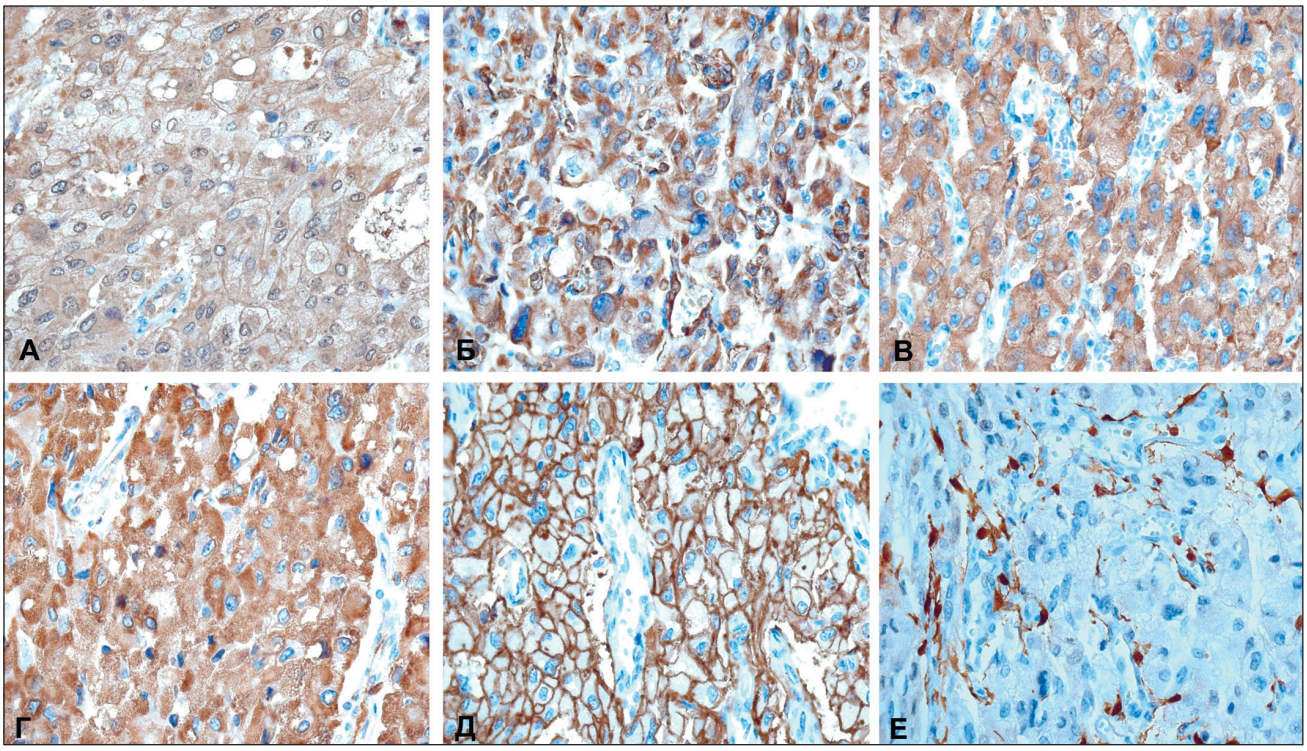
Note: the alveolar structure of the tumor is clearly apparent. Tumor cells with bright fine-grained cytoplasm. A pronounced nuclear and cellular polymorphism is observed.

Figure 8. Immunohistochemical markers of sympathoadrenal paraganglioma



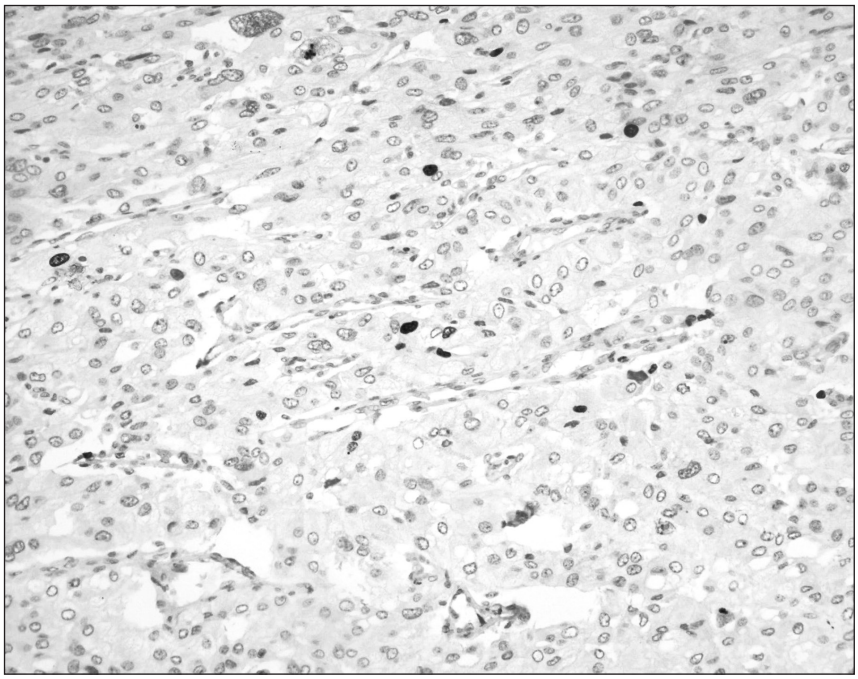
Note: Positive staining for: a — the neuron specific enolase, b — vimentin, c — synaptophysin, d — chromo-granin-A, e — CD 56, f — numerous supporting cells are clearly marked by the reaction to the protein S-100. There is zoom x400 on each fragment (a-f).

Figure 9. The expression of Ki-67 nuclear of proliferating tumor cells, zoom × 400



Note: in the field of view nuclears of isolated proliferating cells are visualized, which indicates the low intensity of tumor cells division.

Figure 10. Fundoscopy of the patient Z., 55 years old (August 2016)



Note: on the right and left there is ehe symptom of arteriovenous crossing II. In the macular region and in the peripheral hard exudates and intraretinal hemorrhages are not defined.

Table 1

PARAGANGLIOMA PATIENT'S INDICES OF ECHOCARDIOGRAPHY DURING DYNAMIC OBSERVATION

Index	LVMI, g/m²	WTR, unit	EF, %	E/A, unit	DT, ms	e', m/s	E/e'	iLA, ml/m²
Source	178	0.81	72	0.7	333	0.04	13	40
1.5 years after removal of paraganglioma	141	0.75	73	0.8	240	0.09	7	36

Note: LVMI — left ventricular mass index, WTR — ratio wall thickness of the left ventricular, EF — ejection fraction, E/A — ratio of velocities of early and late diastolic filling wave of the left ventricle, DT — deceleration time of the of early diastolic filling wave flow, e'- velocity of the early diastolic displacement of the mitral valve's fibrous ring, E/e' — ratio of maximal velocity of the early diastolic filling wave of the mitral flow to the early diastolic motion velocity of the mitral valve's fibrous ring; iLA — volume index of the left atrium.

Table 2

THE CONTENT OF CATECHOLAMINE METABOLITES, CHROMOGRANIN-A IN THE BLOOD OF THE PATIENT WITH PARAGANGLIOMA DURING DYNAMIC OBSERVATION

Index	Bedore the removing of paraganglioma	After 1 month	After 1 year
Normetanephrine, PG/ml	2934	26	87.2
Metanephrine, PG/ml	16.7	90	16.5
Chromogranin-A, nmol/l	16	3.5	2.5

Thus, the problem of diagnosis and treatment of pheochromocytoma/paraganglioma appears to be multidisciplinary and it requires a proper evaluation of biochemical, neurohormonal, radiological, and genetic methods of research. To achieve optimal results, it should be considered at primary visits, a close cooperation of various specialists is required for both diagnostic and treatment decisions, careful follow-up of patients is essential part of the treatment.

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Conflict of interest

The authors declare no conflict of interest.

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