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ADRENAL GLANDS

Anatomy;

The adrenal glands or suprarenal glands are paired, retroperitoneal organs located superior and medial to the kidneys. and weighs 4 to 5 g. They are two endocrine organs in one; an outer cortex, accounts for about 80% to 90% of the gland's volume and an inner medulla, constitutes up to 10% to 20%

The arterial blood supply branches from the aorta and the diaphragmatic and renal arteries. A usually single large adrenal vein drains on the right side into the vena cava and on the left side into the renal vein.

Function of the adrenal glands;

The adrenal glands play a pivotal role in the response to stress. The adrenal cortex is divided into three zones—the zona glomerulosa, zona fasciculata, and zona reticularis.

Mineralocorticoids.

The outer area of the zona glomerulosa is the site of production of the mineralocorticoid hormone, aldosterone. which regulates sodium–potassium homeostasis. The target organs of aldosterone are the kidneys, the sweat and salivary glands and the intestinal mucosa.

Aldosterone secretion is regulated primarily by the renin-angiotensin system. Decreased renal blood flow(haemorrhage, dehydration, renal artery stenosis), decreased plasma sodium, Hyperkalemia, antidiuretic hormone and increased sympathetic tone all stimulate the release of renin and leads to to increase sodium reabsorption and potassium and hydrogen ion excretion at the level of the renal distal convoluted tubule and an increase of plasma volume.

Glucocorticoids.

Cells of the zona fasciculata and zona reticularis synthesise glucocorticoids (cortisol)and the adrenal androgens

The secretion of cortisol, the major adrenal glucocorticoid, is regulated by ACTH secreted by the anterior pituitary, which, in turn, is under the control of corticotrophin releasing hormone (CRH) secreted by the hypothalamus. ACTH secretion may be stimulated by pain, stress, hypoxia, hypothermia, trauma, and hypoglycemia.

there is a diurnal variation in the secretion of cortisol, with peak cortisol excretion also occurring in the early morning and declining during the day to its lowest levels in the evening .

Cortisol has numerous metabolic and immunological effects. It increases gluconeogenesis and lipolysis, decreases peripheral glucose utilisation, inhibits immunological response it also affect connective tissue, bone, cardiovascular, renal, and central nervous systems,

Sex Steroids.

Adrenal androgens are produced in response to ACTH stimulation. They include dehydroepiandrosterone (DHEA) and its sulfated counterpart (DHEAS), androstenedione, and small amounts of testosterone and estrogen.In normal adult males, they are responsible for the development of secondary sexual characteristics at puberty.

Catecholamines.

Catecholamine hormones ;adrenaline (epinephrine), noradrenaline (norepinephrine), and dopamine are produced not only in the central and sympathetic nervous system but also the adrenal medulla. Their effects include the cardiovascular system, resulting in an increase in blood pressure and heart **rate; vasoconstriction , bronchodilatation; and increased glycogenolysis in liver and muscles, all** necessary for the flight/fight response.

DISORDERS OF THE ADRENAL CORTEX;

The Adrenal Incidentaloma;

Definition ;Adrenal lesions discovered during imaging performed for unrelated reasons, not known previously to have been present or causing symptoms.

More than 75% are non-functioning adenomas but Cushing's adenomas, phaeochromocytomas, metastases, adrenocortical carcinomas and Conn's tumours can all be found this way .

Diagnosis;

The main goal is to exclude a functioning or malignant adrenal tumour.

When an incidentaloma is identified, a complete history and clinical examination is required.

Hormonal evaluation includes:

- morning and midnight plasma cortisol measurements;
- 24-hour urinary cortisol excretion;
- a 1-mg overnight dexamethasone suppression test to rule out subclinical Cushing's syndrome
- 12- or 24-hour urine collection for catecholamines, metanephrines, VMA, or plasma metanephrine to rule out pheochromocytoma;
- in hypertensive patients, serum electrolytes, plasma aldosterone, and plasma renin to rule out an aldosteronoma.
- serum DHEAS, testosterone or 17-hydroxyestradiol (virilising or feminising tumour).

Confirmatory tests can be performed based on the results of the initial screening studies

CT or MRI should be performed in all patients with adrenal masses.

FDG-PET or PET-CT scans may distinguish potentially malignant from benign lesions

Treatment;

Non-functioning tumours smaller than 4 cm with benign imaging characteristics should be followed-up after 6, 12 and 24 months by imaging (MRI) and hormonal evaluation. If the tumour remains non-functioning and stable in size, surveillance can be discontinued.

indication of surgical resection are;

A. Any non-functioning adrenal tumour greater than 4 cm in diameter and smaller tumours that increase in size during follow-up.

B. lesions with suspicious features on such as heterogeneity, irregular capsule, or adjacent nodes .
C. Patients with functional tumors or obviously malignant lesions .
D. patients with worsening hypertension, abnormal glucose tolerance, or osteoporosis.

Hyperaldosteronism.

Primary hyperaldosteronism (PHA) , Conn's syndrome ; is defined by hypertension, as a result of hypersecretion of aldosterone. In PHA, plasma renin activity is suppressed. Among patients with hypertension the incidence of PHA is approximately 2%.
Most cases result from a solitary functioning adrenal adenoma (~70%) and idiopathic bilateral hyperplasia (30%).
Hyperaldosteronism may be secondary to stimulation of the renin-angiotensin system from renal artery stenosis and to low-flow states such as congestive heart failure and cirrhosis.

Clinical features

Most patients are between 30 and 50 years , typically present with hypertension, Other symptoms include,muscle weakness, polydipsia, polyuria, nocturia, headaches, and fatigue.
Diagnosis
Laboratory Studies. Hypokalemia and hyperaldosteronism is a common finding, However, it is important to note that up to 40% of patients with a confirmed aldosteronoma were normokalemic. Patients with primary hyperaldosteronism have an elevated plasma aldosterone concentration level with a suppressed plasma renin activity;
MRI or CT should be performed to distinguish unilateral from bilateral disease. because surgery is almost always curative for the former, but usually not the latter

Treatment

The first-line therapy for PHA with bilateral hyperplasia is medical treatment with spironolactone (an aldosterone antagonist), nifedipine (a calcium channel blocker), or captopril (an ACE inhibitor). Unilateral tumors producing aldosterone are best managed by adrenalectomy, either by a laparoscopic approach (preferred) or via a posterior open approach. If a carcinoma is suspected because of the large size of the adrenal lesion or mixed hormone secretion, an anterior transabdominal approach is preferred

Cushing's syndrome

the term Cushing's syndrome refers to a complex of symptoms and signs resulting from hypersecretion of cortisol regardless of etiology.
In contrast, Cushing's disease refers to a pituitary tumor, usually an adenoma, which leads to bilateral adrenal hyperplasia and hypercortisolism.
It can be either ACTH-dependent or ACTH-independent in origin. The most common cause (85%) of ACTH-dependent Cushing's syndrome is Cushing's disease. Ectopic ACTH-producing tumours (small cell lung cancer, foregut carcinoid) and CRH-producing tumours (medullary thyroid carcinoma, neuroendocrine pancreatic tumour) are more infrequent causes of ACTH-dependent Cushing's syndrome.

In about 15% of patients, an ACTH-independent Cushing's syndrome (low ACTH levels) is caused by a unilateral adrenocortical adenoma. Adrenocortical carcinoma and bilateral hyperplasia represent rare causes of hypercortisolism. Excessive or prolonged administration of cortisol-like drugs will produce the same clinical picture.

Symptoms and Signs

Progressive truncal obesity is the most common symptom, occurring in up to 95% of patients. buffalo hump. Purple striae are often visible on the protuberant abdomen. moon facies, and plethora. in combination with hypertension, diabetes

There is an increase in fine hair growth on the face, upper back, and arms, Patients with Cushing's disease also may present with headaches, visual field defects, and panhypopituitarism.

Diagnosis

Cushing's syndrome is characterized by elevated glucocorticoid levels that are not suppressible using the overnight low-dose dexamethasone suppression test. and loss of diurnal variation.

Elevated ACTH levels are found in patients with adrenal hyperplasia due to Cushing's disease and those with CRH-secreting tumors and ectopic sources of ACTH .

In contrast, ACTH levels are characteristically supprressed in patients with primary adrenal tumors.

Therefore, in patients with elevated ACTH, MRI of the pituitary gland, a CT scan of the chest and abdomen is warranted to detect an ectopic ACTH-producing tumour.

In patients with suppressed ACTH levels, a CT or MRI scan is performed to assess the adrenal glands.

Treatment

Medical therapy with metyrapone or ketoconazole reduces steroid synthesis and secretion and can be used to prepare patients with severe hypercortisolism preoperatively or if surgery is not possible.

Laparoscopic adrenalectomy for patients with adrenal adenomas. Open adrenalectomy is reserved for large tumors (≥6 cm) or those suspected to be adrenocortical cancers.

Bilateral adrenalectomy is curative for primary adrenal hyperplasia

Patients with an ectopic ACTH-dependent Cushing's syndrome and an irresectable or unlocalised primary tumour should be considered for bilateral adrenalectomy as this controls hormone excess.

The treatment of choice in Cushing's disease is transsphenoidal excision of the pituitary adenoma,

Patients with ectopic ACTH production are best managed by treating the primary tumor,

Adrenocortical carcinoma

Clinical presentation

Approximately 60% of patients present with evidence of cortisol excess (Cushing's syndrome).

Patients with non-functioning tumours frequently present with an enlarging abdominal mass and abdominal or back pain. Rarely, weight loss, anorexia, and nausea may be present.

Diagnosis

Diagnostic evaluation by measurement of serum electrolyte levels to rule out hypokalemia, urinary catecholamines to rule out pheochromocytomas, an overnight 1-mg dexamethasone suppression test, and a 24-hour urine collection for cortisol, to rule out Cushing's syndrome.

CT and MRI scans are useful to image these tumors

FDGPET or PET-CT scans may have some utility in distinguishing benign from malignant lesions,

Treatment

adrenocortical carcinomas are treated by excision of the tumor en bloc with any contiguously involved lymph nodes or organs such as the diaphragm, kidney, pancreas, liver, or IVC.

Ketoconazole, metyrapone, or aminoglutethimide may also be useful in controlling steroid hypersecretion.

Congenital adrenal hyperplasia (adrenogenital syndrome)

CAH refers to a group of disorders that result from deficiencies or complete absence of enzymes involved in adrenal steroidogenesis. 21-Hydroxylase deficiency is the most common enzymatic defect, accounting for>9o%of cases of CAH.

Deficiency of glucocorticoids and aldosterone leads to elevated ACTH levels and overproduction of adrenal androgens and corticosteroid precursors such as 17- hydroxyprogesterone and Δ4 - androstenedione.

Complete deficiency of 21-hydroxylase presents at birth with virilization, diarrhea, hypovolemia, hyponatremia, hyperkalemia, and hyperpigmentation. CAH may present in girls at birth with ambiguous genitalia

Treatment

Patients with CAH traditionally have been managed medically, with cortisol and mineralocorticoid replacement to suppress the hypothalamic-pituitary-adrenal axis.

DISORDERS OF THE ADRENAL MEDULLA

Phaeochromocytoma

These are tumours of the adrenal medulla , often are called the 10 percent tumor because 10% are bilateral, 10% are malignant, 10% occur in pediatric patients, 10% are extra-adrenal, and 10% are familial.

Pheochromocytomas occur in families with MEN2A and MEN2B in approximately 50% of patients.

Clinical features

Headache, palpitations, and diaphoresis constitute the "classic triad" of pheochromocytomas. Symptoms such as anxiety, flushing, chest pain, shortness of breath, abdominal pain, nausea, vomiting, . Cardiovascular complications such as myocardial infarction and cerebrovascular accidents may ensue.

Pheochromocytomas are one of the few curable causes of hypertension and are found in 0.1% to 0.2% of hypertensive patients. Sudden death may occur in patients with undiagnosed tumors who undergo other surgeries or biopsy.

Diagnosis

Pheochromocytomas are diagnosed by testing 24-hour urine samples for catecholamines and their metabolites metanephrine and normetanephrine as well as by determining plasma -free metanephrine and normetanephrine levels.

localisation of the phaeochromocytoma; MRI is preferred because contrast media used for CT scans can provoke paroxysms. MRI is also the study of choice in pregnant

Treatment

The medical management of pheochromocytomas is aimed chiefly at blood pressure control

Adrenalectomy is the treatment of choice for patients with pheochromocytoma.

Sex Steroid Excess.

Adrenal adenomas or carcinomas that secrete adrenal androgens lead to virilizing syndromes.

Although women with virilizing tumors develop hirsutism, amenorrhea, infertility, and other signs of masculinization, such as increased muscle mass, deepened voice,

Feminizing adrenal tumors are less common and can lead to gynecomastia, impotence, and testicular atrophy.

Treatment

Virilizing and feminizing tumors are treated by adrenalectomy.

Adrenolytic drugs such as mitotane, aminoglutethimide, and ketoconazole may be useful in controlling symptoms in patients with metastatic disease.

Adrenal Insufficiency

Primary adrenal insufficiency is caused by the loss of function of the adrenal cortex.

Symptoms are only evident when about 90% of the adrenal cortex is destroyed.

Secondary adrenal insufficiency is caused by a deficiency of pituitary ACTH secretion.

Acute adrenal insufficiency

Acute adrenal insufficiency usually presents as shock in combination with fever, nausea, vomiting, abdominal pain, hypoglycaemia and electrolyte imbalance. Waterhouse– Friderichsen syndrome is a bilateral adrenal infarction associated with meningococcal sepsis and is rapidly fatalunless immediately treated.

Chronic adrenal insufficiency

When symptoms develop over time, patients present with anorexia, weakness and nausea.

Hypotension, hyponatraemia, hyperkalaemia and hypoglycaemia are commonly observed.

The diagnosis of adrenal insufficiency is made using the ACTH stimulation test. Basal ACTH levels are found to be high with cortisol levels decreased. There is no rise in cortisol levels following the exogenous administration of ACTH (synacthen test).

Treatment

In addition to intravenous administration of hydrocortisone 100 mg every 6 hours, 3 litres of saline is given in 6 hours under careful cardiovascular monitoring.

Once the patient has been stabilized, underlying conditions such as infection should be sought, identified, and treated.