Anterior Pituitary Gland Dysfunction

Dr. B. Paudel

Introduction

- The anterior pituitary gland secretes prolactin, growth hormone, and four trophic hormones: ACTH, TSH, LH, FSH.
- Each trophic hormone stimulates a specific target gland.
- Anterior pituitary function is regulated by hypothalamic hormones that reach the pituitary via portal veins in the pituitary stalk.

Hypothalamic regulation is to stimulate secretion of pituitary hormones, except for prolactin, which is inhibited by hypothalamic dopamine production.

Negative feed back: target organ hormones—neg feed back—stimulation of pituitary hormones including trophins

I. Anterior pituitary dysfunction

- caused by disorders of either the pituitary or hypothalamus.
- Pituitary adenomas are the most common pituitary disorder.
- They are classified by size and function.
- Microadenomas/Macroadenomas and Secretory adenomas /nonsecretory macroadenomas
- Microadenomas: <10 mm in diameter and too small to produce hypopituitarism or mass effects. Clinical manifestations only if they produce excess hormone.

- Macroadenomas: > 10 mm in diameter and may produce pituitary hormone excess, hypopituitarism, and/or mass effects.
- Secretory adenomas produce prolactin, growth hormone, or ACTH.
- Nonsecretory macroadenomas: Cause hypopituitarism or mass effects. Common incidental radiographic findings, seen in approx 10% of the normal population, and do not require therapy.

- Other pituitary or hypothalamic disorders: head trauma, pituitary surgery or radiation, and postpartum pituitary infarction (Sheehan’s syndrome): hypopituitarism.
- Other tumors of the pituitary or hypothalamus (e.g., craniopharyngioma, metastases), inflammatory disorders (e.g., sarcoidosis, histiocytosis X), and infections (e.g., tuberculosis): hypopituitarism or mass effects.
II. Clinical findings.

- may present in several ways.
- Hypopituitarism (deficiency of one or more pituitary hormones),
  1. gonadotropin deficiency is most common,
  2. Secondary hypothyroidism or adrenal failure / adrenal crisis rarely occurs alone.
  3. Secondary adrenal failure --- no hyperkalemia and hyperpigmentation

II. Clinical findings.

- Hormone excess
  1. most commonly results in hyperprolactinemia: secretory adenoma or to nonsecretory lesions damaging hypothalamus or pituitary stalk.
  2. Growth hormone excess (acromegaly): secretory adenomas
  3. ACTH/cortisol excess (Cushing’s disease): secretory adenomas.

II. Clinical findings.

- Mass effects
  1. due to pressure on adjacent structures: headaches and loss of visual fields or acuity.
  2. Hyperprolactinemia: also may be due to mass effect.
  3. Pituitary apoplexy is sudden enlargement of a pituitary tumor due to hemorrhagic necrosis.

II. Clinical findings.

Asymptomatic pituitary adenomas

- Microadenoma: Incidental imaging finding--evaluate for hyperprolactinemia; Cushing’s disease/Cushing’s Syndrome), or acromegaly.
  1. If no pituitary hormone excess exists, therapy is not required.
  2. Incidental imaging of macroadenoma is unusual. Patients should be evaluated for hormone excess and hypopituitarism.

III Diagnosis

- ? Hypopituitarism: clinical signs of target hormone deficiency (e.g., hypothyroidism) or pituitary mass effects.

A. Laboratory evaluation:
- Hypopituitarism: evaluation of target hormone function, including plasma free T4 and a Cortrosyn stimulation test
- In men, plasma testosterone should be measured.
- The best evaluation of gonadal function in women is the menstrual history.

III Diagnosis

B. If a target hormone is deficient
- trophic hormone is measured: secondary/primary target organ dysfunction.
  1. An elevated trophic hormone: indicates primary target gland dysfunction.
  2. In hypopituitarism: trophic hormone levels are not elevated
  3. measurement of trophic hormone levels alone is useless in the diagnosis of hypopituitarism.
Essentials of Diagnosis

- Loss of one, all, or any combination of anterior pituitary hormones.
- ACTH deficiency reduces adrenal secretion of cortisol, testosterone, and epinephrine; aldosterone secretion remains intact.
- Growth hormone (GH) deficiency causes short stature in children; adults experience asthenia, obesity, and increased cardiac mortality.
- Prolactin deficiency inhibits postpartum lactation.
- TSH deficiency causes secondary hypothyroidism.
- LH and follicle-stimulating hormone (FSH) deficiency cause hypogonadism and infertility in men and women.

IV. Anatomic evaluation

- Anatomic evaluation of the pituitary gland and hypothalamus is done best by MRI.
- microadenomas too small to be seen with current techniques.
- The prevalence of incidental microadenomas should be kept in mind when interpreting MRIs.
- Visual acuity and visual fields should be tested when imaging suggests compression of the optic chiasm.

V. Treatment of hypopituitarism.

- Deficient target hormones should be replaced.
- Secondary adrenal failure: early Rx especially if patients are to undergo surgery.
- Infertility due to gonadotropin deficiency may be correctable.

VI. Hyperprolactinemia.

- In women: prolactin-secreting pituitary microadenomas and idiopathic hyperprolactinemia, most common causes of pathologic.
- In men: prolactin-secreting macroadenoma, most common cause.
- Hypothalamic or pituitary lesions that cause deficiency of other pituitary hormones often cause.

Major causes of hyperprolactinemia

- Pregnancy and lactation.
- Prolactin-secreting pituitary adenoma (prolactinoma).
- Idiopathic hyperprolactinemia.
- Drugs:
  1. Dopamine antagonists (phenothiazines, metoclopramide, methyldopa).
  2. Others (verapamil, cimetidine, some antidepressants).
- Interference with synthesis or transport of hypothalamic dopamine.
- Hypothalamic lesions.
- Pituitary macroadenomas.
- Primary hypothyroidism.
- Chronic renal failure.
A. Clinical findings.

Hypogonadotrophic hypogonadism and reduced fertility.

In women:
- amenorrhea or irregular menses and infertility.
- Only approximately half of these women have galactorrhea.
- Prolonged estrogen deficiency: osteoporosis.

In men:
- erectile dysfunction and diminished libido;
- causes androgen deficiency and infertility but not gynecomastia;
- mass effects and hypopituitarism are common.

Pituitary prolactinomas may cosecrete growth hormone and cause acromegaly.
Large tumors may cause headaches, visual symptoms, and pituitary insufficiency.

B. Diagnosis

Hyperprolactinemia is common in young women.

History: medications (metoclopramide)/symptoms of pituitary mass effects or hypothyroidism/pregnancy.

Amenorrhea with/ or galactorrhea: plasma prolactin.
Mild elevations: needs re-confirmed.
Do TSH and a pregnancy test.

C. Therapy

Microadenomas and idiopathic hyperprolactinemia.

- In most patients, hyperprolactinemia does not worsen, and prolactin levels sometimes return to normal.
- Enlargement of microadenomas is rare.
- no Rx: periodic follow-up of prolactin levels and symptoms.
- are treated if infertility or to prevent osteoporosis.
- The dopamine agonists bromocriptine and cabergoline: suppress plasma prolactin and restore normal menses and fertility in most women.
- Initial dosages are bromocriptine, 1.25–2.5 mg PO qhs with a snack, or cabergoline, 0.25 mg twice a week. And monitor prolactin every 2-4 wks.
Microadenomas and idiopathic hyperprolactinemia.
- Maximally effective doses are 2.5 mg bromocriptine tid and 1.5 mg cabergoline twice a week.
- Use barrier contraception, as fertility may be restored quickly.
- Every 2 years, plasma prolactin should be measured after bromocriptine has been withdrawn for several weeks, to determine whether the drug is still needed.
- Transphenoidal resection: who do not respond to or cannot tolerate bromocriptine.

C. Therapy

Prolactin-secreting macroadenomas.
- Must treated with a dopamine agonist: suppresses prolactin levels to normal, reduces tumor size, and improves or corrects abnormal visual fields in 90% of cases.
- Mass effects present: increased to maximally effective levels over a period of several weeks.
- Visual field tests, if initially abnormal, should be repeated 4–6 weeks after therapy is started.
- Pituitary imaging should be repeated 3–4 months after initiation of therapy.

Prolactin-secreting macroadenomas.
- If tumor shrinkage and correction of visual abnormalities are satisfactory—CST
- The full effect on tumor size may take more than 6 months.
- Transphenoidal surgery: is indicated to relieve mass effects and to prevent further tumor growth despite dopamine agonist therapy.
- Surgical cure of macroadenoma is low, so still need further therapy with a dopamine agonist.
- Should not become pregnant unless the tumor has been resected surgically, as the risk of symptomatic enlargement during pregnancy is 15–35%.

VII. Acromegaly & Gigantism
- Excessive GH causes tall stature and gigantism if it occurs before closure of epiphyses. Afterward, acromegaly develops.
- Is mostly due to a GH–secreting pituitary adenoma
- Acromegaly: extremity enlargement, seriously understates the manifestations. The hands enlarge and a doughy, moist handshake is characteristic. The fingers widen, causing patients to enlarge their rings.
- The feet also grow, particularly in width.
- Facial features coarsen since the bones and sinuses of the skull enlarge; hat size increases. The mandible becomes more prominent, causing prognathism and malocclusion. Tooth spacing widens.
- Macroglossia occurs, as does hypertrophy of pharyngeal and laryngeal tissue; this causes a deep, coarse voice
- Arthritis or carpal tunnel syndrome may develop.
- GH-secreting pituitary tumors usually cause some degree of hypogonadism, either by cosecretion of prolactin or by direct pressure upon normal pituitary tissue.
- The pituitary adenoma may cause headaches and vision loss.
- Morbidity from cardiovascular disease is increased.
- Obstructive sleep apnea may occur.
- Secondary hypothyroidism sometimes occurs; hypopituitarism is unusual.
Features of acromegaly/gigantism. A 22-year-old man with gigantism due to excess growth hormone is shown to the left of his identical twin. The increased height and prognathism (A) and enlarged hand (B) and foot (C) of the affected twin are apparent. Their clinical features began to diverge at the age of approximately 13 years.

A. Diagnosis.
- Plasma somatomedin-C (insulin-like growth factor I), which mediates most effects of growth hormone, is the best diagnostic test.
- Marked elevations establish the diagnosis.
- If somatomedin-C levels are elevated only moderately, --- 75 mg glucose orally and measure serum growth hormone q30min for 2 hours--- confirms diagnosis.
- Failure to suppress growth hormone to less than 2 ng/ml confirms the diagnosis of acromegaly.
- Once the diagnosis is made, the pituitary should be imaged.

Essentials of Diagnosis
- Excessive growth of hands, feet, jaw and internal organs; or gigantism before closure of epiphyses.
- Coarsening facial features; deeper voice.
- Amenorrhea, headaches, visual field loss, sweating, weakness.
- Soft, doughy, sweaty handshake.
- Serum GH not suppressed following oral glucose.
- Elevated IGF-1.
- Imaging: Terminal phalangeal "tufting" on radiographs. Computed tomography (CT) or MRI demonstration of pituitary tumor in 90%.

B. Therapy.
- Transsphenoidal resection of the pituitary adenoma: treatment of choice.
- Most patients have macroadenomas, and complete tumor resection with cure of acromegaly often is impossible.
- If somatomedin-C levels remain elevated after surgery, radiotherapy is used to prevent regrowth of the tumor and to control acromegaly.
- The full effect of radiotherapy on growth hormone secretion may take up to 10 years.
- Octreotide can be used to suppress growth hormone secretion while the effect of radiation is being awaited. A dose of 10–30 mg IM monthly suppresses somatomedin-C to normal in most patients.