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CLINICAL EVALUATION, DIAGNOSIS AND TREATMENT OF PHEOCHROMOCYTOMA

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SUMMARY – Pheochromocytomas are rare neuroendocrine tumors that originate in chromaffin cells of the adrenal medulla and excessively secrete catecholamines, which leads to a multitude of different symptoms. The most common symptoms include headaches, palpitations, and sweating. Because of a diverse clinical presentation, pheochromocytomas pose a major diagnostic challenge and often go unidentified. These tumors can occur sporadically or as a part of hereditary syndromes. The diagnosis is confirmed by measuring plasma and 24-hour urinary metanephrine and normetanephrine. Computed tomography, magnetic resonance imaging, and functional morphological examinations are used for tumor localization. The treatment is operative and requires special preoperative patient preparation to prevent hypertensive crisis and arrhythmias. Due to the possibility of recurrence, the patient needs to be monitored. Pheochromocytoma has a high fatality rate if not recognized on time due to the effect of catecholamines on the cardiovascular system.

Keywords: *Pheochromocytoma; Headache; Multiple endocrine neoplasia type 2; Palpitations; Paroxysmal hypertension*

Introduction

Pheochromocytomas are rare neuroendocrine tumors arising from chromaffin cells of the adrenal medulla and producing one or more catecholamines, most commonly norepinephrine and epinephrine, and sometimes dopamine (1). They can also arise from extra-adrenal chromaffin cells of the paravertebral ganglia of the abdomen, pelvis, and chest. In such cases, they are called paragangliomas. They usually do not secrete adrenaline because of their reduced expression of the enzyme that converts norepinephrine to adrenaline (2). They can occur sporadically or as part of hereditary syndromes (3).

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Epidemiology

The incidence rate in the general population is 2-9 per million inhabitants, and it most commonly occurs between the ages of 30 and 50 (3). The frequency is the same in men and women (4). Pheochromocytomas make up approximately 85%, while paragangliomas make up 15% of chromaffin cell tumors (2). They mostly occur sporadically, but in 15% of cases, they

are associated with familial syndromes. In children diagnosed with pheochromocytoma, as many as 70% have a hereditary disease (3). Extra-adrenal tumors are more common in children and reported in 30% of cases. Most tumors are benign, while the malignant ones occur in 10% of pheochromocytomas and 30%-40% of paragangliomas (5). Adrenal incidentaloma is an incidental finding in 3%-4% of abdominal computed tomography (CT) scans (6). In patients diagnosed with adrenal incidentaloma, pheochromocytoma will be detected in 5% of cases (7). According to 54 autopsy findings, pheochromocytoma contributed to patient's death in as many as 55% of cases, while it was not even suspected in 75% of cases, which shows the danger of missed diagnosis (5).

Tumor genetics

Although pheochomocytomas most often occur sporadically, it is important to recognise that 15% of cases are part of familial syndromes. The most common familial syndrome in which pheochromocytoma occurs is multiple endocrine neoplasia type 2 (MEN 2). It is an autosomal dominant disorder characterized by benign or malignant changes occurring in two or more endocrine glands and by changes in nerve, muscle, and connective tissue (8). The frequency is 1:30,000 people in the general population (9). MEN 2A is characterized by the occurrence of medullary thyroid carcinoma in 95% of cases, in combination with pheochromocytoma that occurs in 50% of patients and parathyroid hyperplasia with a frequency of 15%-30%. MEN 2B is associated with medullary thyroid carcinoma in 100% of the cases, with pheochromocytoma that occurs in 50% of the cases (10). Disorders such as mucosal neuromas of the lips and tongue, ganglioneuromatosis of the gastrointestinal tract, and marfanoid habitus are often associated (8,11). It is the MEN 2A syndrome in 90% of the cases. Pheochromocytoma is found after the medullary thyroid carcinoma has already caused symptoms. Most often, these pheochromocytomas are adrenal, benign, and hormonally active. In one-third of the patients, the tumors are bilateral, while half of the patients with unilateral tumor develop the contralateral one within 10 years. Tachycardia, diaphoresis, and headache occur in 40%-80% of the cases. Symptoms are more common and more pronounced than in other hereditary syndromes. Less than 5% of tumors are malignant. The tumor in children with MEN 2B syndrome has a higher potential for malignancy than tumors in MEN 2A syndrome and tumors occurring sporadically (12).

Von Hippel Lindau syndrome is an autosomal dominant hereditary syndrome manifested by a variety of benign and malignant tumors, including the central nervous system, retinal hemangioblastoma, pheochromocytoma, and neuroendocrine tumors of the pancreas. The syndrome affects 1 per 36,000 people in the general population (13). The chances of developing pheochromocytoma are 25%-30% (14). There is a difference between type 1, which involves a low risk of developing pheochromocytoma, and type 2, in which pheochromocytoma often occurs. These are mostly adrenal, and in 50% of the cases, bilateral (10).

The study conducted on subjects with MEN 2 and VHL syndromes showed that patients with MEN 2 syndrome had more pronounced symptoms and a higher incidence of paroxysmal hypertension (15). All patients with MEN 2 syndrome had increased levels of plasma metanephrines, which are metabolites of epinephrine, whereas patients with VHL syndrome exhibited a specific increase in normetanephrine, which are metabolites of norepinephrine. In patients with MEN 2 syndrome, the expression of tyrosine hydroxylase (TH) and phenylethanolamine N-methyltransferase (PNMT) was higher, as well as tissue reserves of epinephrine. Tyrosine hydroxylase is an enzyme that limits the rate of catecholamine synthesis, while phenylethanolamine N-methyltransferase (PNMT) is an enzyme that converts norepinephrine to epinephrine. The difference in biochemical phenotype leads to a difference in catecholamine biosynthesis, which explains the difference in the severity of symptoms in those two syndromes (15).

Neurofibromatosis type 1 (NF1) is an autosomal dominant disease in which pheochromocytoma also occurs with a frequency of 0.1%-5.7%. These are usually benign, unilateral tumors. Malignant tumors occur in 12% of patients. The average age is 42 years. These tumors secrete more epinephrine, so increased levels of plasma and urine metanephrine help distinguish

Table 1. The proportion of sex, age, and frequency of pheochromocytomas in relation to paragangliomas in the most common familial syndromes (17-21)

Syndrome	Gene	Chromosome location	Frequency of germline mutations in apparent sporadic pheochromocytoma	Typical tumor location	Tumor number (multiple versus single)	Average age (years)	Frequency of malignant disease
Multiple endocrine neoplasia type 2	RET	10q11.2	<5%	adrenal medulla	multiple	36	<5%
Von Hippel Lindau syndrome	VHL	3p25-26	2%-11%	adrenal medulla, rarely paraganglioma	multiple	26	5%
Neurofibromatosis type 1	NF1	17q11.2	Unknown	adrenal-periadrenal	single	44	12%
Familiar paraganglioma type 1	SDHD	11q23	4%-7%	head and neck, rarely adrenal medulla	multiple	41	<5%
Familiar paraganglioma type 4	SDHB	1p36.1-35	3%-10%	abdomen and pelvis, rarely adrenal medulla	multiple	35	23%-50%

this syndrome from the VHL syndrome and succinate dehydrogenase (SDH) mutations (10).

Mutations in genes encoding succinate dehydrogenase subunits B and D (SDHD and SDHB) are predisposing factors for type 4 and type 1 paraganglioma syndromes. Pheochromocytomas and head and neck paragangliomas occur in both syndromes. Multifocal paragangliomas are more common in patients with SDHD mutation, whereas in patients with SDHB mutation, malignancy and extraparaganglionic neoplasms are more likely to develop, including renal cell and thyroid carcinoma (16).

Tumor characteristics

The average tumor size is 4.9 cm, while the size of the largest tumor ever described was 29×21×12 cm (22,23). Tumors associated with mutations are smaller than tumors detected due to symptoms (29 vs 50 mm) (24). Although they are generally benign, malignancy is indicated by tumor size greater than 5-6 cm, weight greater than 8 g, abnormal DNA, increased dopamine levels in the blood and the tumor, and persistent hypertension after surgery. The most common metastatic sites are the liver, lymph nodes, and bones (25).

Clinical presentation

Symptoms arise from hypersecretion of catecholamines, most commonly epinephrine and norepinephrine. Sudden secretion occurs intermittently, so symptoms manifest in paroxysmal attacks. The attacks most often occur when getting out of bed, during physical work or excitement, and after meals. Initially, the attacks occur at intervals of several months and later become more frequent. They can be caused by alcohol, drugs, such as adrenaline, and anesthetics. During the attack, the patient is agitated, restless, pale, and sweaty (26). In 80% of cases, the attacks last for about 1 hour, but their duration may range from less than a minute or longer than a week (5). The characteristic triad of symptoms includes headaches, palpitations, and sweating. Hypertension occurs in 80.7% of the patients, headache in 60.4%, palpitations in 59.3%, diaphoresis in 52.4%, and orthostatic hypotension in 23%-50% (27). Pheochromocytoma is the cause of hypertension in 0.1%-1% of cases, while only 5%-10% of hypertension cases are classified as secondary hypertension. Pheochromocytoma should be suspected if the listed symptoms occur before the age of 20 or after 50 and do not respond to treatment (28). Other symptoms and signs are listed in Table 2. If cardiomyopathy, paroxysmal arrhythmias,

or myocardial infarction occur where coronary artery obstruction cannot be detected, pheochromocytoma should be suspected (4). More than 50% of tumors are functional and symptomatic, while the non-functional ones are found by chance (29). Because they cause a variety of symptoms, pheochromocytomas are known as "great imitators", so there is a long list of conditions and diseases that fall under the differential diagnosis of pheochromocytomas (Table 3) (30). This tumor must be recognized and treated in time to avoid hypertensive crisis, arrhythmias, and myocardial infarction (31).

Table 2. Symptoms and signs of pheochromocytomas (3, 5, 18, 19, 32)

Symptoms (frequency)	Signs (frequency)
Headache (60%-90%) Palpitation (50%-70%) Sweating (55%-75%) Fever (60%) Pallor (40%) Fatigue (25%-40%) Weight loss (20%-40%) Anxiety (20%-40%) Fatigue (20%-40%) Flushing (10%-20%) Cold hands and feet Constipation Dyspnea Shaking Pain in the chest, abdomen (usually the epigastrium), lumbar regions, lower abdomen or groin Visual blurring Painless hematuria, nocturia in pheochromocytoma of the bladder Tremor Heat intolerance	Hypertension: sustained (50%-60%) paroxysmal (30%) Orthostatic hypotension (10%-50%) Hyperglycemia (10%) Paradoxical blood pressure response to certain antihypertensive drugs Tachycardia or reflex bradycardia, palpitations, arrhythmias Congestive heart failure Pale face and upper body (rarely redness) Worried, scared look Hypertensive retinopathy Papillary edema Transitory electrocardiographic changes

Pheochromocytoma in children

In 80% of cases, pheochromocytoma in children is associated with gene mutations (33). It occurs at the average age of 11-13 years, and it is twice as common in male children. It is the cause of hypertension in 0.5%-2% of cases. The leading sign is hypertension, occurring in 60%-90% of children, accompanied by headache in 67% of cases, nausea, sweating, palpitations, pallor, and redness in 47%-67% of cases (3, 33). Preoperative preparation is the same as in adults. Lifelong genetic testing and health monitoring are required (3).

Pheochromocytoma in pregnancy

It occurs in 1 per 15,000 to 1 per 54,000 pregnant women (3, 34). If not recognized in time, maternal and fetal mortality can reach 40%-50%. Recent studies have shown that the total maternal mortality rate is 9.8%, while fetal mortality is 16% (3). Pregnancy-related hypertension develops after 20 weeks of gestation. However, if hypertension occurs earlier, pheochromocytoma should be suspected (3). This tumor is difficult to recognize because it mimics preeclampsia (34). Biochemical findings are the same as in non-pregnant individuals. Magnetic resonance imaging (MRI) and ultrasound are used to localize the tumor. Preoperative preparation is the same as in other patients (3). The second trimester is the safest period for surgery as the risk of miscarriage is higher in the first trimester (3, 34). In the third trimester, surgery is often delayed or performed during a caesarean section (34). Preference

Table 3. Differential diagnosis of pheochromocytomas (3, 5, 19, 22, 26)

Neurological disorders	Migraine, Brain tumor, Epilepsy, Cerebrovascular insufficiency, Stroke, Autonomic neuropathy
Psychiatric disorders	Anxiety disorder, Depression, Panic attacks, Hyperventilation
Endocrine disorders	Hyperthyroidism, Hypoglycemia, Menopause, Medullary thyroid carcinoma, Insulinoma, Carbohydrate intolerance, Mastocytosis
Cardiovascular disorders	Coronary insufficiency Essential hypertension Paroxysmal supraventricular tachycardia Postural orthostatic tachycardia syndrome Renovascular hypertension, Syncope, Pulmonary edema
Other	Carcinoid, Preeclampsia (or eclampsia with convulsions), Pseudopheochromocytoma , Sleep apnea , Baroreflux failure, Drug treatment (eg, monoamine oxidase inhibitors, sympathomimetic drugs, withdrawal of clonidine, benzodiazepine withdrawal syndrome), Mercury poisoning

is given to laparoscopic surgery, and it is recommended to avoid vaginal delivery (3).

Table 4. Indications for biochemical testing (30, 35)

Indications for biochemical testing
• Paroxysmal appearance of signs or symptoms
• Resistant hypertension
• Unexplained and unexpected blood pressure response to medication, surgery, or anesthesia
• Hypertension that occurs under the age of 20
• Previous treatment of pheochromocytoma
• Hereditary risk
• Features of the syndrome related to the hereditary syndrome associated with pheochromocytoma
• Incidentaloma with a density above 20 HU

Biochemical tests

If biochemical testing is indicated (Table 4), it should include measurements of plasma free metanephrines or 24-hour urinary fractionated metanephrine level. Plasma free or urinary fractionated metanephrines are more sensitive and, therefore, superior to tests measuring catecholamine excess for diagnosing pheochromocytoma (36). In patients with increased metanephrines, normetanephrines (MN), and 3-methoxytyramine (3MT) levels before surgery, it is recommended to assay plasma or urinary metanephrine and 3-methoxytyramine every year to screen for local or metastatic recurrence or new tumors. Guidelines recommend assaying plasma chromogranin A levels every year in patients operated on for MN-negative, 3MT-negative, and chromogranin A-positive pheochromocytoma to screen for local or metastatic recurrences or new tumors (37). Food, coffee, strenuous physical activity, and smoking are not allowed 8-12 hours before the test (3). Stress and upright body position can also affect the results. Blood sampling in the supine position will result in 30% lower plasma metanephrine values compared to the sitting position. Thus, to reduce the risk of false-positive results, blood samples should be taken from a patient who rested on their back for at least 20 minutes. Plasma metanephrine test showed greater sensitivity when samples were taken after the patient had rested on their back compared to when taken without rest (35). Levels of plasma normetanephrine that are 4 times higher than the reference values and metanephrine levels that are 2.5 times above the normal indicate pheochromocytoma with high certainty (38). Also, urinary catecholamine levels 2-3 times above the reference values support this diagnosis (39). If normetanephrine values are increased less than four times the reference values, a clonidine suppression test may be used. It is useful for distinguishing high levels of plasma norepinephrine caused by sympathetic nerve release from those caused by pheochromocytoma secretion. The clonidine suppression test, which does not reduce elevated plasma normetanephrine levels to <40% after three hours, is highly specific and sensitive for diagnosing tumors (3, 38). Normal metanephrine and normetanephrine test results can be obtained in patients whose tumor secretes only dopamine and its metabolite 3-methoxytyramine. An increase in methoxytyramine alone was found in 70% of patients with mutations in genes encoding SDH. Such patients are generally normotensive and asymptomatic (3). Plasma normetanephrine reference values must be adjusted according to the patient's age. For patients aged up to 17 years, it is 0.47 nmol/L, for those aged between 30 and 39 years, it is 0.70 nmol/L, while in those aged over 60 years, the reference value is 1.05 nmol/L. That is not necessary for metanephrine and 3-methoxytyramine, although they are slightly higher in men than in women (35).

Radiological findings

Adrenal pheochromocytomas are usually first detected on ultrasound, while CT and MRI are used for precise localization and characterization of tumors. Clinical manifestations are present when pheochromocytomas are several centimeters in size and detectable by ultrasound in 90% of the cases. Their appearance on ultrasound varies from solid to mixed and cystic formations (3). CT can detect tumors of 1 cm in size with a sensitivity of 87%-100%. Pheochromocytomas present as a homogeneous or heterogeneous mass, depending on the presence of hemorrhage and necrosis, while calcifications are present in 29% of cases. Cystic regions, fibrosis, and internal bleeding may also be

seen. They are often well defined, with a density of 30-40 Hounsfield units (HU) (3, 40). In newly found suspicious lesions marked by necrosis, irregular edges, and heterogeneous shape, with a density above 10 HU on native scans, a postcontrast CT scan must be taken according to the protocol for differentiating adrenal lesions and to assess the lesion washout. The standard CT protocol for evaluating adrenal incidentaloma includes non-contrast phase, a portal venous phase (60 s after contrast agent administration), and a delayed phase (15 min after contrast agent administration), which is used in calculation of the percentage of absolute and relative washout. Lesions with absolute washout of less than 60% and relative washout of less than 40% rule out adenoma as a differential diagnosis with a sensitivity of 86%–95% and a specificity of 92%–97% (3, 40).The formula for calculating the absolute and relative washout of the adrenal gland formation is shown in Table 5. Figure 1 shows a case of a sharply demarcated heterogeneous mass of the right adrenal gland with a density of 26 HU on a non-contrast scan. Postcontrast CT scans were performed 60 s and 15 min after intravenous contrast administration to measure the degree of opacification and contrast washout rate. In the CT scan performed 60 s after contrast administration, a strong marginal opacification can be observed, while the central area remains hypodense, which indicates central necrosis. The average density 1 minute after contrast administration was 46 HU (Fig. 2). Fifteen minutes postcontrast, the contrast remains in the described lesion, whose average density is 42 HU (Fig. 3). According to the washout calculation formula, a relative washout of 9% and absolute washout of 20% observed in this lesion rule out adenoma as a differential diagnosis.

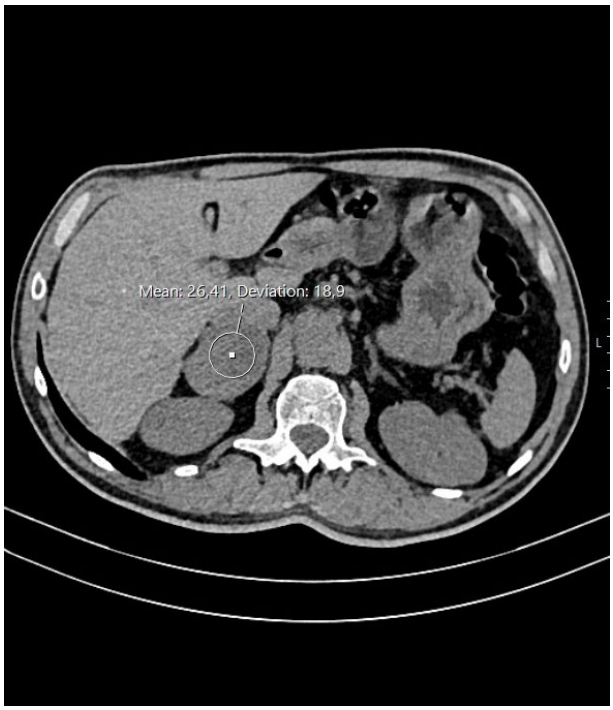

Fig. 1. Computed tomography (CT) non-contrast scan of the abdomen. A sharply demarcated heterogeneous mass of the right adrenal gland with a density of 26 HU is observed, which raises the suspicion of pheochromocytoma.

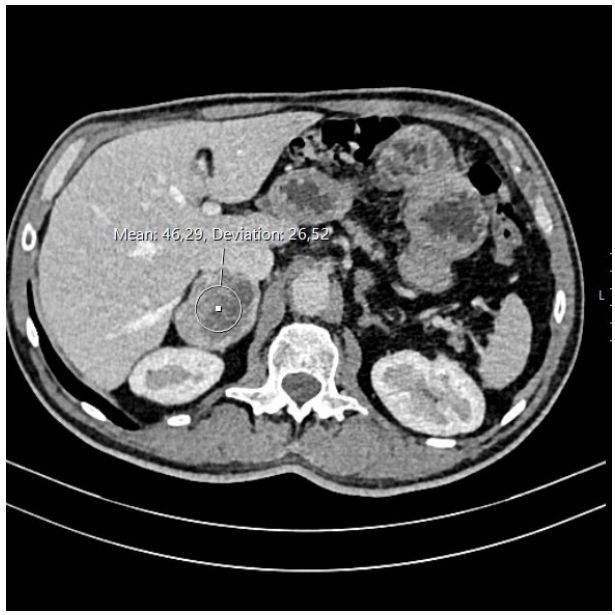

Fig. 2. Abdominal computed tomography (CT) post-contrast image performed 60 seconds after contrast administration to calculate the absolute and relative contrast washout. A strong marginal opacification is observed, while the central area remains hypodense, which indicates central necrosis. The average density of the mass was 46 HU.

Pheochromocytomas are typically hypointense to liver on T1-weighted images and markedly hyperintense on T2-weighted images (lightbulb sign), but that can vary if liquefactive necrosis or hemorrhage are present (41). The characteristic "lightbulb signs", i.e.,

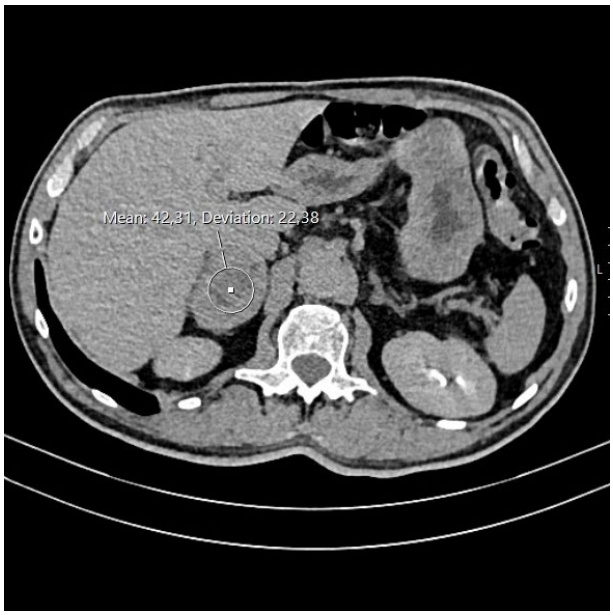

Fig. 3. Abdominal computed tomography (CT) post-contrast image 15 minutes after contrast administration. The contrast remains in the described lesion, whose average density is now 42 HU. Due to the slow washout of the contrast agent in delayed CT sections, adenoma is ruled out as a differential diagnosis.

bright lesions on T2-weighted images, are present in only 30% of cases and are best seen in the fat suppression technique (40). After contrast administration, pheochromocytomas show heterogenous enhancement and delayed contrast washout (6). MRI is the method of choice in children and pregnant women and must be performed in large tumors before surgery to assess vascular invasion (3).

Functional imaging is useful for confirming diagnosis and evaluating metastases (41). It is also recommended after surgery if biochemical tests are inconclusive (3). Functional screening with 123-labelled metaiodobenzylguanidine (MIBG) is characterized by high specificity but not as good sensitivity, so more false-negative test results occur (30, 41). Positron emission tomography (PET) with fluorodeoxyglucose (FDG) has high sensitivity (82.5) for metastatic disease, but the specificity is lower than that of [123I] MIBG (41). In non-metastatic tumors, the sensitivity of FDG-PET CT is 76.8, while the sensitivity of MRI/CT is 95.7, and MIBG 75. Therefore, in non-metastatic diseases, MRI/CT is recommended as the gold standard, while FDG-PET CT is recommended in metastatic disease (43).

Table 5. Formulas for calculating absolute and relative washout of the adrenal gland formation

Parameter	**Formula**
Absolute Washout (APW)	(density in portal venous phase (HU)-density in the delayed phase (HU))/(density in portal venous phase (HU)-density of native sections (HU)) x 100
Relative Washout (RPW)	(density in portal venous phase (HU)-density in the delayed phase (HU))/(density in portal venous phase (HU)) x 100

Table 6. Imaging characteristics of adenomas and pheochromocytomas (40, 42)*

Adrenal gland adenoma	**Pheochromocytoma**
• Homogeneous and well-defined shape • CT: density <10 HU at native cross-sections; absolute washout >60% and relative washout >40% or <35 HU 10-15 min after contrast administration • MRI: loss of signal intensity on out-of-phase T1 weighted images and homogenously isointense or hypointense on T2- weighted images	• Heterogeneous and dense lesion with necrosis and hemorrhage • CT: density >10 HU at native scans; absolute washout <60% and relative washout <40% or density >35 HU 10-15 min after contrast administration • MRI: hypointense on T1-weighted images and markedly hyperintense on T2-weighted images (“lightbulb sign”)

*Abbreviations: CT – computed tomography scan, MRI – magnetic resonance imaging

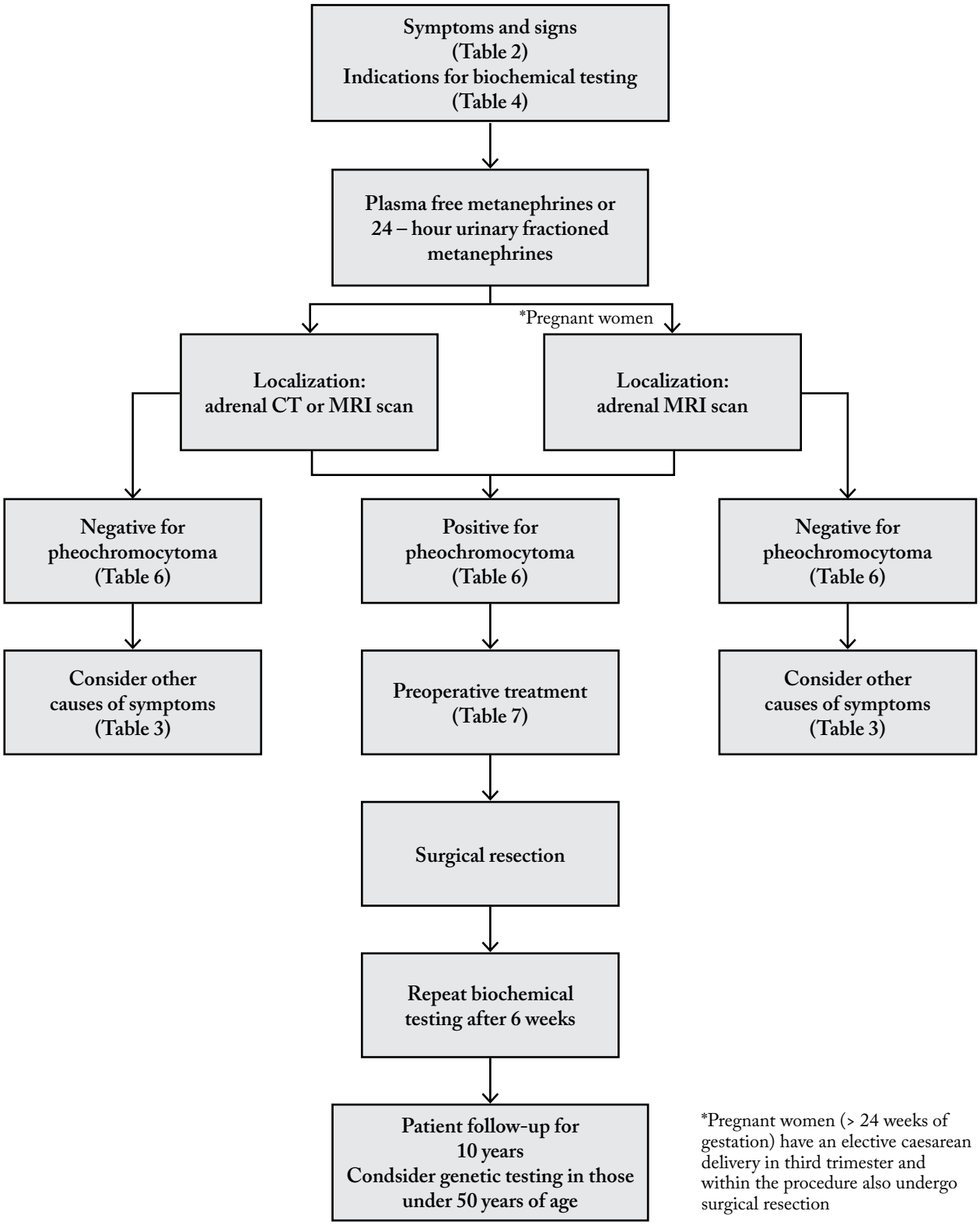

Fig. 4. Algorithm for diagnosing and treating pheochromocytomas.

Treatment

Preoperative preparation is necessary to normalize the patient's blood pressure and pulse, maintain organ function, and prevent catecholamine storm. It is performed 10-14 days before surgery, and even earlier in patients with organ damage due to excess catecholamines, such as cardiomyopathy, vasculitis, recent myocardial infarction (44). The appropriate blockade reduces the number of perioperative complications to less than 3% (3, 44). The most commonly used blocker is phenoxybenzamine, a non-competitive and a non-selective alpha-receptor antagonist with a long-lasting effect that decreases only after α-adrenoceptors have been re-synthesized. The starting dose is 10 mg, given twice a day and increased until clinical manifestations are reduced or side effects occur. A daily dose of 1 mg/kg is usually sufficient. If the initial dose is too high, the patient may experience dizziness, syncope, postural hypotension with reflex tachycardia, and nasal congestion. When the appropriate dose is reached, the patient becomes normotensive or mildly hypotensive (44). During the alpha blockade, it is important to monitor fluid balance to allow the resulting vasodilation to be supported by adequate fluid intake. In addition to phenoxybenzamine, doxazosin, a competitive, short-acting selective alpha-blocker, associated with a lower risk of postoperative hypotension, may also be used (2). Nevertheless, phenoxybenzamine is more commonly used because, in surgery, its non-competitive action prevents separation from the receptor during the release of large amounts of catecholamines, which may occur with doxazosin (6). After alpha-blockers, beta-blockers are introduced for preoperative control of tachycardia and angina pectoris. Propranolol, atenolol, and metoprolol are usually administered (3). They should never be used in the absence of alpha-blockers as they will aggravate the vasoconstriction caused by epinephrine and block its vasodilatory effect. Calcium channel blockers, which also have a role in controlling hypertension and tachyarrhythmias, can also be used for preoperative preparation (44). An example of a preoperative gradual introduction of alpha and beta-blockers is given in Table 7. The criteria for good preoperative preparation include lowering blood pressure below 160/90 mmHg, reducing the number of ventricular extrasystoles to less than 1 in 5 minutes, and achieving normalization of the ST-T changes seven days before surgery (30). Open adrenalectomy is indicated in large or malignant tumors, while the laparoscopic adrenalectomy is indicated in lesions smaller than 4 cm (2). The intraoperative mortality rate is less than 1% (45). Post-operative complications include the risk of hypotension and hypoglycemia (30). Hypoglycemia is a rare complication associated with epinephrine-secreting tumors and prolonged

Table 7. Example of preoperative gradual introduction of alpha- and beta-blockers

Day(s)	Alpha-blocker	Beta-blocker	Sodium chloride
1	phenoxybenzamine 10 mg twice		
2	phenoxybenzamine 10 mg twice		5 g
3	phenoxybenzamine 20 mg twice		5 g
4	phenoxybenzamine 20 mg twice		5 g
5	phenoxybenzamine 30 mg twice		5 g
6	phenoxybenzamine 40 mg twice		5 g
7	phenoxybenzamine 50 mg twice		5 g
8	phenoxybenzamine 50 mg twice	bisoprolol 1.25 tbl.	5 g
9	phenoxybenzamine 50 mg twice	bisoprolol 2.5 mg	5 g
10-20	phenoxybenzamine 50 mg twice	bisoprolol 2.5-5.0 mg*	5 g

*with blood pressure and pulse monitoring. Target blood pressure values 100-110 mmHg.

operative time. In inoperable and malignant tumors, chronic medical treatment is the same as preoperative, while metastases are treated palliatively (3).

Prognosis

The prognosis of benign tumors is excellent, but recurrence rates in 10 years can reach up to 16%, so monitoring is required (24). In malignant tumors, metastases occur in 35% of patients. In 65% of patients, it happens after 5.5 years (45). The expected 5-year survival is 40%-77% (3). High levels of catecholamines, which clinically manifest as hypertension and constipation, are the cause of death in 30% of cases. Some studies show that high doses of I-131 MIBG can lead to long-term survival in patients with malignant tumors (3).

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Sažetak

KLINIČKA SLIKA, DIJAGNOZA I LIJEČENJE FEOKROMOCITOMA

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Feokromocitomi su rijetki neuroendokrini tumori koji potječu iz kromafinih stanica srži nadbubrežne žlijezde i pretjerano luče katekolamine zbog čega dolazi do mnoštva različitih simptoma. Najčešći simptomi uključuju glavobolje, palpitacije i znojenje. Zbog raznolike kliničke slike predstavljaju velik izazov u dijagnostici i često ostanu neprepoznati. Mogu se javiti sporadično ili u sklopu nasljednih sindroma. Dijagnoza se potvrđuje mjerenjem metanefrina i normetanefrina u plazmi i 24-satnom urinu. Za lokalizaciju tumora koristi se kompjutorizirana tomografija, magnetska rezonanca i funkcionalno-morfološke pretrage. Liječenje je operativno i podrazumijeva posebnu preoperativnu pripremu kako ne bi došlo do hipertenzivne krize i aritmija. Zbog mogućnosti recidiva potrebno je pratiti pacijenta. Ako se ne prepozna na vrijeme, ima visoku smrtnost zbog djelovanja katekolamina na kardiovaskularni sustav.

Ključne riječi: *Feokromocitom; Glavobolja; Multipla endokrina neoplazija tipa 2; Palpitacije; Paroksizmalna hipertenzija*