Endocrine Pathology
Pituitary Gland
MHD II 2018-19

Topics
Histology Review
Anterior Pituitary
Posterior Pituitary
Pituitary Gland

Anterior pituitary gland
(Adenohypophysis, Pars Distalis)
Stains: "red-blue"

Posterior pituitary gland
(Neurohypophysis, Pars Nervosa)
Pale staining

Adenohypophysis – high power

The adenohypophysis
contains 3 cell types:
acidophils (stain red)
basophils (stain blue)
chromophobes (pale stain)

The adenohypophysis
stains red-blue on low
power because of the
acidophils and basophils

Normal Anterior Pituitary

Source: Robbins Pathologic Basis of Disease
Neurohypophysis – high power

Resembles neural tissue, with glial cells, nerve fibers, nerve endings, and intra-axonal neurosecretory granules.

Precursors of ADH (vasopressin) and oxytocin synthesized in hypothalamus and transported to pars nervosa where processing is completed.

Hyperpituitarism

- Excess secretion of 1 or more hormones
  - Functional anterior pituitary adenoma
    - Anterior pituitary hyperplasia
      - Pregnancy
    - Carcinoma
    - Extrapituitary tumors
    - Hypothalamic pathology

Anterior Pituitary Adenoma

- Most common cause of hyperpituitarism
- Functional vs nonfunctional
- Microadenomas <1cm in diameter
- Macroadenomas >1cm in diameter
Pituitary Adenoma

- Clinical manifestations
  - Depend on hormone(s) secreted
  - Mass effect
    - Bitemporal hemianopsia
    - Headache

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### Table H-1: Classification of Pituitary Adenomas

<table>
<thead>
<tr>
<th>Pituitary Cell Type</th>
<th>Hormone</th>
<th>Tumor Type</th>
<th>Associated Syndrome</th>
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<tr>
<td>Corticotroph</td>
<td>ACTH</td>
<td>Dense granulated</td>
<td>Cushing syndrome</td>
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<tr>
<td>Somatotroph</td>
<td>GH</td>
<td>Dense granulated</td>
<td>Gigantism (children)</td>
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<tr>
<td>Lactotroph</td>
<td>Prolactin</td>
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<td>Galactorrhea and amenorrhea (in females)</td>
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<td>Mammosomatotroph</td>
<td>Prolactin, GH</td>
<td>Mammosomatotroph</td>
<td>Combined features of GH and prolactin excess</td>
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<tr>
<td>Thyrotroph</td>
<td>TSH</td>
<td>Thyrotroph</td>
<td>Hyperthyroidism</td>
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<tr>
<td>Granulotroph</td>
<td>PRF-LH</td>
<td>Granulotroph *pituitary adenoma*</td>
<td>Hypogonadism, hypothyroidism and hypopituitarism</td>
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</tbody>
</table>

ACTH: adrenocorticotropic hormone, TSH: thyroid-stimulating hormone, LH: luteinizing hormone, FSH: follicle-stimulating hormone, PRF: proopiomelanocortin, \*Pituitary adenoma: a type of tumor that develops from the pituitary gland.
Pituitary Adenomas

- Majority sporadic
  - ~5% familial
    - MEN I (parathyroid, pancreas, pituitary)
Pathogenesis

- **GNAS1 Gene Mutation**
  - Constitutive activation of stimulatory G protein
  - Unchecked cellular proliferation

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Prolactin Secreting Adenomas (Prolactinoma)

- Most common functioning adenoma

**Female**
- Galactorrhea
- Amenorrhea, infertility
  - Elevated prolactin inhibits LH surge
    - Decreases the hypothalamic drive for pulsatile luteinizing hormone (LH) secretion, inhibiting ovarian folliculogenesis

**Male**
- Impotence, infertility
  - Low testosterone (in part)

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Prolactinomas

- DDX elevated prolactin level
  - Hypothalamic/Stalk pathology
    - Hypothalamic dopamine inhibits prolactin
  - Drugs
  - Pregnancy, breast feeding
Prolactinomas

- Treatment
  - Dopamine agonists
    - Cabergoline, Bromocriptine
  - Surgery for macroadenomas

Growth Hormone Secreting Adenoma (Somatotroph Cell Adenoma)

- 2nd most common type functioning adenoma
- Persistent GH stimulation → stimulation of hepatic insulin-like growth factor I (somatomedin C) in liver
  - Mitogenic, anabolic effects on multiple organs

GH secreting adenoma

- Prepubertal
  - Gigantism

- Post pubertal
  - Acromegaly
Facial aspect of a patient with acromegaly. Nose is widened and thickened, cheekbones are obvious, forehead bulges, lips are thick and facial lines are marked. The forehead and overlying skin is thickened, sometimes leading to frontal bossing.

GH Adenomas

- Diagnosis
  - Elevated insulin-like growth factor I (IGF-1)
  - Elevated growth hormone
  - Lack of growth hormone suppression by oral glucose (oral glucose tolerance test)
GH Adenomas

- Treatment
  - Surgery
  - Somatostatin (growth hormone-inhibitory hormone) analogs
    - Inhibit GH secretion by binding to specific receptors for somatostatin and its analogs
    - Octreotide, lanreotide

Adrenocorticotropic Hormone Producing Adenoma (Corticotroph Adenoma)

- Secrete ACTH
- Clinically silent vs hypercortisolism
- Cushing DISEASE
  - Hypercortisolism via pituitary adenoma
  - Hyperpigmentation
    - Prohormone melanocyte stimulating hormone

Clinical features of Cushing's syndrome.

- Note central obesity and broad, purple stretch marks (B. close-up).
- Note thin and brittle skin in an elderly patient with Cushing's syndrome.
- Hyperpigmentation of the knuckles in a patient with ectopic adrenocorticotropic hormone (ACTH) excess.

Legend:

Cushing Disease = Cushing Syndrome caused by ACTH producing pituitary adenoma

- Round face
- "Buffalo hump"
- Osteopenia
- Hypertension
- Atherosclerosis
- Glucose intolerance
- Hyperlipidemia
- Increased susceptibility to infections
- Depression
Nelson Syndrome

• Adrenal glands removed for treatment of hypercortisolism due to Cushing Disease
• Persistence of corticotroph adenoma
• What do you think happens?

Nelson Syndrome

– No inhibitory effect of adrenal corticosteroids on pituitary adenoma (adrenal glands have been removed)
– Adenoma continues to grow into a clinically aggressive mass
  • Mass effect
    • Visual field defects, headache, cavernous sinus invasion
  • Hyperpigmentation
    • Marked elevated levels ACTH produced by adenoma
  • No cortisol secreted

accelerated growth of ACTH-secreting cells in preexisting microadenomas when the effect of glucocorticoid negative feedback inhibition is reduced.

No adrenals – no cortisol
*Hyperpigmentation from ACTH
Pituitary Adenomas

- LH, FSH, TSH secreting adenomas
  - Extremely rare
- Nonfunctioning pituitary adenomas
  - Clinically silent though producing hormone
    - May be poorly differentiated; produce and secrete hormones inefficiently
  - Mass effect

Pituitary Carcinoma

- Extremely rare

HYPOPITUITARISM

- Deficiency of pituitary hormones
  - Nonfunctional pituitary adenoma
  - Ischemic injury
  - Surgery, radiation
  - Inflammatory conditions
Hypopituitarism

• Pituitary adenoma
  – Mass effect
  – Pituitary apoplexy
    • Acute hemorrhage into adenoma

Hypopituitarism

• Ischemic necrosis
  – Sheehan Syndrome
    • Post partum necrosis of anterior pituitary
      – Obstetrical hemorrhage, shock
        » Hypotension ➔ vasospasm ➔ ischemic necrosis
    • Initial clinical clue: lactation failure
      • Life threatening secondary adrenal insufficiency

Hypopituitarism

• Ischemic necrosis
  – Destruction of >75% of pituitary
    • DIC
    • Sickle cell disease
    • Traumatic injury
    • Shock
Hypopituitarism

- Empty Sella Syndrome
  - Enlarged sella turcica not filled (entirely) with pituitary tissue
    - Primary
      - Defect in diaphragm of the sella leads to CSF leak
      - ↑ CSF pressure around pituitary gland
      - Causes pituitary atrophy
    - Secondary
      - Identifiable disease/therapy which results in “empty sella”

EMPTY SELLA

Hypopituitarism

- “Injury”
  - Pituitary surgery, radiation, trauma
- Infiltrative lesions
  - TB, sarcoid, hemochromatosis, metastases
- Hypothalamic disease
  - Hypopituitarism + s/s of posterior pituitary dysfunction (ie diabetes insipidus)
Posterior Pituitary Syndromes

- Antidiuretic Hormone (ADH)
  - Promotes free H2O absorption in collecting tubules
  - ADH deficiency
    - Diabetes insipidus
  - ADH excess
    - Syndrome of inappropriate antidiuretic hormone secretion (SIADH)

Diabetes Insipidus

Central
- ADH deficiency
  - Pituitary, hypothalamic pathology
- Response to ADH analogue (Desmopressin)

Nephrogenic
- Renal tubules unresponsive to ADH
- No response to ADH analogue (Desmopressin)
**Diabetes Insipidus**

- Excessive loss of free water
  - Polyuria → Dilute urine
- Compensatory increased thirst
  - Polydypsia

- Patient unable to compensate with free water
  - HYPERnatremia
  - Dehydration
    - Inappropriately low urine specific gravity

**Dr. Leehey’s Lecture**

**SIADH**

- Excess absorption free water
  - Euvolemic HYPOnatremia
    - Total body water increased, blood volume remains nearly normal
      - No peripheral edema
Dr. Leehey’s Lecture

SIADH

- Ectopic secretion
  - Small cell carcinoma lung (paraneoplastic syndrome)
- Non-neoplastic lung pathology
- CNS injury
- Drugs
  - SSRIs, carbamazepine, chlorpropamide, cyclophosphamide
- Idiopathic

Other Pituitary Pathology

Background embryology review:
- What is “Rathke’s pouch”?
Pituitary gland forms from two separate embryonic structures:

- **Week 3** - a hypophyseal pouch (Rathke pouch = future anterior pituitary) grows from roof of the pharynx/oral ectoderm; a neurohypophyseal bud (future posterior pituitary) forms from the diencephalon.
- **Month 2** – Rathke pouch detaches from the roof of the pharynx and merges with the neurohypophyseal bud.

During the fetal period, anterior and posterior parts of pituitary complete development.

**Other Pituitary Pathology**

- **Craniopharyngioma**
  - Benign tumor
  - Arises from vestigial remnants of Rathke’s pouch
  - Primarily suprasellar location
  - 10-20% intrasellar

*Adamantinomatous Craniopharyngioma Containing Teeth*

[Image of medical diagrams related to pituitary pathology]
Craniopharyngioma

- Histology
  - Solid, cystic components
  - Calcifications common
  - Palisading of squamous epithelial cells

Other Sellar/Suprasellar Tumors

- Rathke cleft cysts
  - Developmental Failure of Rathke's pouch obliteration
  - Lined by cuboidal epithelium with cilia and/or goblet cells
  - Growth may compromise pituitary gland

- Germ cell tumors/dermoid cyst
  - Primary CNS tumors arise along midline (pineal and suprasellar)
  - "rests" of germ cells vs migrate late in development
A 30-year-old woman, who has three healthy children, notes that she has had no menstrual periods for the past 6 months, but she is not pregnant and takes no medications. Within the past week, she has noted some milk production from her breasts. She has been bothered by headaches for the past 4 months. After nearly hitting a bus while changing lanes driving her vehicle, she is concerned with her vision. On physical examination she is afibrile and normotensive. Her lateral vision is reduced. Which of the following laboratory test findings is most likely to be present in this woman?

A. Increased serum cortisol  
B. Lack of growth hormone suppression  
C. Hyperprolactinemia  
D. Hyponatremia  
E. Abnormal glucose tolerance test  
F. Decreased serum TSH

A 24-year-old presents with the onset of labor at 38 weeks gestation. As a consequence of placenta accreta she develops severe hemorrhage. She remains hypotensive for 4 hours and requires transfusion of 10 packed RBC units. Postpartum, she becomes unable to breast-feed the infant. She does not have a resumption of normal menstrual cycles. She becomes more sluggish and tired. Laboratory findings include hyponatremia. Which of the following pathologic lesions is she most likely to have had following delivery?

A. Bilateral adrenal hemorrhage  
B. Pituitary necrosis  
C. Metastatic choriocarcinoma  
D. Subacute thyroiditis  
E. Posterior pituitary adenoma