Management of hyperprolactinemia

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Case 1

- A 33-year-old lady is seen for delayed menses
- Married for 2 years
- No pregnancy despite attempts
- Prolactin 120 ng (or mcg) (normal < 25) [1520 mIU (normal <530)]
- **How would you approach?**

Causes of hyperprolactinemia

- Prolactinoma
- Drugs:
  - antipsychotics, SSRI, estrogen, methyldopa, metoclopramide, domperidone, verapamil
- Pituitary/hypothalamic tumors or disorders
- Hypothyroidism
- CKD
- Chest wall injury
- Idiopathic

Manifestations of hyperprolactinemia

- Oligomenorrhea
- Amenorrhea
- Infertility (can occur with normal menses)
- Galactorrhea
- Erectile dysfunction (in men)
- Headache

Evaluation of high prolactin

- Are there symptoms?
- Always do TSH, serum creatinine
- How high is the prolactin level?
  - > 200 is suggestive of prolactinoma
  - Mild increase (26 -40) can be due to: physical or emotional stress, meal, breast stimulation
  - If mild increase, repeat test fasting

Evaluation of high prolactin

- If high TSH (primary hypothyroidism):
  - Treat with thyroxine
  - Once TSH is normal, repeat prolactin
  - If prolactin is still high, do MRI pituitary with contrast

Evaluation of high prolactin

- If there is a suspicion of a drug effect:
  - History is very important
    - **Relation of high prolactin to starting the medication**
  - Stop the drug if possible
  - If not possible, switch to another medication with similar action
  - Consult psychiatrist before stopping antipsychotic medications
  - Check prolactin after 3 days

Evaluation of high prolactin

- **Do NOT start treatment before doing MRI**

1)If MRI showed pituitary lesion:

  - **If prolactin is > 200**
    - Suggestive of prolactinoma
  - **If prolactin 26-200:**
    - Still can be prolactinoma
    - Or pituitary tumor

Evaluation of high prolactin

1) If MRI is **NORMAL**:

- Rule out other causes
- If no cause is found:
  - **Idiopathic hyperprolactinemia**
  - Can try treatment if there are symptoms
  - If no symptoms: no treatment is needed

Prolactinoma

- **Size < 1 cm = microprolactioma**
- **Size ≥ 1 cm = macroprolactinoma**

When to treat high prolactin?

1) Symptoms of hypogonadism (amenorrhea, oligomenorrhea, infertility, erectile dysfunction)
2) Neurologic symptoms due to the size of the tumor (impaired vision or headache)
3) Macroadenoma or if the tumor extends outside the sella, or elevates optic chiasm, or invades cavernous or sphenoid sinuses
4) Disturbing galactorrhea

Treatment of hyperprolactinemia

- **Dopamine agonists:**

  1) Bromocriptine

  - Low cost
  - Start 1.25 mg at bedtime
  - ↑ after 1 week to 1.25 mg bid
    - After breakfast, after dinner
  - Switch to cabergoline if intolerance or inadequate response

Treatment of hyperprolactinemia

2) Cabergoline

- 1st choice
- More effective than bromocriptine
- Less side effects than bromocriptine
- Higher cost
- Start by 0.25 mg twice weekly at bedtime
- Safe in pregnancy
- If using > 2 mg/week, consider cardiac echo monitoring for valve disease

Follow up after treatment of hyperprolactinemia

- Advise the patient to **stop** treatment if she gets pregnant
- Check prolactin after 1 month
- Assess symptoms (menses, headaches,…)
- Assess for side effects (nausea, dizziness)
- If intolerance or resistance to bromocriptine, switch to cabergoline

Follow up after treatment of hyperprolactinemia

- Increase drug dose according to prolactin level
- Target is normal prolactin level and ↓ symptoms
- Decreasing tumor size is NOT the target

1) If normal prolactin:

  - Continue same dose of medication
  - Gonadal function may take **few months** to return

Follow up after treatment of hyperprolactinemia

2) If prolactin is still high :

- Increase dose of medications
  - Bromocriptine up to 5 mg bid
  - Cabergoline 1.5 mg twice/week (higher dose can be used)
- Continue same dose once prolactin is normal
- Some patients will have no symptoms with mildly high prolactin. Can keep same dose

Long term follow up of hyperprolactinemia

- Check prolactin initially every month
- Stop treatment if pregnancy
- Repeat MRI at 6-12 months (if prolactinoma)
- Treatment for at least 1 year
- **Prolactinoma**:
  - If prolactin is normal for 1 year & no adenoma on MRI:
    - Reduce dose of drug
    - Check prolactin every 3 months
  - If prolactin is normal and no adenoma on MRI for 2 years
    - Stop drug and monitor

Follow up of idiopathic hyperprolactinemia

- High prolactin and normal MRI
- Some may have small adenomas not visible on MRI
- If no symptoms, no treatment is needed
- If symptoms, treat
- Check prolactin every 2-3 months
- Reduce drug dose to keep prolactin normal
- If normal prolactin for 2 years, try stopping the drug

Hyperprolactinemia: difficult cases

- No response to treatment
  - **25% with bromocriptine**
  - **10% with cabergoline**
- May respond to ↑↑ doses of cabergoline (> 2 mg/week)
- Intolerance to both bromocriptine & cabergoline
- Refer to gynecology:
  - Clomiphene to help with pregnancy
  - Estrogen & progesterone (if pregnancy is not an issue)
- For men:
  - hCG if attempting fertility
  - Testosterone if fertility is not desired

Prolactinoma: when to do surgery?

1. Intolerance to medical therapy
2. Inadequate response to medical therapy
3. Pituitary apoplexy (hemorrhage) with neurological deficits

Endocrine society guideline. J Clin Endocrinol Metab 2011;96:273.

Prolactinoma in pregnancy

- Stop treatment
- Those with microprolactinoma usually do fine
- Do not follow prolactin (it will be high)
- Generally, no need for MRI
- If macroprolactinoma, some may need treatment
- Patients with new symptoms: do formal visual field exam and MRI **without** contrast
- Refer to specialist