Pituitary Disorders

Pearls

Whitney Woodmansee M.D.
Director, Clinical Neuroendocrine Program
Brigham and Women's Hospital / Harvard Medical School
Boston, MA
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Learning Objectives

Lecture is a general neuroendocrine review.
Goal is to discuss:
- Neuroendocrine physiology
- Diagnostic approach and management of pituitary disorders

Pituitary Gland

Anterior Pituitary
- Adenohypophysis
- 80% of the gland
- Derived from Rathke’s pouch (oral ectoderm)
- Comprised of 5 cell types
- Secretes 6+ neuropeptides
- Controlled by RH from the hypothalamus & feedback from target organs.

Posterior Pituitary
- Neurohypophysis
- 20% of the gland
- Direct extension of the hypothalamus.
- Terminal axons from SON and PVN of hypothalamic neurons
- Hormone produced in hypothalamus, stored in pituitary.

Pituitary Physiology

Anterior Pituitary
- Hypothalamic releasing hormone
- Produces anterior pituitary hormone
- Target organ

Posterior Pituitary
- Hypothalamus
- Supraoptic nc
- Paraventricular nc
- Axons
- Posterior pituitary
- AVP
- Oxytocin

Approach to Pituitary Disorders

Evaluate:
- Mass effects
- Pituitary hyperfunction
  - “Suppression tests”
- Pituitary hypofunction
  - “Stimulation tests”
Pituitary Disorders

- **Anterior Pituitary**
  - Sellar Masses
    - Pituitary Adenoma
    - Mass effect
    - Hyperfunction
    - Hypofunction
  - Apoplexy
  - Hypopituitarism

- **Posterior Pituitary**
  - Overproduction of AVP
    - Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH)
  - Underproduction of AVP
    - Diabetes Insipidus
      - Central (pituitary)
      - Nephrogenic

History:
- Question regarding endocrine hypo or hyper function. Think of anterior & posterior pituitary function.

- **Hypofunction**
  - Hypothyroidism
  - Hypogonadism
  - Adrenal Insufficiency
  - GH Deficiency
- **Hyperfunction**
  - Hyperthyroidism
  - Prolactin excess
  - GH excess
  - Neurological symptoms: HA, visual disturbance.

Patient Evaluation

- **History:**
  - Question regarding endocrine hypo or hyper function. Think of anterior & posterior pituitary function.

- **Deficiency:**
  - Hypothyroidism: dry skin, puffy, delayed DTR's
  - Hypogonadism: loss of body hair, testicular softness.
  - Adrenal insufficiency: low BP. (Recall no hyperpigmentation as with Addison's)
  - GH deficiency: central adiposity

- **Excess:**
  - Hyperthyroidism: hypermetabolic, soft skin, tremor, lid lag, increased DTR's, tachycardia
  - Hypergonadism: Not much to see.
  - Cortisol excess: Cushings' syndrome features.
  - GH excess: Acromegaly features.
  - Prolactin excess: hypogonadism, galactorrhea

Patient Evaluation

- **Physical Exam:** Look for clues of hormone status.

  - **Deficiency:**
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Patient Evaluation

- **Physical Exam (continued):**
  - Good neurologic exam:
    - look for cranial nerve palsies
    - assess visual acuity.
  - Visual fields by confrontation.

Patient Evaluation

- **Differential Diagnosis of Sellar/Parasellar Lesions**

<table>
<thead>
<tr>
<th>Benign Tumors</th>
<th>Granulomatous, Infectious, and Inflammatory</th>
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<tbody>
<tr>
<td>Pituitary adenoma (carcinoma)</td>
<td>Lymphohistiocytic hypophysitis</td>
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<td>Meningioma</td>
<td>Abscess</td>
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<td>Cell Rest Tumors</td>
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<td>Cranopharyngioma</td>
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<td>Primitive Germ Cell Tumors</td>
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<td>Astrocytoma</td>
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Pituitary Adenomas: Epidemiology

- Pituitary adenomas are the 3rd most common brain tumor.
- They account for 10-15% of all intracranial tumors.
  - MRI studies 14.4%
  - Autopsy series 12-22.5%
- They are classified according to size.
  - Microadenomas - < 10mm
  - Macroadenomas - > 10 mm

Pituitary Tumorigenesis

- Chromosomal lesions
- Oncogene Activation
- Aberrant Signal Transduction
- Aberrant Growth Factors
- Loss of Tumor Suppressors

Case 1-1

- 24 yr old woman G2P2, menses never resumed after d/c OCP’s. ROS: HA’s, no visual or other neuro c/o. + fatigue, depression, and cold intolerance. Can’t seem to lose weight she gained with last pregnancy. + galactorrhea x 6 mos.
- Meds: none
- PE: normal. What should you look for on PE? What is the differential diagnosis?

Case 1-2

Labs
- E2 11; LH 6; FSH 5
- IGF-1 nl 183, GH 1
- α SU 0.8 (nl)
- cortisol 8
- FT4 1, TSH 1.5
- Prolactin 283
- What is the single most important test to order to exclude a physiologic cause of elevated prolactin?
  - Hematocrit
  - Ferritin
  - Pregnancy test
  - Chest Xray

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Case 1-3

**Labs**
- E2 11; LH 6; FSH 5
- IGF-1 nl 183, GH 1
- α SU 0.8 (nl)
- HCG negative
- cortisol 8
- FT4 1, TSH 1.5
- Prolactin 283

- How do you interpret the lab values?
- What is the next step?
- What is the diagnosis?
- What are the treatment options?

Clinical Presentation of Hyperprolactinemia

- Galactorrhea **
- Hypogonadism **
  - Amenorrhea / menstrual irregularities
  - Infertility
  - Erectile dysfunction
  - Growth arrest / delayed puberty
- Hirsutism
- Gynecomastia
- Mass effects if tumor is large

DDx: Hyperprolactinemia

- Pregnancy (Normal) - Need to rule out in women.
- Drugs - Take a good history.
  - DA depletion or antagonists-usually psychoactive
  - Estrogens
- Primary Hypothyroidism - Check TSH
- Pituitary tumor (prolactinoma) - Pituitary MRI
- Neurogenic - chest wall lesion, suckling
- Cirrhosis
- Ectopic production - ovarian tumors
- Idiopathic

Prolactinomas: Treatment

**Treatment Options:**
Medical Therapy with DA agonists *****
- Bromocriptine, Cabergoline

- Micros: 90-96% response, Macros: 60-75% response

Transsphenoidal resection
- 36-53% cure rate for micros, lower for macros.
- Up to a 40% recurrence rate.

Radiation
- Works in a minority of patients over a long time.


Case 2-1

57 yr old male with multiple medical problems who recently presented to PCP with SOB, CP. Found to have new onset CHF, hypoxia
- LVEF 25%, cardiac cath normal.

PMH: Rheumatoid arthritis, gout, nephrolithiasis, colon polyps, carpal tunnel syndrome, COPD.

Meds: Captopril, allopurinol, ASA, prednisone 5mg/d, methotrexate.

Case 2-2

PE: 126/88 P82.

Neck: 25g thyroid.

Lungs: bibasilar rales. RRR +S3

Abd: obese o/w normal.

Ext: Large doughy hands. Size 13 feet, wide. No active joint inflammation. Multiple skin tags.

What diagnosis are you considering?
What lab tests would you like?
Clinical Features of Acromegaly

- Soft tissue hypertrophy
- Arthritis / Carpal tunnel syndrome
- Increased hand, head, foot size.
- Organomegaly
  - Cardiomegaly with CHF
- Metabolic Disturbances
  - Diabetes Mellitus
- Obstructive Sleep Apnea
- Colon polyps/cancer
- Increased mortality

Case 2-3

Labs:
GH 2.4; IGF-1 985 (high)
FT4 = 0.7 (normal 0.7-2.7), TSH 0.4
α SU 3.1 (high)
FSH 11, LH 7.4, testosterone 234 (low normal)
prolactin 7 (normal)

What diagnosis are you considering now?
Would you order any radiologic tests at this time?

Case 2-4

What test can be used to confirm GH hypersecretion?
A. Midnight salivary GH
B. Oral glucose tolerance test for GH suppression
C. Urinary IGF-1
D. Serum IGFBP-3

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Acromegaly: Treatment

- Surgery
- Medical Therapy
  - Somatostatin Analogs
    - Octreotide LAR
    - Lanreotide
  - Pegvisomant
- Radiation
  - Conventional
  - Radiosurgery

Goal is “biochemical cure”
Normal IGF-I
Normal GH suppression

Case 3-1

- 50 yr old woman referred to evaluate weight gain.
Reports rapid 50lb wt gain.
No HA, visual, neuro complaints.
“Dr. you must do something about this weight!!!”
PMH: hypothyroidism, HTN, “borderline DM.”
FMH: obesity, thyroid disease
Meds: LT4, lisinopril, ASA

PE: 176/90 P72
Moon face, dorsocervical and supraclavicular fat pads
Thyroid 30g pebbly
CTA B, RRR
Central obesity
Abd: “purple striae
1+ edema
Neuro: normal

What would you recommend?
Clinical Features of Cushing’s Syndrome

- Central obesity
- Skin changes
- Hirsutism
- Menstrual irregularities
- Hypertension, CAD
- Muscle weakness
- Osteoporosis
- Mood disturbances

Case 3-1

You are concerned about Cushing’s syndrome in this patient. What is the best first step in evaluating this patient?

A. Screen for hypercortisolism
B. Obtain a pituitary MRI
C. Obtain a CT scan of the adrenal glands
D. Perform inferior petrosal sinus sampling to determine if the source of excess cortisol is an ACTH producing pituitary adenoma

Cushing’s Syndrome

Step 1: Document syndrome of hypercortisolism
- Screening tests for hypercortisolism include:
  - 24 hour urine free cortisol
  - Late night salivary cortisol levels
  - 1mg overnight dexamethasone test

Step 2: Determine whether it is ACTH dependent or independent.

Step 3: Localize tumor and remove.

Thyrotropinomas

- Very rare (approx. 0.5-1% of pituitary adenomas)
- Clinical presentation:
  - Hypothyroidism, goiter
    - Patients often treated previously with thyroidectomy / I131
  - 70% present with macroadenomas
- Diagnosis:
  - Elevated T4, T3
  - Inappropriately NORMAL or elevated TSH
- Treatment:
  - Surgery (treatment of choice), Somatostatin analogs

Nonfunctioning Adenomas

- Appear clinically inactive.
- Often secrete α subunit, β subunit or intact gonadotropins.
- One third of all pituitary tumors.
- Often present with mass effect symptoms only and no evidence of hormonal overactivity.
- Some patients with large tumors present with panhypopituitarism.
- Treatment of choice is surgery
### Pituitary Adenoma

**Therapeutic considerations**

- Treating symptoms related to mass effects
  - Restoration or preservation of vision
  - Neurologic improvements – cranial nerves, headaches
- Correcting pituitary hyperfunction.
  - Aim for biochemical cure
  - Medical therapy for hormonal replacement

### Hypopituitarism

**Management**

- Treatment based on correcting hormonal deficiencies.
  - Thyroid - levothyroxine (** remember TSH cannot guide Rx**)
  - Adrenal - HCC or prednisone. Use lowest dose possible.
  - Gonad - Men require testosterone, women require HRT (OCP)
  - Growth hormone - Can treat with rhGH.
  - Prolactin - no replacement available or required.
  - Posterior pituitary – Desmopressin (DDAVP)
- Medical Alert Jewelry

### Pituitary Disease

**Summary**

**Main “take home” messages:**

1. When evaluating patients with pituitary disorders, let pituitary physiology be your guide. Evaluate:
   - Mass effects (headache, visual dysfunction)
   - Pituitary hyperfunction
     - GH (Acromegaly)
     - ACTH (Cushing’s disease – hypercortisolism)
     - Prolactin (galactorrhea, menstrual disorders, erectile dysfunction)
     - TSH (hyperthyroidism)
   - Pituitary hypofunction – all hormonal systems
2. Treatment is aimed at restoring normal pituitary function and can include: surgery, hormonal replacement, medications

### General References

- Best Pract Res Clin Endocrinol Metab. 2009 Oct;23(5): - This volume has multiple chapters on various pituitary topics.