43 year old man with low libido

Katie Stanley, MD

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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

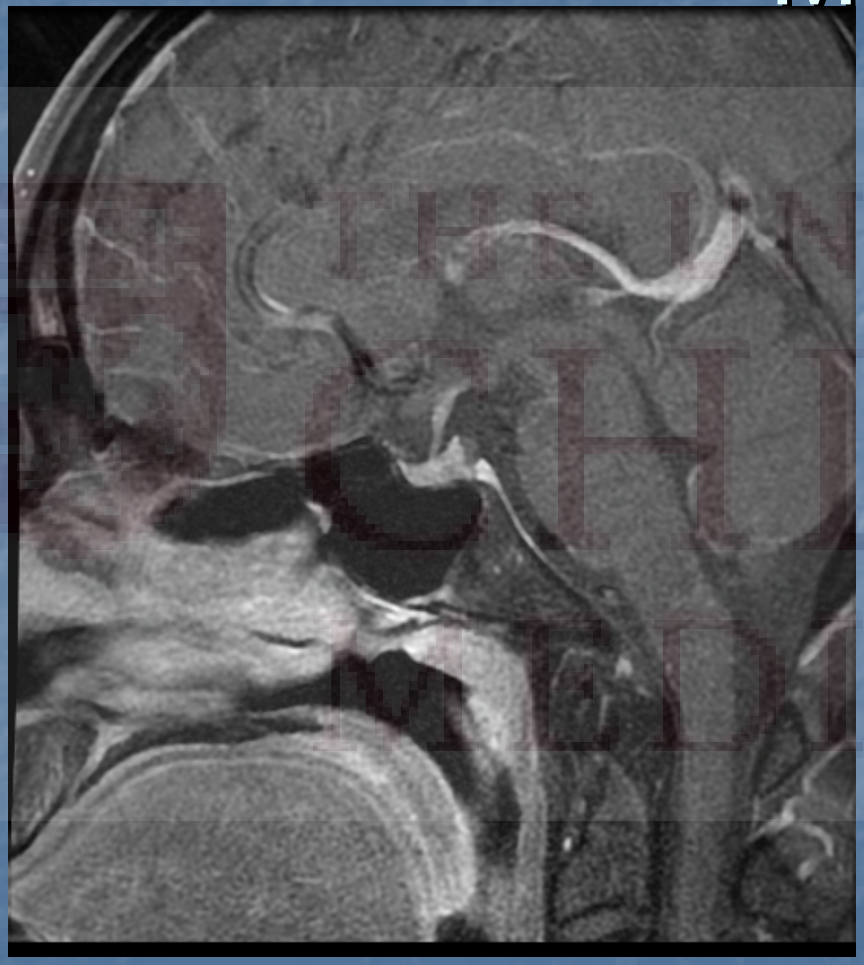
Differential diagnosis of low testosterone

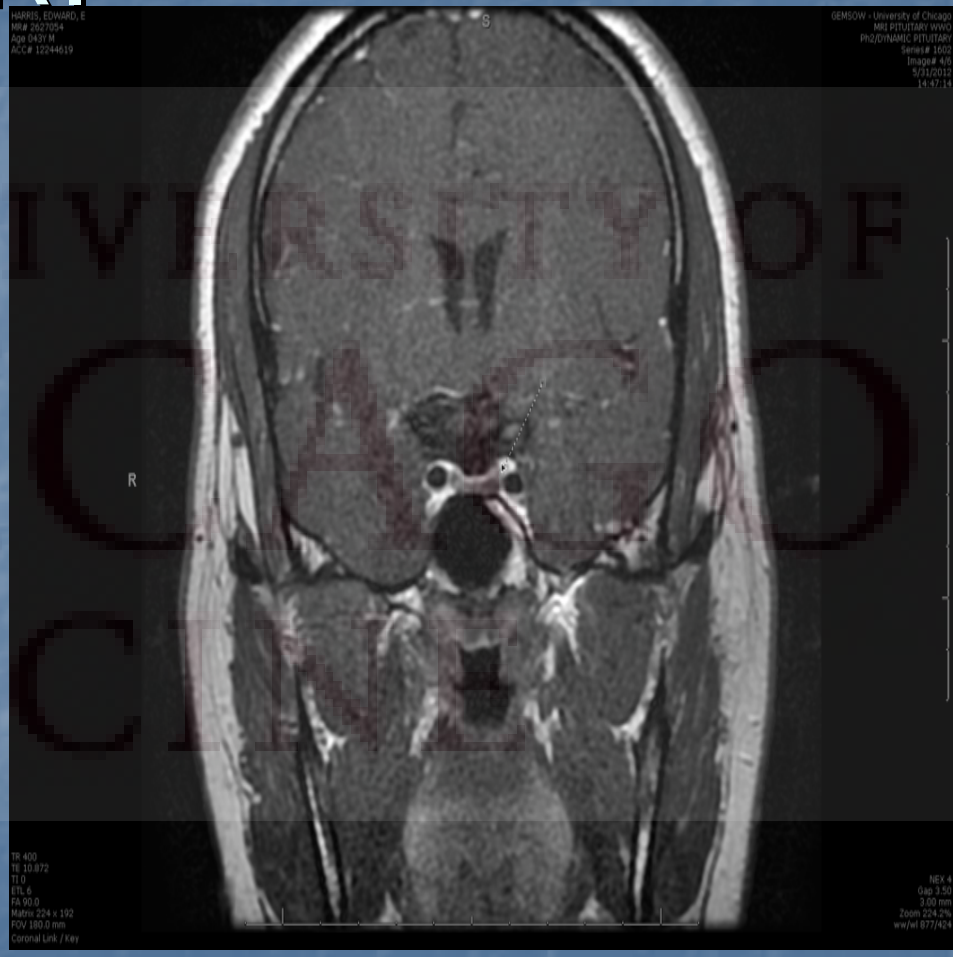
- Primary hypogonadism
  - Congenital: Klinefelter, cryptorchidism, LH receptor mutations, etc.
  - Infections, eg mumps
  - Radiation
  - Alkylating agents
  - Ketoconazole
  - Torsion
  - Trauma
  - Autoimmune
  - Chronic renal failure
  - Idiopathic
- Secondary hypogonadism
  - Congenital: Kallman,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

MRI





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 work-up

- 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 Hypogonadotropic 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

Type of inflammation	Pt Characteristics	Endo Characteristics	Associated Sxs	MRI Appearance	Histological Appearance
TB hypophysitis	Developing world, other signs of active TB usually but not always present	Often presents with ant pit dysfxn incl hyperPRL, DI	HA common and early, visual disturbances	Sellar mass, thickening/ nodularity of stalk	Central necrosis surrounded by infl cells
Pituitary abscess	Rare, chronic and indolent sxs	60% ant hypopit (GH>GT>>ACTH/TSH), DI 28%, hyperPRL 15%	Long standing HA, visual disturbances (50%), meningitic signs,fever/WBC	Round sellar cystic lesion, hypo or iso on T1, iso or hyper on T2, peripheral gad enhancement	Gram positive bacteria
Fungal hypophysitis	Rare, often immunocompromised (aspergillosis)	Depends on extent, rare	Visual sxs prominent, HA, fever	Mass lesion	
Sarcoidosis	Young and middle-aged adults	DI 25-55% neurosarcoid, hyperPRL 3-32%, ant deficiencies esp hypogonadism	Variable- cough, dyspnea, CP, skin lesions	Absence of T1 hyperintensity, lesions iso on T1, gad enhanced	Non-caseating granulomas
Wegener's granulomatosis	Female>male have pituitary involvement	Pituitary involvement <1%, usually DI, rare ant pit dysfxn, can precede other sxs	Oral ulcers, cavitary lung lesions, hematuria	Enlarged pit w/homogenous enhancement, thickening of stalk, esp sup	Necrotizing granulomatous small vessel vasculitis
Langerhans' cell histiocytosis	Children>adults, mean adult age 33	Ant pit dysfxn in 20%, almost invariably assoc with DI, GH>GT>>ACTH/TSH	Variable- bone pain, rashes	Stalk thickening, absence of PP bright spot	Collections of Langerhans cells with eos, small lymphs, histiocytes
Lymphocytic hypophysitis	Female:male 0.91, mean female age 39.7, male 46.3	Ant pit dysfxn 66-95%, ACTH, thyroid, GT>GH, DI 14-48%, hyperPRL 16%	HA/impaired vision (50-70%), N/V, weakness, other autoimmune dzs	Symmetric enlargement, homogenous contrast enhancement, stalk thickening, cystic lesions	Diffuse polyclonal lympocytic infiltration with T cell predominance
Granulomatous hypophysitis	F:M 1, 40s	ACTH>TSH=GT>GH, DI 48%, hyperPRL 33%	HA+vis sxs 83%	Triangular mass, T1 iso	Granulomas and lymphs
Xanthomatous Hypophysitis	3:1 F, 20s	GT>GH, TSH>ACTH, DI 25%, hyperPRL 25%	HA 75%, visual sxs rare, longer duration sxs	Round, hypointense	Lipid laden macrophages

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References

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