Recognition and management of phaeochromocytoma

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Abstract

Phaeochromocytomas are catecholamine-secreting neuroendocrine tumours arising from the chromaffin cells in the adrenal medulla. These tumours may be identified incidentally, as part of a workup for multiple endocrine neoplasia or during unrelated surgery. Better understanding of catecholamine physiology and advances in preoperative preparation has significantly reduced surgical mortality from around 40% to less than 3%. Surgery is the definitive treatment in most cases and laparoscopic resection is associated with reduced hospital stay and earlier mobilisation. Phaeochromocytomas are of particular interest to anaesthetists as it presents a unique haemodynamic challenge both before and after adrenal resection. In this article we describe the physiology of these tumours, their diagnosis and perioperative management.

Keywords α-blockers; β-blockers; calcium channel blockers; catecholamines; incidentalomas; metanephrines; metyrosine; paraganglioma; phaeochromocytoma

Royal College of Anaesthetists CPD matrix: 1A01, 1A02, 2A03, 2A04, 2A05, 2A06, 2A07, 3A03

Learning objectives

After reading this article, you should be able to:

- describe the pathophysiology of phaeochromocytomas
- describe the preoperative management of patients with phaeochromocytomas
- describe the intraoperative anaesthetic management of the tumour resection
- explain the immediate and long-term postoperative complications

Background

Phaeochromocytomas are tumours that arise from the chromaffin tissue derived from the neural crest. Nearly 80% arise from the adrenal gland, the rest are extra-adrenal and known as paragangliomas. Paragangliomas can be found in the para-aortic region, pelvis, chest and rarely the heart.

The incidence of phaeochromocytoma is 1–8/million in the general population. It is present in approximately 5% of patients presenting with an incidental mass in the adrenal gland – giving such tumours the name of incidentalomas. The incidence of malignancy is approximately 10% in tumours arising from the adrenals. This incidence rises to 25% in larger and extra-adrenal tumours. Although there are no known risk factors for this tumour, almost a fifth occur in hereditary syndromes. This includes syndromes such as multiple endocrine neoplasia types 2A and 2B as well as hereditary paraganglioma syndrome, in which specifically affected genes are identified. Other conditions associated with phaeochromocytoma include von Hippel–Lindau disease and neurofibromatosis type 1. Ten different genes have been associated with the development of these tumours.[1]

Clinical features

Clinical features of phaeochromocytoma are varied and sometimes non specific. Hypertension is found in 70–90% of patients. When hypertensive patients present with the classical triad of headache, palpitations and excessive sweating, the combination is highly specific (93.8%) and sensitive (90.9%) for phaeochromocytoma. They can also present with hypertensive crisis either with or without a background of sustained hypertension. About 13% of patients with high circulating catecholamines are asymptomatic, possibly due to receptor downregulation.[2]

Catecholamine-secreting tumours can present for the first time, as unexplained hypertension, tachycardia and arrhythmia during diagnostic procedures or other unrelated surgery.

Less common features include weight loss, orthostatic hypotension and cardiomyopathy, hypercalcaemia, diarrhoea and fluid and electrolyte imbalance. It can be associated with metabolic disorders such as diabetes.

Importantly, phaeochromocytoma may present as a medical emergency characterized by multiple organ failure, encephalopathy, hypertension or hypotension. In addition to intensive therapy, emergency tumour removal may be indicated.

Pathophysiology

The WHO defines phaeochromocytoma as a tumour arising from chromaffin cells in the adrenal medulla. Paragangliomas are closely related tumours in extra-adrenal sympathetic and parasympathetic ganglia.

The significantly raised blood pressure that often characterises this tumour results from raised circulating catecholamines and an enhanced sympathetic nervous system. Sympathetic vesicles are loaded with catecholamines due to increased production. There is also an increased frequency of sympathetic neuronal impulse and selective desensitisation of pre-synaptic α2-adrenergic receptors resulting in excess release of neuronal norepinephrine during stimulation. The dual mechanism explains the severe hypertension that may result from relatively small increments in circulating norepinephrine as well as the paroxysmal nature of the hypertension that is triggered by stressful stimuli such as pain, intubation, and surgical incision.

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The effect of sustained hypertension on the heart can lead to hypertrophic or dilated cardiomyopathy. Both types are fortunately reversible following tumour resection.

Chronic vasoconstriction leads to decreased intravascular volume and these patients can be severely volume depleted.

Diagnosis

Priority is given to establishing evidence of increased catecholamine production by the tumour. All symptomatic patients, those with adrenal incidentalomas and those with hereditary risk of developing a catecholamine secreting tumour should be investigated for phaeochromocytoma. Identifying the tumour's location then follows.

Figure 1 shows the synthesis and metabolism of catecholamines.

Historically, there was a reliance on the direct assay of plasma concentrations of catecholamines and catecholamine metabolites in the urine. Unfortunately these tests suffered poor sensitivity and specificity. The catecholamines are quickly metabolized to metanephrines in the tumour by catechol-O-methyltransferase (COMT), thus potentially producing deceptively normal plasma and urine assays. More sensitive tests include, metanephrine screening. Table 1 gives an indication of the sensitivity and specificity of biochemical tests for phaeochromocytomas and paragliomas.[2]

Blood sample for biochemical markers should be taken with the patient supine, about 15–20 minutes after venous cannulation. Patients should avoid food, caffeinated beverages, strenuous physical activity, or smoking for at least 8 hours before testing. Metanephrine levels greater than four times the reference normal level is considered diagnostic of phaeochromocytoma. Severity of increase also indicates need for urgent management.

Unfortunately, despite the tests mentioned, diagnostic uncertainties remain. When levels are borderline in patients whose presentation is strongly suggestive of phaeochromocytoma, the clonidine suppression test is helpful. Plasma catecholamines are measured before and 3 hours after oral administration of 0.3 mg clonidine. If the test fails to reduce catecholamine levels to more than 50%, this is strongly indicative of phaeochromocytoma.

CT and MRI scans are the initial tools for localization of the tumour. MRI scans are more sensitive in detecting extra-adrenal tumours. MRI is also preferred in pregnant patients and children

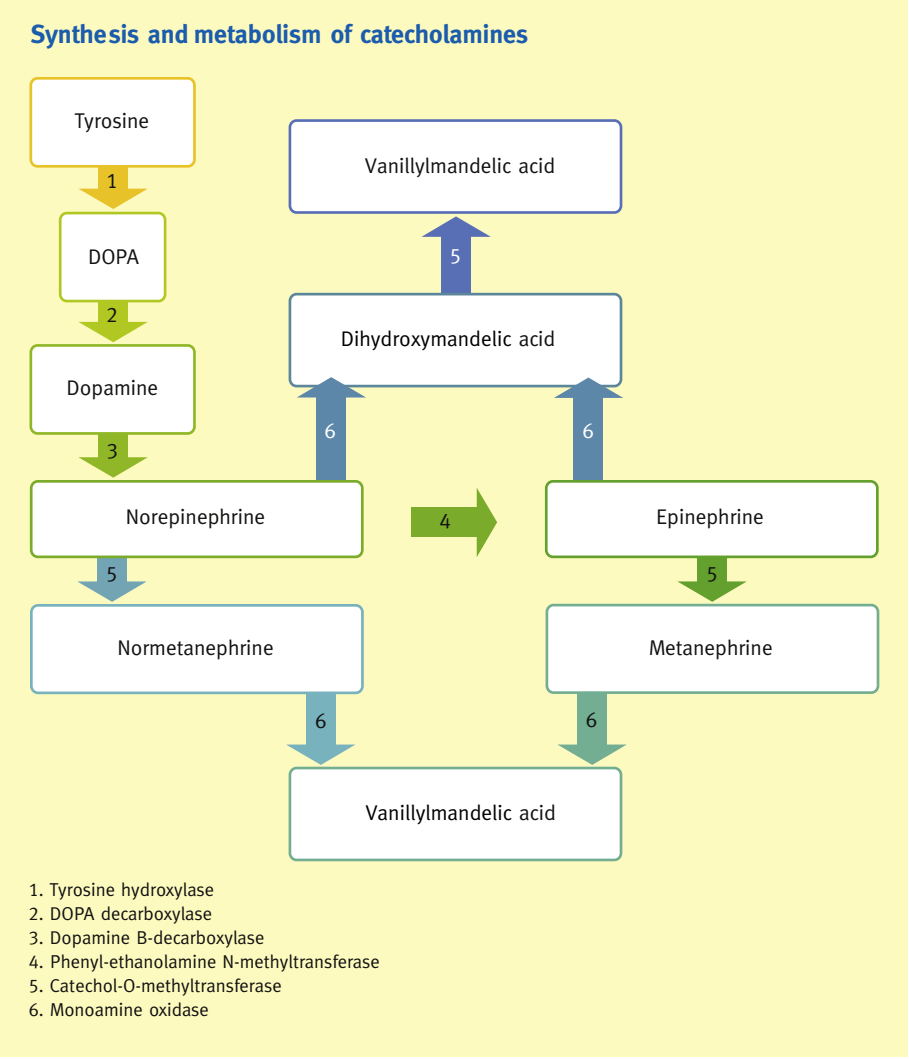

Figure 1