Pathology of adrenal glands

DR.AYSER HAMEED

LEC.4

Normal histological notes

- Adrenal glands consist of two regions (cortex & medulla).
- Cortex consists of three zones:-
  1. Zona glomerulosa, which secretes mineralocorticoids (aldosterone).
  2. Zona fasiculata, which secretes glucocorticoids (cortisol).
  3. Zona reticularis, which secretes androgens.
- Both zones 2 &3 are under the control of ACTH of pituitary gland, while zone 1 is under the control of renin.

Pathology of Adrenal glands Cortex

I. Hyper functioning of cortex, which includes:-
   1. Cushing syndrome (increase cortisol).
   2. Hyperaldosteronemia (increase aldosterone).
   3. Virilizing syndromes (increase androgens).

II. Hypo functioning of adrenal cortex, like Addison disease.

Cushing syndrome (Hypercortisolism)

- Either exogenous or endogenous.
- Most cases of Cushing syndrome are exogenous (due to administration of steroid drugs).
- Causes of endogenous Cushing syndrome are:-

1. Disorders of pituitary gland & hypothalamus (ACTH dependent Cushing syndrome).
2. Disorders of adrenal cortex (ACTH independent Cushing syndrome) & this type of Cushing syndrome is due to hyperplasia or adenomas of adrenal cortex.
3. Cushing syndrome due to ectopic ACTH secretion by nonadrenal neoplasms.

ACTH dependent Cushing syndrome

- This also called Cushing disease.
- Form 90% of cases of endogenous Cushing syndrome.
- Female/ Male 3/1, mostly at the 3rd- 4th decades of life.
- Most of cases are due to Micro adenomas of pituitary gland (ACTH producing pituitary adenomas).
- As a result of increase ACTH secretion, most of patients have bilateral nodular cortical hyperplasia, which result in hypercortisolism.

ACTH independent Cushing syndrome

- Form 20%- 30% of cases of endogenous Cushing syndrome.
- ***Causes***
  1. Adrenal neoplasms (adenomas or carcinomas, both are unilateral).

2. Bilateral adrenal hyperplasia (rare).

Cushing syndrome due to ectopic ACTH secretion by nonadrenal neoplasms

- These tumors are:-
  1. Small cell carcinoma of lung.
  2. Carcinoid tumors.
  3. Medullary carcinoma of thyroid.
  4. Islets tumors of pancreas.

Clinical features of Cushing syndrome

- Most cases of Cushing syndrome develop the symptoms gradually except (those due to small cell carcinoma of lung).
- Early symptoms are weight gain & hypertension.
- With time there is truncal obesity like moon face, buffalo hump, this obesity is due to centripetal fat distribution.
- Decreased Muscle mass & limb weakness due to atrophy of type II myofibers.
- D.M like symptoms like hyperglycemia, which is due to stimulation of gluconeogenesis & inhibit uptake of glucose by cells & glucosuria & polydipsia.
- Osteoporosis, which is due to increase protein breakdown & increase osteoclastic activity.
- Others include (cutaneous striae, decrease immune response, hirsutism, and menstrual abnormality, psychosis & increase skin pigmentation.

Lab.findings

1. Increase 24 hrs of urinary free cortisol level.
2. Loss of normal diurnal pattern of cortisol secretion.
3. For localizing the cause of Cushing syndrome by:-
   I. Level of serum ACTH.
   II. Urinary steroid excretion after administration of the synthetic glucocorticoid dexamethasone.

Morphology of Cushing syndrome

- Those of exogenous Cushing syndrome are associated with increase blood level of exogenous cortisol, which result in block the secretion of pituitary ACTH, which in turn result in decrease stimulation of adrenal cortex, so result in bilateral adrenal cortices atrophy.
- Those of secondary Cushing syndrome are usually associated with bilateral adrenal glands hyperplasia or adenomas, the cortices are diffusely thickened & yellow (due to increase number of lipid rich cells).
- Increase weight of adrenal glands to between 25 to 40 grams with some degree of nodularity (nodular hyperplasia).

Pituitary gland changes in Cushing syndrome

1. *Crock hyaline changes*, this is the most common change seen in pituitary gland in all forms of Cushing syndrome. In this condition, the normal granular, basophilic cytoplasm of the ACTH producing cells in the pituitary is replaced by homogenous, lightly basophilic material (cytokeratin filaments deposition).
2. *Pituitary Adenomas* or foci of *ACTH cell hyperplasia*.

Adrenal insufficiency (hypoadrenalism)

- Either primary or secondary hypoadrenalism.
- Primary hypoadrenalism is either acute or chronic.
- ***Causes of acute primary hypoadrenalism:-***
    1. Waterhouse- friderichsen syndrome (bilateral adrenal hemorrhage follow meningococcemia).
    2. Sudden withdrawal of long term corticosteroid treatment.
    3. Stress in patients with underlying chronic adrenal insufficiency.

- ***Causes of chronic primary hypoadrenalism(Addison disease)***
    1. Autoimmune diseases.
    2. Tuberculosis.
    3. AIDS.
    4. Metastatic diseases.
    5. Fungal infection.
    6. Sarcoidosis.
    7. Systemic amyloidosis.

Addison Disease

- It is uncommon disorder resulting from progressive destruction of the adrenal cortex.
- Clinical features of Addison disease do not appear until at least 90% of adrenal cortex has been destructed.
- 50% of cases are associated with other autoimmune disorders like Hashimoto's thyroiditis, pernicious anemia, type I D.M……etc.

Morphology of hypoadrenalism

Gross.

- In Addison disease, adrenal glands are shrunken; while in secondary hypoadrenalism (due to diseases of pituitary & hypothalamus) adrenal glands are reduced to small, flattened, yellow structure.

Mic.

- In Addison disease, the cortex of adrenal glands contains only scattered residual cortical cells within the network of connective tissue, with lymphoid infiltration of the cortex.
- In secondary hypoadrenalism; there is atrophy of cortical cells with loss of cytoplasmic lipid particularly in zona fasciculata.

Clinical features of Addison disease

1. Insidious onset of weakness & easy fatigability.
2. Nausea, vomiting & diarrhea.
3. Hyperpigmentation in primary hypoadrenalism (due to increase level of ACTH).
4. Hypotension due to decrease level of aldosterone.
5. Hypoglycemia & glycosuria.

Pathology of adrenal medulla

The most important pathological process in adrenal medulla is ***Pheochromacytoma***.

Pheochromacytoma.

- Neoplasm composed of chromaffin cells, which like the non-neoplastic chromaffin cells synthesize & release catecholamine's (epinephrine, norepinephrine).
- Pheochromacytoma can describe by a rule of 10s:-
  1. 10% of pheochromacytoma are familial.
  2. 10% are extra- adrenal in their sites (Paraganglioma).
  3. 10% of cases are bilateral.
  4. 10% are biologically malignant.

Gross

Range from small, circumscribed to large hemorrhagic mass.

Mic.

- Composed of polygonal to spindle cells with their supporting cells, which divide the tumor into small nests (zellaballen) pattern by a rich vascular network.
- Cytoplasm of neoplastic cells is granular (due to their contents of catecholamine's granules).
- Even in benign cases, there is vascular & capsular invasion, so the diagnosis of malignant pheochromacytoma depends on presence of metastases (to lymph nodes, lung, liver & bones).

Clinical features

- The most characteristic clinical feature of pheochromacytoma is ***isolated, paroxysmal, episodes of hypertension*** in 50% of cases, **with associated symptoms** like (tachycardia, palpitation, headache, tremor, sudden abdominal symptoms).
- All these symptoms are due to overproduction of catecholamines by the neoplastic cells.
- Laboratory data (increase urinary excretion of free catecholamine's & their metabolites like Vanilyl Mndelic Acid (VMA).

Endocrine tumors of Pancreas

- Less common than exocrine tumors.
- **Most** of these tumors are **functioning** (some of them are nonfunctioning).

- **Three common syndromes** associated with functioning tumors:-

1. **Hyperinsulinism.**
2. **Hypergastrinemia (Zollinger – Ellison syndrome).**
3. **Multiple Endocrine Neoplasia**.

Hyperinsulinism:
Islet cells **tumors secrete insulin…… hypoglycemia**.
Clinical features
Characterized by:-

1. **Neuropsychiatric disorders** like confusion, nervousness & stupor.
2. **Hypoglycemic attacks** precipitating by fasting or exercises & relieved by administration of glucose or eating.
3. **High level of circulating insulin (C- peptide) & hypoglycemia**.

Islet cells tumors giving rise to these symptoms are called Insulinoma.

Morphology of insulinoma:

- Most of these tumors are within pancreas & benign (10% are carcinomas).
- Most of these tumors are solitary (some are ectopic tumors).

Gross
Insulinoma are solitary (less than 2cm) & encapsulated, red – brown nodules anywhere in the pancreas.

Mic:
Benign insulinoma characterized by **Giant islets** with preservation of normal orientation of islet cells.

Malignant tumors characterized by local invasion, metastases & less common anaplasia.

Zollinger – Ellison Syndrome & Gastrinoma:

- Tumors characterized by excess secretion of gastrin (Gastrinoma).
- Gastrinoma either in duodenum or in pancreas.
- More than half of cases of gastrinoma are invasive & metastasized at time of diagnosis.
- Multiple gastrinoma are associated with MEN type 1.

Z- E syndrome is association of pancreatic tumor, increased gastric acid secretion with severe peptic ulcer (mostly duodenal ulcer).

Characteristics of ulcer associated with Z- E syndrome:

1. **Multiple** ulcers (D. U & G. U).
2. Intractable ulcers (**resist treatment**).
3. Presence in **abnormal site (jejunum & second part of duodenum**).
4. More than **50% of cases are associated with diarrhea (other hormones secretion).**

Multiple endocrine neoplasia (MEN)

- Are group of **inherited disorders** resulting from proliferative lesions **(hyperplasia, adenomas & carcinomas) of multiple endocrine organs**.
- **Characteristics of MEN;**
  1. Occur **at younger age than the sporadic cases.**
  2. Involve **multiple endocrine organs**.
  3. **Even in the one organ, the tumors are often multifocal.**
  4. They are usually more **aggressive than the sporadic cases.**
- **Types of MEN;**

1. MEN I:

- **Autosomal dominant disease, with mutation in a gene MEN1 on chromosome 11.**
- Include **i. Parathyroid hyperplasia.**
  ii. Pancreatic endocrine tumors.
  iii. Pituitary prolactinoma.

.MEN II:

- Autosomal dominant disorder, due to mutation of RET gene located on chromosome 10.
- Include two subtypes;

MEN IIA: which include:-

i. Thyroid medullary carcinoma.
ii. Pheochromacytoma.
iii. Parathyroid hyperplasia.

MEN IIB:

Similar to MENA but differ by:-

i. Do not develop primary hyperparathyroidism.
ii. Develop extra endocrine manifestation like ganglioneuromas of lips, GIT, tongue.

THANKS DEAR AND GOOD LUCK