Pituitary Pathology

ANTERIOR PITUITARY

Hyperpituitarism
- Excess secretion of 1 or more hormones
- Most common etiology – Pituitary adenoma

Pituitary Adenoma
- Benign neoplasm arising from a specific anterior pituitary cell type
- Pituitary adenomas may be functional – exhibit autonomous hormone secretion
  Or they may be clinically nonfunctional- they do not actively secrete hormones

  - Prolactin secreting adenomas are the most common type of functioning adenoma followed by growth hormone secreting adenomas followed by ACTH secreting adenomas
  - TSH, LH, FSH secreting adenomas are RARE

  - Pituitary “microadenomas” measure <1cm in diameter;
  - “Macroadenomas” measure >1cm in diameter

Clinical Presentation
- Pituitary adenomas can cause symptoms by secreting hormones or by impinging on adjacent pituitary tissue and structures
- Symptoms due to local effects include:
  - Pituitary failure (usually clinically nonfunctional macroadenomas)
  - Headache by stretching the dural plate
  - Visual field defects by pressing on the optic chiasm – classically bitemporal hemianopsia

Pathogenesis
- The majority of pituitary adenomas are sporadic.
  ~5% may be associated with MEN I (parathyroid, pancreatic, pituitary adenomas)

- Mutation of the GNAS1 gene, which results in constitutive activation of a stimulatory G protein, is one of the more common genetic alterations.

Histology
- Pituitary adenomas are composed of relatively uniform, polygonal cells arranged in sheets, cords.
- Cellular monomorphism and the absence of the significant reticulin network distinguish pituitary adenomas from non-neoplastic anterior pituitary parenchyma.
Summary of specific types of Pituitary adenomas

PROLACTINOMA
-Most common type of functioning adenoma

Clinical presentation:
-Women – hyperprolactinemia results in loss of pulsatile LH secretion, blunting of LH peak, hypoestrogenism, and anovulation; oligomenorrhea, amenorrhea
-Galactorrhea

Men – hyperprolactinemia attenuates LH secretion leading to low testosterone levels; Diminished libido,
- 30% galactorrhea

Other causes of elevated prolactin levels - should be considered in the differential
-Pregnancy, lactation, nipple stimulation, chest wall lesions
-Compression of the pituitary stalk decreases dopamine suppression of prolactin as do hypothalamic tumors
-Drugs - dopamine receptor antagonists such as Haldol, metoclopramide
  Methyldopa inhibits dopamine synthesis, reserpine inhibits dopamine storage

Treatment
-Medical – dopamine antagonists such as bromocriptine, cabergoline
-Surgical resection for prolactinomas not responding to medical treatment or large macroadenomas with local effects

GROWTH HORMONE SECRETING ADENOMAS (SOMATOTROPH ADENOMAS)
-Growth hormone - most abundant anterior pituitary hormone, produced by the pituitary somatotroph cells
-Growth hormone’s predominant action is to stimulate hepatic synthesis and secretion of IGF-1, a potent growth and differentiation factor

Brief Growth Hormone (GH) review: GH induces protein synthesis and nitrogen retention and impairs glucose tolerance by antagonizing insulin action. GH also stimulates lipolysis. Linear bone growth occurs as a result of complex hormonal and growth factor actions, including those of IGF-I. GH stimulates epiphyseal prechondrocyte differentiation. Although GH exerts direct effects in target tissues, many of its physiologic effects are mediated indirectly through IGF-I, a potent growth and differentiation factor. The liver is the major source of circulating IGF-I. In peripheral tissues, IGF-I also exerts local paracrine actions that appear to be both dependent on and independent of GH. Thus, GH administration induces circulating IGF-I as well as stimulating local IGF-I production in multiple tissues.
Clinical manifestations
- Children - before the epiphyses of long bones are fused, linear growth increases; result is **pituitary gigantism**.

Adults – **acromegaly**
- Features of acromegaly - Acral and soft tissue overgrowth, skin thickening, enlarged jaw (macrognathia), enlarged, swollen hands and feet
- Cardiovascular abnormalities include hypertension, left ventricular hypertrophy, and cardiomyopathy.
- Hyperinsulinism, insulin resistance, overt diabetes in 10 to 15 percent of cases

Diagnosis
- Measurement of serum IGF-1 levels - elevated
- Random growth hormone level measurement not as useful (pulsatile secretion)
- Glucose tolerance test – failure to suppress growth hormone levels after glucose load

Treatment
- Surgical resection
- Medical therapy with synthetic somatostatin analogue – octreotide, lanreotide

ADRENOCORTICOTROPH HORMONE PRODUCING ADENOMA - (CORTICOTROPH ADENOMA)
- Clinical – Cushing Disease – excess ACTH induces adrenal cortical hypersecretion and signs/symptoms of cortisol excess

  (note that Cushing Syndrome refers to hypercortisolism from any cause. Cushing Disease is reserved for excess ACTH secretion by pituitary corticotrope tumors)

- What is Nelson Syndrome?
  Patients who have had bilateral adrenalectomy for Cushing's Syndrome may have residual pituitary corticotroph tumor/adenoma with subsequent growth. Pathogenesis: tumors likely represent accelerated growth of ACTH-secreting cells in preexisting microadenomas when the effect of glucocorticoid negative feedback inhibition is reduced.
**Hypopituitarism**
Deficiency of pituitary hormones

**Differential:**

- Nonfunctional pituitary adenoma:
  Causes mass effect and pituitary parenchyma compression

- Pituitary apoplexy:
  - Acute intrapituitary hemorrhage, often into adenoma
  - Can present with sudden onset of excruciating headache, diplopia due to pressure on the oculomotor nerves, and hypopituitarism.
  - All pituitary hormonal deficiencies can occur; sudden onset of ACTH, cortisol deficiency can cause life threatening hypotension

Sheehan syndrome:
- Infarction of the pituitary gland after postpartum hemorrhage
- Common initial clinical manifestation – failure to lactate postpartum

**Empty Sella**
- 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”

**Pituitary Surgery, radiation**

**Infiltrative, Inflammatory conditions**
- TB, sarcoid, hemochromatosis, metastases

**Hypothalamic disease**
- Suspect when have signs of Hypopituitarism + s/s of posterior pituitary dysfunction (Diabetes insipidus)
POSTERIOR PITUITARY

- Principle disorders are associated with deficiency of antidiuretic hormone (diabetes insipidus) or syndrome of inappropriate diuretic hormone secretion (SIADH)

Diabetes Insipidus

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<th>Central</th>
<th>Nephrogenic</th>
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<td>• ADH deficiency</td>
<td>• Renal tubules unresponsive</td>
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<tr>
<td>- Pituitary, hypothalamic pathological</td>
<td>to ADH</td>
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<tr>
<td>• Response to ADH analogue</td>
<td>• No response to ADH analogue</td>
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<tr>
<td>(Desmopressin)</td>
<td>(Desmopressin)</td>
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Clinical manifestations
- Patients with central DI typically present with polyuria, nocturia, polydipsia.
- The serum sodium concentration is often in the high normal range, which is required to provide the ongoing stimulation of thirst to replace the urinary water losses.
- Marked hypernatremia can develop when thirst is impaired or cannot be expressed i.e., patients who are debilitated, infants/young who cannot independently access free water; postoperative period

Diagnosis
- Examining the response (urine volume and osmolality) to water restriction and subsequent, administration of exogenous ADH

SIADH
- Disorder of impaired water excretion caused by the inability to suppress the secretion of antidiuretic hormone
- The excess free water results in hyponatremia
- Patients are euvoletic: Though the total body water is increased, blood volume remains nearly normal; there is no peripheral edema

Why? Antidiuretic hormone secretion results in a concentrated urine and therefore a reduced urine volume. The higher the plasma ADH, the more concentrated the urine. In most patients with SIADH, ingestion of water does not adequately suppress ADH, and the urine remains concentrated. This leads to water retention, which increases total body water (TBW). This increase in TBW lowers the plasma sodium concentration by dilution. In addition, the increase in TBW transiently expands the extracellular fluid volume and thereby triggers increased urinary sodium excretion, which both returns the extracellular fluid volume toward normal and further lowers the plasma sodium concentration.
Causes of SIADH

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

Management
- Treat the underlying cause
- Free water restriction

What is a craniopharyngioma?
- Tumor of childhood that may cause hypopituitarism
- Supratentorial mass
- Arises from epithelial remnants of Rathke’s pouch
- May encroach on the optic chiasm leading to bitemporal hemianopsia
  “Tooth” like calcifications may be seen on imaging
- Histology - Solid and cystic components; Calcifications common; Palisading of squamous epithelial cells
- Benign but tend to recur after resection