Pheochromocytoma

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Pheochromocytoma facts

- Catecholamine-secreting tumor of the neuroectodermal cells of the adrenal medulla (chromaffin cells of the neural crest)
- Central torso location along the sympathetic chain
- Incidence = 0.1-0.4% of HTN patients;
- M=F and found in the 4th-5th decade of life
- 25% found incidentally; 4-8% of incidentalomas
- Can be asymptomatic (10-20%) and normotensive (10-20%)
- Delay of 3 years from initial symptoms to diagnosis
- Hereditary forms – MEN2, Von Hippel Lindau, Neurofibromatosis type 1 and familial paraganglioma
Pheochromocytoma

?? Still the “Tumor of 10’s”

- 10% Bilateral (higher in MEN2 pts. and children)
- 10% Malignant (higher in extra-adrenal tumors)
- 10% Extra-adrenal (most [98%] are in the abdomen)
- 10% Children
- 10% Familial – incidence probably 10-24%
Adrenal medulla

Catecholamine synthesis

- PNMT (phenylethanolamine-N-methyltransferase) present only in adrenal medulla and organ of Zukerkandl
- Most extra-adrenal pheos can only make norepinephrine
Clinical presentation of Pheochromocytoma

- Episodic headaches
- Sweating
- Tachycardia/Palpitations
- Chest pain/MI
- Anxiety/panic attacks
- Abdominal pain/N & V
- Precipitated “spells”
- Sustained HTN
- Paroxysmal HTN
- Sustained/Paroxysmal HTN
- HTN crisis
- Fever
- Glucose intolerance
- GI dysmotility
Pheochromocytoma principles

- Biochemical diagnosis first then imaging
- Biochemically screen all retroperitoneal masses
- Episodic catecholamine production, but continuous metabolism of byproducts allows diagnosis. Distinguishing true positive from false positive biochemical testing remains a challenge
- Always alpha block before beta – unopposed alpha stimulation can result in catastrophic HTN crisis, CVA, Pulmonary edema, CHF, sudden death, etc.
- No FNAB without biochemical screening
  - Only for patients with primary extra-adrenal malignancy (breast, lung, renal, ovarian, melanoma, lymphoma, etc.)
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Biochemical diagnosis

- 24 hour urine collection is 98% sensitive and 98% specific and is usually elevated 4-fold above upper reference limits
  - Free catecholamines, total/fractionated metanephrine, VMA
  - Plasma free metanephrines
    - Easy to obtain and frequently is first test performed
    - Highly sensitive (99%) to exclude pheo with normal values, but not as specific (85%) as 24-hour urinary testing
- Plasma epinephrine & norepinephrine levels variable
- Chromogranin A levels – limited s/s but useful in assessing tumor burden and disease progression in patients with malignancy
- Clonidine suppression test rarely used – lowers plasma catecholamines after 0.3 mg oral dose administers
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Who should undergo biochemical screening?

- Paroxysmal HTN
- Therapy resistant HTN
- Volatile HTN
- Severe intraoperative HTN
- Younger patients < 40 years of age
- Hereditary predisposition
- Sudden anxiety attacks
- Incidentalomas
Preoperative medical blockade
Lowered perioperative mortality from 45% to < 2%

- Alpha blockade started 2-4 weeks preoperatively in all pheo patients and always prior to beta blockade (if needed)
  - Phenoxybenzamine – non-selective, non-competitive with 24-hr. half-life and possible tachycardia; goal is mild orthostasis and nasal congestion
  - Doxazocin (Cardura) – selective, but ? less effective in highly active tumors
  - Terazosin & Prazosin – shorter half life needing more frequent dosing
  - Phentolamine, Labetalol, α-methyltyrosine, etc.
  - Calcium channel blockers (Amlodipine, Nifedipine, Nicardipine) – no tachycardia and may limit coronary spasm
- Beta blockade – only after alpha blockade to treat tachyarrythmias
  - Propranolol, Atenolol, Esmolol (intra-op), Labetalol, etc.
Pheochromocytoma imaging

- Abdominal/Pelvic CT scanning
- Abdominal MRI
  - High intensity T2-weighted images
  - Evaluate IVC and hepatic invasion
- MIBG – $^{123}$I-MIBG ideal & $^{131}$I-MIBG for ablation
- PET scanning - DOTATATE
When do we need a $^{123}$I-MIBG scan?

- Marginal biochemical diagnosis
- Extra-adrenal tumors
- Multiple tumors
- Suspicion of malignancy
- Normal adrenal imaging
- PET scanning may be superior
- Therapeutic ablation with $^{131}$I-MIBG
- Unnecessary in most sporadic benign tumors
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Surgical management

- Hemodynamic monitoring and IV agents available
- Pre, intra, and postoperative volume expansion
- Anesthesia expertise – enflurane or isoflurane to limit catecholamine release
- Early adrenal vein ligation with minimal tumor manipulation
- Laparoscopic adrenalectomy advisable
  - Expect a highly vascular tumor
  - Avoid capsular rupture
  - Appropriate for larger tumors – poor size correlation for malignancy
- Manage po hypotension and hypoglycemia
Laparoscopic adrenalectomy

- Route of choice for most removal of most pheochromocytomas
- Advanced laparoscopic procedure
- Transperitoneal vs. retroperitoneal approach
- High success rates (R/L/B); similar OP times as open
- Decreased pain, hospitalization, and morbidity with earlier return to activity, & ? lower cost
- Combine with other laparoscopic procedures
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Who should undergo genetic screening?

- Young patients < 35 years of age
- Bilateral tumors
- Extra-adrenal tumors
- Paragangliomas
- Malignant tumors
- Family history of genetic syndromes
- ?? All patients
Malignant pheochromocytoma

- Benign vs. malignant often difficult
- Recurrence = 0-17% after resection for “benign” tumors
  - Long term surveillance with biochemical testing essential
- Operative vs. pathologic diagnosis
- Resection/debulking may lower catecholamine production and allow more effective medical control of HTN
- Metastases to bone, lung, liver, CNS, lymph nodes, etc.
- MIBG, chemotherapy, RFA, chemo/arterial embolization, & RT are options with limited success
- 5-year survival 30-60% - goal is palliation of HTN symptoms
- Cortical sparing may increase recurrence rates