Pheochromocytoma

Michael F. Roizen

Risk

- Incidence in USA: 0.03–0.04% (~80,000) by autopsy of nonselected individuals.
- Prevalence: 0.1–0.3% of individuals with sustained Htn have pheochromocytoma. At least 20% are now diagnosed when the tumor is incidentally found during abdominal MRI or CT for other reasons.
- Race with highest prevalence: Caucasian.

Perioperative Risks

- In the case of emergency (life-threatening trauma, ruptured viscus), use α- and β-blockers and nitroprusside and keep pt in ICU until worst pain has passed or adrenergic control is achieved.
- Risk of hypertensive crisis is increased with bleeding into myocardium, brain, or kidney or with ischemia.
- Mortality rate of 0–3% even if pt is appropriately prepared for tumor resection and in "good" hands for adrenalectomy; it may be higher for undiscovered cases undergoing nonadrenal surgery.
- 25–50% of those who die in hospital of pheochromocytoma crisis do so during induction of anesthesia, during stressful periop periods, or during labor and delivery, often in surgery for other problems
- Associated with cholelithiasis and renal stones.

Worry About

- Pheochromocytoma (catecholamine excess) crisis with hemorrhage/infarcts in vital organs.
- Major goal is to avoid pheochromocytoma crisis; preop and intraop goals in management of extra-adrenal surgery are same as for adrenal surgery. If adrenergic blockade is not present prior to surgery, try to delay operation until pt has an appropriate degree of α-blockade. Judge appropriate blockade by:
  - No BP readings >165/90 mm Hg for 48 h
  - Presence of orthostatic hypotension, but BP on standing should not be <80/45 mm Hg
  - ECG free of ST-T changes
  - Absence of other signs of catecholamine excess and presence of signs of α-blockade

Overview

- Tumor of catecholamine-producing tissue (90% in adrenals). Painful (stressful) events in daily living or if a pt is less than perfectly anesthetized cause exaggerated stress response. Even small stresses can lead to blood catecholamine levels of 2000 to 20,000 pg/mL. However, infarction of tumor, with release of products onto retroperitoneal surfaces or pressure causing release of products, can result in blood levels of 200,000–1 million pg/mL, a situation that should be anticipated during tumor resection.
- Endocrinopathy associated with CV disease: Tachycardia, CHF, dysrhythmias (AFIB).
- Need α-blocker prior to β-blocker unless vasoconstrictive effects of latter go unopposed, thereby increasing risk of dangerous Htn. β-blockade is suggested if persistent arrhythmias or tachycardia fail to resolve with α-blocker or are aggravated by α-blocker.
- If α-blockade is used appropriately, risk of crisis diminished by >90%.
- Calcium channel blockers (nicardipine) are second in frequency for preparation, and metatyrosine is used as an alternative for malignant pheochromocytoma or for rapid preparation, but it has major adverse effects, including somnolence, movement disorder, and orthostatic effects and may be best confined to use in the hospital. These drugs, both phenoxybenzamine and metatyrosine, have recently become much more expensive.

Indications and Usual Treatment

- 60–90% of cases arise spontaneously and 10–40% are familial (autosomal dominant genetics involving chromosome 7 implicated in many).
- Associated with MEA IIA (medullary thyroid carcinoma; primary hyperparathyroidism) and IIB (medullary thyroid carcinoma and mucosal neuromas) with mutation often at chromosome location 17q11.2.
- Associated with neurofibromatosis, von Hippel–Lindau disease (retinal and cerebellar hemangioblastoma), ataxia-telangiectasia syndrome, Sturge-Weber syndrome, with mutation often at the VHL gene localized to chromosome 3p25–26.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT		Nasal stuffiness (from α-adrenergic blockade)		
CV	Htn; dysrhythmias; AFIB, sinus tachycardia, mitral valve prolapse; CHF, myocardial fibril necrosis or myocarditis	SOB, poor exercise tolerance, palpitations, Htn (50% sustained, 40% paroxysmal)	Standard exam including BP measurement for 1 min in stressful environment plus orthostatic maneuvers with BP/HR measured for 1 min	ECG, ECHO (if cardiomyopathy is suspected)
GI	90% of tumors adrenal or abdominal	Weight loss, diarrhea Dehydration	Palpation of abdomen can trigger crisis	No different from normal
HEME		Mild polycythemia, thrombocytopenia (secondary to reduced intravascular fluid)		Hgb (reduced polycythemia is a way to judge volume expansion by α-blocker)
GU	Renal stones from dehydration			
CNS	Increased catecholamine effects	Headache, tremor, anxiety, lowered pain threshold, fatigue		
METAB	Associated with hyperparathyroidism	Glucose intolerance from α-adrenergically induced gluconeogenesis and reduced insulin secretion		Insulin Rx often before Dx is made; Ca^{2+}

Key References: Witteles RM, Kaplan EL, Roizen MF: Safe and cost-effective preoperative preparation of patients with pheochromocytoma, *Anesth Analg* 91(2):302–304, 2000; Amar L, Servais A, Gimenez-Roqueplo AP, et al.: Year of diagnosis, features at presentation, and risk of recurrence in patients with pheochromocytoma or secreting paraganglioma, *J Clin Endocrinol Metab* 90(4):2110–2116, 2005; Lenders JW, Duh QY, Eisenhofer G, et al.: Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline, *J Clin Endocrinol Metab* 99(6):1915–1942, 2014.

Perioperative Implications

Preoperative Preparation

- Prehydrate liberally over 6–60 d if CV status will tolerate it; expand with high salt/fluid diet while increasing α-adrenergic blockade over 7–60 d (some use calcium channel blockers, but increased complications are associated with this process epidemiologically).

Monitoring

- Temperature.
- Arterial line placement prior to induction is difficult and painful but desired because of variations in BP.
- PA cath or TEE if CV system severely affected; CVP used in a minority of cases.

Anesthetic Technique

- No technique/group of agents associated with a better outcome; use of droperidol controversial; agents that block reuptake (ketamine) or cause catecholamine release might be avoided.

Induction/Maintenance

- Prehydrate liberally if CV status will tolerate it.
- Gentle induction with nitroprusside infusion plugged into an IV line and running slowly.
- Dopamine infusion in reserve for ready use.
- Painful or stressful events often cause an exaggerated response due to release of catecholamines from nerve endings that are "loaded" by the reuptake process.

Postoperative Period

- If catecholamine-producing tumor has been removed or α-adrenergically blocked, do not chase or force a high UO with large crystalloid infusions; pts have tendency to develop CHF because they have been on endogenous inotropes for many years.
- Early mobilization and deep breathing a must but fraught with difficulty; disturbed mentation often follows the removal of catecholamines for a lengthy period.

Adjuvants

- Drug interactions possible with chronic antiadrenergic agents, such as between verapamil or diltiazem and β-blockers in depressing AV nodal conduction if pt is chronically or acutely receiving a β-blocker or has decreased clearance of phenytoin, barbiturates, rifampicin, chlorpromazine, or cimetidine.

Anticipated Problems/Concerns

- Important to interview family members and perhaps advise them to inform their future anesthesiologists about the potential for such a familial disease.