43 year old man with low libido

Katie Stanley, MD
August 16, 2012
HPI

- 43 yo M with history of heroin addiction on methadone maintenance
- Reported low libido to PCP
- PCP checked testosterone and found to be low per pt
- Erectile function decreased
- Shaves 1x/wk but unchanged
- Has multiple children but none for 14 yrs despite unprotected sexual activity with wife
HPI continued

- Notes increased HA x 3 yrs, mild
- No visual changes
- No galactorrhea
- +snoring but feels refreshed after sleep
- 100 lb weight gain since quitting heroin
- No history of testicular torsion, infection, no masses or change in size
Past Medical History

- Type 2 DM
- Pt reports BGs 90s-low 100s
- Heroin addiction on methadone wean
Medications

- Metformin 500 mg daily
- Methadone 70 mg daily
Family History

- No known hypogonadism, pubertal disorders, brain or pituitary tumors
Social History

- Married
- Has 13 children but none with current wife
- History of heroin use
  - Inhaled, never injected
- No current tobacco or alcohol use
Physical Exam

- Wt 123.2 kg, Ht 170.2 cm, BMI 42.5
- P 59, R 18, BP 128/66
- Gen: Well appearing, obese, NAD
- HEENT: PEERL, EOMI, visual fields intact to confrontation
- Neck: NL thyroid
- CV: RRR, nl heart sounds
- Resp: CTAB
- GI: Soft, ND/NT, nl BS
- MSK: No edema, nl ROM
- Neuro: A+O x 3, nl reflexes
- Skin: No rashes or lesions
- GU: Testes 5 cm bilaterally, nl consistency, no masses, normal male distribution of pubic hair
Differential diagnosis of low testosterone

Primary hypogonadism
- Congenital: Klinefelter, cryptorchidism, LH receptor mutations, etc.
- Infections, eg mumps
- Radiation
- Alkylating agents
- Ketoconazole
- Torsion
- Trauma
- Autoimmune
- Chronic renal failure
- Idiopathic

Secondary hypogonadism
- Congenital: Kallman, GNRH mutation
- Hyperprolactinemia
- Chronic glucocorticoids
- Chronic opioids
- Chronic systemic illness
- Obesity
- OSA
- Tumors, eg pituitary adenomas, craniopharyngioma
- Infections, eg TB, syphilis, fungal
- Infiltrative, eg LCH, sarcoidosis, lymphocytic hypophysitis, hemochromatosis
- Trauma
- Idiopathic
Labs

- Total testosterone 45 ng/dL
- Free testosterone 16 pg/mL
- LH 3.6
- FSH 2.2
- Prolactin 8.62
- CBC: WBC 6.7, Hgb 12.5, HCT 38.5, RBC 5.60, MCG 68.8, Plts 281
- Fe 44, ferritin 199, TIBC 263, % saturation 16.7
- PSA 1.04
- BMP: Na 139, K 3.7, Cl 104, HCO3 25, BUN 9, Cr 1.1, Glu 115, Ca 9.0
Pituitary gland moderately atrophic with heterogeneous, mildly diminished enhancement, suggestion of nodularity within left aspect of gland, no discrete post pit identified, ? Of prior insult Including granulomatous disease
Further history:
- No night sweats/fever
- TB risk factors: +homelessness, incarceration, has been previously tested and negative
- No chronic cough
- No diarrhea
- No bone pain, arthralgias
- Does note nocturia 3-4x/night, drinking 2x/night x ~ 3 yr
Further work-up continued

- CMP: Na 138, K 4.0, Cl 103, HCO 26, BUN 12, Cr 1.1, Glu 94, Ca 8.9, Prot 7.6, Alb 3.9, Bili 0.1, Alk phos 103, AST 18, ALT 29
- Serum osm 280 (urine osm not done)
- CRP 22 (<5), ESR 31 (0-15)
- Quantiferon gold negative
- ACE 36.5 (8-52)
- TSH 2.62, FT4 0.92, T3 122
- ACTH 19.9, cortisol 10.4
- IGF-1 134 (101-267)
- CXR: No signs of sarcoid, TB, LCH
- Plain films of skull, mandible, femurs, humerus: No signs of LCH
Questions

- Yield of MRI in secondary hypogonadism?
- How do opioids cause hypogonadism?
- Does his MRI suggest a diagnosis?
- Any other workup to do?
- When to repeat MRI?
- Biopsy?
MRI in Hypogonadotrophic Hypogonadism

- 1996 study of 167 men with testosterone <230 ng/dL
  - Empty sella in 6.7%, macroadenoma 2.4%, microadenoma 6%, hypothalamic lesion 1.2%
  - TT 121 +/-66 vs. 177+/1 40
  - 21.2% in lowest quintile of total testosterone

- 2003 study of 51 men with TT<300 or FT< 1.5 ng/dL
  - 4 with pit adenoma: 3 with elevated PRL, 1 with TT<200
  - 9 with empty sella

- 2004 study of 120 men with idiopathic HH found 10.7% with irregularly contrasting pituitary
  - No healthy controls had this finding
  - Not typical of LCH; CXR, PPD, ACE to r/o sarcoid and TB
  - Planned “close follow up”
Opioids and Hypogonadism

- 103 men on maintenance treatment, 64.5% on methadone vs. 27.8% on buprenorphine had low testosterone.
- 54 men on opioids for chronic pain had significantly lower free and total testosterone than controls.
- Chronic heroin use may be associated with increased pituitary volume, decreased response to GnRH stimulation testing.
- Mechanisms:
  - GnRH
  - Negative feedback
<table>
<thead>
<tr>
<th>Type of Inflammation</th>
<th>Pt Characteristics</th>
<th>Endo Characteristics</th>
<th>Associated Sxs</th>
<th>MRI Appearance</th>
<th>Histological Appearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB hypophysisis</td>
<td>Developing world, other signs of active TB usually but not always present</td>
<td>Often presents with ant pit dysfxn incl hyperPRL, DI</td>
<td>HA common and early, visual disturbances</td>
<td>Sellar mass, thickening/ nodularity of stalk</td>
<td>Central necrosis surrounded by infl cells</td>
</tr>
<tr>
<td>Pituitary abscess</td>
<td>Rare, chronic and indolent sxs</td>
<td>60% ant hypopit (GH&gt;GT&gt;ACTH/TSH), DI 28%, hyperPRL 15%</td>
<td>Long standing HA, visual disturbances (50%), meningitic signs, fever/WBC</td>
<td>Round sellar cystic lesion, hypo or iso on T1, iso or hyper on T2, peripheral gad enhanced</td>
<td>Gram positive bacteria</td>
</tr>
<tr>
<td>Fungal hypophysisis</td>
<td>Rare, often immunocompromised (aspergillosis)</td>
<td>Depends on extent, rare</td>
<td>Visual sx sx prominent, HA, fever</td>
<td>Mass lesion</td>
<td></td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>Young and middle-aged adults</td>
<td>DI 25-55% neurosarcoid, hyperPRL 3-32%, ant deficiencies esp hypogonadism</td>
<td>Variable cough, dyspnea, CP, skin lesions</td>
<td>Absence of T1 hyperintensity, lesions iso on T1, gad enhanced</td>
<td>Non-caseating granulomas</td>
</tr>
<tr>
<td>Wegener’s granulomatosis</td>
<td>Female&gt;male have pituitary involvement</td>
<td>Pituitary involvement &lt;1%, usually DI, rare ant pit dysfxn, can precede other sx</td>
<td>Oral ulcers, cavitary lung lesions, hematuria</td>
<td>Enlarged pit w/homogenous enhancement, thickening of stalk, esp sup</td>
<td>Necrotizing granulomatous small vessel vasculitis</td>
</tr>
<tr>
<td>Langerhans’ cell histiocytosis</td>
<td>Children&gt;adults, mean adult age 33</td>
<td>Ant pit dysfxn in 20%, almost invariably assoc with DI, GH&gt;GT&gt;ACTH/TSH</td>
<td>Variable bone pain, rashes</td>
<td>Stalk thickening, absence of PP bright spot</td>
<td>Collections of Langerhans cells with eos, small lymphs, histiocytes</td>
</tr>
<tr>
<td>Lymphocytic hypophysisis</td>
<td>Female:male 0.91, mean female age 39.7, male 46.3</td>
<td>Ant pit dysfxn 66-95%, ACTH, thyroid, GT&gt;GH, DI 14-48%, hyperPRL 16%</td>
<td>HA/impaired vision (50-70%), N/V, weakness, other autoimmune dzs</td>
<td>Symmetric enlargement, homogenous contrast enhancement, stalk thickening, cystic lesions</td>
<td>Diffuse polyclonal lymphocytic infiltration with T cell predominance</td>
</tr>
<tr>
<td>Granulomatous hypophysisis</td>
<td>F:M 1:40s</td>
<td>ACTH&gt;TSH=GT&gt;GH, DI 46%, hyperPRL 33%</td>
<td>HA + vis sx sx 83%</td>
<td>Triangular mass, T1 iso</td>
<td>Granulomas and lymphs</td>
</tr>
<tr>
<td>Xanthomatos Hypophysitis</td>
<td>3:1 F, 20s</td>
<td>GT&gt;GH, TSH&gt;ACTH, DI 25%, hyperPRL 25%</td>
<td>HA 75%, visual sx sx rare, longer duration sx</td>
<td>Round, hypointense</td>
<td>Lipid laden macrophages</td>
</tr>
</tbody>
</table>
Questions

- Yield of MRI in secondary hypogonadism?
- How do opioids cause hypogonadism?
- Does his MRI suggest a diagnosis?
- Any other workup to do?
- When to repeat MRI?
- Biopsy?
References