Endocrine Emergencies

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Diabetes and Nutrition Center
February 17, 2017
Headache and vision changes

• 50 year old man admitted for elective AVR
• ROS + for decrease libido and ED
• Post-op he c/o decrease vision left eye, and headache. On exam BP 88/60 right eye ptosis, inability to adduct right eye and patient was drowsy

• Diagnosis.....
PITUITARY APOPLEXY

- Age 10-90, peak: 50
- men > women
- Most undiagnosed pituitary adenoma
- Headache: 80%
- Visual change: 50%
- Ophthalmoplegia: 50%
  - CN III most common
- Other
  - Photophobia: 40%
  - Nausea/vomiting: 57%
  - Altered consciousness
- Precipitating factors 10-40%
  - Angiography
  - Surgery
  - Head trauma

NEJM 2003 349:21:2034
Hormonal Deficiencies

- Corticotropic deficiency: 50-80%
- Give empiric corticosteroids in all patients
- 30-70% thyrotropic deficiency
- 40-75% gonadotropin deficiency
- Almost all GH deficiency
- Diabetes Insipidus rare: 5% patients

Endocrine Reviews 2015,36(6):622-645
Treatment

- Hydrocortisone 50 mg IV q 6 hrs or 100-200 mg bolus then 50-100 mg q 6 hrs
- Surgical decompression to be considered for significant neuro-ophthalmic signs or reduced consciousness. Surgery should be done within first week after symptom onset. 86% improvement versus 46% visual improvement surgery prior/after 1 week

*Endocrine Reviews 2015,36(6):622-645*
PITUITARY TUMOR

• WHAT IS IT?

• IS IT SECRETING ANY HORMONE IN EXCESS?

• ARE THERE ANY HORMONAL DEFICIENCIES?

• IS THERE COMPRESSION OF THE OPTIC CHIASM?

• HAS AN ENDOCRINOLOGIST BEEN CONSULTED PRIOR TO A NEUROSURGEON?
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• HAS AN ENDOCRINOLOGIST BEEN CONSULTED PRIOR TO A NEUROSURGEON?

“Neurosurgery on a patient with a nonfunctional pituitary tumor without mass effect leads to two possible outcomes: patient is the same or worse.” James W. Findling, MD
Altered Mental Status
Altered Mental Status

- 52 year old woman with type 1 DM for 20 years lost to follow-up uses OTC NPH and Regular insulin split dose. HgA1c 7-8%
- AM husband could not arouse her for 45 minutes. Glucose was 77 increased to 144 mg/dl
- Complains of fatigue for 2 months. No fever, no cough, no dysuria, no chest pain.
- Has history of migraine headaches and complains of severe HA in ER. CT scan negative
Altered Mental Status

PMH: type 1 DM, migraine headache
Social: 20 pack years
PE: 127/74 80 sat 88-94% room air
Heart: RRR
No edema
Delayed response to questions, confused
Skin dry, Delayed reflexes
## Altered Mental Status

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<th>Test</th>
<th>Result</th>
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<td>WBC</td>
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<td>Platelets</td>
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<td>Na</td>
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<tr>
<td>Cortisol</td>
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<tr>
<td><strong>TSH</strong></td>
<td><strong>60.1</strong></td>
</tr>
<tr>
<td>Free T4 (0.50-1.2 ng/dl)</td>
<td><strong>0.60</strong></td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>Normal</td>
</tr>
<tr>
<td>CT head</td>
<td>Normal</td>
</tr>
<tr>
<td>UA</td>
<td>No WBC, proteinuria</td>
</tr>
<tr>
<td>Lumbar puncture</td>
<td>Negative: 0 RBC, 4 Nucl cells, clear</td>
</tr>
</tbody>
</table>
Myxedema Coma

• Lethargy…Stupor….Coma
• Respiratory Failure
• Hypothermia
Myxedema Coma

- Lethargy…Stupor….Coma
- Respiratory Failure
- Hypothermia

Our patient altered mental status, hypoxia and hypothyroid. Consider evolving myxedema coma or at very least hypothyroid crisis
Precipitating Event

- Hypothermia
- CVA
- CHF
- Infection
- Sedatives
- Trauma
Findings

- Respiratory
  - Reduced hypoxic respiratory drive
  - Reduced ventilatory response to hypercarbia
- Neuropsychiatric
  - < 90 degrees worst prognosis
  - Lethargy, poor memory, depression
- Dry Skin
  - Hoarse voice
  - Enlarged tongue
  - Delayed tendon reflexes
  - Nonpitting edema
  - Sinus bradycardia
  - Low voltage complexes
  - Pericardial effusions
  - Nomocytic anemia
  - Hyponatremia
  - ↑ CPK
  - ↑ LDH
Myxedema Coma Treatment

- Supportive care
- Loading dose of levothyroxine 200-400 micrograms IV (lower older, CHD, smaller)
- LT4 > 500 and LT3 > 75 mcg/day associated with increase mortality
- Daily replacement 75% of 1.6 micrograms/kg body weight IV then 100% PO.
- Can consider T3 5-20 micrograms loading then 2.5-10 micrograms every 8 hours until improved clinical status
- Empiric glucocorticoids ideally cortisol prior to dosing
- Check T3 and T4 levels 1-2 days after onset of treatment.

_Thyroid_ 2014:24:1670-1748
Altered Mental Status

• Given type 1 DM and smoking, concerned with underlying hearts disease.
• She was treated with 200 mcg Levothyroxine IV then 75% of 1.6 mcg/kg LT4 IV x 2 days then change to PO
• Improved within 24 hrs, confusion resolved at 48 hrs.
Myxedema Coma Summary

• Medical emergency
• Hypothermic, altered mental status, hypoxia/hypercarbia and hypothyroid
• Evaluate for precipitating cause
• LT4 200-400 mcg IV +/- T3
• Glucocorticoids until confident normal function
• Supportive care
Emergent Surgery
Emergent surgery case

- 20 year old G1P0 at 4 weeks gestation developed vaginal bleeding and passing clots.
- US: Abnormal echogenicity within endometrium 14.5 cm max dimension. No discrete fetal pole. Bilateral ovarian cysts
- Beta HCG > 400,000 mIU/ml
- Admitted for surgery for concerns molar pregnancy.
Emergent Surgery

• c/o 1 month of fatigue
• Weight loss 15 pounds/3 weeks
• Palpitations
• Muscle weakness
• Daily Nausea/vomiting
• No fever
• No hallucinations
• No eye complaints
• No neck pain
• No family history of thyroid disease

• 98.6 133/74 pulse 94-120
• No stare, no lid lag
• Thyroid not enlarged, nontender, no nodules, diffuse bruit
• Heart: RRR
• No tremor
Emergent Surgery

- c/o 1 month of fatigue
- Weight loss 15 pounds/3 weeks
- Palpitations
- Muscle weakness
- Daily Nausea/vomiting
- No fever
- No hallucinations
- No eye complaints
- No neck pain
- No family history of thyroid disease

- 98.6 133/74 pulse 94-120
- No stare, no lid lag
- Thyroid not enlarged, nontender, no nodules, diffuse bruit
- Heart: RRR
- No tremor
- LAB:
  - TSH 0.01
  - Free T4 3.2 (0.50-1.2 ng/dl)
  - Free T3 8.7 (2-2-4.0 pg/ml)
  - Thyrotropin Receptor AB: neg
Molar Pregnancy and Hyperthyroidism

- Gestational Trophoblastic disease 1.5/1000 UK pregnancies
- Molecular mimicry between HCG subunits and TSH
- Potency for HCG and TSH receptor 4000 times less than TSH

*British Journal of Cancer* 2011:104:1665-1669
Hyperthyroid emergency

• Thyroid Storm
  – Clinical diagnosis
  – Temp >103, mental status changes, nausea/vomiting or jaundice
• Unstable angina/MI
• Emergent Surgery: Can precipitate thyroid storm, adverse cardiovascular outcomes. Postpone elective surgery. Provide optimal medical management for urgent surgery
Medical Treatment Hyperthyroidism

Propylthiouracil: 200-400 mg every 4-6 hours
- decrease synthesis
- decrease T4 to T3 conversion

Dexamethasone
- decrease release of thyroid hormone
- decrease T4 to T3 conversion

Supersaturated potassium iodine
- decrease release of thyroid hormone.

Beta blockers
- control heart rate
Medical Treatment Hyperthyroidism

**Propylthiouracil**: 200-400 mg every 4-6 hours  
- decrease synthesis  
- decrease T4 to T3 conversion

**Dexamethasone**  
- decrease release of thyroid hormone  
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**Supersaturated potassium iodine**  
- decrease release of thyroid hormone.

<table>
<thead>
<tr>
<th></th>
<th>Day 0</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 10</th>
<th>Day 30</th>
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<tr>
<td>TSH</td>
<td>0.01</td>
<td></td>
<td></td>
<td>Stop methimazole</td>
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<tr>
<td>Free T3</td>
<td>2.2-4.0 pg/ml</td>
<td>8.7</td>
<td>3.8</td>
<td>1.9</td>
<td>2.7</td>
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<tr>
<td>Free T4</td>
<td>0.5-1.2 ng/dl</td>
<td>3.2</td>
<td>3.0</td>
<td>2.6</td>
<td>1.0</td>
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<tr>
<td>HCG</td>
<td>&gt;400,000</td>
<td></td>
<td></td>
<td>1,846</td>
<td>35.6</td>
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</table>
Hypertension case
Hypertension case

• A 38 year old woman has had hypertension for 9 years.
• She had preeclampsia with her first pregnancy.
• Current antihypertensive regimen:
  – Lisinopril, 20 mg/day
  – Triamterene/hydrochlorothiazide, 37.5/25 mg/day
  – Metoprolol, 50 mg/day
Hypertension case

- Examination: Ht 66 inches (1.68 m), Weight 157 pounds (71.4 kg) BMI 25.3, BP 164/92 mm Hg. P 72 bpm
  - Grade II systolic ejection murmur
  - There was no pedal edema
  - Normal pulses throughout

- Laboratory
  - Na+ 146 135-145 mmol/L
  - K+ 3.6 3.5 to 5.0 mmol/L
  - HCO3 30 23 to 30 mmol/L
  - Creatinine 1.0 0.7 to 1.4 mg/dl
  - eGFR >60
Hypertension case

• Definition of resistant hypertension
  – The blood pressure is above goal despite the use of three antihypertensive medications of different classes, including a diuretic.

• She was screened for secondary forms of hypertension after the triamterene/HCTZ was stopped for 3 weeks.
  – Aldosterone 24 ng/dl
  – Plasma renin activity (PRA) 0.6 ng/ml/hr
  – Potassium 2.9 mmol/L

Confirmation testing-she underwent salt loading and had an elevated urinary aldosterone level.
1.3 cm homogeneous appearing right adrenal nodule. The left adrenal appeared normal.
Outcome

• She underwent a right laparoscopic adrenalectomy.
  – Pathology: 1.8 cm yellow adrenal nodule
• Following surgery:
  – BP 122/72
  – She was taking 10 mg of lisinopril per day.
Laboratory
  – K+ 4.5 mmol/L
  – Aldosterone 4.2 ng/dl
  – PRA 3.4 ng/ml/hr
Evaluation of resistant hypertension

Consider screening for:

– Hypercortisolism
  • Two late night salivary cortisols
  • Overnight 1 mg dexamethasone suppression test

– Pheochromocytoma
  • Plasma metanephrines
  • Or 24 hr urine for free metanephrines

– Primary aldosteronism.
  • Morning PRA, aldosterone and K+
  • Confirmation: 24 hr urine for aldosterone, sodium and creatinine collected at the end of a 3-day oral salt load.
Primary aldosteronism


- Occurs in 5-13% of patients with ‘essential hypertension.’
- Occurs in ~20% of patients with resistant hypertension.
- In the last 15 years –the majority of patients diagnosed with hyperaldosteronism have normal potassium levels.
- A clue is the K+ often is in the low normal range.
- The K+ level has to be evaluated in the context of the medications the patient is taking.
  - ACE inhibitors and ARBS raise the K+.
  - Triamterene and amiloride raise the K+.
  - Regular use of NSAIDs will raise the K+.
Abdominal pain and hyponatremia
Abdominal pain and hyponatremia

A 34 yo woman with a 6 yr history of Crohn’s disease on variable dosing of entocort or prednisone (up to 30-40 mg/d), complains of cycles of lower abdominal pain resolved with IV hydration and narcotics. There are 50 ER visits in the past 3 years for abdominal pain, tachycardia, hypotension, and hyponatremia. Labs: Na 111-135, K 3.8-6.1, Creatinine and TSH normal

<table>
<thead>
<tr>
<th>#1</th>
<th>#2</th>
<th>#3</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTH &lt;5</td>
<td>ACTH &lt;5</td>
<td>ACTH 275</td>
</tr>
<tr>
<td>Cortisol 11.3 → 15.7</td>
<td>Cortisol &lt;0.2 → &lt;0.2</td>
<td>Cortisol &lt;0.2 → &lt;0.2</td>
</tr>
</tbody>
</table>

While hypotensive Na 120, K 5.3, renin 56, aldosterone 2.1.
While hypotensive: Na 125, Urine Na 109 mmol/l.
Abdominal pain and hyponatremia

Her prednisone of 5 mg/d is held for a 4\textsuperscript{th} anticipated cosyntropin stimulation test.

She is found by her husband unresponsive. She survives a 10-15 minute code. She is discharged on hydrocortisone 20 mg twice daily.

**On exam:** She is Cushingnoid, BP 102/60, P 77, Wt 145 lbs

No hyperpigmentation.

**Past history:** amenorrhea and FSH of 82.

**Meds:** percocet, fentanyl, hydrocortisone 20 mg BID.

BMD shows Z-scores near -4.
Abdominal pain and hyponatremia

Why is she having multiple episodes of hypotension, hyponatremia and abdominal pain?

A) She requires a larger dose of prednisone to treat her Crohn’s disease.

B) She is noncompliant with corticosteroids and is having adrenal crisis from secondary AI.

C) She has primary adrenal insufficiency and needs mineralcorticoids.

D) She is abusing laxatives and is drug seeking.
Abdominal pain and hyponatremia

Why is she having multiple episodes of hypotension, hyponatremia and abdominal pain?

A) She requires a larger dose of prednisone to treat her Crohn’s disease.

B) She is noncompliant with corticosteroids and is having adrenal crisis from secondary AI.

C) **She has primary adrenal insufficiency and needs mineralcorticoids.**

D) She is abusing laxatives and is drug seeking.
Abdominal pain and hyponatremia

- She has primary adrenal insufficiency and needs mineralcorticoids.
- She has had multiple episodes of adrenal crisis
- She shows salt wasting when hypovolemic, consider laxative abuse, and primary AI
- ACTH should be elevated with primary but can be suppressed with high dose long acting corticosteroids and with narcotics
- Despite hypotension and elevated PRA, minimal aldosterone. Further testing showed positive 21 hydroxylase antibodies
- Always consider adrenal insufficiency with hyponatremia...often there is a prolonged delay
Adrenal Insufficiency

- Volume depletion
- Hypotension
- Hyponatremia
- Hyperkalemia
- Fever
- Abdominal pain

- Weight Loss
- Failure to thrive
- Postural dizziness
- Hypoglycemia
- Hyperpigmentation (primary) sun-exposed areas

*JCEM* 2016 101(2): 364-389
Adrenal Insufficiency Diagnosis

- Cosyntropin stimulation 250 micrograms. Peak cortisol at 30 or 60 minutes >18 micrograms/dL.
- Or morning cortisol < 5 micrograms/dL with elevated ACTH (primary)
- Plasma ACTH > 2 fold upper limit of reference range is consistent with PAI
- Ensure not on corticosteroids measured in cortisol assay
Delay in Diagnosis: too common

- < 30% woman and 50% men with AI diagnosed within 6 months after onset symptoms.
- 20% patients suffered > 5 years prior to diagnosis
- >67% consulted with at least 3 physicians
- 68% initial diagnosis was false: psychiatric and GI diseases.
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<table>
<thead>
<tr>
<th>Symptom</th>
<th>Frequency</th>
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<tbody>
<tr>
<td>Hyponatremia</td>
<td>100%</td>
</tr>
<tr>
<td>Lack Appetite</td>
<td>100%</td>
</tr>
<tr>
<td>Weight Loss</td>
<td>100%</td>
</tr>
<tr>
<td>Orthostatic Hypotension</td>
<td>100%</td>
</tr>
<tr>
<td>Hyperpigmentation</td>
<td>95%</td>
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</table>

Delay in Diagnosis of AI is a frequent cause of adrenal crisis, *Inter J Endocrinology* 2013

*Am J Med Sci* 2010;339(6)525-31
Adrenal Insufficiency Management

Crisis
• If suspected immediate 100 mg IV hydrocortisone
• Fluid resuscitation 1 liter isotonic within 1st hour or 5% glucose in NS followed by continuous IV
• 200 mg hydrocortisone/24 hours IV or 6 hourly injections
• Hypoglycemia: 2-4 ml/kg of D25W max single dose 25g
• Dexamethasone is the least preferred glucocorticoid

Chronic
• Hydrocortisone 12-25 mg in 2-3 divided doses
• Hormonal monitoring not helpful (i.e. ACTH)
• Fludrocortisone 50-100 micrograms/d
• Follow BP, BMP
• PRA upper limit normal
• Do not restrict salt
• Sick day education
Adrenal Insufficiency Summary

• Think about diagnosis in every patient with hyponatremia. Especially weight loss and pain.
• Do not delay treatment for crisis.
• Educate patients regarding sick day management.
Hypercalcemia
Hypercalcemia Diagnosis

**PTH Mediated**
- Primary Hyperparathyroidism
- Lithium
- Familial Hypocalciuric Hypercalcemia

**Non PTH mediated**
- Malignancy
  - Humoral
  - Direct bone mets
- Calcitriol Induced
- Milk Alkali Syndrome
- Hyperthyroidism
- Vitamin D toxicity
- Vitamin A toxicity
- Adrenal Insufficiency
EVALUATION

• Stepwise

• Calcium, albumin, creatinine, PTH, PTHrP, phosphorus, 25-hydroxyvitamin D and 1, 25 dihydroxyvitamin D.
Actions of PTH

- Activates 1-alpha-hydroxylase enzyme
  - Converts 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D
- Stimulates calcium reabsorption in the distal nephron
- Stimulates renal phosphorus excretion
- PTH leads to calcium mobilization from the bone with help from 1,25 dihydroxyvitamin D
Actions PTHrp

- Nearly all human tissues
- Functions within microcirculation to regulate smooth muscle tone and transepithelial calcium transport
- Leads to osteoclast generation and activation
- Does not augment 1,25 dihydroxyvitamin D production.
Actions 1,25 dihydroxycholecalciferol

• Activated from 25-hydroxyvitamin D in the kidneys via 1-alpha-hydroxylase (which is activated by PTH)
• Increases absorption of calcium and phosphate from GI tract
• Decreases renal excretion of calcium and phosphate
• With PTH increases calcium release from bone
## Etiology of Hypercalcemia

<table>
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<tr>
<th>Condition</th>
<th>PTH</th>
<th>PTHrP</th>
<th>PO4</th>
<th>25 D</th>
<th>1,25 D</th>
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<tr>
<td>Primary Hyperparathyroidism</td>
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<td>‡</td>
<td>‡</td>
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<td>HN to ‡</td>
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<tr>
<td>Humoral Hypercalcemia Malign</td>
<td>‡</td>
<td>‡</td>
<td>N to ‡</td>
<td>-</td>
<td>‡</td>
</tr>
<tr>
<td>Direct Bone Invasion</td>
<td>‡</td>
<td>‡</td>
<td>N to ‡</td>
<td>-</td>
<td>‡</td>
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<tr>
<td>Calcitriol Induced</td>
<td>‡</td>
<td>‡</td>
<td></td>
<td>Not ‡</td>
<td>N to ‡</td>
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</table>
Hypercalcemia Case

67 yo woman referred for hypercalcemia

- Hypercalcemia noted late June 2010 when hospitalized with calcium 17 mg/dl and creatinine 3.0 mg/dl. She was given IVF/calcitonin/Zoledronic acid

- Early June 2010 calcium normal, creatinine 1.0

- + Fatigue, nausea, anorexia, arthralgias, weight loss

- No h/o cancer

- Calcium intake <500 mg daily

- Routine calcium/D supplements stopped
Hypercalcemia Case

PE
- Somewhat ill-appearing

Labs
- Calcium 12.1 mg/dl
- PTH <3 pg/ml (15-65)
- Phos 3.2 mg/dl
- Creatinine 1.3
- SPEP, UPEP, TSH, 25D, cortisol, CXR normal
What diagnostic test would you do next?

a. Parathyroid scan with sestimibi
b. PTHrP and 1,25(OH)2D
c. CT scan of chest, abdomen, and pelvis
d. ACE level
What diagnostic test would you do next?

a. Parathyroid scan with sestimibi
b. PTHrP and 1,25(OH)2D
b. CT scan of chest, abdomen, and pelvis
d. ACE level
PTH-Independent Hypercalcemia

- Malignancy
- Calcitriol mediated (granulomatous, inflammatory)
- Hyperthyroidism
- Milk-alkali syndrome or calcium-alkali syndrome
- Immobilization
- Adrenal insufficiency
- Rare causes
Hypercalcemia case

- Additional studies
- $\text{PTHrP} \ 0.4 \text{ pmol/l} \ (<2)$
- $1,25 \ (OH)2 \ D \ 275 \ \text{pg/ml}$
Hypercalcemia Case

- Additional studies
- PTHrP 0.4 pmol/l (<2)
- 1,25 (OH)2 D 275 pg/ml (<100 pg/ml)
- CT – *gastric mass*
- Bx – *large B cell lymphoma*
Calcitriol-Mediated Hypercalcemia

- Sarcoid
- Lymphoma
- Tuberculosis
- Fungal disease
- Wegener’s granulomatosis
- Crohn’s
- Nephrogenic systemic fibrosis after gadolinium
- Mineral oil injection (oleogranulomatous mastitits – paraffinoma)
- Silicone-induced granuloma
- Lipoid pneumonia
- Seminoma
- Leprosy
- Cat-scratch fever
- Acute granulomatous pneumonia
- BCG therapy
- Subcutaneous fat necrosis of the newborn
- Hepatic granulomatosis
- Talc-induced granuloma
- Inflammatory arthritis
Hypercalcemia of Malignancy

- 2.7% of cancer patients
- 50% survival of 30 days regardless of treatment
- Tumor-induced bone resorption mediated by an increase in osteoclasts
  - Systemic secretion of PTHrP
  - Local osteolytic bone resorption

*J Clin Endocrinol Metab* 2014: 99(9): 3144-3152
Etiology of Hypercalcemia of Malignancy

- PTHrP mediated hypercalcemia
- Osteolytic metastases mediated hypercalcemia
- Hypercalcemia secondary to overproduction of 1,25 vitamin D
- PTH mediated hypercalcemia (parathyroid carcinoma and ectopic production)
Etiology of Hypercalcemia of Malignancy

- Squamous Cell Cancers
- Urinary Tract Cancers
- Breast Cancer
- NonHogkin’s lymphoma
- Ovarian Cancer

- PTHrP mediated hypercalcemia
- Osteolytic metastases mediated hypercalcemia
- Hypercalcemia secondary to overproduction of 1,25 vitamin D
- PTH mediated hypercalcemia (parathyroid carcinoma and ectopic production)
Etiology of Hypercalcemia of Malignancy

- Breast Cancer
- Multiple Myeloma
- PTHrP mediated hypercalcemia
- Osteolytic metastases mediated hypercalcemia
- Hypercalcemia secondary to overproduction of 1,25 vitamin D
- PTH mediated hypercalcemia (parathyroid carcinoma and ectopic production)
Etiology of Hypercalcemia of Malignancy

Lymphomas
Ovarian germ cell tumors
Etiology of Hypercalcemia of Malignancy

- Parathyroid Carcinoma
- Small Cell Lung Cancer

- PTHrP mediated hypercalcemia
- Osteolytic metastases mediated hypercalcemia
- Hypercalcemia secondary to overproduction of 1,25 vitamin D
- PTH mediated hypercalcemia (parathyroid carcinoma and ectopic production)
Hypercalcemia Treatment

- Mild: calcium < 12 mg/dl
- Moderate: calcium 12-14 mg/dl
- Severe: calcium > 14 mg/dl
Treatment

• Isotonic crystalloid 200-300 ml/min
• Furosemide if fluid overload occurs
• Calcitonin 4-8 units/kg q 6-12 hours
  – Onset within 4 hours
  – Max drop about 2 mg/dl
• Bisphosphonates: Zoledronic acid
  – 4 mg over 15-30 minutes
  – Onset 2-4 days, duration about 30 days
• Denosumab
Denosumab for Treatment of Hypercalcemia of Malignancy

*JCEM* 2014, 99(9):3144-3152

- By day 10, 36% CR
- Median time for response 9 days
- Median duration of response ≈100 days
Hypercalcemia
Case 2
Hypercalcemia Case 2

- 66 year old woman with history of GERD
- Longterm H2 blockers and proton pump inhibitor. She stopped lansoprazole 10/16.
- Historically would use 6 Tums Ultra per day.
- No past kidney stones, No fractures, no history of cancer, no weight loss, mild lower back pain.
- Total calcium was normal 2011 and 2015
Hypercalcemia Case 2

• 11/8/16 routine labs: creatinine 0.80, calcium 10.7, albumin 4.1
• Became lightheaded, nausea/vomiting
• Family members thought her odd on the phone and brought her to the ER dated 11/22 and calcium increased to 17.2 mg/dl
• CT abdomen/chest/pelvis was normal
Hypercalcemia Case 2

- Past History: CVA, esophagitis, HTN, hyperlipidemia.
- Meds: simvastatin, losartan, amlodipine, MVI, zolpidem, ASA, ferrous sulfate
- Former smoker quit decades ago
### Hypercalcemia case 2

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<tr>
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<th>11/22/16</th>
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<td>10.7</td>
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<tr>
<td>Creatinine</td>
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<tr>
<td>CO2 (21-32)</td>
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<td>39</td>
</tr>
<tr>
<td>Albumin</td>
<td>4.1</td>
<td>3.6</td>
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<tr>
<td>Phosphorus</td>
<td></td>
<td></td>
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<tr>
<td>PTH intact</td>
<td></td>
<td>17</td>
</tr>
<tr>
<td>PTH rP</td>
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<tr>
<td>25 OH D (30-100)</td>
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<td>34</td>
</tr>
<tr>
<td>1,25 OH D (18-79 pg/ml)</td>
<td></td>
<td>14</td>
</tr>
<tr>
<td>TSH</td>
<td>0.80</td>
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</tbody>
</table>

SPEP normal, CT scan chest/abdomen/pelvis negative
Treated with Calcitonin and IV hydration
What is the cause of her severe hypercalcemia?

A) Primary hyperparathyroidism as her PTH intact was not suppressed.

B) Direct bone metastases from some unclear metastatic bone disease

C) Past mild hypercalcemia from unclear etiology exacerbated by milk alkali syndrome

D) Probable granulomatous disease as PTH and PTHrP are not increased

E) Familial Hypocalciuric hypercalcemia
Hypercalcemia Case 2

• Additional history requested. After stopping the proton pump inhibitor the patient increased her consumption of TUMS ultra (1000 mg calcium carbonate) to 20 or more tablets per day.
What is the cause of her severe hypercalcemia?

A) Primary hyperparathyroidism as her PTH intact was not suppressed.

B) Direct bone metastases from some unclear metastatic bone disease

C) Past mild hypercalcemia from unclear etiology exacerbated by milk alkali syndrome

D) Probable granulomatous disease as PTH and PTHrP are not increased

E) Familial Hypocalciuric hypercalcemia
# Hypercalcemia case 2

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<tr>
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<th>11/8/16</th>
<th>11/22/16</th>
<th>1/27/17</th>
<th>2/6/17</th>
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<tbody>
<tr>
<td>calcium</td>
<td>10.7</td>
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<td>10.1</td>
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<td>Creatinine</td>
<td>0.80</td>
<td>1.94</td>
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<td>CO2 (21-32)</td>
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<td>39</td>
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<tr>
<td>Albumin</td>
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<td>3.6</td>
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<tr>
<td>Phosphorus</td>
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<td>3.0</td>
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<tr>
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<td>29</td>
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<tr>
<td>24 hour urine calcium</td>
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<td>160 mg/d</td>
<td>Creat=680 mg</td>
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</table>
Hypercalcemia Case 2

1) Severe calcium PTH independent but PTH not as low as expected for calcium of 17.
2) Not Humoral PTHrP from a cancer
3) No evidence of granulomatous disease as 1,25 not high normal to high with suppressed PTH and negative PTHrP
4) Persistent high calcium with nonsuppressed PTH supports primary hyperparathyroidism. Documentation of past normal calcium rules out FHH
5) Negative imaging less likely bone mets
6) She had high calcium, excessive calcium carbonate, alkalosis, and acute renal insufficiency: Milk Alkali Syndrome
Milk Alkali Syndrome

- 3rd most common inpatient hypercalcemia
- 9-12% of hospitalized patients with ↑ Calc
- Most common cause for calcium >14 mg/dl
- Typically at least 4-5 grams of calcium carbonate per day
- Renal insufficiency
- Alkalosis
- 1,25 D low, PTH low (although variable levels reported), low-normal PO4
- Treat with hydration.

Hypercalcemia Summary

1) Determine if PTH dependent or independent.

2) Consider cancer Humoral via PTHrP or bone mets

3) If not PTH dependent and not PTHrP. Review 1,25 Vit D and consider if inappropriately high normal to increased, ensure not 25 OH Vit D toxic

4) Consider other causes such as Milk Alkali, hyperthyroidism, AI