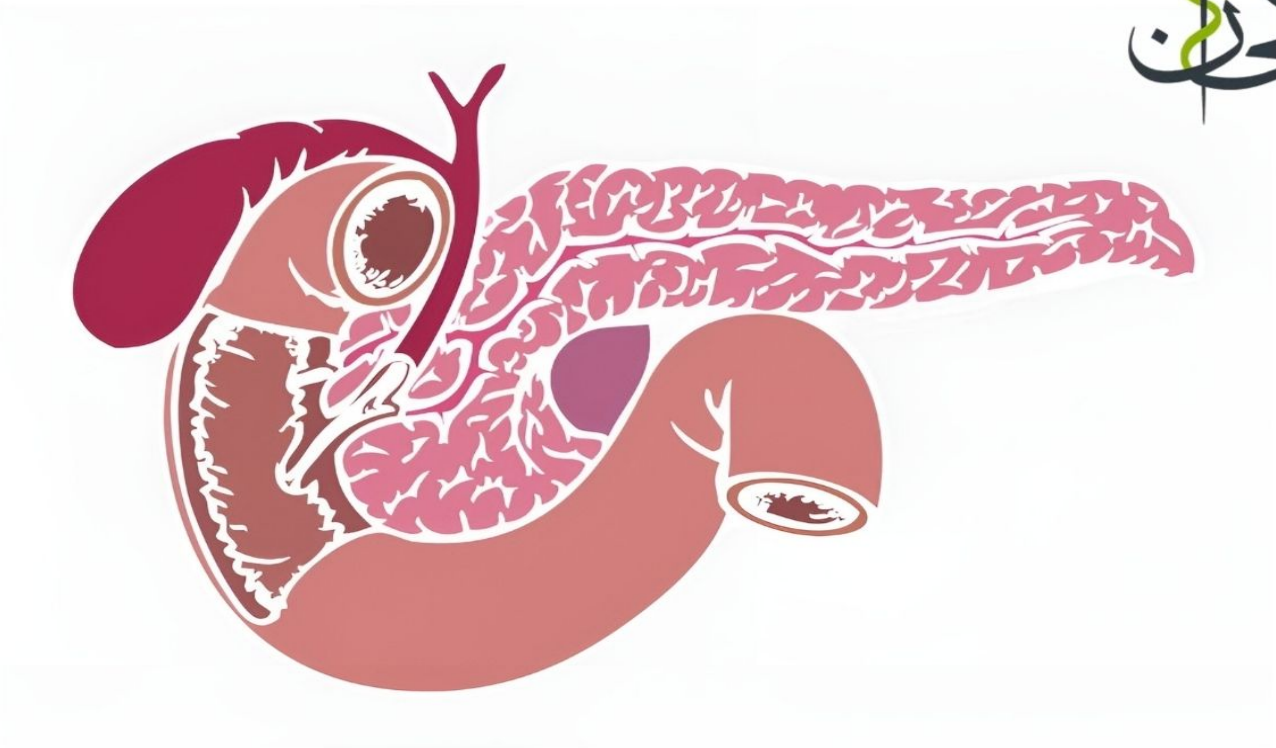
Endocrine system

5

Pathology



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Diseases of the pituitary gland

We classify diseases of the pituitary gland into:

1- Anterior pituitary gland diseases.
2- Posterior pituitary gland diseases.

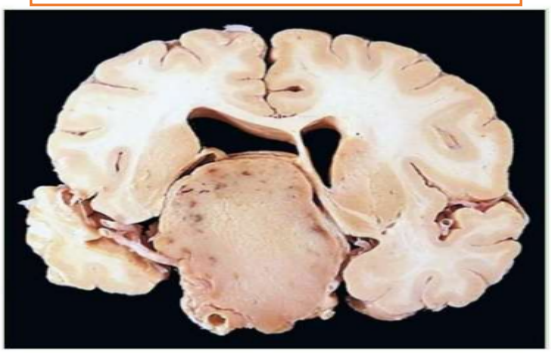
(Anterior pituitary gland diseases)

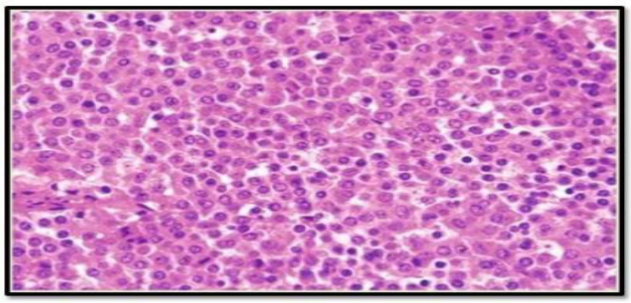
1) Anterior Pituitary adenoma

- Considered the most common pituitary adenoma.
- Can be functional (secretory of hormones leading to hyperpituitarism) or nonfunctional (symptoms are related to tumor mass-effect).
- Called **microadenoma** if size ≤1cm, very common (20% of the population harbors silent forms), incidental finding, can be functioning in certain cases.
- Called macroadenoma if size >1cm which can cause:
  1- **Tumor mass effects** (**increased intracranial pressure** leading to nausea, vomitus and headache, **optic nerve compression** leading to blurry vision and blindness and finally **hydrocephalus** which is accumulation of CSF in the brain).
  2- **Large non-functional adenoma can cause Hypopituitarism** by compressing and destroying the surrounding normal tissue.
- Histologic morphology doesn't correlate (indicate) the functional status of the adenoma. (For instance, Gonadotropic adenoma despite having gonadotropic proliferation is considered silent with no hormone production.

MORPHOLOGY

Notice the enlargement and shifting of the brain as mass effect





❖ There are subtypes of Anterior pituitary adenoma:

1- Lactotrophic adenoma (Prolactinoma)

- The **most common functioning pituitary adenoma** (30%)
- Extracellular **Dystrophic calcification** is common (appears as pituitary stones on X-ray)
- Causes **amenorrhea** (Cessation of menstrual cycle), **galactorrhea** (engorgement of the breast with milk), **infertility and loss of libido** (due to suppression of sexual hormones).
- **Symptoms are less obvious in men and post-menopausal women** (more chance to reach large size).
- **High prolactin causes endothelial dysfunction** (leading to **cardiovascular diseases**) and **insulin resistance** (leading to **DM** and therefore complicates patients already diagnosed with DM).
- Diagnosis: **Pituitary mass and very high level of serum prolactin.**
- Other etiologies leading to increased serum Prolactin: (Not related to adenoma and here there is a mild increase in serum prolactin while in prolactinoma there is a high increase with obvious symptoms)
  1- **Mild increase in serum prolactin may accompany other types of pituitary adenoma or hypothalamic diseases** due to interference with the normal inhibitory control of dopamine and thus causing **lactotroph hyperplasia** (less severe since hyperplasia can be reversed).
  2- **Chronic renal failure: decreased clearance of prolactin.**
  3- **Primary hypothyroidism: high TRH increases prolactin secretion.**
  4- **Drugs blocking dopamine receptor (anti-depressants).**

2- Somatotrophic adenoma

- **Growth-hormone secreting adenoma.**
- **Second most common functional PA, non-functional SA is rare.**
- Commonly reach large size.
- **Gigantism in children** (long bones)
- **Acromegaly in adults** (skin coarse facial features, soft tissue, visceral growth).
- Also causes **diabetes** (GH functions as an Insulin antagonist)**, hypertension, GI cancer** (By inducing cellular growth)**, gonadal dysfunction.**
- **May accompany lactotrophic adenoma** (hence termed **Mammo somatotrophic adenoma**)
- Microscopy: **densely** and **sparsely granulated variants** with the latter being more aggressive and non-responsive to somatostatin therapy and therefore requiring surgical interventions.

3- Corticotroph Adenoma

- **Functional adenomas** produce ACTH causing hypersecretion of adrenal cortisol causing Cushing Disease (Characterized by Elevated levels of cortisol in serum).
- Commonly microadenoma occurs in 3 forms

1) **densely granulated**
2) **Sparsely granulated**
3) **Crooke cell adenoma**: another variant, showing ring-like cytokeratin protein inside the cells, clinically aggressive

> Insight: The 4 Antagonists for insulin are: **glucagon, adrenaline, cortisol and growth hormone**

- **Proopiomelanocortin (POMC)**: precursor of ACTH, stains positive for PAS stain.
- **Cushing Syndrome manifestations: central obesity, hypertension, hyperglycemia** (Recall that Cortisol is one of the antagonists of insulin leading to hyperglycemia).
- **Nelson syndrome**: occurs secondary to bilateral adrenalectomy (Past-methodology for treating of Cushing syndrome) characterized by progressive enlargement of PA causing tumor effect, skin hyperpigmentation (POMC leads to production of melanotropin which stimulates Melanocytes of the skin).

4- Gonadotrophic Adenoma

- Can manifest in 3 forms:
  1) Usually produces small amounts LH and FSH hormones **(silent)** and therefore Most symptoms are related to mass-effect
  2) **(Hypopituitarism)** due to destruction of the surrounding normal cells (impaired secretion of LH leading to loss of libido, amenorrhea)
  3) Rarely reported in literature **(Hyperpituitarism)**, some cases secrete large amount of LH/FSH leading to macroorchidism (Enlargement of testis), hyperspermia, ovarian hyperstimulation.

5- Thyrotrophic Adenoma

- TSH-producing adenoma, uncommon (<1% of PA).
- Rare causes of hyperthyroidism.

6- Plurinominal adenoma

- Secrete multiple hormones, clinically aggressive

7- Null cell adenoma

- Do not express any markers of hormones, not differentiated (Histological examination only shows stem cell with nuclei, no other prominent features).

- **Pituitary Apoplexy**

- Rare condition that arises as a complication of pituitary adenoma further complicating its case.
- Sudden hemorrhage in pituitary gland causing acute enlargement and damage
- Symptoms of increased intracranial pressure (severe periorbital headache, nausea, vomiting, visual disturbance)
- Later, patients develop symptoms of **hypopituitarism** due to compression and destruction of surrounding normal cells.
- **Loss of ACTH causes hypotension** (No secretion of Aldosterone) **and hypoglycemia** (No secretion of Cortisol which can be fatal).
- **Critical condition, neurosurgical intervention is needed**.

- **Sheehan syndrome** is a similar but milder condition results from **pituitary infarction secondary to ischemia**, virtually it can lead to deficiency of any of the Ant. pituitary gland hormones. It occurs due to 2 contributing factors:
  1- Severe post-partum hemorrhage (thus it occurs post-partum).
  2- Normal physiological hyperplasia of the pituitary gland during pregnancy.

- **Pituitary Carcinoma**

- Rare, <1% of pituitary tumors.
- Most are functional (prolactin or ACTH-secretion is most common).
- Differentiated from PA by metastasis.

- **Pituitary Blastoma**

- Malignant pituitary tumor arises in children <2 years.
- Morphologically undifferentiated cells (blastema).
- Cushing syndrome is common.

(Posterior pituitary gland diseases)

- ## Diabetes Insipidus (DI)

➢ Deficiency in anti-diuretic hormone (ADH), called "central DI".
➢ Results in inability of kidneys to reabsorb fluids (**polyurea**, **polydipsia** (increased thirst), **dehydration**, **Pale tasteless urine** but **NORMAL Blood glucose levels**).
➢ Results from:
  1- **head trauma (including brain surgery), hypothalamic diseases (tumors, inflammation).**
  2- Can be **Genetic: mutation in arginine vasopressin (ADH) or its receptor.**
  3- **Nephrogenic DI**: kidney is unresponsive to ADH (similar symptoms).

- ## Syndrome of inappropriate antidiuretic hormone secretion (SIADH)

➢ **Results in over-reabsorption of water in kidneys** (oliguria, hyponatremia (dilutional), **cerebral edema**, brain dysfunction).
➢ Although total body fluid is increased, blood volume remains normal, **no peripheral edema**.
➢ **Usually caused by a paraneoplastic syndrome** (small cell carcinoma of lung).
➢ Also **caused by drugs, CNS inflammation (Hypothalamic inflammation for example) or trauma.**

- ## Craniopharyngioma

➢ **Suprasellar tumor, arises from the vestigial epithelium of Rathke pouch** (composed of stratified squamous non keratinized epithelium).
➢ **Slowly growing tumor**
➢ **Bimodal age distribution** (children 5-15, old >65 years)
➢ Presentation: **hypopituitarism (Dwarfism in children), DI, tumor effect (in adults).**
➢ **Adamantinomatous CPh**: a form characterized by squamous cell with keratin, common in children, also shows dystrophic calcification, may produce cyst or becomes inflammatory producing (machine oil) material.
➢ **Papillary CPh**: a form characterized by squamous cells show papillae formation, no keratin, no cyst, no calcification seen in adults.

- **Practice problems:**

1- An X ray of a 55-year-old lady showed expansion of the Sella turcica with associated bony erosions. She complained of vision problems. The MOST COMMON cause of her symptoms is:

A- Pituitary macroadenoma, Prolactinoma type
B- Pituitary microadenoma, prolactinoma type.
C- Prolactinoma that can be of any size.
D- Non-functioning pituitary macroadenoma
E- Non-functioning pituitary adenoma of any size.

2- A 66-year-old patient complained of polyuria and polydipsia. His fasting blood sugar was 70 mg/dl in three occasions. A blood test of this patient will show:

A- hypernatremia
B- hyponatremia
C- hypercalcemia
D- hypocalcaemia
F- normal calcium and sodium levels

3- A 32-year-old pregnant lady delivered by a caesarean section. She lost 2 litres of blood during the operation and her systolic blood pressure dropped significantly. She developed hypothyroidism and adrenal insufficiency. Which of the following statements is CORRECT about her disease?

A- An X ray would show expansion of Sella turcica
B- Her symptoms are caused by ischemic necrosis of 50% of the anterior pituitary
C- The presence of a pre-existing large non-functioning pituitary adenoma makes her more vulnerable to develop hypopituitarism
D- Her symptoms are caused by hemorrhage within the anterior pituitary.
E- Her symptoms could've been better if bleeding of the same amount and duration occurred during pregnancy rather than during delivery

4- Which of the following is NOT a feature of central diabetes insipidus?

A- Characterized by polyuria.
B- Characterized by ADH deficiency.
C- Hyponatremia.
D- Can be caused by chronic inflammation of the pituitary gland and hypothalamus.
E- The urine shows inappropriate low specific gravity.

Answers:

1- D
2- A
3- C
4- C