Pheochromocytoma & Paraganglioma

Biochemistry before imaging, imaging before surgery · and alpha blockade before any beta blocker, without exception

Alpha first *always*

WHEN TO SUSPECT IT *rare, but catastrophic when it is missed*

THE CLASSIC TRIAD

Episodic headache, palpitations and sweating, in spells lasting minutes, often with pallor rather than flushing and a sense of doom. **The spells are paroxysmal**, so the patient is frequently normal in clinic, and blood pressure between episodes can be entirely normal.

THE OTHER ROUTES IN

Resistant hypertension, **hypertension in a young patient**, marked blood pressure lability, and **an adrenal incidentaloma**, which is now one of the commonest ways it is found. Also a **hypertensive crisis during anesthesia or a procedure**.

DO NOT BIOPSY THE MASS

Biopsying an unsuspected pheochromocytoma can precipitate a fatal hypertensive crisis. Exclude it biochemically before any adrenal biopsy, which is the reason the workup order on this sheet is not negotiable.

DIAGNOSIS *biochemistry first, and interpret it properly*

Step	Detail
1. Plasma free metanephrines *or 24-hour urinary fractionated metanephrines*	**Metanephrines, not catecholamines.** Tumors metabolize catecholamines continuously, so metanephrines are raised between spells while catecholamines may be normal. **Draw supine after 30 minutes of rest**: an upright or stressed draw is a common cause of a false positive that then triggers an unnecessary imaging cascade
2. Interpret the magnitude	**A level more than three times the upper limit is highly suggestive.** Mild elevations are frequently false positives and should prompt a repeat under proper conditions before anything else happens
⚠ Exclude the interfering drugs first	**Tricyclic antidepressants and SNRIs are the biggest offenders**, along with levodopa, decongestants, amphetamines, buspirone, and **labetalol and sotalol**, which interfere with some assays. Also acetaminophen with certain methods. **Where safe, withdraw the drug and repeat before diagnosing**. Physiological stress, including acute illness in an ICU patient, raises levels too
3. Then image	**CT or MRI of the abdomen and pelvis only after biochemical confirmation.** If nothing is found, or disease is multifocal or metastatic, functional imaging with **DOTATATE PET** or MIBG locates it

PREOPERATIVE PREPARATION *the part that kills patients when it is rushed*

Step	Detail
⚠ Alpha blockade FIRST never beta first	**Start an alpha blocker for 7 to 14 days before surgery**: phenoxybenzamine, or a selective agent such as doxazosin. **Giving a beta blocker first leaves alpha-mediated vasoconstriction unopposed and can precipitate a hypertensive crisis, pulmonary edema and death.** This is the single most examined and most clinically important point in the whole topic
Then salt and volume	**Liberal salt intake and generous fluids** once alpha blockade has begun. These patients are chronically vasoconstricted and **profoundly volume depleted**, and expanding the volume is what prevents the severe hypotension that follows tumor removal
Add a beta blocker only afterward	Once alpha blockade is established, add a beta blocker **only if tachycardia or arrhythmia requires it**. It is an optional second step, not a routine one
Anticipate the intraoperative swings	Severe hypertension on tumor handling, then **abrupt hypotension the moment the venous drainage is ligated**. Warn the anesthetic team, and expect vasopressors and volume at that point
After surgery	**Hypotension and hypoglycemia** are both expected: catecholamine withdrawal removes the vasoconstriction and releases the suppression of insulin. **Monitor glucose actively** rather than waiting for symptoms. Recheck metanephrines a few weeks later to confirm cure

GENETICS & FOLLOW-UP *a much more inherited disease than it used to be taught*

REFER EVERYONE FOR TESTING

Around 40% are hereditary, so genetic testing is now recommended in **all** patients, not only the young or those with a family history. Key syndromes: **MEN2** (with medullary thyroid cancer and hyperparathyroidism), **von Hippel-Lindau**, **neurofibromatosis type 1**, and the **SDHx** family.

WHY IT CHANGES CARE

A germline result triggers **screening of relatives** and alters surveillance. **SDHB in particular carries a higher risk of malignant and metastatic disease**, so it changes how closely the patient is followed. **In MEN2, exclude and treat the pheochromocytoma BEFORE any thyroid surgery.**

LIFELONG FOLLOW-UP

There is no reliable histological marker of malignancy: it is defined by metastasis, which can appear years later. **Annual biochemical surveillance is therefore lifelong** for everyone, and indefinite in hereditary and paraganglioma cases.

THE SPELL DIFFERENTIAL *most patients tested do not have it, so know what else does this*

Alternative	What points to it instead
Panic disorder	**By far the commonest explanation for episodic palpitations, sweating and doom.** Favors panic: prominent dyspnea and paresthesia, an identifiable trigger or agoraphobia, and **normal blood pressure during a witnessed spell**. Testing is still reasonable when spells are stereotyped and hypertension is documented
Thyrotoxicosis	Heat intolerance, weight loss with preserved appetite, tremor, a **wide pulse pressure** and goiter. **Check TSH in every patient investigated for spells**, since it is cheap and frequently the answer
Carcinoid syndrome	**Flushing rather than pallor**, plus secretory diarrhea and wheeze. The flush is the discriminator: pheochromocytoma classically causes **pallor** during the spell
Drugs and withdrawal	Cocaine, amphetamines, decongestants and excess caffeine; **abrupt clonidine withdrawal** and alcohol withdrawal both produce a convincing adrenergic picture. Also **MAO inhibitor plus tyramine**
Hypoglycemia and mastocytosis	Hypoglycemia gives adrenergic symptoms that **resolve with carbohydrate**, so check a glucose during a spell. Mastocytosis brings **urticaria, flushing and anaphylactoid features** with a raised tryptase

CRISIS TRIGGERS & PEARLS

- **Know the drugs that can trigger a crisis in an unprepared patient: beta blockers given alone**, **glucagon**, **metoclopramide**, anesthetic induction agents, opiates, and unopposed **tyramine**-rich food with MAO inhibitors. In an acute crisis, **phentolamine** or a nitroprusside or nicardipine infusion is used, never a beta blocker alone.
- **Paragangliomas are the extra-adrenal version**, arising along the sympathetic chain and in the head and neck, where they are often **non-secretory** and present as a painless mass with cranial nerve signs instead of spells.
- **It belongs on the differential of an unexplained cardiomyopathy**, since sustained catecholamine excess causes a reversible catecholamine cardiomyopathy that improves once the tumor is removed.

References: Endocrine Society clinical practice guideline on pheochromocytoma and paraganglioma · published guidance on perioperative alpha blockade and on genetic testing in pheochromocytoma-paraganglioma syndromes.

Educational aid; verify against current guidance, local formulary and patient factors.

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