Sellar Masses

Focus on Hyperprolactinemia

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Disclosures: No conflicts related to hyperprolactinemia

If mentioned, investigational agents will be noted as such

Objectives:
1. Review physiologic and pathologic causes of hyperprolactinemia
2. Identify the indications for treatment of hyperprolactinemia
3. Illustrate the importance of pituitary imaging and other tests to exclude the possibility of “pseudoprolactinoma”
Normal head MRI, coronal view

Patient facing us

Cavernous sinus (R)

Optic chiasm

Pituitary gland
Pituitary Tumor Types

Thyrotroph (1%)
Hyperthyroidism

Corticotroph (10-15%)
Cushings Disease

Gonadotroph (15-40%)
“Clinically nonfunctioning”
Visual field loss
Hypopituitarism

Somatotroph (10-20%)
Acromegaly

Lactotroph (40-50%)
Hyperprolactinemia

“Clinically nonfunctioning”
Physiology - control of PRL secretion
Causes of hyperprolactinemia

**Physiological**
- Pregnancy, postpartum
- Nursing
- Sleep
- Physical exertion
- Food
- Stress

**Pharmacological**
- Antihypertensives
- Psychotropics
- Metoclopramide
- Opiates
- Cocaine
- Protease Inhibitors

**Pathological**

*Pituitary-hypothalamic*
- Pituitary tumors
- Other sellar masses/cysts
- Infiltrative disorders
- Hypothalamic disease

**Other**
- Primary hypothyroidism
- Seizures
- Polycystic ovary disease
- Neurogenic/ chest wall causes
- Renal insufficiency
- Cirrhosis
Hyperprolactinemia cases

CASE

• 28 year old woman referred by primary care provider (PCP) for prolactin (PRL) of 55 ng/ml (nl<20) found in evaluation of amenorrhea

• Healthy, no meds, periods were previously regular

• Normal physical exam except trace galactorrhea
Hyperprolactinemia

**SYMPTOMS**

- Hypogonadism
  - amenorrhea, other abnormalities
  - infertility
  - decreased libido
  - erectile dysfunction

- Galactorrhea, gynecomastia

- Hirsutism, acne

- Mass effect (macroadenomas)

What is the next step?
Hyperprolactinemia

EVALUATION

• Repeat PRL

• Exclude other causes of high PRL
  - pregnancy
  - primary hypothyroidism
  - medications
  - miscellaneous

The PRL is high again and all of these are absent. What next?
Hyperprolactinemia

EVALUATION FOR PROLACTINOMA

• Repeat PRL

• Exclude other causes of high PRL
  - pregnancy
  - primary hypothyroidism
  - medications
  - miscellaneous

• Obtain head MRI
5mm hypolucency in left side of pituitary; probable microadenoma

What is the next step?
Is there an indication for treatment (Tx)?

Unlike other pituitary tumor subtypes, not always, but yes, if:

1. Macroadenoma (tumor >1cm)
2. Hypogonadism
3. Infertility
4. Enlarging microadenoma
5. Bothersome galactorrhea, androgenic symptoms, ?HA

Natural history studies: most microadenomas remain stable without Tx
But all patients should be followed for the small chance of progression
Low spinal BMD in women with hyperprolactinemic amenorrhea

CT Spine Mineral Content (mg/K$_2$HPO$_4$/cm$^3$)

Klibanski JCEM 1988
Hyperprolactinemia

CASE

• Cabergoline (cbg) initiated

• PRL normal on ½ pill weekly (0.25 mg/wk)

• Periods resumed in 3 months

• Lesion on MRI decreased in size at 1 year

This is a typical, simple case in which everything went well, but……
Dopamine Agonists and the Risk of Cardiac-Valve Regurgitation

René Schade, M.D., Frank Andersohn, M.D., Samy Suissa, Ph.D., Wilhelm Haverkamp, M.D., Ph.D., and Edeltraut Garbe, M.D., Ph.D.

A patient taking cbg 1mg/wk would reach Zanettini’s study cumulative dose in 77.2 yrs.
A patient on 0.25mg/wk would reach this dose in 308.8 yrs!

The majority of studies in hyperprolactinemia patients on cabergoline show no increased risk.
Each of these patients had mild to moderate hyperprolactinemia and many had already been diagnosed as having a prolactinoma. In some cases, treatment with a dopamine agonist had already been initiated. Provide a second opinion after reviewing the scan.
Hyperprolactinemia

CASE

• 35 yo F c/o galactorrhea, irregular pds
• Gyn measured PRL: 54 ng/ml (nl<20)
• Dx: PRL’oma → dopamine agonist initiated
• PRL normal, periods more regular; c/o HA
• Head MRI obtained → referred for further Tx

What is the next step?
CASE

- 41 yo F with persistent postpartum galactorrhea, PRL 55.9
- Periods regular on oral contraceptive pills (OCPs), 15 lb weight gain, mild depression
- Normal physical exam except trace galactorrhea, blood pressure (BP) 146/90

Given a prescription for cabergoline

Sees you for a second opinion. What do you say?
Hyperprolactinemia

CASE

• 24 yo marathon runner c/o amenorrhea
• Dx’d as 2° exercise; stopped running; achy, tired

• Age 32 saw endocrinologist for temperature intolerance
• PRL 33.3 ng/ml (nl<20)

• Dx: PRL’oma → bromocriptine initiated
• PRL normal, persistent amenorrhea

• Pt read about PRL, asked for scan; not done
• Changed endocrinologists → head MRI obtained
CASE

32 yo woman with postpartum galactorrhea complained of (c/o) fatigue, cold intolerance

Primary care physician (PCP) questioned possibility of Sheehan’s; measured hormones
- PRL 48 ng/ml (<20)
- Free T4 index 1.2 (4-12)
- Cortrosyn stimulation test normal

Head MRI: Brain tumor -> referred for med Tx

Could this be Sheehan’s? What would you like to do next?
Hyperprolactinemia

CASE

- 19 yo F referred for prolactinoma treatment
  “I’m here to get started on a pill for my brain tumor”
- Amenorrhea: PRL by PCP: 25 ng/ml (nl <20)
- Head MRI abnormal → referred for treatment of PRL’oma
- Positive ROS (depression, HA, dizziness, bruising, nocturia, fatigue, weight gain, hot flashes)
- PEx: borderline postural blood pressure, no Cushingoid or acromegalic features, no galactorrhea

Does she leave with the prescription?
45 yo M saw primary care physician (PCP) requesting sildenafil for erectile dysfunction

PCP performed blood tests:
- testosterone low 167 ng/dl (nl 240-950)
- PRL high 84 ng/ml (nl<20)
- told patient tx with dopamine agonist likely (instead of sildenafil) → referred to endocrinologist → MRI
25 YO F MIT graduate student presents to university health service with blurred vision

PMH: healthy (remote history of seizures)

Gyn Hx: recent amenorrhea (since arriving in Boston for grad school)

PEx: 5’4”, 148 lbs, BP 110/70, P 70, no evidence of hormone excess or deficiency
Hyperprolactinemia

**CASE**

- hCG negative, fasting glucose 82, chemistries essentially nl (Na+ 134)
- PRL high - 49, repeated 57 ng/ml (nl <20)
- LH 1.5, FSH 1.3, androgens nl
- Normal TSH, free T4, morning cortisol
- Negative eye exam → referred to Massachusetts Eye & Ear Infirmary (MEEI)
CASE

38 yo F presented requesting GH replacement

Past hx: 1982 amenorrhea, galactorrhea → transsphenoidal surgery (TSS) for PRL’oma → cured

Years later, amenorrhea, HAs, PRL 37 (nl \( \leq 20 \)); MRI “slightly abnormal” → recurrence

Bromocriptine (bcr) → fainted → tested for hypoadrenalism → hypopituitarism dx’d & tx’d; felt better, but not normal

F/U MRI on 1 year bcr: “30% decrease in size to 1cm”
CASE

• Read about GH replacement on internet; noted similarities (abdominal weight gain, fatigue)
• Requested testing by endocrinologist; he declined
• IGF-I 110 ng/ml (nl 106-368)
• ITT: glucose nadir 21, peak GH 1.5 ng/ml
• Very eager to begin GH; asks when she can start

Will you start growth hormone?
Sellar masses are not always pituitary adenomas

~1500 transsphenoidal procedures performed at MGH 1998 – 2009

116 cases (7.9%) were not pituitary adenomas

*Other includes chondrosarcomas, germinomas, osteogenic sarcoma, fibrosarcoma, ependymoma, hyperplasia, hemangioma, infection, papilloma, squamous carcinoma, fibrous dysplasia, sphenoid sinusitis, sinonasal undifferentiated carcinoma and unspecified cyst

One third had hyperprolactinemia and many were initially misdiagnosed as prolactinoma
Hyperprolactinemia

THESE CASES ILLUSTRATE THE IMPORTANCE OF

➢ Obtaining a head scan when PRL is elevated - even mildly (and not due to pregnancy, meds, 1° hypothyroidism, misc causes)

➢ Considering other hormone-secreting pituitary abnormalities (Cushing’s, acromegaly, TSHomas)

➢ Being sure the degree of PRL elevation is appropriate for the size of the lesion (ie R/O pseudoprolactinoma)
Sellar Masses

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QUESTIONS?