Morning Report 2012

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• I have no disclosures to report.

Image of the Day

• 25 year old gentleman comes to see you for better control of his diabetes.

• His past medical history is notable for type 2 diabetes first diagnosed 6 years ago and hypertension diagnosed 3 years ago.

• Initially, he was placed on metformin but due to gradually poorer control of his diabetes, he was started on insulin.

Image of the Day

• Current regimen:
  – Metformin 1000 mg bid
  – Lantus 20 U qhs

• Very motivated, carefully follows an ADA diet and exercises on a regular basis.

• Frustrated that his lifestyle changes are not making a difference in his diabetes control. His blood sugars are in the 200s again.

What would you do next?
Signs and Symptoms of Acromegaly

- Enlarged jaw
- Enlarged, swollen hands and feet
- Coarse facial features
- Nose enlargement
- Spreading of teeth
- Joint pains
- Skin tags
- Macroglossia
- Voice deepening
- Diabetes
- Hypertension
- LVH
- Organomegaly
- Colonic polyps and colon cancer
- Sleep apnea

Diagnosis of Acromegaly

- Insulin growth factor -1 (IGF-1)
- If IGF-1 elevated
  - OGTT with growth hormone levels
  - Suppression of GH to < 1ng/mL in normals

Patient Course

- IGF-1 and Growth Hormone levels were elevated
- Imaging confirmed a pituitary tumor
- Transphenoidal surgery with cure

Secondary Causes of Hyperglycemia

- Acromegaly
- Cushing's Syndrome
- Pheochromocytoma
- Adrenal Insufficiency
- Hyperthyroidism
- Glucagonoma
- Somatostatin-secreting tumors
- Pancreatic disease
- Medications (i.e. glucocorticoids, atypical antipsychotics, HIV protease inhibitors)

Case

62 year old housewife and mother of four children came in for evaluation of hair loss.

“If I go bald, I will kill myself.”

She was in good general health.

She did have a history of hypothyroidism. Positive thyroid peroxidase antibodies. Euthyroid on replacement.

Tonsillectomy. Appendectomy. Scarlet fever as a child.
First noticed symptoms 3 weeks ago—fair amount of hair in her comb.

Two days prior, she saw her hairdresser who told her “you have huge bald spots” and asked her if she was ill.

No weight loss, fevers, chills, sweats, rash, weight change, change in urinary or bowel habits, bruising, change in skin pigmentation.

Her husband and children were well. Her mother had died of breast cancer at age 56 and her father from pneumonia and Alzheimer’s disease at age 82.

BP 105/65  HR 64  RR 10

Several 2 to 6 cm bald spots with broken off hairs at the edges.

No hair loss over her body.

Normal female escutcheon.

No thyroid nodules.

No lymphadenopathy.

Breast, lung, cardiovascular, and abdominal exams were unremarkable.

Stool was brown and guaiac negative.

Gait, speech, and cranial nerves all intact.

WBC 3100/μL (62 P, 28 L, 7 M, 3 E)

Hematocrit 36%

Platelets 224,000/μL

Kidney and liver function tests normal.

What additional tests would you want to perform?

Iron 18 μg/dL (40-159)

TIBC 380 μg/dL (250-450)

Transferrin saturation 5%

B12 111 pg/mL (250-900)

MMA 0.6 μmol/L (0-0.40)
Hair Growth Cycle

- **Anagen**
  - Growth phase
  - 2-3 years
  - 80-90% of follicles

- **Catagen**
  - Involution phase
  - 2-3 weeks
  - 1-3% of follicles

- **Telogen**
  - Resting phase
  - 3-4 months
  - Hair shed at end of telogen (75/day)
  - Mature root sheath or club at proximal end
  - 5-10% of follicles

Alopecia

- **Scarring**
  - Associated fibrosis, inflammation, and loss of hair follicles
  - Smooth scalp with decreased # of follicular openings

- **Non-scarring**
  - Hair shafts gone but follicles preserved
  - Potentially reversible

Non-scarring and Scarring Hair Loss

Scarring Alopecia

- Discoid lupus
- Sarcoidosis
- Lichen Planus

Non-scarring Alopecia

- Androgenetic telogen effluvium
- Alopecia areata
- Tinea capitis
- Traumatic alopecia
- SLE
- Secondary syphilis
- Hypothyroidism, hyperthyroidism
- Hypopituitarism
- HIV
- Deficiencies of protein, iron, biotin, zinc
- Medications

Androgenetic Alopecia

- Most common type of hair loss: 30-40% of adult men and women
- Genetically determined shortening of anagen phase (shorter, thinner hair shafts)
- Increased sensitivity of the hair follicles to androgens or increased levels of androgens
- Anterior/midline scalp
- Polygenic inheritance/variable penetrance
Androgenetic Alopecia

- Women less than men
  - Fewer androgen receptors in hair follicles
  - Less 5α-reductase activity (T → DHT)
  - Increased aromatase (T → E2)

- Rule out androgen excess in women
  - Acne
  - Hirsutism
  - Male escutcheon
  - Clitoromegaly

Telogen Effluvian

- Most common cause of diffuse hair loss
- Diffuse shedding of normal hairs (clubbed hairs)
- Often follows major illness or postpartum
- Pull test
  - Grasp around 30 hairs. If more than 5 club hairs come out – abnormal
- Thyroid disease, iron deficiency, lupus
- Usually regrows in 3-4 months

Alopecia Areata

- Common (1/1,000)
- T cell infiltrates around hair follicles
- Associated with other autoimmune diseases (vitiligo, thyroiditis, and pernicious anemia)
- Smooth, circular discrete area of complete hair loss
- Black dots of hair broken a few mm from scalp at edge of lesion

Alopecia: Pull Test

- Grasp around 30 hairs. If more than 5 club hairs come out – abnormal

Alopecia Areata

- May have hair loss on body and/or pitted nails
- Plucked hairs look like exclamation points (narrow, rather than clubbed at the base)
- Develops over a few weeks, regrows in a few months (90%)
Clubbed Hairs

Alopecia Evaluation
- TSH
- Iron/TIBC
- Rule out trauma
- Meds: warfarin, heparin, PTU, vitamin A, lithium, beta blockers, clonidine, amphetamines
- ANA, VDRL
- Vitamin B12

EKG of the day

Brugada Syndrome
- Elevated J point, ST segment in V1-2
- Brugada Syndrome vs. Brugada Pattern
- Inverted T Type 1; upright T in Types 2-3.
- Polymorphous VT/sudden death
- Often familial
- Channelopathy – usually Na+ channelopathy
- Occasionally can be provoked by Type 1 anti-arrhythmics, stress
- See similar ST-T abnormalities in lateral leads in hypothermia, hypercalcemia.

Case
59 year old man with an extensive cardiac history including CAD and VT, who presented with epistaxis.

He had been quite ill over the last 4 weeks.

4 weeks previously
- The patient was hospitalized for AICD interrogation due to multiple discharges.
- During his 10-day hospital stay both a fractured lead and malfunctioning epicardial patch were replaced via thoracotomy.
4 weeks previously

- Post-operative fevers were treated with 5 days of vancomycin, cefazolin and levofloxacin. All cultures were negative, and antibiotics were discontinued.
- The patient was still having low grade temperatures when he was discharged.

Presentation

- In the post-discharge period, the patient experienced malaise, fatigue, anorexia with an 8 lb weight loss, and diarrhea.
- He reported no tactile fevers.
- One day prior to admission, he developed a right-sided headache, without visual changes, nuchal rigidity, altered speech or local weakness.

Day of admission

- On the day of admission, the patient developed new epistaxis that did not resolve with local compression. He also noticed blood in the sclera of his right eye.
- On route to the ED, family members noted left leg and right arm shaking associated with mild confusion but no loss of consciousness.

Additional ROS

- No bladder or bowel incontinence.
- No chest pain, orthopnea or palpitations.
- No head trauma.

Past Medical History

- DM2
- CAD (s/p MI and CABG in 1996)
- ICM (EF=40%)
- VT (s/p AICD placement in 1999, revised 4 weeks previously)
- Diverticulitis
- CVA in 1997
- Hypertension
- Hypercholesterolemia
- Obesity

Medications

- Lisinopril 40 mg po qd
- Atenolol 50 mg po qd
- Amiodarone 200 mg po qd
- Warfarin 5mg po qd
- Aspirin 325 po qd
- Ranitidine 150 mg po bid
**Allergies:** NKDA

**Soc Hx:** Lived in the North End with a stable male partner. No known TB risk factors. No tobacco, intravenous drugs, or significant alcohol use.

**Fam Hx:** Father- lung cancer, Mother - stroke

**Physical Exam**

T-101.4°F P-80 BP-146/60 RR-20

**General:** Awake, diaphoretic, soaked through his clothes, confused but followed simple commands.

**Skin:** Multiple ecchymoses. Mild incisional erythema, but no evidence of external chest wound breakdown or drainage. Poor skin turgor.

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**PHYSICAL EXAM (CONTD)**

- **HEENT:** Right conjunctival hemorrhage. EOMI.

- **Neck:** supple. JVP flat.

- **Lungs:** Bibasilar crackles.

- **CV:** RRR. 2/6 SEM. No peripheral edema.

- **Neuro:** Tremulous. Reflexes 3-4+.

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**Labs**

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<th>10.5</th>
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<td>4.4</td>
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MCV- 87

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<th>55.6</th>
<th>107</th>
<th>55</th>
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</thead>
<tbody>
<tr>
<td>PTT</td>
<td>243</td>
<td>139</td>
<td>132</td>
</tr>
</tbody>
</table>

Ca-9.5 Mg-1.6 PO4-4.4 TP-5.9 Alb-4.7 CKMB (-)

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**Studies**

**CXR** - Cardiomegaly, no infiltrates, AICD in place

**ECG** - Old anterior-septal MI. No change from previous study

**Head CT** - Subdural hematomas affecting bilateral frontal areas; right internal capsule CVA (likely old)

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**Hospital Course**

- FFP and vitamin K therapy were initiated.

- Persistent fevers developed with Temps 101-102°F. Blood, sputum and stool samples were obtained for microbiologic study. Pan CT scans showed no source on infection.

- ID and Neurology consultations were obtained.

- Phenytoin was initiated for question of seizure-like activity.
Hospital Course (cont’d)

• The patient remained febrile.

• Blood cultures, lumbar puncture, echocardiography and serologies for HIV and syphilis failed to explain the fevers.

• By hospital day 5, severe hypernatremia developed (Na 163) with worsening mental status.

• Temp was 104.5. RR 40

What would you do next?

• >38.0°C for 3 days

Roth, AFP, 2003

Rare Miscellaneous Causes

• Atrial myxoma
• Familial Mediterranean Fever
• Histiocytosis
• Pheochromocytoma
• Whipple’s disease
• Thyroiditis and Thyrotoxicosis

Hospital Course

• TFTs ordered:
  • TSH <0.01 (0.5-5 uU/mL)
  • T4 18.5 (4.5-10.9 ug/dL)
  • THBI 2.51 (0.77-1.23)
  • FT4I 46.4 (4.5-10.9)
  • T3 343 (60-181 ng/dL)

• Concern was for amiodarone induced hyperthyroidism
Treatment

• Methimazole 30 mg per rectum q6 hrs was initiated, but later changed to propythiouracil (PTU) 400 mg pngt q 6 hrs.
• Solumedrol 60 mg iv q12 hrs
• Iopanoic acid 1 gm qd

• Pulmonary aspiration was felt to have occurred in the setting of delirium and agitation.
• Despite anti-thyroid therapy, the patient developed hyperpyrexia (T=107°F) and increased clonus.
• A diagnosis of Thyroid Storm was made, and the patient underwent thyroidectomy.

Follow-up

• The patient’s temp dropped quickly after the thyroidectomy.
• The patient was discharged after a 3 week hospital course.
• At follow-up, he had returned to his previous level of function.

Amiodarone

• 75 mg of iodine per 200 mg tablet
• 10% of iodine released as free iodide daily
• Average daily iodine intake in US is 0.15-0.30 mg.
• ½ life is 100 days

Thyroxine and Amiodarone

Amiodarone and Thyroid Function

(Daniels, JCEM, 2001; Basaria and Cooper Am J Med, 2005)
Chronic Amiodarone Treatment

Probability of Thyroid Disease with Amiodarone Treatment

Amiodarone and Hyperthyroidism

Severe Hyperthyroidism - Treatment

• Thyroid gland
  - Inhibit synthesis – PTU, Methimazole
  - Inhibit TH release – Iodine, Lithium
  - Surgery

• Peripheral Effects of TH
  - Inhibit T4 to T3 conversion – PTU, steroids, iopanoic acid, propranolol
  - Removal of excess thyroid hormone – plasmapheresis

• Systemic Decompensation
  - Treat hyperthermia – Tylenol, cooling
  - Correct dehydration and nutritional deficits – fluids, electrolytes
  - Supportive therapy – pressors, treat CHF, steroids

Anticoagulation and Hyperthyroidism

• Hyperthyroidism increases metabolism of vitamin K-dependent clotting factors

• Altered protein binding of warfarin

• Enhanced affinity of warfarin for its receptors

Lab of the Day

• 36 year old woman with diabetes, liver disease, and HIV comes to see you in follow-up.

• She says that her blood glucose has been very elevated – consistently in the 250s.

• She believes this is due to poor diet.

• You counsel her regarding diet and exercise, refer her to a nutritionist, and order a hemoglobin A1c.

(Melmed et al., JCEM, 1981)

(Trip MD et al., Am J Med, 1991)

(Daniels, JCEM, 2001)

(Daniels, JCEM, 2001)

(Chute et al., Endo Practice, 1997)

(Chute et al., Endo Practice, 1997)
Lab of the Day (cont’d)

• Her Hgb A1c returns at 6.8%.

• You are surprised at this hemoglobin A1c. What value did you expect?

<table>
<thead>
<tr>
<th>Hemoglobin A1c (%)</th>
<th>Average blood glucose (mg/dL)</th>
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<tbody>
<tr>
<td>6</td>
<td>135</td>
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<tr>
<td>7</td>
<td>170</td>
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<td>8</td>
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<td>9</td>
<td>240</td>
</tr>
<tr>
<td>10</td>
<td>275</td>
</tr>
</tbody>
</table>

(Hemoglobin A1c x 33) - 60

Lab of the Day (cont’d)

• Why is there a discrepancy?
  – Glucometer
  – Timing of testing
  – Assay
  – Treatment of iron, folate, or vitamin B12 deficiency
  – Hemolysis

Hemoglobin A1c

• Red blood cells are freely permeable to glucose
• Glucose irreversibly attaches to the hemoglobin
• The hemoglobin A1c represents 3 months of blood sugar readings because of the lifespan of red blood cells
• Increases in red blood cell turnover → falsely low hemoglobin A1c

Our patient

• Hct 36%
• Iron studies, folate, and B12 all normal and not on recent treatment for deficiencies
• LDH 285 (107-235 U/L)
• Haptoglobin <8 (30-200 mg/dL)
• She has hemolysis – probably from her liver disease.
• How could you check her blood sugar control?

Fructosamine

• Measure of glycosolated end products
• Her level was 538 (0-285 umol/L).
Case

44 year old private investor presented to his PCP with low libido of one year’s duration.

He has been married for seven years. Had his first child one year ago.

The decline in his libido was gradual.

He is healthy and active, loves outdoor activities and building ships.

Increasing fatigue over the past year has limited his time outdoors.

Does not feel depressed. Has no other signs or symptoms of a systemic illness including no fevers, chills, headaches, weight changes, changes in his hair or skin texture, bowel movements.

His only medical problem is mild hand arthritis.

Low libido

- Psychiatric: depression, anxiety disorder
- Medications: SSRIs, anticonvulsants, antihypertensive medications
- Systemic illness
- Recreational drugs
- Androgen deficiency
- Thyroid disease
- Hyperprolactinemia
- Erectile dysfunction

Normal pubertal development.

In addition to the low libido, he has noticed decreased morning erections and decreased ejaculatory volume.

No change in frequency of shaving, no breast enlargement, or change in testicular size.

No headaches, vision changes.

No medications.

No tobacco, rare ETOH, no illicit drug use.

Family history unremarkable for thyroid disease, delayed puberty, infertility.
• Ht 6’4”, Wt 162 lb, BP 128/82, P 84, RR 10
• Gen: non-eunochoidal
• HEENT: PERRL, EOMI, Visual fields full
• Thyroid: normal in size and without nodules.
• No gynecomastia
• Lung, cardiovascular, and abdominal exams normal.
• GU: testes 10 cc bilaterally, nl phallus
• Hair: No change in male distribution of body hair
• Neuro: normal muscle bulk and strength.

Labs
• Testosterone 36 ng/dL (270-1190)
• TSH and prolactin normal

What would you do next?

Male Hypothalamic-Pituitary-Gonadal Axis

Labs
• Testosterone 40 ng/dL
• LH 1.5 U/L (2.4-5.9)
• FSH 1.3 (0.9-15.0)

What would you do next?

Further Evaluation
• MRI of the pituitary gland revealed no masses.
• Bone density scan: spine T score -2.5
• Semen analysis – azoospermia
• CBC Hct 36.1%
Secondary Hypogonadism: Acquired

- Benign tumors & cysts
- Malignant tumors
- Infiltrative diseases
- Infections
- Pituitary apoplexy
- Trauma
- Radiation
- Hyperprolactinemia

Infiltrative Diseases

- Critical Illness
- Chronic systemic illness
- Glucocorticoids
- Chronic opiate use
- Adult-onset Hypogonadotropic Hypogonadism

- Hemochromatosis
- Sarcoïdosis
- Eosinophilic granulomatosis

- Fe = 219 ug/dL (40-159 ug/dL)
- TIBC = 257 ug/dL (250-450 ug/dL)
- Transferrin saturation = Fe/TIBC = 85.2%
- Ferritin = 2435 ug/L (20-400 ug/L)
- HFE testing: C282Y homozygote

Hemochromatosis and hypogonadism

- Secondary
  - Deposition in the pituitary gland
- Primary – much less common
  - Deposition in the testes

Hemochromatosis and recovery of function

- Little, if any, data
- Most say that if >40 years old, gonadal function does not recover

(Cundy et al., Clin Endo, 1993)

Summary

- Secondary causes of diabetes
- Acegaly
- Alopecia evaluation
- Brugada Syndrome
- Fever of unknown origin
- Amiodarone and the thyroid
- Extreme hyperthyroidism/thyroid storm
- Potential inaccuracies in hemoglobin A1c
- Hypogonadism
- Hemochromatosis

References
