Adrenal Insufficiency

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Normal Function - Adrenal Gland

Anterior pituitary

ACTH

Hyperplastic adrenal

Cholesterol

Progrenolone

17-Hydroxyprogrenolone

Dehydroxyepiandrosterone

Androstenedione

11-Deoxycorticosterone

Progesterone

Corticosterone

Aldosterone

11-Deoxycortisol

17-Hydroxyprogestosterone

MINERALOCORTICORTICIDS

GLUCOCORTICORTICIDS

SEX STEROIDS

Testosterone

Up

21

17

Block

11
• Zona Glomerulosa

• Zona Fasiculata

• Zona Reticularis
(c) Capsule
Adrenal cortex
Adrenal medulla

(d) Capsule
Zona glomerulosa
Zona fasciculata
Zona reticularis
Adrenal medulla

LM 35x
Steroid Hormones

- **Glucocorticoids**
  - CHO, lipid & fat metabolism
  - Increases blood glucose levels & gluconeogenesis
  - Increases protein breakdown
  - Inhibits protein synthesis

- **Mineralcorticoids**
  - Electrolyte & fluid balance
  - Increases sodium & water retention
  - Regulated by renin & angiotensin

- **Sex Steroids**
  - Low synthesis in adrenals compared to gonads
  - Virilising hormones may be secreted
Adrenal gland Insufficiency

- Can be caused by
  - Primary adrenal disease
  - Decreased adrenal stimulation from low ACTH
- Clinical Patterns of presentation
  - Primary acute adrenocortical insufficiency – Adrenal Ciris
  - Primary chronic adrenocortical insufficiency – Addison disease
  - Secondary adrenocortical insufficiency
Primary Acute Adrenocortical Insufficiency

- Clinical Presentation
  1. Commonly present as **Adrenal Crisis**
     - in pts with chronic adrenocortical insufficiency
     - Precipitated by stress requiring immediate increase in steroid output but adrenal glands incapable of responding
  2. In pts on exogenous corticosteroids
     - Occurs in rapid drug withdrawal
     - Failure to increase glucocorticoid output by atrophic glands
Primary Acute Adrenocoritcal Insufficiency

3. As a result from massive adrenal haemorrhage destroying adrenal cortex
Adrenal Haemorrhage - adrenal crisis

• New borns high risk – especially after prolonged and difficult labor.
  ▫ Deficient in prothrombin for several days after birth increases risk of bleeding
• Pts on anticoagulant therapy
• Post-surgical pts who develop DIC
• Complication of sepsis – Waterhouse-Friderichsen syndrome
  ▫ N.meningitidis, pseudomonas, pneumococci, H.influenzae or staphylococci infections
Waterhouse-Friderichsen Syndrome

- Rapidly progressive hypotension leading to shock
- DIC with widespread purpura
- Rapidly developing adrenocortical insufficiency due to massive bilateral haemorrhage
- High risk in children
- Basis: direct bacterial seeding of small vessels in adrenal, endotoxin-induced vasculitis or hypersensitivity vasculitis
Waterhouse-Friderichsen Syndrome

- Adrenal gland pathology: adrenals converted to sacs of clotted blood
- Histology: haemorrhage from medulla in thin walled sinusoids & extending to cotex
- Islands of cortical cells may be recognised
Morphology
Massive adrenal haemorrhage, resulting in primary acute adrenal insufficiency.
Primary Chronic Adrenocortical Insufficiency (Addison Disease)

- Results from destruction of adrenal cortex
- Clinical symptoms appear when 90% of cortical tissue has been damaged
- Causes:
  - Autoimmune disorder
  - Infections
  - Metastatic cancers
Autoimmune cause - Addison Disease

- 60-70% of primary chronic adrenocortical insufficiency
- Can occur in sporadic cases or familial disorder
- 50% of cases only adrenal gland affected
- Other 50% adrenal gland + other endocrine gland affected
  - Thyroid (Hashimoto disease)
  - Type I DM
  - Parathyroid gland – idiopathic hypoparathyroidism
  - Pernicious anaemia
Addison Disease - Pathogenesis

- Antibody directed against adrenal gland resulting in autoimmune adrenitis
Infective Causes of Addison Disease

- TB common cause in PNG population
- Fungal infections also can cause Addison Disease
  - *Histoplasma capsulatum* & *coccidioides immitis*
Metastatic Causes - Addison Disease

- Breast
- Lung
- GIT
- Melanoma
- Haematopoietic neoplasms
Clinical Features - Addison Disease

• Insidious onset
  ▫ Symptoms appear when 90% of gland destroyed
• Progressive weakness
• Easy fatigability
• Non-specific GIT symptoms – anorexia, nausea, vomiting, wt loss & diarrhoea
• **Hyperpigmentation of skin**
• Electrolyte abnormalities – High K & low Na from mineralocorticoid deficiency
• Hypoglycaemia – glucocorticoid deficiency
Features of Addison’s d.

Addison's disease:

- Note the generalised skin pigmentation (in a Caucasian patient) but especially the deposition in the palmer skin creases, nails and gums.

- She was treated many years ago for pulmonary TB. What are the other causes of this condition?
Addison Disease - Morphology

• Irregular shrunken adrenal glands – autoimmune
  ▫ Histology: scattered residual cortical cells in a collapsed network of tissue
  ▫ Variable lymphoid infiltrate present in cortex, may extend into subjacent medulla

• Infection – TB or fungal infection
  ▫ Granulomatous inflammation

• Metastatic Ca
  ▫ Adrenals enlarged
  ▫ Architecture obscured
This is a caseating granuloma of tuberculosis in the adrenal gland. Tuberculosis used to be the most common cause of chronic adrenal insufficiency. Now, idiopathic (presumably autoimmune) Addison's disease is much more often the cause for chronic adrenal insufficiency.
Granulomatous inflammation
The pair of adrenals in the center are normal. Those at the top come from a patient with adrenal atrophy (with either Addison's disease or long-term corticosteroid therapy). The adrenals at the bottom represent bilateral cortical hyperplasia. This could be due to a pituitary adenoma secreting ACTH (Cushing's disease), or Cushing's syndrome from ectopic ACTH production, or idiopathic adrenal hyperplasia.
Metastatic breast carcinoma affecting the adrenal gland and causing primary chronic adrenal insufficiency
Secondary Adrenocortical Insufficiency

• Due to
  ▫ Disorder of hyothalamus & pituitary gland resulting in low ACTH synthesis and secretion
  ▫ Prolonged exogenous administration of glucocorticoids
    • Suppress ACTH production & adrenal function resulting in adrenal atrophy

• Signs & symptoms similar to Addison Disease
• NO SKIN PIGMENTATION
• Mild electrolyte abnormality due to normal aldosterone synthesis
Laboratory findings.

1. A low serum Na level and a high serum K level together with a characteristic clinical picture suggest the possibility of Addison’s disease.

2. Adrenal insufficiency can be specifically diagnosed by:
   - low levels of plasma glucocorticoids and mineralocorticoids, or urinary 17 – hydroxycorticosteroid (17 – OHCS) or 17 – ketogenic steroid (17 – KGS);
   - demonstrating failure to increase plasma cortisol levels, or urinary 17 – OHCS or 17 – KGS excretion, upon administration of ACTH in patients with primary adrenal insufficiency
     (those with secondary adrenocortical insufficiency will have a significant increase in plasma cortisol or 24 - h urinary corticosteroid levels.)

3. To distinguish between primary and secondary adrenal insufficiency, have to find the level of plasma ACTH: primary shows increased, and secondary shows decreased level.
Diagnosis & Treatment

- Diagnostic test
  - Synacthen test

- Treatment
  - Cortisol replacement
    - Hydrocortisone/Cortisone
  - Aldosterone replacement
    - Fludrocortisone
Synacthen test

- Baseline cortisol may be normal in Addison’s disease
- Synacthen test: uses synthetic ACTH analogue
- Normal response: rise in cortisol
END

References: Robins Pathological Basis of Diseases

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