69 year old woman with hypercalcemia

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HPI

- 69 yo F with CLL and SCC of bladder
- Presented with abdominal pain, decreased PO intake, fatigue, generalized weakness, constipation, pelvic pain
- Symptoms worsening x 1-2 weeks
- Neither she nor husband note mental status changes
- Found to have Ca of 11.8 (corrected 12.4)
- No prior hypercalcemia
- On MVI, no other Ca or vit D
Oncologic history

- Presented 9/2013 with difficulty urinating, dysuria, vaginal spotting, wt loss, bloody diarrhea
- CT showed extensive retroperitoneal LAD and splenomegaly, severe bilateral hydronephrosis with level of obstruction at bladder
- CBC showed 62% lymphocytes with some cells suspicious for malignant lymphoid cells
Oncologic history

- Inguinal LN bx and BM cx c/w small lymphocytic lymphoma/CLL
- Cystoscopy -> 4 cm bladder mass resected c/w squamous cell carcinoma of bladder
- Bilateral nephrostomy tubes placed
- Has received 3 cycles of bendamustine/rituximab with subsequent decrease in LAD
- Seeking coverage for ibrutinib to further decrease LAD prior to cystectomy, pelvic LN dissection, ileal conduit
Other History

- **Other PMH**
  - HTN
  - DM2
  - H/o GI bleed x 2

- **Family History**
  - No calcium disorders

- **Social History**
  - Married
  - Used to work as nurse’s aid
  - Former smoker ½ ppd x 4 yrs, quit 2010

- **Home Medications**
  - Acyclovir
  - Amlodipine
  - ASA
  - Dapsone
  - Nexium
  - MVI
  - Metoprolol
  - Lantus and Novolog
  - Metformin
  - Remeron
  - Miralax
  - Peri-Colace
  - Tramadol prn
Review of Systems

- Constitutional: Positive for appetite change, fatigue and unexpected weight change. Negative for fever.
- Respiratory: Negative for shortness of breath.
- Cardiovascular: Positive for chest pain. Negative for leg swelling.
- Gastrointestinal: Positive for abdominal pain, constipation and abdominal distention. Negative for nausea and vomiting.
  - B/L nephrostomy tubes
- Musculoskeletal: Negative for joint swelling.
- Skin: Negative for rash.
- Hematological: CLL
- Psychiatric/Behavioral: Negative for confusion and decreased concentration.
Physical Exam

- Wt 42 kg, Ht 162.6 cm, BMI 15.9, T36.8, HR 70, RR 16, BP 116/39, SaO2 98% RA
- Constitutional: No distress. Cachectic appearing
- Head: Normocephalic and atraumatic. Tachy MM
- Eyes: Conjunctivae normal are normal.
- Neck: Neck supple. No thyromegaly present.
- Cardiovascular: Normal rate, regular rhythm, normal heart sounds and intact distal pulses.
- Pulmonary/Chest: Effort normal and breath sounds normal.
- Abdominal: Soft. She exhibits distension. There is no tenderness.
- Musculoskeletal: She exhibits no edema.
- Neurological: She is alert. She has normal reflexes. Poor historian but answered questions appropriately
- Skin: Skin is warm and dry. She is not diaphoretic. Cap refill < 2sec
- Psychiatric: She has a normal mood and affect.
Initial Labs

- Na 122 K 5.8 Cl 85 HCO3 29 BUN 26 Cr 1.1 Ca 11.8
- Prot 7.2 Alb 2.7 Bili 0.5 Alk phos 121 AST 23 ALT 8
- WBC 10.3 Hgb 10.6 Plts 345
- PTH 22 with Ca 11.4 Mg 2.1 PO4 3.5
Differential Diagnosis

- PTH-mediated
  - Primary hyperparathyroidism
  - Tertiary hyperparathyroidism
  - PTHrp mediated
- Non PTH mediated
  - 1,25OH-vitamin mediated
    - CLL
    - Granulomatous disease
  - Milk alkali syndrome
  - Vitamin D intoxication
  - Hyperthyroidism
  - Adrenal insufficiency
  - Renal insufficiency
  - Osteolytic metastases
Further workup and initial management

- IVF at 150 ml/hr
- TSH 3.65 FT4 1.18
- Cortisol 17.3 ACTH 19.5
- 25OH-D, 1,25OH-D, PTHrp pending
- Bisphosphonate or steroids?
  - Start with bisphosphonate, but…
  - Make sure not vitamin D deficient first
## Course

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25OH-D 36

Pamidronate 60 mg IV x 1 given 2/13 pm

1,25OH-vitamin D 38
## Course

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2/15 Fluid overload -> stopped IVF, started Lasix
2/15 Started calcitonin 4 mcg/kg q12h
2/17 CT showing progression of disease with peritoneal carcincomatosis
Increased calcitonin to 8 mcg/kg q12h
Course

• 2/18 Recommended denosumab 120 mg x 1
  - Not given because not on formulary
• 2/19 am Found unresponsive
  - Intubated and transferred to MICU
• 2/20 Made comfort care and extubated
• PTHrp 5.9 (<2.0)
• 2/21 Pt expired
Does level of PTHrp determine response to pamidronate?

- Prospective study of 44 patients with malignant disease and hypercalcemia
- Measured PTHrP, nephrogenous cAMP, TmCa, TmP, phosphate
- All treated with 2-3 L NaCl followed by pamidronate
- Defined good response as nl Ca for 14 days or more, poor response as elevated Ca within 14 days
Does level of PTHrp determine response to pamidronate?
Is there a better treatment for PTHrp-mediated hypercalcemia?
What about using denosumab?

- Open label single arm study of patients with malignancy and Ca >12.5 7-30 days after receiving bisphosphonate
- Denosumab 120 mg on days 1, 8, 15, 29 then q4wks
References


• S Morony et al.  The inhibition of RANKL causes greater suppression of bone resorption and hypercalcemia compared with bisphosphonates in two models of humoral hypercalcemia of malignancy.  *Endocrinology.* 2005: 3235-43.