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Pheochromocytoma with severe cardiac complications

Feochromocitoma: širdies ir kraujagyslių sistemos komplikacijos

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Introduction

Pheochromocytoma is a rare and usually benign catecholamine-secreting tumor with a broad variety of signs and symptoms, the most common being palpitations, headaches, and sweating. Rarely, pheochromocytoma can cause severe cardiac complications such as myocardial infarction, pulmonary edema or cardiogenic shock.

Case report

We report a case of a 42-year-old male who presented with acute chest pain, dyspnea, and general weakness. He had a history of episodical high blood pressure and panic attacks, which were unsuccessfully treated with antidepressants. The patient developed a severe left ventricular function impairment with pulmonary edema and cardiogenic shock. Coronary angiography showed a spasm of the right coronary artery. We suspected pheochromocytoma and performed computed tomography of the abdomen, which showed a large tumor in the right adrenal gland. It was confirmed to be a pheochromocytoma. The patient was treated with α-blockers, and a successful laparoscopic surgical removal of the pheochromocytoma was carried out eighteen days later. The patient recovered well, and symptoms of pheochromocytoma disappeared.

Conclusion

Pheochromocytoma can cause severe cardiac complications in different mechanisms, such as coronary spasm and direct catecholamine toxic effect on cardiomyocites. Diagnosing and treating pheochromocytoma with cardiac complications remains a challenge for a physician.

Key words: pheochromocytoma, hypertension, acute myocardial infarction, catecholamine-induced cardiomyopathy

Įvadas
Feochromocitoma yra retas dažniausiai nepiktybinis katecholaminus sekretuojantis navikas, kuriam būdinga didelė simptomų įvairovė. Širdies plakimo jausmas, galvos skausmas bei gausus prakaitavimas – būdingiausi pacientų skundai. Retais atvejais feochromocitoma komplikuojasi gyvybei grėsmingomis širdies ir kraujagyslių sistemos ligomis – miokardo infarktu, plaučių edema bei kardiogeniniu šoku.

Klinikinis atvejis

Į priėmimo skyrių atvykęs 42 metų amžiaus vyras skundėsi intensyviu krūtinės skausmu, dusuliu ir bendru silpnumu. Pastaruoju metu pacientas buvo nesėkmingai gydomas antidepresantais dėl besikartojančių panikos atakų, kurių metu padidėdavo arterinis kraujospūdis. Priėmimo skyriuje paciento būklė sparčiai blogėjo, progresavo ūminis kairiojo skilvelio nepakankamumas, išsivystė plaučių edema bei kardiogeninis šokas. Atlikus vainikinių arterijų angiografiją, pastebėtas dešiniosios vainikinės arterijos distalinės dalies spazmas. Įtarus feochromocitomą, buvo atlikta pilvo kompiuterinė tomografija – rastas didelis navikas kairiajame antinkstyje. Laboratoriniais tyrimais patvirtinta feochromocitomos diagnozė. Aštuoniolika dienų pacientas buvo gydytas α-blokatoriais, vėliau sėkmingai atlikta naviko šalinimo operacija. Pooperaciniu laikotarpiu komplikacijų nebuvo, feochromocitomos simptomai išnyko.

Išvados

Feochromocitoma gali sukelti sunkių širdies ir kraujagyslių sistemos komplikacijų dėl įvairių katecholaminų pertekliaus poveikio mechanizmų. Aprašytu atveju tai buvo vainikinių arterijų spazmas bei tiesioginis toksinis katecholaminų poveikis kardiomiocitams. Labai didelė nespecifinių simptomų įvairovė bei galimos sunkios komplikacijos lemia tai, kad feochromocitomos diagnostika bei gydymas tebėra nelengvas iššūkis gydytojui.

Reikšminiai žodžiai: feochromocitoma, hipertenzija, ūmus miokardo infarktas, katecholaminų sukelta kardiomiopatija.

Introduction

Pheochromocytoma is a rare and usually benign catecholamine-secreting tumor with an incidence of 1 to 8 cases per 1 million annually [1]. The signs and symptoms are associated with an increased concentration of catecholamines – usually noradrenalin or adrenalin, although some tumors produce dopamine. Classical symptoms of pheochromocytoma are due to intermittent catecholamine secretion and include palpitations, headaches, sweating, and severe hypertension, lasting from seconds to hours. However, the presentation of pheochromocytoma can be much more diverse, varying from panic attacks to potentially life-threatening cardiac complications such as acute coronary syndrome and pulmonary edema [2]. The diagnosis is usually made biochemically by evaluating the levels of catecholamines and their metabolites metanephrines in blood plasma or urine. The second step in establishing the diagnosis is localization of the tumor, which is done by means of computed tomography (CT) scan or magnetic resonance imaging (MRI). The treatment of choice is the surgical removal of pheochromocytoma, which usually results in the disappearance of symptoms. In this paper, we report a case of pheochromocytoma presenting with severe cardiac complications.

Case report

A 42-year-old male was admitted to the Klaipeda Seamen's Hospital emergency department with acute chest pain, dyspnea, nausea, and general weakness. He had a history of psychomotor agitation attacks which went together with an increased blood pressure (BP) to 240/120 mm Hg and heart rate (HR) to 130 beats per minute (bpm). The patient had been having this type of attacks 2–3 times per week for one year. He had been diagnosed with an anxiety disorder and panic attacks. He had been using antidepressants. The patient had one episode of paroxysmal atrial fibrillation. Coronary angiography had been performed 6 months ago in another hospital and showed no pathology of coronary arteries.

On examination, the patient was cyanotic, his respiratory rate was 30 breaths per minute, there were a lot of pulmonary crackles in all the lung auscultation area, blood oxygen saturation was 82–88%. He had tachycardia of 140 bpm, normal heart sounds without cardiac murmurs; BP was 166/117 mm Hg.

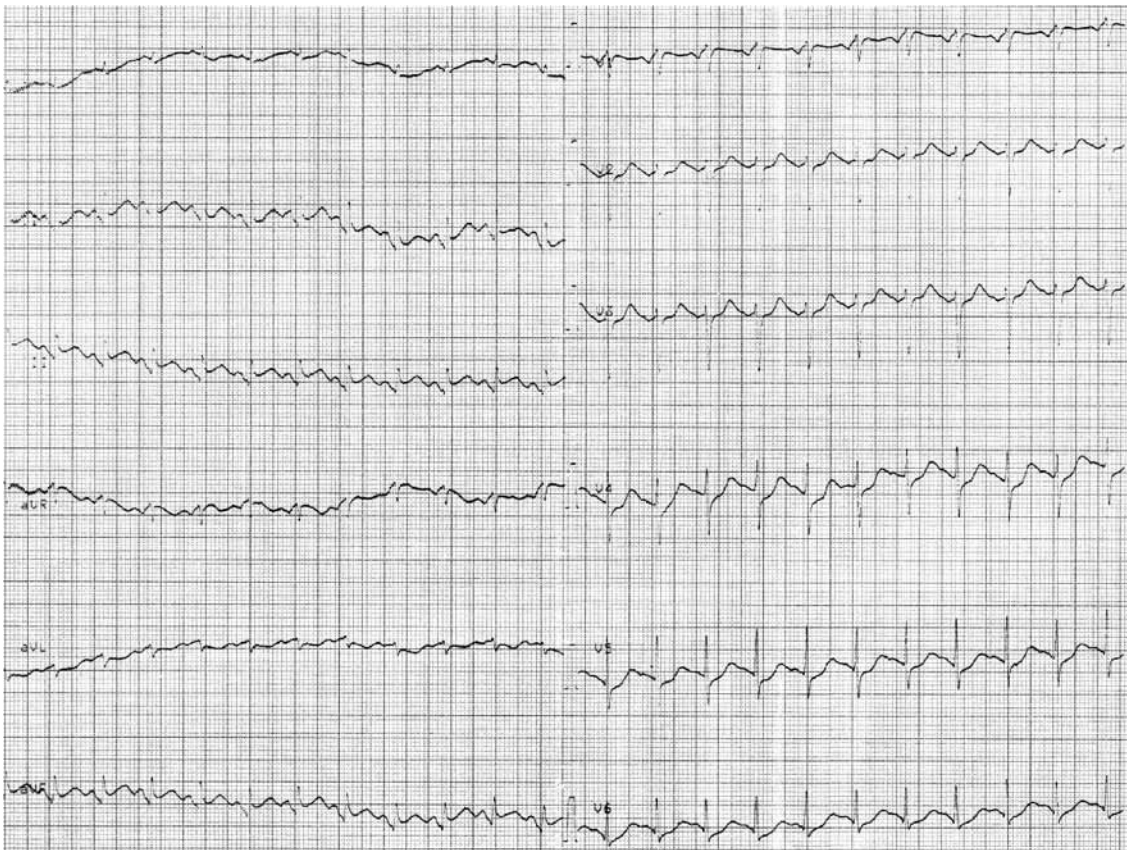

Fig. 1. ECG on admission, showing sinus tachycardia and ST segment elevation by 2 mm in leads III, aVF and ST segment depression by 1 mm in leads V4, V5, V6

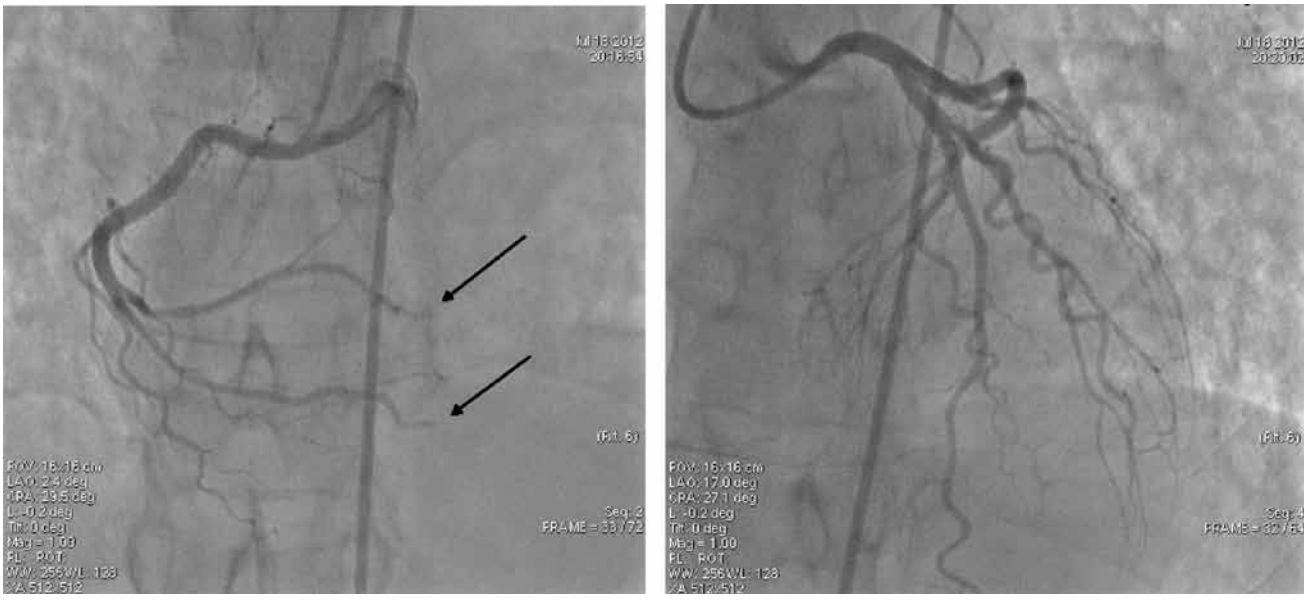

Fig. 2. Coronary angiography views showing a spasm of the right coronary artery and the normal left coronary artery

The abdomen was painful in the epigastrium. There was no neurological deficit. The ECG showed sinus tachycardia of 145 bpm and ST segment elevation by 2 mm in leads III, aVF (Fig. 1). Due to progressive respiratory deterioration, mechanical ventilation was started. We suspected acute myocardial infarction with ST segment elevation. Coronary angiography revealed a distal occlusion of the right coronary artery; other coronary arteries were normal (Fig. 2). We tried intracoronary nitrate injections, thromboaspiration, low-pressure balloon dilatation, but the flow was not restored. During the procedure, the patient developed a cardiogenic shock with a drop of blood pressure, so an intra-aortic balloon pump (IABP) was used together with dopamine infusion in inotropic doses. The sonoscopy of the heart showed an akinetic apex of the heart, akinetic inferior wall and hypokinetic middle segments of the left ventricle. The ejection fraction of the left ventricle was reduced to 20%. The sonoscopic view was similar as seen in stress-induced cardiomyopathy, except for the inferior wall which was absolutely akinetic, including basal segments. The patient's cardiac biomarkers (cTnI) were elevated to 7.3 ng/ml; the NT-ProBNP concentration of 21800 ng/ml showed a severe heart failure.

Having in mind the patient's medical history, we had a preliminary diagnosis of catecholamine-secreting tumor with catecholamine-induced cardiomyopathy (CIC), complicated by a cardiogenic shock. Abdominal sonoscopy revealed a large tumor with signs of necrosis in the right adrenal gland. A CT scan of the abdomen showed a right-sided adrenal tumor 7 cm x 6.5 cm in size, suspected pheochromocytoma (Fig. 3). The diagnosis was confirmed by the 24-hour urinary metanephrine level test, which found severely increased catecholamine metabolite levels. We had the clinical diagnosis of the right adrenal gland pheochromocytoma, complicated by CIC, myocardial infarction of the inferior wall with ST elevation, and cardiogenic shock.

On the 3rd day of hospitalization dopamine infusion was stopped, on the 4th day IABP was removed and mechanical ventilation was discontinued. On the same day we started the α1-selective alpha blocker doxazosin 4 mg once daily. Three days later we changed doxazosin to phenoxybenzamine 10 mg twice daily and continued until the surgery. The patient was also on loop diuretics, spironolactone, ACE inhibitors, beta blockers and aspirin – standard treatment of myocardial infarction with heart failure. Sonoscopy of the heart was repeated on the 9th day of hospitalization. It showed the hypokinetic inferior wall, the ejection fraction of the left ventricle being 45%. The apex and middle segments of the left ventricle were fully recovered.

The surgical removal of the right adrenal gland (right adrenalectomy) was planned. The patient was prepared for surgery and operated on the 18th day of hospitalization. Right adrenalectomy was done laparoscopically. The adrenal vein was ligated first, and tumor together with the adrenal gland was removed. The surgical procedure was successful, though there were some BP fluctuations. The histological analysis of the tumor confirmed it was pheochromocytoma.

On the 1st postoperative day we had to discontinue all the antihypertensive treatment due to the low blood pressure. Without the drugs, the systolic blood pressure was between 120 and 90 mm Hg and the diastolic between 80 and 70 mm Hg. The patient was discharged on the 8th post-operative day.

Later, genetic testing was performed for mutations in the VHL and RET genes. No mutations were found.

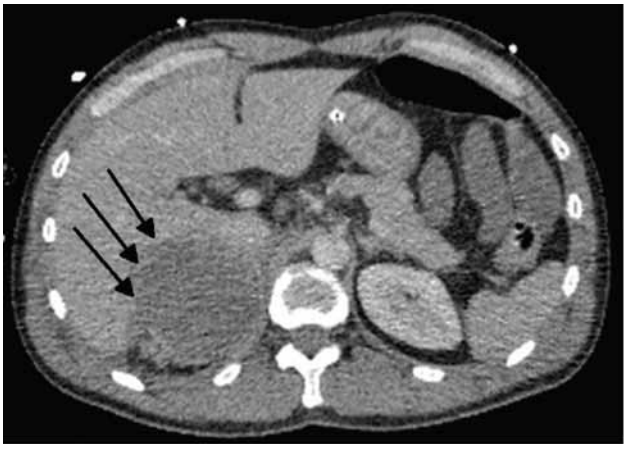

Fig. 3. CT view of the tumor in the right adrenal gland

Discussion

Pheochromocytomas originate from chromaffin cells of the adrenal medulla and secrete excessive amounts of catecholamines, most commonly noradrenalin. Due to the broad variety of symptoms, the most challenging issue in diagnosing pheochromocytoma is suspecting it. Only less than 0.2% of patients with hypertension have pheochromocytoma [3]; other most common symptoms such as palpitations, headaches, and sweating also lack specificity. Less common symptoms include orthostatic hypotension, visual blurring, papilledema, weight loss, polyuria, polydipsia, constipation, increased erythrocyte sedimentation rate, hyperglycemia, leukocytosis, psychiatric disorders and, rarely, secondary erythrocytosis due to erythropoietin overproduction [4, 5]. Sometimes pheochromocytoma can manifest with severe cardiac complications such as myocardial infarction or cardiac failure [2, 6, 7]. The pathophysiology of myocardial dysfunction associated with pheochromocytoma has been linked to either a direct toxic effect of catecholamines on cardiomyocytes or the supply–demand mismatch and myocardial stunning due to microvascular dysfunction and the spasms of epicardial coronary arteries [8]. The more recently published hypothesis gives convincing evidence that cardiac dysfunction in stress-induced cardiomyopathy is caused by a direct toxic effect of a high catecholamine concentration on cardiomyocites. High levels of circulating epinephrine trigger a switch in intracellular signal trafficking from Gs protein to Gi protein signaling through the β2-adrenoreceptors. This change in signaling is negatively inotropic, and the effect is greatest at the apical myocardium in which the density of β-adrenoceptors is highest [9].

We suspect that the occlusion of the right coronary artery was due to a vasospasm. However, the spasm did not resolve quickly and the duration was long enough to cause a permanent myocardial damage. Therefore, repeated sonoscopy of the heart showed the remaining hypokinesia of the inferior wall. On the other hand, akinesia of the apex cannot be explained by a vasospasm, because coronary angiography revealed a normal blood flow in the left anterior descending artery. The akinesia of the apex disappeared completely after more than one week. We think that there might have been involved two different mechanisms of myocardial damage, which are a coronary spasm and the direct toxic effect of catecholamines on cardiomyocites. The present case shows that excessive amounts of catecholamines can damage the myocardium in both ways at the same time.

Though rarely, pheochromocytoma can compromise the cardiac function so severely that it leads to a cardiogenic shock with the need of mechanical support. There are reports in the literature, which illustrate a successful use of IABP or even extracorporeal membrane oxygenation (ECMO) in such cases [10, 11]. The use of inotropes or vasopressors in catecholamine-induced cardiomyopathy with a cardiogenic shock is debatable. Pheochromocytoma itself produces excessive amounts of catecholamines, so whether additional infusion is beneficial for the patients remains doubtful. In the case of severe left ventricular dysfunction with cardiogenic shock, mechanical support seems to be the method of choice. The calcium-sensitizing agent levosimendan might be a second-line pharmacological support [9]. Our patient was stabilized with IABP, and he received also dopamine infusion. The infusion was stopped as soon as we confirmed the diagnosis of pheochromocytoma.

A widely accepted medical treatment of pheochromocytoma before the surgery is α-adrenergic blockade. Phenoxybenzamine is an irreversible, long-acting, non-selective α-blocking agent and usually is a drug of choice, although other α-blocking agents, such as doxazosin, may be used. After achieving an adequate α-adrenergic blockade, the β-adrenergic blockade should be initiated. The latter blockade should not be started first, because it can lead to a hypertensive crisis by blocking peripheral vasodilatory receptors with unopposed alpha-adrenergic receptor stimulation.

Surgical removal of pheochromocytoma is usually planned at least 10 days after the initiation of an adequate α- and β-adrenergic blockade. The key points of a successful surgical resection of pheochromocytoma are minimizing tumor manipulation, avoidance of tumor spillage, complete removal of the tumor, early ligation of the adrenal vein, and a good coordination with the anesthesiology team for the control of perioperative hemodynamics. The laparoscopic approach to the adrenal gland is the procedure of choice for patients with solitary intra-adrenal pheochromocytomas that are not

suspected to be malignant. Although the laparoscopic procedure might be safely performed in the majority of cases, sometimes laparotomy might be necessary to stabilize the hemodynamics [12].

Up to 24% of pheochromocytomas are familial, most commonly associated with multiple endocrine neoplasia type 2 (MEN-2) or the von Hippel-Lindau (VHL) disease [13]. Our patient was tested for mutations in VHL and RET genes. No mutations were found, so, most likely, this was a case of a sporadic pheochromocytoma.

Conclusion

The case we have presented shows that pheochromocytoma can cause severe cardiac dysfunction by different mechanisms. We believe that the prolonged vasospasm might have caused the infarction of the inferior left ventricular wall, and apical akinesia might have been a form of catecholamine-induced cardiomyopathy due to the direct toxic catecholamine effect on cardiomyocites. Diagnosing and treating pheochromocytoma with cardiac complications remains a challenge for a physician.

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