Pituitary Tumors

Pituitary tumors are common neoplasms, and recognition of their presentation is critical since a favorable therapeutic outcome is dependent on early identification of the lesion.

Classification
- Microadenoma: (< 1 cm in diameter)
- Macroadenoma: (> 1 cm in diameter)
- Can be classified:
  - (a) chromophobic
  - (b) chromophilic

The endocrinologic morbidity that is associated with pituitary tumors is dependent on the specific underproduction or overproduction of a hormone or hormones associated with the tumor.

Hormonal deficiencies - Clinical effects

Growth hormone deficiency:
- Adults - Increased rate of cardiovascular disease, obesity, reduced muscle strength and exercise capacity, and increased cholesterol
- Infants - Hypoglycemia
- Children - Decreased height and growth rate

Gonadotrophin deficiency:
- Men - Diminished libido and impotence; testes shrink in size, but spermatogenesis generally preserved
- Women - Diminished libido and dyspareunia; breast atrophy in chronic deficiency
- Children - Delayed or frank absence of puberty
- Adolescent girls - Present similarly to adult women
Thyrotropin deficiency:
- Malaise, weight gain, lack of energy, cold intolerance, and constipation

Corticotrophin deficiency:
- Unlike primary adrenal insufficiency, mineralocorticoid function (which is dependent on the angiotensin-renin axis) not affected; deficiency limited to glucocorticoids and adrenal androgens
- Initially, symptoms nonspecific (eg, weight loss, lack of energy, malaise); severe adrenal insufficiency may present as a medical emergency

Pan-hypopituitarism:
- Refers to deficiency of several anterior pituitary hormones; may occur in a slowly progressive fashion (eg, pituitary adenomas)

Hormonal overproduction - Clinical effects

Prolactin:
- Hypogonadism, if hyperprolactinemia sustained
- Women - Amenorrhea, galactorrhea, and infertility
- Men - Decreased libido, impotence, and rarely galactorrhea

Growth hormone:
- Children and adolescents - May result in pituitary gigantism
  - Adults - Acromegaly Changes in the size of the hand and feet, coarseness of the face, frontal bossing, and prognathism result. Further changes in the voice, and hirsutism, confirm the diagnosis.
- Acromegaly frequently results in glucose intolerance, with 20% of patients progressing to diabetes mellitus.
- Respiratory difficulty and sleep apnea are fairly common.

Growth hormone
- Cardiac complications result from acromegalic cardiomyopathy.
- Although patients have a bulky appearance, they are generally weak as a result of associated myopathy.
- Carpal tunnel syndrome is seen frequently.
- Lumbar canal stenosis can present with a syndrome resembling amyotrophic lateral sclerosis.
- Acromegaly may be associated with colonic polyps, although an
increased colon cancer incidence has not been shown definitively

Cushing disease:

- Weight gain, centripetal obesity, moon facies, violet striae, easy bruisability, proximal myopathy, and psychiatric changes
- Other possible effects - Arterial hypertension, diabetes, cataracts, glaucoma, and osteoporosis

Epidemiology

- **Frequency**
- **United States**
  - Pituitary tumors represent anywhere between 10% and 15% of all intracranial tumors.
  - Incidental pituitary tumors are found in approximately 10% of autopsies.
  - The incidence of acromegaly is approximately 3 per million. Acromegaly has no sex predilection.
- **International**
  - The incidence of pituitary tumors is probably the same worldwide.
- **Morbidity**
  - Mortality rate related to pituitary tumors is low. Advances in medical and surgical management of these lesions and the availability of hormonal replacement therapies have contributed to successful management.
  - Pituitary apoplexy can be a lethal complication.
  - Morbidity associated with macroadenomas may include permanent visual loss, ophthalmoplegia, and other neurological complications.
  - Tumor recurrence is also a possibility.
  - CNS metastases and, rarely, distant metastases occur with pituitary tumors.
  - Endocrine abnormalities are amenable to correction. However, damage in many organ systems as a result of long-standing uncorrected deficiencies may be irreversible.
- **Race**
• No racial predilection.

• **Gender.**
  • Symptomatic prolactinomas are found more frequently in women.
  • Cushing disease also is more frequent in women (female-to-male ratio 3:1).

• **Age**
  • Most pituitary tumors occur in young adults, but they may be seen in adolescents and elderly persons.
  • Acromegaly usually is seen in the fourth and fifth decades of life.

  **Presentation**
  • The presentation of a pituitary macroadenoma relates to its mass effect and pressure on surrounding structures.
  • Fifty to sixty percent present with visual symptoms due to compression of optic nerve structures.
  • Nonspecific headache can be seen.
  • Lateral extension can result in compression of the cavernous sinuses and may cause ophthalmoplegia, diplopia, and/or ptosis. Talkad et al recently reported an isolated, painful, postganglionic Horner syndrome as the initial sign of lateral extension of a large prolactinoma.\(^{[6]}\)
  • Extension into the sphenoid sinuses can cause spontaneous cerebrospinal fluid (CSF) rhinorrhea.

  **Physical Examination**
  • Macroadenomas can compress optic nerve structures.
  • The optic chiasm is the most frequently affected structure.
  • Bitemporal field defects are the most common findings.
  • **Prolactinomas**
  • In females, galactorrhea may be present on clinical examination. Women undergoing an infertility evaluation may be found to have a prolactinoma.
  • In males, galactorrhea is infrequent; testicles may be decreased in size and may be soft to palpation.

  • **Acromegaly**
  • A multitude of clinical signs can be appreciated by comparing the current facial appearance with prior photographs.
• These changes include large hands and feet (with thick fingers and toes) and coarse facial features with frontal bossing. Women may appear masculinized. Other findings might include prognathism, carpal tunnel syndrome, and voice quality changes.

• Cushing disease:
  • Findings are prominent and include obesity, centripetal fat deposition, proximal myopathy, moon facies, buffalo hump, posterior subcapsular cataracts, arterial hypertension, bruises, and skin striae

Hypopituitarism
Chronic hypopituitarism: results in hypotension, generalized weakness, hypothermia, malaise, and depression.
Acute sudden hypopituitarism (ie, pituitary apoplexy): is associated with shock, coma, and death.
Work up

- **Laboratory studies:** Pituitary mass Visual fields and ophthalmologic evaluation are critical in defining the presence of a chiasmal syndrome.

  - **Prolactinomas:** Serum prolactin levels should be measured in any patient with a suspected sellar or suprasellar mass.

    - If elevated, investigate the possibility of pharmacologic and other factors prior to ordering extensive neuroimaging studies.

    - Serum prolactin level >200 mcg/L in a patient with a macroadenoma greater than 10 mm in size is diagnostic of a prolactinoma. Levels below that range in a macroadenoma suggest hyperprolactinemia secondary to hypothalamic compression.

- **Growth hormone abnormalities:** Growth hormone (GH) levels are elevated in acromegaly but can fluctuate significantly.

- Intravenous (IV) GH levels every 5 minutes for 24 hours may show consistent elevation of GH.

- This is not a practical diagnostic method, but does indicate that a single GH value is not sufficient to make a diagnosis.

  - **IGF-1**

    - **Serum insulinlike growth factor 1 (IGF-1) level:** is the best endocrinologic test for acromegaly. IGF-1 reflects GH concentration in the last 24 hours. Technical factors may limit its usefulness in some laboratories.

    - Oral glucose tolerance test is the definitive test for the diagnosis of acromegaly; a positive result is the failure of GH to decrease to < 1 mcg/L after ingesting 50-100 g of glucose.

      - Thyrotrophin-releasing hormone (TRH), 200 mcg, can be given to increase the test's accuracy. A GH level > 5 mcg/L suggests acromegaly.

      - Failure to decrease the GH concentration to < 2 mcg/L after a glucose load and after TRH stimulation is highly suggestive of acromegaly.
• **Cushing disease and Cushing syndrome:** Twenty-four hour urine is collected for free cortisol. Usually 2 baseline values are obtained.

• **Dexamethasone suppression test:** The physiological basis of this test is a decrease in adrenocorticotropic hormone (ACTH) secretion by the pituitary because of exogenous glucocorticoid administration. One mg of dexamethasone is administered. Serum cortisol level is measured the next morning; it should be < 138 nmol/L (ie, < 5 mcg/dL).

• **Standard low-dose dexamethasone:** Two-day baseline serum and urine cortisol levels are determined. The patient is then given 4 doses of 0.5 mg of dexamethasone at 6-hour intervals. Normal suppression is a serum cortisol level of < 138 nmol/L or a urine level of less than 55 nmol/L.

• If cortisol levels are increased abnormally, corticotrophin-releasing factor (CRF) in a dose of 100 mcg can be given to differentiate between Cushing disease and other causes of hypercortisolism (ie, Cushing syndrome). With pituitary adenomas, cortisol secretion is increased over the baseline.

• **High-dose dexamethasone suppression confirms diagnosis of a pituitary adenoma.** It suppresses the pituitary gland even in the presence of an adenoma. If cortisol levels remain unchanged, the cause of increased cortisol is not a pituitary adenoma.

• **Serum levels of ACTH:** The serum concentration of ACTH is higher than normal (>5.5 pmol/L at 9 am and >2.2 pmol/L at midnight).

• **MRI of the brain** and sellar region with multiplanar thin sections is of critical importance. This provides axial, coronal, and sagittal sections of the sellar contents.

• **CT scan of the brain** with sellar images may be sufficiently specific and can detect tumor calcifications. However, the detail is generally inferior to that of MRI.
• **Cerebral angiography**: is not performed routinely in the workup of sellar mass lesions. It generally is performed when vascular

**Medical Care**

• **Prolactinomas**: The majority of these lesions respond to dopamine receptor agonists. Improvement in visual field abnormalities, resolution of symptoms associated with hyperprolactinemia, and visible diminution of the actual mass can result with treatment.

• **Acromegaly**: Somatostatin analogues (octreotide) can be helpful in the treatment of increased postoperative levels of GH. In some cases, the tumor may shrink modestly.

• Gallstones are a frequent complication of somatostatin-analogue therapy. Dopamine agonists also have been used.

**Surgical Care**

• **Transsphenoidal surgery**: Transsphenoidal microscopic surgery is the most frequent surgical approach for the resection of pituitary tumors. With larger lesions, a transfrontal approach may become necessary to decompress the visual pathways.

• Minimally invasive endoscopic surgery using a 4-mm endoscope through a nostril is a possibility in selective cases.

• The main complication after transsphenoidal surgery (from the endocrine standpoint) is **hypopituitarism**

• **Prolactinomas**: 

  **Microprolactinomas**: Transsphenoidal resection of the tumor offers a chance for a cure without the need for long-standing dopamine agonist therapy; however, many patients choose dopaminergic therapy.

• **Macroadenomas**: that secrete prolactin are best treated with dopamine agonists
• Acromegaly:
  • Transsphenoidal surgery decreases GH levels to less than 5 mcg/L in 60% of cases.
  • Radiotherapy is an alternative, although GH levels may not decrease for 2-4 years.
  • Elevated GH levels may be treated with somatostatin analogues and dopamine agonists