Lecture 9 Adrenal gland pathology
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PRIMARY HYPERALDOSTERONISM

a. *Bilateral idiopathic hyperaldosteronism*,
   - bilateral nodular hyperplasia of adrenals
   - the most common underlying cause (60% of cases)

b. *Adrenocortical neoplasm*, adenoma (the most common cause) or, rarely, an adrenocortical carcinoma.
- In approximately 35% of cases, the cause is a solitary aldosterone-secreting Aldosterone-producing adrenocortical adenoma referred to as **Conn syndrome**

c. Rarely, familial hyperaldosteronism may result from a genetic defect that leads to overactivity of the *aldosterone synthase* gene, *CYP11B2*. 
Features of aldosterone producing adrenocortical adenoma

• Solitary
• Encapsulated
• Well circumscribed
• Histology: can show endocrine atypia
• May contain spironolactone bodies if treated with spironolactone
Adrenocortical adenoma
Adrenocortical adenoma/ note the endocrine atypia
Spironolactone bodies

• Aldosterone producing adenomas contain eosinophilic, laminated cytoplasmic inclusions= spironolactone bodies which appear after treatment with spironolactone (an aldosterone antagonist)
Spironolactone bodies
Spironolactone bodies
CLINICAL FEATURES OF HYPERALDOSTERONISM

The clinical hallmark is hypertension

- Hyperaldosteronism may be the most common cause of secondary hypertension
- Hypokalemia
Adrenal insufficiency

- Decreased hormonal production from the adrenal
- Divided into three types
  1. Acute insufficiency
  2. Chronic insufficiency = Addison disease
  3. Secondary insufficiency
Acute Adrenocortical Insufficiency:

Occurs in the following situations:

a. Crisis in patients with chronic adrenocortical insufficiency precipitated by stress
b. In patients maintained on exogenous corticosteroids.. Sudden withdrawal, or stress
c. Massive adrenal hemorrhage
3. Massive adrenal hemorrhage

May destroy enough of the adrenal cortex to cause acute adrenocortical insufficiency.

- This condition may occur:
  1. In patients maintained on anticoagulant therapy
  2. Patients suffering from sepsis: a condition known as the Waterhouse-Friderichsen syndrome

- Sepsis due to: *Neisseria meningitidis*, *Pseudomonas* spp., and *Haemophilus influenzae*

- *Underlying cause* involves endotoxin-induced vascular injury.
Massive adrenal hemorrhage
primary chronic adrenocortical insufficiency (Addison disease):

- Uncommon disorder resulting from progressive destruction of the adrenal cortex.

Causes:
- Autoimmune adrenalitis.
- Infections
- Metastatic tumors
ADDISON DISEASE

1. Autoimmune adrenalitis

- 60% to 70% of Addison disease cases and is the most common cause of primary adrenal insufficiency in developed countries.

- There is autoimmune destruction of steroid-producing cells, and autoantibodies to several key steroidogenic enzymes have been detected in affected patients.
Addison disease

2. Infections: Tuberculosis and Fungal infections

- Tuberculous adrenalitis, which once accounted for as many as 90% of cases of Addison disease, has become less common with the advent of anti-tuberculosis therapy.

- Disseminated infections caused by *Histoplasma capsulatum* and *Coccidioides immitis* also may result in chronic adrenocortical insufficiency.
ADDISON DISEASE

- Patients with AIDS are at risk for the development of adrenal insufficiency from several infectious (cytomegalovirus and TB) and noninfectious

3. Metastatic neoplasms involving the adrenals:
   Carcinomas of the lung and breast are the most common primary sources.
Secondary adrenocortical insufficiency

Hypothalamic-pituitary diseases including:

- Metastasis
- Infection.
- Infarction
- Irradiation

- Can be part of pan hypopituitarism.
Clinical features of adrenal insufficiency

- Clinical manifestations of adrenocortical insufficiency do not appear until at least 90% of the adrenal cortex has been compromised.

a. progressive weakness and easy fatigability.

b. *Gastrointestinal disturbances* are common and include anorexia, nausea, vomiting, weight loss, and diarrhea.
c. In patients with **primary adrenal disease**, increased levels of ACTH precursor hormone stimulate melanocytes, with resultant *hyperpigmentation* of the skin and mucosal surfaces: The face, axillae, nipples, areolae, and perineum are mainly affected

**Note:** *hyperpigmentation is not seen in patients with secondary adrenocortical insufficiency.*
d. Decreased aldosterone in primary hypoadrenalism results in potassium retention and sodium loss, with consequent hyperkalemia, hyponatremia, volume depletion, and hypotension.

- In secondary hypoadrenalism is characterized by deficient cortisol and androgen output but normal or near-normal aldosterone synthesis. This is because ACTH doesn’t affect the production of aldosterone.
Adrenal medulla

- Chromaffin cells... derived from the neural crest.
- Secrete catecholamines.
- Most important disease: neoplasms.
TUMORS OF THE ADRENAL MEDULLA

Pheochromocytoma
- gives rise to a surgically correctable form of hypertension.
- Pheochromocytomas usually subscribe to "rule of 10s":
  a. 10% of pheochromocytomas are extraadrenal, called paragangliomas,
  b. 10% of adrenal pheochromocytomas are bilateral; this proportion may rise to 50% in cases that are associated with familial syndromes.
c. 10% of adrenal pheochromocytomas are malignant,

d. 10% familial. Now we think up to 25% might be familial.
pheochromocytoma
pheochromocytoma

Fig. 20.44  Pheochromocytoma. The tumor is enclosed within an attenuated cortex and demonstrates areas of hemorrhage. The comma-shaped residual adrenal gland is seen (lower portion).
On microscopic examination

- Are composed of polygonal to spindle-shaped chromaffin cells and their supporting cells, compartmentalized into small nests, or Zellballen, by a rich vascular network.

- The cytoplasm has a finely granular appearance, because of the presence of granules containing catecholamines.

- The nuclei of the neoplastic cells are often pleomorphic.
pheochromocytoma
Pheochromocytoma..

- The definitive diagnosis of malignancy in pheochromocytomas is based exclusively on the presence of metastases.
Clinical Features

- The predominant clinical manifestation is *hypertension*

- Sudden cardiac death may occur, probably secondary to catecholamine-induced myocardial irritability and ventricular arrhythmias.