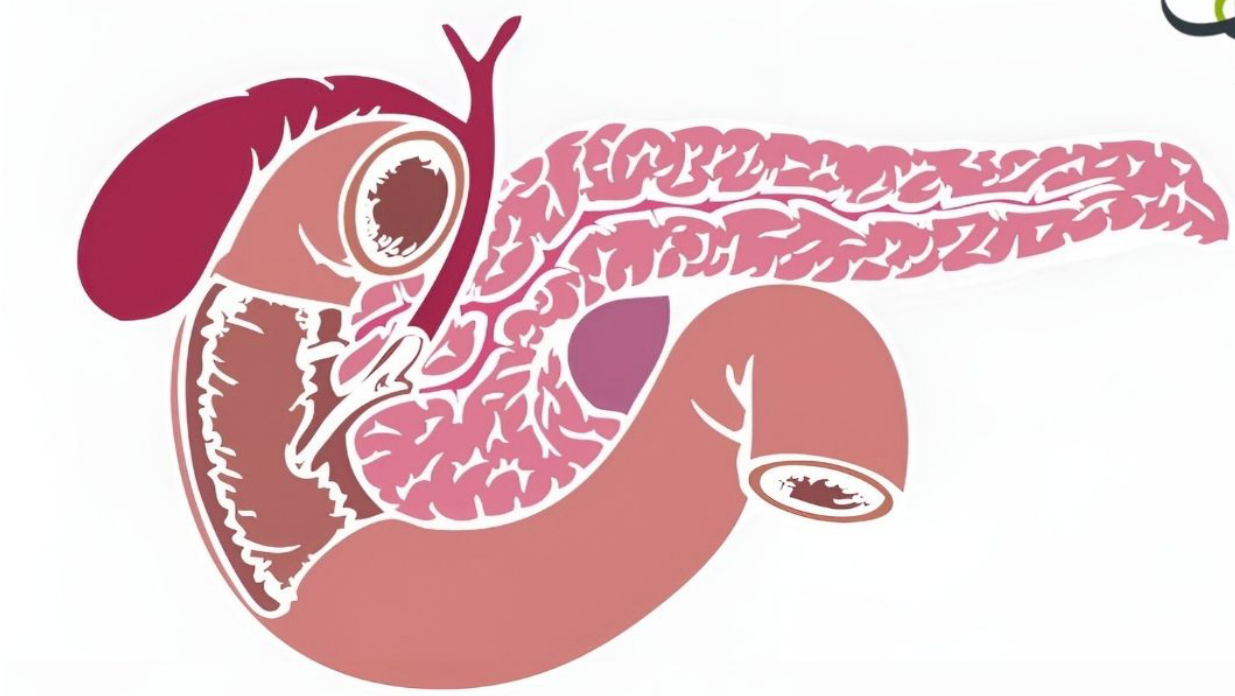
Endocrine system 6

Pathology



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Slides in black // DR. in blue

DISEASES OF ADRENAL GLAND-1

Hypercortisolism

- most common disease of adrenal gland; which means increasing secretion of cortisol
- **AKA Cushing syndrome**
- **Can be exogenous (iatrogenic) most common; when the person is taking steroids (medical treatment) or endogenous (less common) the cause is from the body.**
- **Endogenous causes are divided into ACTH-dependent and indepedendent**

ACTH-secreting PA (pituitary adenoma)

- **is the most common cause of endogenous hypercorticolism (60%), AKA Cushing Disease, more common in women, young adults, functional microadenoma ACTH dependent**
- **In rare cases, corticotroph hyperplasia (excessive CRH secretion from hypothalamic tumor) which lead to increase ACTH secretion**
- **Adrenal glands show bilateral nodular hyperplasia (because ACTH activate both glands)**

Ectopic ACTH production

- **5-10% of endogenous Cushing syndrome cases (ACTH dependent)**
- **More common in men, middle age**

- Causes: Small cell carcinoma of lung (it can secrete ADH,ACTH,CRH), carcinoid tumor, medullary carcinoma of thyroid, pancreatic neuroendocrine tumors
- In some cases, ectopic production of CRH
- Again, bilateral adrenal nodular hyperplasia
- Pathologic changes is less prominent than pituitary cause, secondary to poor prognosis of accompanied cancer

Primary adrenal adenoma

Adenoma in the gland that secretes cortisol without the need of ACTH

- 10-20% of ACTH-independent cases
- Low ACTH level (negative feedback on pituitary)
- PRKAR1A genetic mutation
- The other adrenal gland is atrophic due to low ACTH the other gland get suppressed

Adrenal carcinoma

- 5-7% of ACTH-independent cases
- Very large size of adrenal glands larger than adrenal adenoma
- Produces very high level of cortisol result in prominent symptoms
- Genetic mutations in: activation of beta-catenin (CTNNB1), inactivation of TP53, MEN1 and PRKAR1A
- The other adrenal gland is atrophic

Primary adrenal hyperplasia

- Independent of ACTH
- Rare
- Shows bilateral adrenal cortical hyperplasia, multiple nodules are larger than 1 cm
- Familial disease: inherited mutation in the tumor suppressor gene: armadillo repeat containing 5 (ARMC5)
- Sporadic disease: 50% show ARNC5 mutation, others show ectopic production of G-protein coupled hormone receptors (similar action of ACTH) (lead to proliferation of the gland without the need to ACTH)
- Syndromic disease: McCune Albright syndrome (multiple endocrine diseases that appear early in life) , germline activating mutation in GNAS, produces excessive cAMP (cause proliferation of the cells of the endocrine system) multisystemic disease

Micronodular bilateral adrenal hyperplasia

- ACTH-independent
- Small nodules (<1 cm)
- Two variants: primary pigmented nodular adrenocortical disease (brown small nodules) or Carney complex (multisystemic disease of endocrine and non-endocrine neoplasms (multiple tumers))
- Both variants harbor mutation in cAMP-dependent protein kinase (PRKAR1A gene), producing excessive cAMP

Morphology

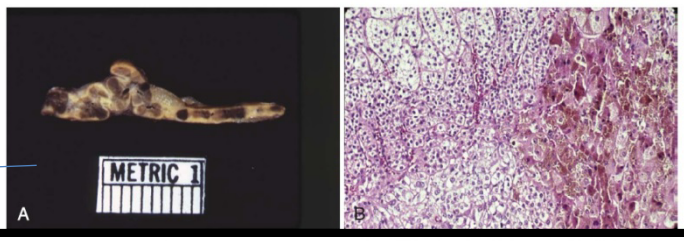
- **Pituitary gland shows Crooke hyaline change (homogenous pale color of corticotroph cells instead of normal granular basophilic cytoplasm), seen in all cases of Cushing syndrome**
- **Adrenal atrophy (fasciculata and reticularis) is seen in exogenous cause of Cushing syndrome**
- **ACTH-dependent hyperplasia shows bilateral diffuse enlargement of adrenal glands (mixture of cells are seen in contrast to adenoma) , variable nodularity and yellow color (grossly), zona reticularis is expanded, eosinophilic and is "lipid poor", surrounded by outer vacuolated "lipid-rich" zona fasciculata. Nodules can be seen and contain "lipid-rich" cells**
- **Macronodular hyperplasia: multiple large nodules (mixed lipid-rich and poor cells), separated by small nodules**
- **Micronodular hyperplasia: small dark nodules (black or brown), the pigment is lipofuscin (it is a degenerative material that accumulate in cells during aging)**

Normal adrenal gland

Hyperplastic adrenal gland (thick, bigger, contain multiple nodules)

Diffuse hyperplasia of the adrenal gland contrasted with a normal adrenal gland (top). In cross-section, the hyperplastic adrenal cortex is yellow and thickened, and a subtle nodularity is seen in this gland from a patient with ACTH dependent Cushing syndrome.

Pigmented adrenal hyperplasia, multiple brown nodules, lipofuscin pigment is seen microscopically



(A) Micronodular adrenocortical hyperplasia with prominent pigmented nodules in the adrenal gland. (B) On histologic examination, the nodules are composed of cells containing lipofuscin pigment, seen in the right part of the field.

- **Adrenal adenoma (single mass/nodule)can be functional (Cushing syndrome) which suppress ACTH production or non-functional (incidental), both have the same appearance**
- **Adrenocortical adenoma is surrounded by a capsule (benign tumer), weighs <30g, yellow, microscopically is similar to zona fasciculata cells**
- **Adrenocortical carcinoma is large (commonly >200 g), not capsulated, anaplastic cells if functioning it well suppress ACTH and the other glad well be atrophic**
- **Both diseases are more common in women, middle age, show contralateral adrenal atrophy (when functioning)**

Clinical symptoms of Cushing disease

- **Hypertension**
- **Fat redistribution: Central obesity, moon face, buffalo hump (fat in the back and neck)**
- **Proximal muscle weakness (atrophy); cortisol is a catabolic hormone so it damages the muscles**
- **Hyperglycemia, glucoseurea, polyurea, polydipsia; hypercortisolism antagonize insulin which cause diabetes**
- **Bone resorption (osteoporosis); catabolism**
- **Collagen degradation (thin skin, easy bruise, poor wound healing, striation تشققات**
- **Hisrutism: excesive hair growth over the body , in ACTH dependent hypercortisolism sex hormones well increase (Androgens)**
- **Menstrual abnormalities**
- **Immune suppression: increased cortisol suppress T cells**
- **Mental and psychotic disturbances (very high levels of cortisol)**