Pheochromocytoma

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36.1 Key Points

A pheochromocytoma is a tumor of chromaffin cells, which secrete catecholamines, predominantly norepinephrine, as well as epinephrine, and rarely dopamine. The majority of pheochromocytomas are sporadic, but up to 25 % of cases are hereditary [1]. It may be associated with multiple endocrine neoplasia syndrome, type IIA and type IIB (also known as MEN IIA and MEN IIB), von Hippel-Lindau disease, neurofibromatosis type 1 (von Recklinghausen disease), phakomatosis, and paraganglioma syndromes.

Clinical signs and symptoms result from excessive catecholamine levels, the most common of these features is hypertension. The classic symptom triad of episodic headaches, tachycardia, and sweating may be present.

Diagnostic tests of choice are 24-h urine metanephrines and plasma fractionated metanephrines. Imaging studies should be performed after biochemical studies have confirmed the diagnosis of pheochromocytoma.

36.2 Background

Pheochromocytomas may occur in persons of any age. The peak incidence is between the third and the fifth decades of life, but approximately 10 % occur in children.

Tumors are normally located in the adrenal medulla, but approx. 10–20 % are located elsewhere – usually throughout the sympathetic chain in the thorax, abdomen, and pelvis.

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About 10 % of pheochromocytomas are malignant; this goes up to 33 % in extra-adrenal pheochromocytomas. There are no reliable histopathological methods for distinguishing benign from malignant tumors. Instead, malignancy requires evidence of metastases at non-chromaffin sites distant from the primary tumor. The most common sites of metastasis are lymph nodes, bones, lungs, and liver. Malignant pheochromocytomas carry a very poor prognosis.

The pheochromocytoma "rule of 10": 10 % bilateral, 10 % malignant (higher in familial cases), 10 % extra-adrenal, and 10 % in children.

36.3 Therapy

Surgical resection of the tumor is the treatment of choice, along with preoperative management hypertension with full α-blockade (phenoxybenzamine, prazosin, doxazosin) for at least 2–3 weeks prior to surgery. In select cases, beta-blockers may be added after adequate alpha-blockade has been established in order to reduce tachycardia, a side effect of α-blockade [2]. That way permits the surgery to proceed while minimizing the likelihood of severe, life-threatening intraoperative hypertension, which might occur when the tumor is manipulated. Laparoscopic adrenalectomy is the procedure of choice today.

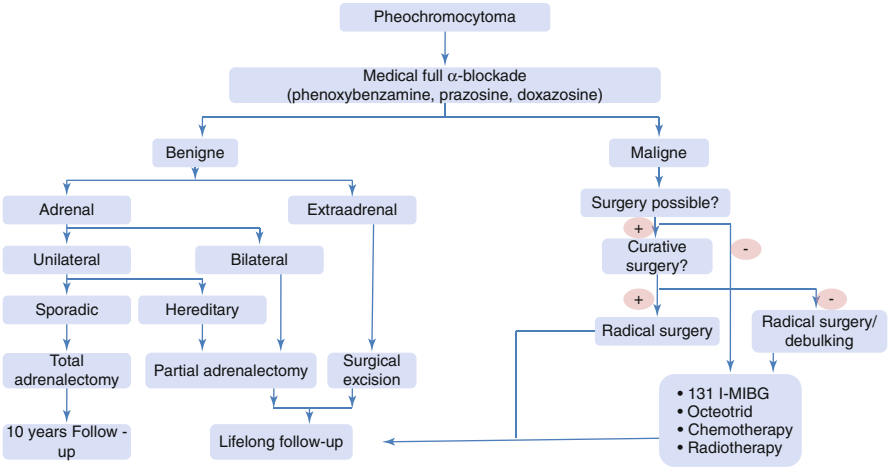
Hormone levels of norepinephrine and epinephrine return to normal after surgery.

In case of malignant pheochromocytoma, a multimodal treatment is required.

After aggressive surgery has been carried out, adjuvant treatment options include [3]:

- Combination chemotherapy: Chemotherapy with a combination of cyclophosphamide, vincristine, and dacarbazine provides partial remission and improvement of symptoms in up to 50 % of patients with malignant pheochromocytoma.
- External beam radiation therapy: Only in case of skeletal metastasis in order to prevent pathologic fractures.
- High-dose 131I-meta-iodobenzylguanidine (MIBG) radionuclide therapy: 131 I- MIBG is transported into the cell via the cell membrane norepinephrine transporter present on most neoplastic chromaffin cells. Overall, about 75 % of patients treated with 131 I-MIBG show improvement in symptoms, 50 % have reductions in hormonal activity, and 22 % show objective tumor responses.
- Somatostatin analogs: In patients with endocrine tumors expressing somatostatin receptors, targeted treatment with analogs of the natural ligand (e.g., octreotide, lanreotide) can lead to marked biochemical and, in part, radiological improvements.

For surgical follow-up, obtain plasma metanephrine levels yearly for 10 years. Ensure that blood pressure is under control. In patients with an underlying genetic mutation or malignant disease, lifelong follow-up is mandatory.



36.4 Complications

Untreated pheochromocytoma causes substantial morbidity and mortality, usually caused from a lethal hypertensive paroxysm. Cardiovascular complications may include hypertensive crisis (treatment: sodium nitroprusside, phentolamine, uradipil), cardiac arrest, sudden death, stroke, myocardial infarction, congestive heart failure, and renal insufficiency.

Complications of surgery for pheochromocytoma are primarily due to severe preoperative hypertension, high secretion tumors, or repeat intervention for recurrence. In case of bilateral adrenalectomy, adrenal insufficiency can occur.

In individuals with benign tumors, the 5-year survival rate after surgery is above 95 %. In case of malignant tumor, the 5-year survival rate after surgery is less than 50 %.

References

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