# Endocrinology
# L:6


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- Hyperaldosteronism
- Pheochromocytoma

# Hyperaldosteronism

- The prevalence of primary hyperaldosteronism is controversial.
- If only hypertensive patients with hypokalaemia are investigated, then fewer than 1% of patients with hypertension will be found to have primary hyperaldosteronism. Around half of these have an adrenal adenoma secreting aldosterone (Conn's syndrome).
- Recent studies in which hypertensive patients have been screened using aldosterone/renin ratios suggest that the prevalence may be as high as 5%. Most of these 'extra' patients have bilateral adrenal hyperplasia rather than Conn's syndrome and many have normal plasma potassium.
- Glucocorticoid-suppressible hyperaldosteronism is a rare autosomal dominant disorder caused by inappropriate secretion of aldosterone from the adrenal in response to normal levels of ACTH, despite suppression of renin and angiotensin II levels.
- In a few conditions, the mineralocorticoid receptor in the distal nephron is activated even though aldosterone levels are low. Either the receptors are activated by cortisol (ectopic ACTH syndrome or 11β-HSD2 deficiency) or 11-deoxycorticosterone (rare congenital adrenal hyperplasias or tumours),

# Hyperaldosteronism (Mineralocorticoid excess)

- Indications to test for mineralocorticoid excess in hypertensive patients include
- Hypokalaemia
- Poor control of blood pressure with conventional therapy,
- presentation at a young age.
- Excessive activation of mineralocorticoid receptors most often results from enhanced secretion of renin (secondary hyperaldosteronism) in response to inadequate renal perfusion and hypotension.
- Secondary hyperaldosteronism may be associated with hypertension in renovascular disease and in very rare renin-secreting renal tumours.
- Less commonly, mineralocorticoid excess and hypertension occur in suppressed renin secretion primary hyperaldosteronism

# Mineralocorticoid excess causes

Secondary hyperaldosteronism (With renin high and aldosterone high)

Inadequate renal perfusion, e.g. diuretic therapy, cardiac failure, liver failure, nephrotic syndrome, renal artery stenosis- most common causes

- Primary hyperaldosteronism: (With renin low and aldosterone high)
- Adrenal adenoma secreting aldosterone (**Conn's syndrom**)
- Idiopathic bilateral adrenal hyperplasia
- Glucocorticoid-suppressible hyperaldosteronism (rare)
- Renin-secreting renal tumour (very rare).
- With renin low and aldosterone low (non-aldosterone-dependent activation of mineralocorticoid pathway)
- Ectopic ACTH syndrome
- **Liquorice** misuse (inhibition of 11β-HSD2-) 11 β -hydroxysteroid dehydrogenase type 2
- Deoxycorticosterone-secreting adrenal tumour
- Rare forms of congenital adrenal hyperplasia and 11β-HSD2 deficiency

# **Hyperaldosteronism:** clinical assessment

- Many patients are asymptomatic,
- They may have features of sodium retention or potassium loss.
- Sodium retention may cause edema
- Hypokalaemia causes muscle weakness (or even paralysis, especially in Chinese),
- Polyuria (secondary to renal tubular damage which produces nephrogenic diabetes insipidus)
- Occasionally tetany (because of associated metabolic alkalosis and low ionized calcium

# Hyperaldosteronism:Investigations

- **Biochemical**

- Electrolytes may show hypokalaemia and elevated bicarbonate.
- Plasma sodium is usually towards the upper end of the normal range in primary mineralocorticoid excess, but is characteristically low in secondary hyperaldosteronism (because low plasma volume stimulates ADH release and high angiotensin II levels stimulate thirst
- The key measurements are plasma renin activity and aldosterone
- Almost all antihypertensive drugs interfere with these hormones (e.g. β-blockers inhibit, whilst thiazide diuretics stimulate renin secretion), so these should be stopped for at least 6 weeks beforehand.
- If renin is low and aldosterone levels are high, then Conn's adenoma can be differentiated from bilateral adrenal hyperplasia by tests of aldosterone response to angiotensin II; in Conn's adenoma aldosterone does not rise on standing or with furosemide administration.
- In the rare circumstance when renin and aldosterone are both low, further tests include measurement of urinary cortisol and its metabolites, and 11-deoxycorticosterone

# Hyperaldosteronism:Investigations

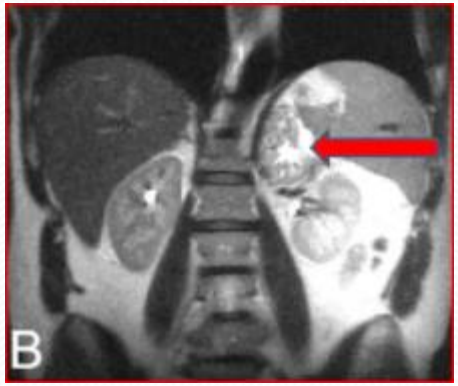
- **Localisation**
- Abdominal CT for The only cause of primary hyperaldosteronism which is usually treated by surgery
- - the test is required to localise the tumour ,but it is important to recognise that non-functioning adrenal adenomas are present in about 20% of patients with essential hypertension, and adrenal CT should only be performed when the biochemistry supports the diagnosis of adrenal tumor.
- If the scan is inconclusive, then adrenal vein catheterisation with measurement of aldosterone (and cortisol to confirm positioning of the catheters) may be helpful

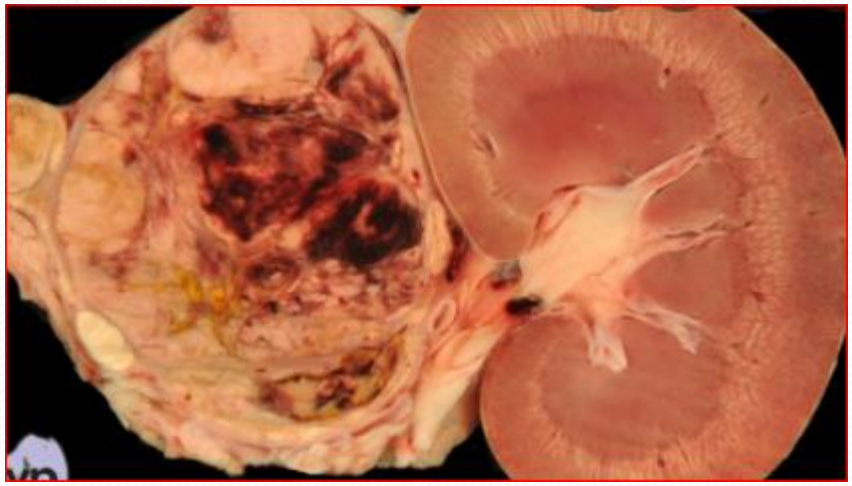
# Hyperaldosteronism: management

- Mineralocorticoid receptor antagonists (spironolactone or eplerenone) are valuable in treating both hypokalaemia and hypertension in all forms of mineralocorticoid excess.
- High doses of spironolactone (up to 400 mg/day) may be required. Up to 20% of males develop gynaecomastia on spironolactone.
- Amiloride (10-40 mg/day), which blocks the epithelial sodium channel regulated by aldosterone, or eplerenone can be used when such problems arise.
- Glucocorticoid-suppressible hyperaldosteronism is treated by suppression of ACTH, e.g. with dexamethasone
- In patients with Conn's adenoma, medical therapy is usually given for a few weeks to normalise whole-body electrolyte balance before unilateral adrenalectomy.
- Laparoscopic surgery cures the biochemical abnormality but hypertension remains in as many as 70% of cases, probably because of irreversible damage to the systemic microcirculation

# PHAEOCHROMOCYTOMA

- This is a rare tumor of chromaffin tissue that secretes catecholamines and is responsible for less than 0.1% of cases of hypertension.
- There is a useful 'rule of tens' in this condition: 10% are malignant, 10% are extra-adrenal (i.e. elsewhere in the sympathetic chain) and 10% are familial



# Phaeochromocytoma Clinical features

These depend on the pattern of catecholamine secretion

Clinical feature:

the classic triad of symptoms are headache, chest pain, and diaphoresis

- Some patients present with a complication of hypertension, e.g. stroke, myocardial infarction, left ventricular failure, hypertensive retinopathy or accelerated-phase hypertension.
- The apparent paradox of postural hypotension between episodes is explained by 'pressure natriuresis' during hypertensive episodes so that intravascular volume is reduced.
- There may be features of the familial syndromes associated with phaeochromocytoma including neurofibromatosis, von Hippel - Lindau syndrome and MEN type 2.
- Hypertension (usually paroxysmal; often postural drop of blood pressur-
- Paroxysms of:Pallor (occasionally flushing, Palpitations, Sweating, Headache,Anxiety (fear of death-angor animi) ,
- Abdominal pain, vomiting, Constipation
- Weight loss
- Glucose intolerance

# Phaeochromocytoma Investigations:

## Biochemical

- Excessive secretion of catecholamines can be confirmed by measuring the hormones (adrenaline/epinephrine, noradrenaline/norepinephrine and dopamine) in plasma or their metabolites (e.g. vanillyl-mandelic acid, VMA; conjugated metanephrine and normetanephrine) in urine.
- Catecholamine secretion is usually paroxysmal and sometimes the paroxysms are infrequent. Therefore, false-negative results may be obtained if samples are collected during a period when symptoms or hypertension are absent .
- Increased urinary catecholamine excretion occurs in stressed patients and is induced by some drugs .
- For this reason, a suppression test may be valuable.
- Normal adrenomedullary secretion is suppressed by administration of drugs which interfere with sympathetic outflow, such as *clonidine or **pentolonium tartrate.
- In phaeochromocytoma these drugs do not suppress plasma catecholamines.

- *Clonidine : is an $\alpha_2$-adrenergic agonist medication used to treat high blood pressure.*
- ***pentolonium a ganglionic blocking agent inhibits release of adrenaline and noradrenaline from adrenergic nerves*

# Phaeochromocytoma Investigations:2

## Localization

- Phaeochromocytomas are usually identified by abdominal CT or MRI .
- -Difficulty can arise with the localisation of extra-adrenal tumours.
- -Scintigraphy using meta-iodobenzyl guanidine (MIBG) can be useful.
- -Selective venous sampling with measurement of plasma noradrenaline (norepinephrine) may be required

# Phaeochromocytoma Management:

- Medical therapy is required to prepare the patient for surgery, preferably for a minimum of 6 weeks to allow restoration of normal plasma volume.
- The most useful drug in the face of very high circulating catecholamines is the α-blocker phenoxybenzamine (10-20 mg orally 6-8-hourly) because it is a non-competitive antagonist, unlike prazosin or doxazosin.
- If α-blockade produces a marked tachycardia, then a β-blocker (e.g. propranolol) or combined α- and β-antagonist (e.g. labetalol) can be added.

# Phaeochromocytoma Management:

**During surgery**

- Sodium nitroprusside and the short-acting α-antagonist phentolamine are useful in controlling hypertensive episodes which may result from anaesthetic induction or tumour mobilisation.

**Post-operative** hypotension may occur and require volume expansion and, very occasionally, noradrenaline (norepinephrine) infusion. This is uncommon if the patient has been prepared adequately with phenoxybenzamine