

# 67 yo man with kyphosis

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Endorama

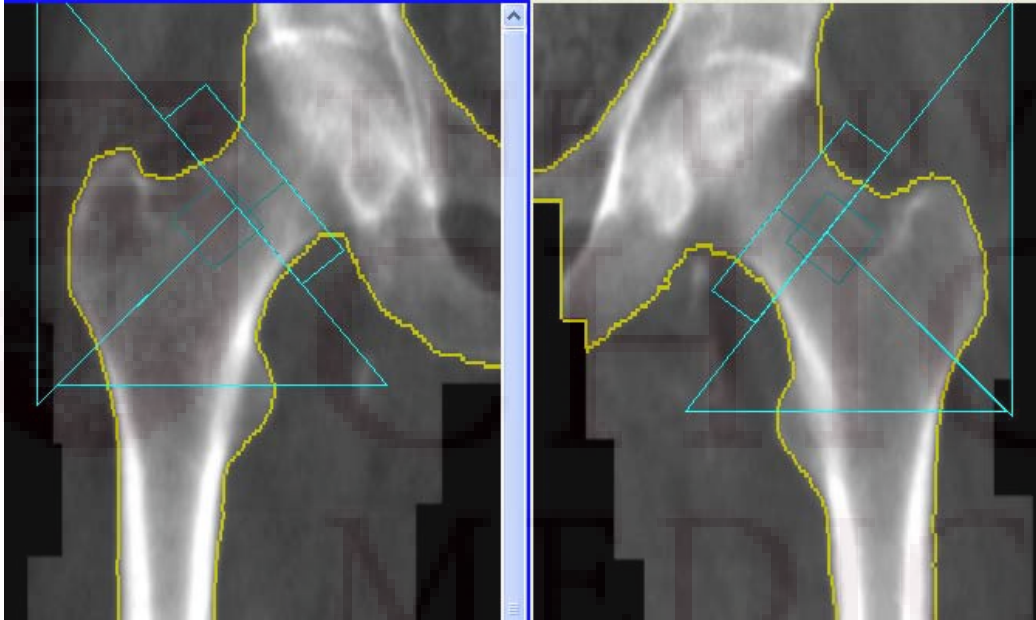
2/14/13



# History of Present Illness

- 67 yo man with PMHx sig. for T4N2b pyriform sinus squamous cell carcinoma who was admitted for chemoradiation cycle 1/5 TFHX.
  - Noted to have kyphosis on physical exam
  - Inpatient BMD was obtained

# Bone Mineral Density



- L femoral neck -3.1, L total neck -2.9
- R femoral neck -2.8, R total neck -3.2
- L1-4 spine -2.9

Endocrine was consulted for osteoporosis.



CXR



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# History of Present Illness

- Per patient and sisters, his kyphosis has been chronic since childhood
- Tallest height was 6'2", now 5'10"
- No back pain
- Lost 40 lbs in the past year
- Fracture history: L wrist at age 10 while jumping out of a window playing a cowboy
- Fall history: once in the past year, after receiving chemotherapy for the first time



# Past Medical History

- T4N2b pyriform sinus squamous cell carcinoma
  - Diagnosed in 10/2012
  - Induction chemotherapy: cisplatin/paclitaxel/cetuximab ± everolimus
  - TFHX (paclitaxel, infusional 5-fluorouracil, hydroxyurea, and twice-daily radiation therapy)
- Barrett's esophagus with high grade dysplasia
- Hypertension
- Chronic obstructive pulmonary disease



# Medications

- Lisinopril 40 mg daily
- Carvedilol 12.5 mg BID
- Esomeprazole 40 mg daily
- Mirtazapine 15 mg daily
- Hydrocodone-acetaminophen
- Combivent inhaler
- Fluticasone inhaler
- Calcium carbonate 1250 mg BID
- Magnesium hydroxide 1200 mg BID
- Potassium chloride 40 mEq daily
- Ferrous sulfate 325 mg daily



# Medical History

- Social History:
  - Not married, no children
  - Lives with his sister
  - Previously worked as a carpenter
  - Smoked for 40 pack-years, quit 1 year ago
  - Drank 6-12 beers on the weekends
- Family History:
  - Maternal grandmother, mother, and 2 maternal aunts with osteoporosis.
  - No family history of hip fractures.
  - Father died of oral cancer, smoker.
  - Maternal grandmother and maternal aunt with colon cancers.



# Physical Exam

- BP 176/86 | Pulse 83 | Temp(Src) 36.1 °C (97 °F)| Resp 20 | Ht 171 cm (5' 7.32") | Wt 70.2 kg (154 lb 12.2 oz) | BMI 24.01 kg/m<sup>2</sup> | SpO<sub>2</sub> 98%
- Constitutional: Patient appears thin, in no acute distress.
- Eyes: Conjunctivae are not injected. Sclerae anicteric. Pupils are equal, round, and reactive to light. Extraocular movements are intact.
- ENT: Mucous membranes moist.
- Neck: Supple. No thyromegaly or nodules palpated.
- Cardiovascular: Regular rhythm and rate. No murmurs appreciated. Intact distal pulses.
- Respiratory/Chest: Normal respiratory effort. No wheezes or crackles.
- Gastrointestinal/Abdomen: Normoactive bowel sounds. Soft, nontender, nondistended.
- Musculoskeletal/extremities: +Kyphosis, able to straighten.
- Neurological: Alert and oriented to person, place, and date. Normal deep tendon reflexes. + Chvostek's sign.
- Skin: Skin is warm and dry. Macular rash throughout.
- Psychiatric: Normal mood and affect.



# Laboratory Data

|     |     |     |     |      |     |
|-----|-----|-----|-----|------|-----|
| 139 | 105 | 16  | 113 | 9.6  | 403 |
| 4.1 | 22  | 1.0 |     | 10.9 |     |

Ca 7.4, Phos 2.9, Mg 0.7

29.9

Total protein 6.4, alb 3.4,  
tb 0.2, alk phos 107,  
AST 19, ALT 15

# Trends

Mg(OH)<sub>2</sub> 500 mg TID  
CaCarb

Mg(OH)<sub>2</sub> 1200 mg TID  
CaCarb 1250 mg BID

Mg 4 mg

Mg 6 mg

Day 1

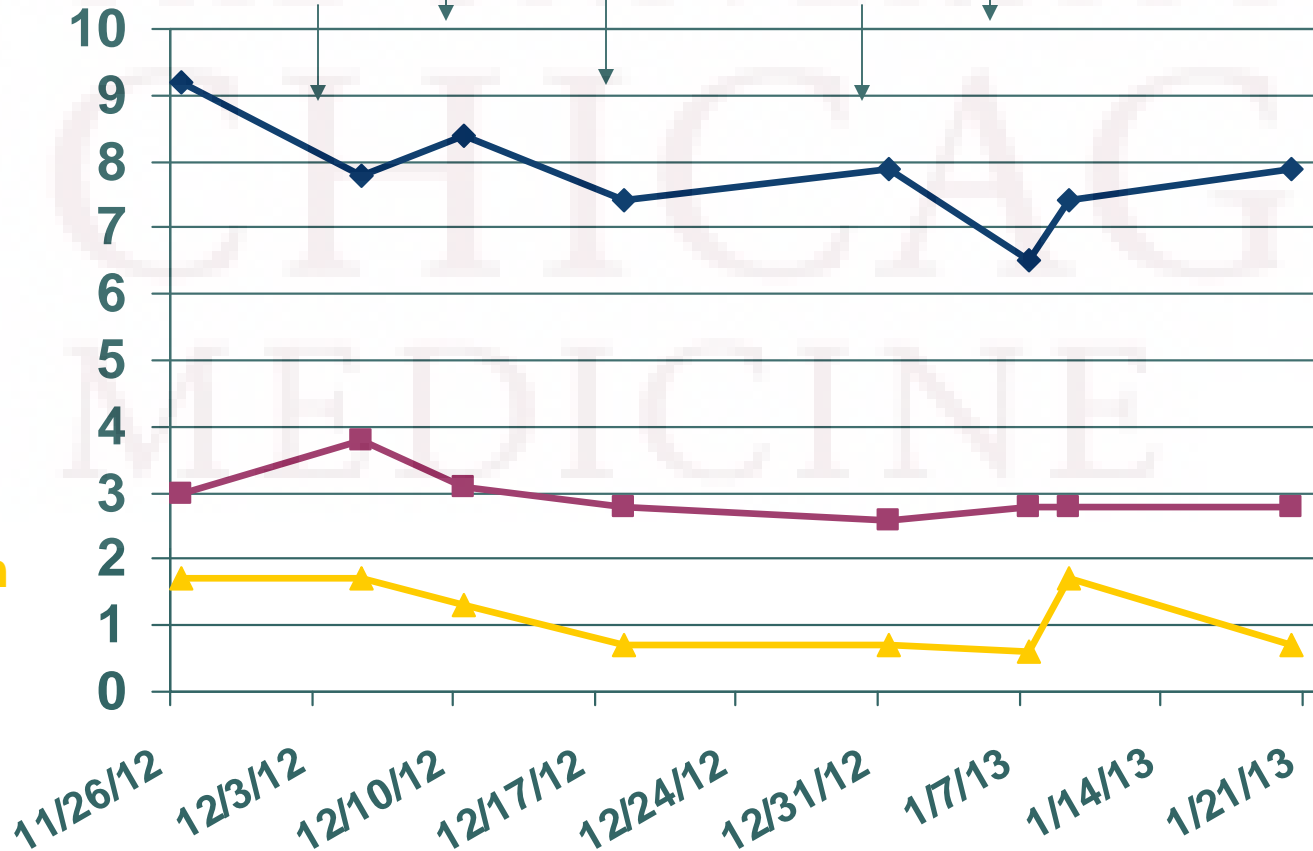
Mg 8 mg

Mg 6 mg

Calcium

Phosphate

Magnesium





# Additional Labs

- PTH 157 (15-75)
- Calcium 7.8 (8.7)
- Phos 3.5
- Mg 1.5
- 25 OH 16
- TSH 0.52
- 24 hour urine Ca 15 mg (100-300), Cr 662 mg (1000-2000)



# Assessment & Plan

- 67 yo man with PMHx sig. for T4N2b pyriform sinus squamous cell carcinoma admitted for chemoradiation cycle 1/5 TFHX. He was noted to have kyphosis. BMD showed severe low BMD.
  - Osteoporosis: He has no history of atraumatic fractures. Risk factors include family history of osteoporosis, sig. weight loss, tobacco use.
    - Can consider checking testosterone, FSH, LH as outpatient.
    - Currently with hypocalcemia and vitamin D insufficiency, hold off on treatment until normalized.
  - Hypocalcemia: Likely due to hypomagnesemia from chemotherapy (cetuximab, cisplatin), chronic ETOH. 5-FU may also cause hypocalcemia. Also has vitamin D insufficiency.
    - Please aggressive replete Mg.
    - Restart calcium carbonate 1250 mg BID.
    - Replete with vitamin D2 50,000 weekly x 8 weeks followed by vitamin D3 1000 daily.



# My questions:

- How does cetuximab affect magnesium balance?
- What is the relationship between hypomagnesemia and hypocalcemia?

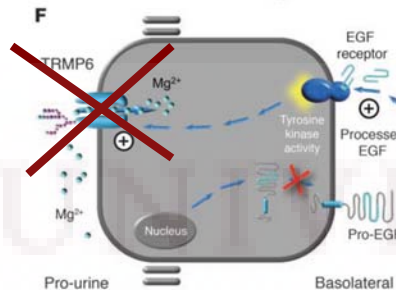
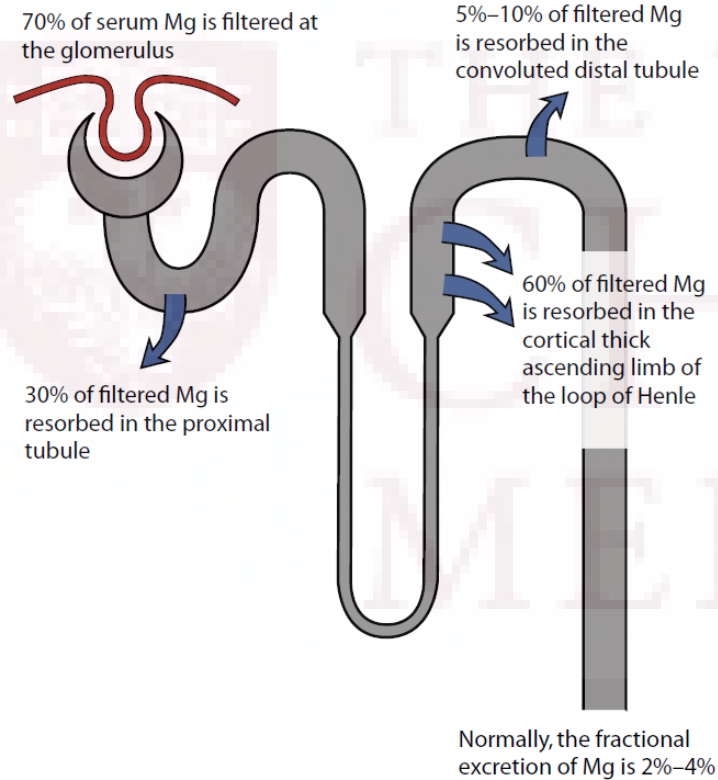


# Cetuximab

- Chimeric monoclonal antibody that binds and inhibits epidermal growth factor receptor
- Fakih et al. performed a retrospective review on 48 pts with colorectal cancer on cetuximab and normal baseline Mg level.
  - 8% with grade 2, 8% with grade 3, 19% with grade 4 hypomagnesemia
- Risk Factors:
  - Longer duration of treatment, older age, higher baseline Mg

Fakih et al. [Clin Colorectal Cancer](#). 2006 Jul;6(2):152-6.  
Saif. [J Support Oncol](#). 2008 May-Jun;6(5):243-8.

# Mechanism of Action



- EGFR is highly expressed in the apical membrane of the loop of Henle and DCT.
- Cetuximab inhibits the activity of epithelial Mg channel TRPM6 in the DCT.



# Hypomagnesemia

## Clinical Manifestations of Hypomagnesemia

|   |
|---|
| Tremor  |
| Hyperactive deep tendon reflexes  |
| Hyperreactivity to sensory stimuli  |
| Muscular fibrillations  |
| Positive Chvostek sign  |
| Positive Trousseau signs  |
| Carpopedal spasms progressing to tetany   |
| Mental status changes: <ul style="list-style-type: none"><li>Irritability</li><li>Disorientation</li><li>Depression</li><li>Psychosis</li></ul> |
| Reversible respiratory muscle failure may occur in severe hypomagnesemia  |



# Magnesium and PTH Secretion

- Mild hypomagnesemia increases PTH secretion.
- Severe hypomagnesemia can cause hypoparathyroidism and resultant hypocalcemia.
  - Biphasic:
    - >2.4 mg/dL: Stimulation of CaSR
    - <1.2 mg/dL: Disinhibition of G $\alpha$ -subunits, thereby mimicking activation of CaSR
- Parenteral Mg results in rapid rise in PTH levels.

Vetter et al. [Curr Opin Nephrol Hypertens.](#) 2002 Jul;11(4):403-10.  
Agus. [J Am Soc Nephrol.](#) 1999 Jul;10(7):1616-22.



# Magnesium and PTH Resistance

- Freitag et al. studied isolated perfused bones from dogs fed a low Mg diet.
  - Hypomagnesemia was found to decrease uptake of PTH and diminish cAMP generation in response to PTH.
- Rude et al. studied 17 patients with mean serum Ca 6.7 mg/dL and Mg 0.75 mg/dL.
  - PTH was undetectable in 7 patients, normal in 7 patients, and high in 2 patients.
  - PTH increased within 24 hours after initial magnesium therapy.
    - In 3 patients, within 1 min after IV Mg, PTH rose from undetectable to 3600 and 1725 and from 425 to 937.
  - Calcium normalized after 4 days.

Freitag et al. J Clin Invest. 1979 Nov;64(5):1238-44.

Rude et al. Clin Endocrinol (Oxf). 1976 May;5(3):209-24.



# Hypomagnesium and Bone

- Epidemiologic studies have shown a positive correlation between Mg intake and bone mineral density.
- Rude et al. placed mice on a low Mg diet.
  - Lower serum Mg and skeletal Mg content
  - Slightly higher serum Ca
  - Similar PTH levels
  - Reduced bone growth
    - Decreased tibial growth plate width by 33%
    - Decreased number and length of chondrocyte columns
  - Decreased trabecular bone volume in the metaphysis of the tibia
  - Decreased osteoblast number.
  - Increased osteoclast number by 135%.
    - Increased IL-1 and TNF $\alpha$  levels in osteoclasts.



# Take Home Points

- Not all kyphosis is due to vertebral fractures.
- Magnesium can affect both PTH secretion and sensitivity, resulting in hypocalcemia.
- Magnesium may be important in bone health.



# References

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