52 yo F w/a “cold foot”, found to have hypercalcemia

Jess Hwang
10/31/13
HPI

- Admitted for a “cold foot” x 3 days
- Weight loss of 50 lb in the last 6 months
CT Angio Aorta

- Found to have acute thrombosis of L ext iliac, distal SFA
• Acute thrombosis of L popliteal artery
Hospital course

- LLE thrombectomy... complicated by:
  - Melena post-op
  - Bradycardia and PEA arrest
  - Oliguria → CVVH from 7/30-8/1
- Consulted for abnormal TFTs
• PMH
  HTN
  CHF
  Dyslipidemia
  C-section x 2
  Ectopic pregnancy

• Social History
  1 PPD x years
  No EtOH

• Family History
  Mom - lung cancer
  Sister - ovarian cancer
  Brother - prostate cancer

• Medications
  Aspirin 81 mg
  Coreg 3.125 BID
  Lasix 40 mg
  Simvastatin 10 mg
Physical Exam

• Vitals: 36.3, 114/86, 96, SpO2 97%, BMI 24.6,
• Gen: no apparent distress
• HEENT: no scleral icterus, no exophthalmos
• Neck: no thyromegaly, no palpable nodules
• CV: borderline tachycardia
• Pulm: crackles at bases
• GI: soft, non-tender, +ascites/abd distension
• Ext: LLE- wound vac
• Neuro: alert & oriented
• Psych: normal mood
<table>
<thead>
<tr>
<th>TSH 0.24 (RR 0.3-4)</th>
<th>FT4 1.38 (RR 0.9-1.7)</th>
<th>TT3 69 (RR 80-195)</th>
<th>rT3 268 (RR 160-353)</th>
<th>TPO/Tg Ab neg</th>
</tr>
</thead>
<tbody>
<tr>
<td>137</td>
<td>107</td>
<td>17</td>
<td>110</td>
<td>8.7</td>
</tr>
<tr>
<td>4.4</td>
<td>22</td>
<td>0.9</td>
<td>10.9</td>
<td>124</td>
</tr>
<tr>
<td>5.1</td>
<td>2.4</td>
<td>1.7</td>
<td>1.7</td>
<td>40</td>
</tr>
<tr>
<td>2.8</td>
<td>77</td>
<td>1.6</td>
<td>1.6</td>
<td></td>
</tr>
<tr>
<td>65</td>
<td>94</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Differential Diagnosis Hypercalcemia

- Hyperparathyroidism
  o Primary HPT
    - Solitary adenoma
    - Parathyroid hyperplasia
  o Secondary/tertiary hyperparathyroidism
  o Lithium therapy
  o Familial benign hypocalciuric hypercalcemia
- Malignancy-associated hypercalcemia
  o PTHrP-mediated
  o Vit D mediated
  o Lytic bone metastasis
- Vitamin D related
  o Vitamin D intoxication
  o Sarcoidosis or other granulomatous diseases
- Endocrine disorders
  o Thyrotoxicosis
  o Addison’s disease
- Miscellaneous
  o Immobilization
  o Thiazide diuretics
  o Vitamin A intoxication
  o Milk-alkali syndrome

Hypercalcemia

- Diagnosed with hypercalcemia 1 year ago
- Was on Sensipar 30 mg for a year
- 1 episode nephrolithiasis years ago
- No bone fractures
- Never evaluated for osteoporosis
- No history of sarcoid
- Not on medications causing this
More labs

- Ca 10.9 → 12.2
- Ionized Ca 5.9
- Mg 1.6
- Phos 1.7
- PTH 160 (RR 15-75)
- 25-OH vit D 6
- PTHrp 0.8 (RR <2)
- 1,25-OH vit D 15 (RR 18-78)
SPEP/UPEP

- Monoclonal IgG lambda
- 1 gm of proteinuria in 24 hr urine with a significant proportion of monoclonal free lambda light chains
Bone Marrow Biopsy

- Plasma cell dyscrasia involving a hypocellular bone marrow (25% cellular, 10% clonal plasma cells, lambda restricted) with concurrent amyloid deposition.

Skeletal Survey

- No discrete lesions of myeloma.
Transthoracic Echo

- Mild concentric LVH. LVEF 35.9%. RV systolic performance is mild-moderately reduced. LA severely dilated.

Cardiac MRI

- LVEF 35%. RV moderate systolic dysfunction. RVEF 36%. Late GAD enhancement circumferentially, strongly suggestive of cardiac amyloidosis.
EGD

- Stomach: focally inflamed antral mucosa with amyloid deposition
- Duodenum: focal mildly active duodenitis with amyloid deposition and features suggestive of ischemia.

Colonoscopy

- Ascending colon: ischemic colitis with ulceration and amyloid deposition.
Thyroid US

R LOBE: 5.5x2.1x2.1 cm. L LOBE: 4.3x1.6x2.0 cm. ISTHMUS: 0.7 cm. Homogeneous parenchymal echogenicity bilaterally.

PARATHYROID GLANDS: Post/inf to R thyroid lobe → hypoechoic extrathyroidal nodule, represents hyperplastic parathyroid glands vs parathyroid adenomas. Inf to the L thyroid lobe → extrathyroidal, hypoechoic nodule represents a hyperplastic parathyroid gland or parathyroid adenoma.
Thyroid Ultrasound

**L lobe**

**R lobe**
DXA scan

- L1-L4 spinal BMD = 0.802 g/cm² (T = -3.2)
- Total hip BMD = 0.752 g/cm² (T = -2.0)
- Forearm BMD = 0.740 g/cm² (T = -1.6)
Our Patient

- Diagnosis: Primary lambda- AL amyloidosis with cardiac, GI, bone marrow, possible endovascular and mild renal involvement, with 10% marrow monoclonal plasma cells
- Treated with Sensipar 60 mg daily
- Started chemotherapy with Bortezemib

Future tests
- 24h urine Ca/Cr
- Sestamibi scan→referral to endocrine surgery
Clinical Questions

• Association between PHPT and Monoclonal Gammopathy?
• Medical management PHPT
  ▫ Cinacalcet
  ▫ Severe vitamin D deficiency
• PTH as a biomarker in heart failure?
PHPT and Monoclonal Gammopathy

- Objective: to prospectively determine presence of monoclonal gammopathy in PHPT
- Cohort: 101 PHPT, 127 non-PHPT surg controls, 101 age/sex matched thyroid surg controls
- Results: monoclonal Ig was detected in 10% with PHPT compared with 2% of surgical controls (p = 0.005) and 3% of benign thyroid controls

Medical Management PHPT

- CI to parathyroidectomy or persistent PHPT have few non surgical options
- Cinacalcet is FDA approved for treating 2° hyperparathyroidism in patients with CKD on HD and patients with parathyroid cancer.
  - Calcimimetic agent that levels by binding to CaSR on PTH cells → causes L-shift in CaSR set point
  - ↓PTH (neg feedback) → ↓Ca

Medical Management PHPT

- Objective: to establish efficacy of cinacalcet (up to 4.5 yrs) in ↓Ca in patients with PHPT
- Patients: 1) failed PTHx (n=29), 2) 1+ criteria for PTHx-no surgery (n=37), 3) mild asx PHPT (n = 15)
- Results: ↓Ca, ↓PTH, and ↑Phos were similar. No significant changes in BMD. Efficacy maintained for up to 4.5 yr of f/u
- Conclusions: cinacalcet is equally effective in the medical management of PHPT patients

J Clin Endocrinol Metab, January 2011, 96(1):E9–E18
Vitamin D Deficiency in PHPT

- Vitamin D inadequacy is more common in patients with PHPT
- Initiation of vitamin D therapy if 25-hydroxy vitamin D < 20 ng/mL in PHPT
- Well-designed trials are needed to better define the safety and efficacy of vitamin D therapy in patients with concomitant vitamin D deficiency and PHPT

Vitamin D Deficiency in PHPT

- The causes of low circulating levels of 25-OHD in patients with PHPT are not totally understood.
  - Accelerated conversion $25\text{-OH} \rightarrow 1,25\text{-OH \, vitD}$?
  - Increased catabolism of 25-OH vit D?
  - Increased adiposity?

PTH as a biomarker in HF?

- **Objective:** to investigate whether PTH could identify patients with advanced HF
- **Cohort:** 150 outpatients w/systolic HF.
- **Results:** PTH = 43, 84, 121, and 161 pg/ml in NYHA functional classes I, II, III, and IV, respectively (p < 0.001). PTH levels were correlated with BNP level and LVEF (p < 0.001). Optimal cut-off value of PTH to predict advanced HF was > 96.4 pg/ml, with 93.3% Sn and 64.2 Sp.

Altay H. Am J Cardiol 2012;109:252–256
PTH as a biomarker in HF?

Altay H. Am J Cardiol 2012;109:252–256
Take Home Points

• Consider SPEP in patients with PHPT
• In patients with monoclonal gammopathy and hypercalcemia w/no other symptoms of progressive disease ➔ check for PHPT
• Replete 25-OH vit D to >20 in PHPT
• PTH is being studied as a biomarker in HF
References