Phaeochromocytoma

Dr Mousa Tuwati Alfakhri

15/7/2020

Phaeochromocytoma

- Rare neuro-endocrine tumours , they are chromaffin tumours arising from adrenal medulla and secreting catecholamines.(adrenaline/epinephrine,noradrenaline/ norepinephrine).
- 80% occur in adrenal medulla while 20% arise elsewhere in body in sympathetic ganglia (paragangliomas).
- Most caese benign – only 10-15% malignant .
- Around 40% associated with inherited disorders(neurofibromatosis , von Hippel–Lindau syndrome, and MEN 2)

Genatic syndromes associated with Phaeochromocytomas

MEN-2A and 2B	**❖ Mutation in RET proto-oncogene (chromosome 10)** **❖ Primary hyperparathyroidism and medullary thyroid carcinoma associated with phaeochromocytoma** **❖ MEN-2B also associated with marfanoid phenotype and mucosal neuromas (tongue)**
Von Hippel–Lindau syndrome	❖ Mutation of VHL tumour suppressor gene (chromosome 3) ❖ Renal cell carcinoma, cerebellar haemangioblastoma, retinal angioma, renal and pancreatic cysts
Neurofibromatosis	❖ Autosomal dominant condition caused by mutations of *NF1* gene on chromosome 17 ❖ Phaeochromocytomas in 1.0% and mostly late presentation (>30 years)

Epidemiology

- Pheochromocytomas are rare, reportedly occurring in 0.05–0.2% of hypertensive individuals.
- Equal sex distribution, and most commonly present in the third and fourth decades.
- Up to 50% may be diagnosed post-mortem.
- Tumours may be bilateral, particularly where part of an inherited syndrome

Prognosis

- 5-year survival rate for people with nonmalignant pheochromocytomas **>95%.**
- for malignant pheochromocytomas, **the 5-year survival rate < 50%.**
- Although pheochromocytomas are rare, making the diagnosis is critical because malignancy rate is **10-15%**, and pheochromocytomas may precipitate life-threatening hypertension, and patient may be cured completely with their removal

Pathophysiology

- Clinical manifestations of pheochromocytoma result from excessive catecholamine secretion by tumor.
- Secretion may occur either intermittently or continuously. Catecholamines typically secreted are norepinephrine and epinephrine; some tumors produce dopamine
- **Biologic effects of catecholamines:**

❑ Stimulation of alpha-adrenergic receptors results in elevated blood pressure, glycogenolysis, gluconeogenesis, and intestinal relaxation.

❑ Stimulation of beta-adrenergic receptors results in an increase in heart rate and contractility

Clinical features of phaeochromocytoma

Classically, pheochromocytoma manifests as spells with the following 4 characteristics: present in only 30-40% of cases

- Headaches
- Palpitations
- Diaphoresis
- Severe hypertension

The following may also occur during spells:

- Tremor
- Nausea
- Weakness
- Anxiety
- Epigastric pain
- Flank pain
- Constipation

Clinical signs associated with pheochromocytomas

- Hypertension
- Postural hypotension: From volume contraction
- Hypertensive retinopathy
- Tachyarrhythmias
- Pulmonary edema
- Cardiomyopathy
- Weight loss
- Fever
- Tremor
- Paralytic Ileus
- Neurofibromas
- Café au lait spots

Hypertension in phaeochromocytoma

- It is rare cause of HTN(resposible only for 0.05–0.2% of HTN) .
- 40% episodic HTN
- 40% persistent
- 10-15% of cases are normotensive
- 5% assocaited with orthostatic hypotension

Precipitants of hypertensive crisis

Precipitants of a hypertensive crisis include the following:

- ✓ Anesthesia induction
- ✓ Opiates
- ✓ Dopamine antagonists:(metoclopramide)
- ✓ Cold medications
- ✓ Beta blockers
- ✓ Drugs that inhibit catecholamine reuptake: Eg, tricyclic antidepressants and cocaine
- ✓ Childbirth

Differential Diagnoses

- ✓ Angina Pectoris
- ✓ Anxiety Disorders
- ✓ Hyperthyroidism and Thyrotoxicosis
- ✓ Hypoglycemia
- ✓ Insulinoma
- ✓ Intestinal Carcinoid Tumor
- ✓ Menopause

When to suspect pheochromocytoma

- Hyperadrenergic spells (eg, self-limited episodes of nonexertional palpitations, diaphoresis, headache, tremor, or pallor)
- Resistant hypertension
- A familial syndrome that predisposes to catecholamine-secreting tumors (MEN2, NF1, VHL)
- A family history of pheochromocytoma
- An incidentally discovered adrenal mass
- Onset of hypertension at a young age (eg, <20 years)
- Idiopathic dilated cardiomyopathy

Investigations

- Excessive secretion of catecholamines can be confirmed by measuring metabolites in plasma and/or urine (metanephrine and normetanephrine).
- high ‘false-positive’ rate metanephrine concentrations may be seen during acute illness, following vigorous exercise or severe pain and following ingestion of some drugs such as tricyclic antidepressants.

Biochemical diagnosis of pheochromocytoma

- 24 hr urine of catacholamines
  - Epinehprine
  - Nor epinephrine
  - Dopamine
- 24 hr urine for metanephrines (metabolites of catacholamines)
  - Metanephrine
  - Nor metanephrine
- Plasma metanephrines (but not plasma catacholamines because of their short half live and difficult to assess)

Biochemical diagnosis of Pheochromocytoma....Cont

- **24-hour urinary collection for catecholamines and metanephrines**
  - 87.5% sensitivity, 99.7% specificity
  - Used in patients at lower risk
- **Vanillylmandelic acid** — The 24-hr urinary (VMA) excretion has poor diagnostic sensitivity and specificity compared with 24-hour urinary metanephrines.
- **Plasma metanephrine testing**
  - 96% sensitivity, 85% specificity
  - Used in patients at high risk (those with predisposing genetic syndromes or family or personal history of pheochromocytoma)

Imaging and Localisation

- Abdominal CT scanning: Has accuracy of 85-95% for detecting adrenal masses of 1 cm or greater
- MRI: Preferred over CT scanning in children and pregnant or lactating women; has reported sensitivity of up to 100% in detecting adrenal pheochromocytomas
- Scintigraphy: **MIBG (meta-iodobenzyl guanidine)scan** Reserved for biochemically confirmed cases in which CT scanning or MRI does not show a tumor,and for paraganglinomas (extra-adrenal)

Screening for associated conditions

MEN 2

- Serum calcium.
- Serum calcitonin
- Screening for mutations in the *ret* proto-oncogene

VHL

- Ophthalmoscopy—retinal angiomas
- MRI—posterior fossa and spinal cord.
- US of kidneys

NF1

Clinical examination for *café-au-lait* spots and cutaneous neuromas

Management

- Surgical resection of tumor is treatment of choice and usually cures hypertension. Careful preoperative treatment with alpha and beta blockers is required to control blood pressure and prevent intraoperative hypertensive crises.
- **Preoperative medical stabilization :**

➢ Start alpha blockade with phenoxybenzamine 7-10 days preoperatively

➢ Provide volume expansion with isotonic sodium chloride solution

➢ Encourage liberal salt intake

➢ Initiate a beta blocker only after adequate alpha blockade, to avoid precipitating a hypertensive crisis from unopposed alpha stimulation

Conclusion

- Pheochromcytoma is rare tumours of adrenal medulla secreting catecholamines
- 80% in adrenal medulla 20% in sympathetic ganglia(paragangliomas)
- Benign tumor ,Only 10-15% malignant
- Around 40% associated with inherited disorders(neurofibromatosis , von Hippel–Lindau syndrome, and MEN 2)
- only 30-40% of cases presented with the classical symptoms
- It is rare cause of HTN
- diagnosis by measuring catacholamines and its metabolites metanephrines in urine or plasma metanephrines
- CT,MRI and MIBG are used for localization of pheochromocytoma
- Surgical resection of tumor is treatment of choice
- Careful preoperative treatment with alpha and beta blockers required to control blood pressure and prevent intraoperative hypertensive crises.

THANKS