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Pheochromocytoma associated with neurofibromatosis type 1: a clinical case

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A clinical case of pheochromocytoma in combination with neurofibromatosis type 1 is presented in a man admitted to the cardiology department with acute coronary syndrome on the background of hypertensive crisis. The crisis was complicated by myocardial ischemia, myeloid leukemoid reaction, hyperglycemia and acute renal damage. Pheochromocytoma was verified by blood metabolites of catecholamines test and histological method. Surgical adrenalectomy was performed.

Key words: pheochromocytoma, neurofibromatosis type 1, hypertensive crisis.

Conflicts of Interest: nothing to declare.

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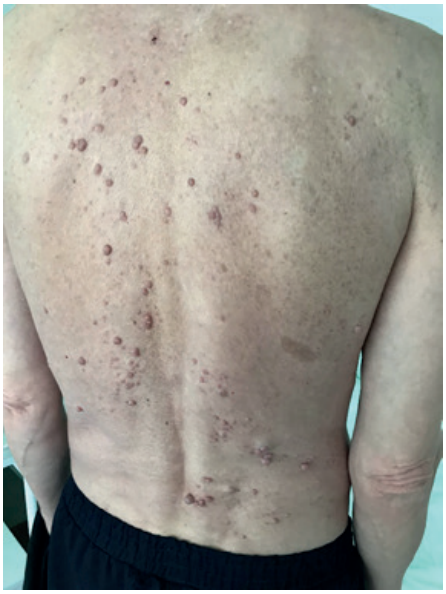

Fig. 1. Multiple neurofibromas of the skin in patient P.

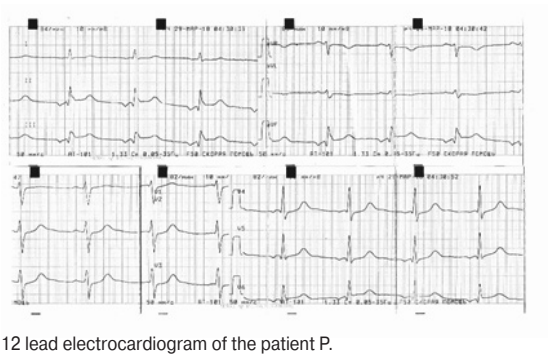

Fig. 2. 12 lead electrocardiogram of the patient P.

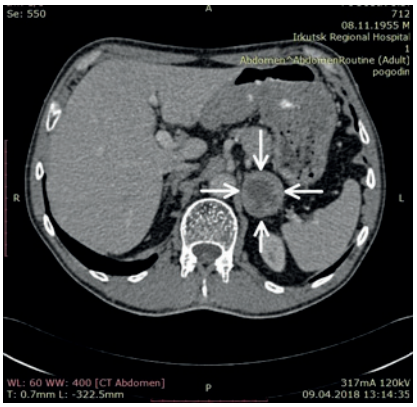

Fig. 3. Multispiral computed tomography of the abdominal cavity of patient P.
Note: axial section. Arrows indicate a tumor of the left adrenal gland.

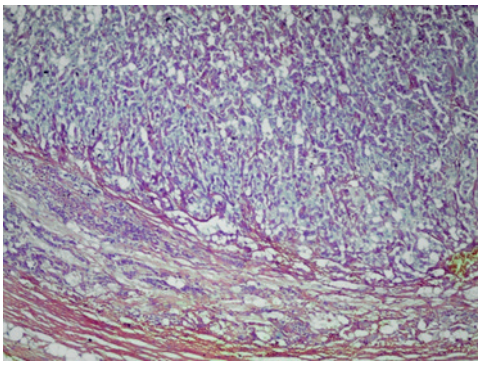

Fig. 4. Micrograph of a fragment of an adrenal tumor.
Note: hematoxylin-eosin stain, x40.

Pheochromocytoma is a tumor of the adrenal medulla that produces catecholamines. Every year, 3-6 new cases of the disease are detected per 1 million people. The prevalence among patients with arterial hypertension (AH) is 0,5-2%. Up to 30-40% of pheochromocytoma cases may have a genetic nature. Pheochromocytoma associated with neurofibromatosis type 1 (NF1) belongs to the hereditary one [1]. NF1 is an autosomal dominant disease, the skin manifestations of which are multiple pigmented cafe-au-lait macules and neurofibromas. A genetic defect in NF1 is localized on the 17th chromosome (17q11.2). This gene encodes a neurofibromin protein, which is a tumor suppressor. The incidence is 1 in 3 thousand children. Pheochromocytoma is diagnosed in 0,1-5,5% of patients with NF1, however, when NF1 is combined with hypertension, the frequency increases to 20-56% [2, 3].

We present a case of pheochromocytoma and NF1 in a patient with hypertensive crises and suspected acute coronary syndrome (ACS).

Patient P., 62 years old, in March 2018 was admitted to the cardiology department of the Irkutsk Regional Clinical Hospital with complaints of intense pain behind the sternum, trembling in the body, sweating, headache, increased blood pressure (BP) with a diagnosis of ACS. For 6 years, hypertensive crises with a BP rise to 220/120 mm Hg were observed 1 time in 1-2 months. Patient did not underwent examination and not taking antihypertensive drugs. The patient noted spots on the skin since childhood, tumor growths on the skin from a young age, but the NF1diagnosis was not previously made.

Condition on admission was severe. The heart rate was 92 per minute, BP — 164/100 mm Hg. The skin is moist. On the skin were neurofibromas (Fig. 1). On the ECG, low atrial rhythm, ST segment elevation in leads III, avF, ST depression in V2-V4 (Fig. 2).

An emergency coronary angiography was performed. Pathology of the coronary bed is not revealed. Troponin T at admission was 0,12 mg/L, after a day — 0,024 mg/L (0,01-0,17). According to echocardiography, the valves are not changed. Estimated pressure in the right ventricle was 30 mm Hg. The size of the cavities of the heart was not increased. Left ventricular ejection fraction was 64%,

interventricular septum, posterior wall of the left ventricle are not thickened. Zones of hypo- and akinesis were not identified. The filling pattern of the left ventricle is rigid.

In the clinical blood analysis on the second day from the onset, leukocytosis of 29,2x109, neutrophils of 90% was detected. After two days, the number of leukocytes decreased to 7,9x109. Upon receipt, fasting glycemia was 18,8 mmol/L, after a day — 3,8 mmol/L without treatment. On the day of admission, blood creatinine level was 320 μmol/L, on the 6th day it decreased to 100 μmol/L. Diuresis did not decrease.

The combination of cutaneous signs of NF1 and complicated hypertensive crisis with transient neutrophilic leukocytosis and hyperglycemia suggested pheochro-mocytoma.

Multispiral computed tomography of the abdominal organs was performed (Fig. 3). In the left adrenal gland, a heterogeneous round formation (hypo-intensive in the central sections (8 HU) and hyper-intensive on the periphery (31 HU), 37x38 mm sized, intensively accumulating contrast around the periphery (up to 72 HU) with the preservation of avascular central sections. Conclusion: space-occupying lesion of the left adrenal gland (pheochromocytoma?).

Parameters of secretion of catecholamine metabolites: methanephrine >900,00 pg/ml (⩽120 pg/ml), normetanephrine — 370,6 pg/ml (⩽200 pg/ml). Levels of alstosterone, cortisol, adrenocorticotropic hormone in the blood, plasma renin activity are normal.

In May 2018, the patient underwent a left-sided adrenalectomy with laparotomy access. Protocol of pathological and anatomical examination of the surgical material: adrenal gland 32 g 8,0x4,5x4,0 cm with a clearly delimited tumor 4,0 cm in diameter. Histologically, adrenal tissue with nodular hyperplasia of the cortical substance, the tumor is constructed of round, elongated and polygonal cells with granular cytoplasm, with the formation of solid, trabecular and alveolar structures, with an abundant network of sinusoidal vessels, with hemorrhage focuses, areas of sclerosis, surrounded by a capsule. Conclusion: Pheochromocytoma (Fig. 4).

The clinical picture of pheochromocytoma is diverse. The presence of crises in a patient with skin manifestations of NF1 maximizes the disease risk [1-3]. With pheochromocytoma, various variants of myocardial damage are possible: direct damage with catecholamines, ischemia and type 2 infarction due to spasm of the coronary arteries and increased oxygen demand against tachycardia and hypertension, takotsubo cardiomyopathy [2, 4, 5].

The absence of coronary artery pathology in coronary angiography made it possible to exclude coronary artery disease. The absence of violations of local contractility on echocardiography contradicts takotsubo cardiomyopathy. Type 2 myocardial infarction is excluded according to the results of troponin test. Severe neutrophilic leukocytosis on admission required considering of the infectious process, however, a rapid decrease in leukocytes in dynamics made it possible to associate it with pheochromocytoma [5]. Acute renal damage was probably due to severe vasoconstriction and ischemia of the renal parenchyma against the background of hypercatecholaminemia. Our data are confirmed by the description of isolated cases of acute renal failure associated with pheochromocytoma [6].

Thus, this case demonstrates a late diagnosis of pheochromocytoma, despite the presence of skin manifestations of NF1 and hypertensive crises.

Conflicts of Interest: nothing to declare.

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