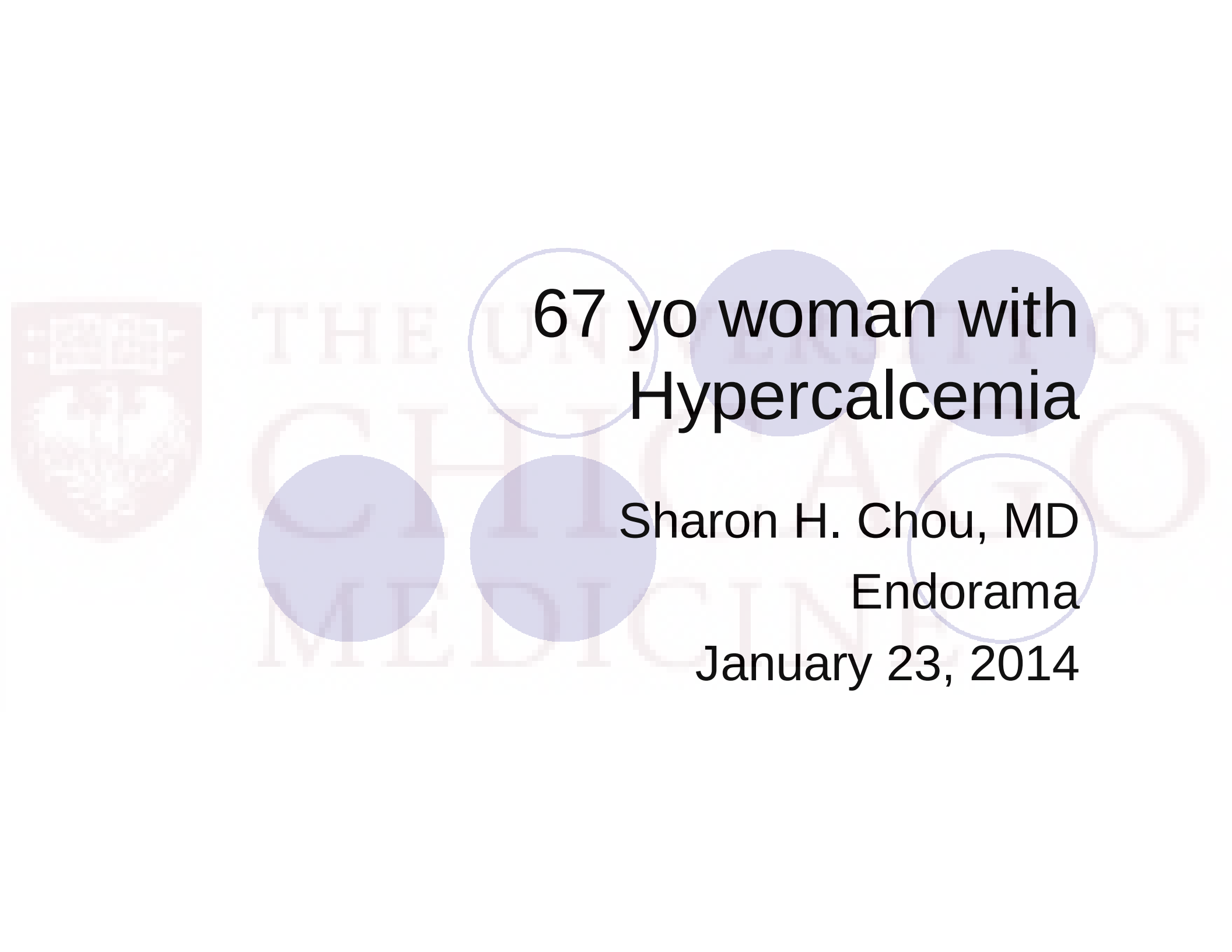




67 yo woman with Hypercalcemia

Sharon H. Chou, MD

Endorama

January 23, 2014

History of Present Illness

- | 67 yo woman with PMHx sig. for CAD, HTN, and stroke in 1996 who presented with 4 days of worsening fatigue and weakness.

- | Ca 22.3!

History of Present Illness

| Per daughter:

- | Nauseous, vomited once, and had poor po intake
- | Urine output may have been decreased
- | Last BM 2 days ago
- | Progressively more confused
- | No history of kidney stones
- | History of traumatic clavicle fracture at age 40

Past Medical History

| Past Medical History

- | Coronary artery disease, s/p CABG in 1998
- | Stroke in 1996
- | Peripheral vascular disease, s/p aortobifemoral bypass in 1999
- | Hypercholesterolemia
- | Hypertension

| Medications:

- | Aspirin 325 mg daily
- | Atorvastatin 40 mg daily
- | Niacin 1000 mg daily
- | Atenolol 25 mg daily
- | Losartan 100 mg daily
- | Chlorthalidone 25 mg daily
- | Calcium and vitamin D supplement 1 tab BID

Medical History

| Social History:

- | Lives with her husband and daughter
- | Previously worked in a department store
- | Smokes ½ ppd x 35 yrs
- | Occasional brandy

| Family History:

- | No calcium disorders, kidney stones

| ROS:

- | +lethargy
- | Weight stable
- | +chills, no fevers
- | +thirsty
- | +nausea, vomiting

Physical Exam

- | BP 150/62 | Pulse 71 | Temp 36 °C (96.8 °F) (Tympanic) | Resp 16 | Ht 170.2 cm (5' 7") | Wt 78.019 kg (172 lb) | BMI 26.94 kg/m² | SpO₂ 97%
- | Constitutional: Patient **extremely lethargic**, 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 dry with thick secretions.**
- | Neck: Supple. No thyromegaly or nodules palpated.
- | Cardiovascular: Regular rhythm and rate. No murmurs appreciated. Intact distal pulses.
- | Respiratory/Chest: Normal respiratory effort. No wheez crackles.
- | Gastrointestinal/Abdomen: Normoactive bowel sounds. Soft, nontender, nondistended.
- | Musculoskeletal/extremities: No peripheral edema. Diffusely weak.
- | Neurological: **Lethargic, oriented to person only.**
- | Skin: Skin is warm and dry.

Labs

141 91 95 } 136
3.2 32 5.9

Ca 22.3

Ionized Ca 10.12 (4.60 - 5.40)

Phos 3.3, Mg 1.9

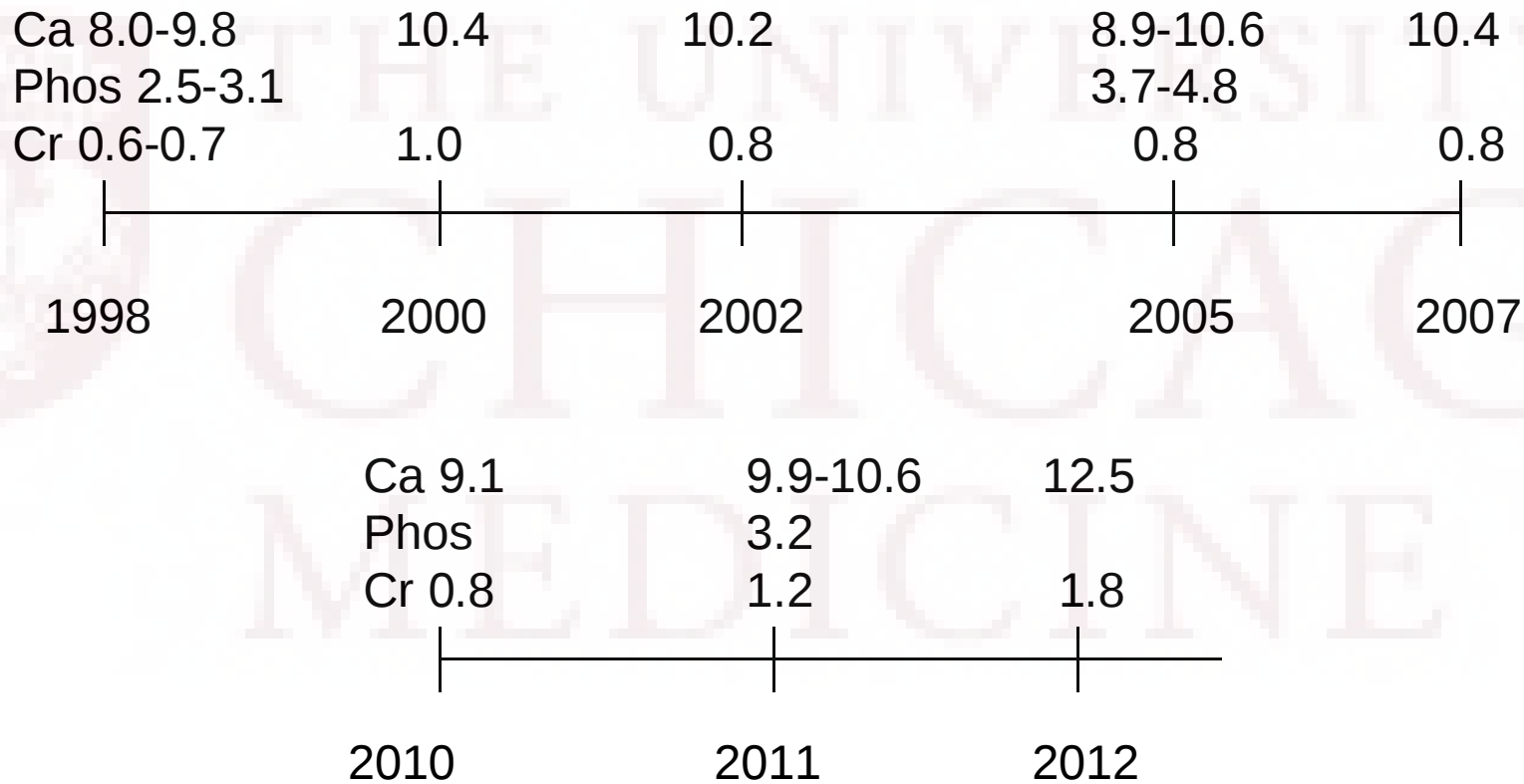
Albumin 4.8, alk phos 48, ast 43, alt 12

~~14.7
19.9 322
42.5~~

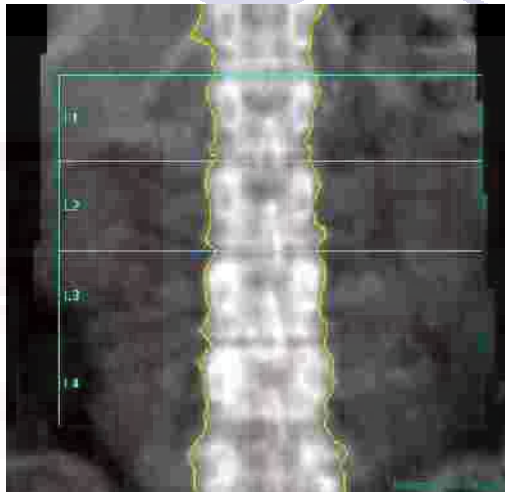
74N, 5B, 14L, 6M

Urine sp gr 1.017, neg LE, neg nitrate, neg protein, neg glucose, tr ketones

History of Labs



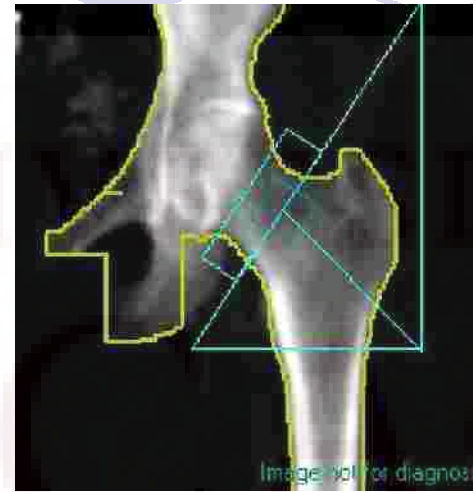
Prior DEXA



L1-L4

T-score 0.7

Z-score 1.5



Region	T-score	Z-score
L neck	-1.9	-1.3
R neck	-1.3	-0.7
L total	-1.5	-1.5
R total	-1.3	-1.3

Labs

- | Ca 22.4
- | Ionized Ca 10.56
- | Phos 3.2
- | Mg 1.9
- | Albumin 4.8
- | PTH (15-75) 37

- | PTHrP (<2) 0.7
- | 25OH vit D 60
- | 1,25 vit D (18-78) 11
- | Angiotensin-1-converting enzyme (8-52) 22
- | SPEP: MGUS
- | TSH 0.36

Assessment & Plan

- | Underlying primary hyperthyroidism given the nonsuppressed PTH of 37, exacerbated by chlorthalidone use and acute on chronic renal failure.
- | Initial recommendations:
 - | Malignancy work-up
 - | Cardiac monitoring
 - | Continue to hold chlorthalidone
 - | IV hydration as tolerated by cardiac and renal status. May need Lasix to prevent volume overload
 - | Consider calcitonin in this acute setting
 - | Pamidronate contraindicated in renal failure
 - | Consult Renal for possible need of HD

Hospital Course

PTH 190

Ca	22.3 à 18.5	16.4 à 12.6	11.5 à 10.0	9.8 à 8.8	8.2 à 8.1
Phos	3.3	3.0 à 1.6	1.1 à 1.2	0.8 à 1.8	2.1 à 1.4
Cr	5.9 à 5.0	4.3 à 2.9	2.5 à 2.3	2.2 à 1.9	1.9 à 1.9

Day 1

2

3

4

5

3L NS
bolus

NS 250 cc/hr à 83 cc/hr

Calcitonin

Post-hospitalization Follow Up

- | Endo Clinic: 1 week follow up

- | Ca 7.5, Cr 1.4
- | PTH 289

- | Heme/Onc Clinic: 2 week follow up

- | Ca 10.5, Phos 4.5, Cr 1.5
- | PTH 37
- | Alk phos 94, bone specific alk phos 17 (>22), CTX 694 (104-1008)
- | Bone marrow bx: mild marrow plasmacytosis with a population of aberrant plasma cells (CD19 -/partial CD56 +) with marked kappa light chain excess, worrisome for a plasma cell dyscrasia
- | Skeletal survey: No discrete myelomatous lesions

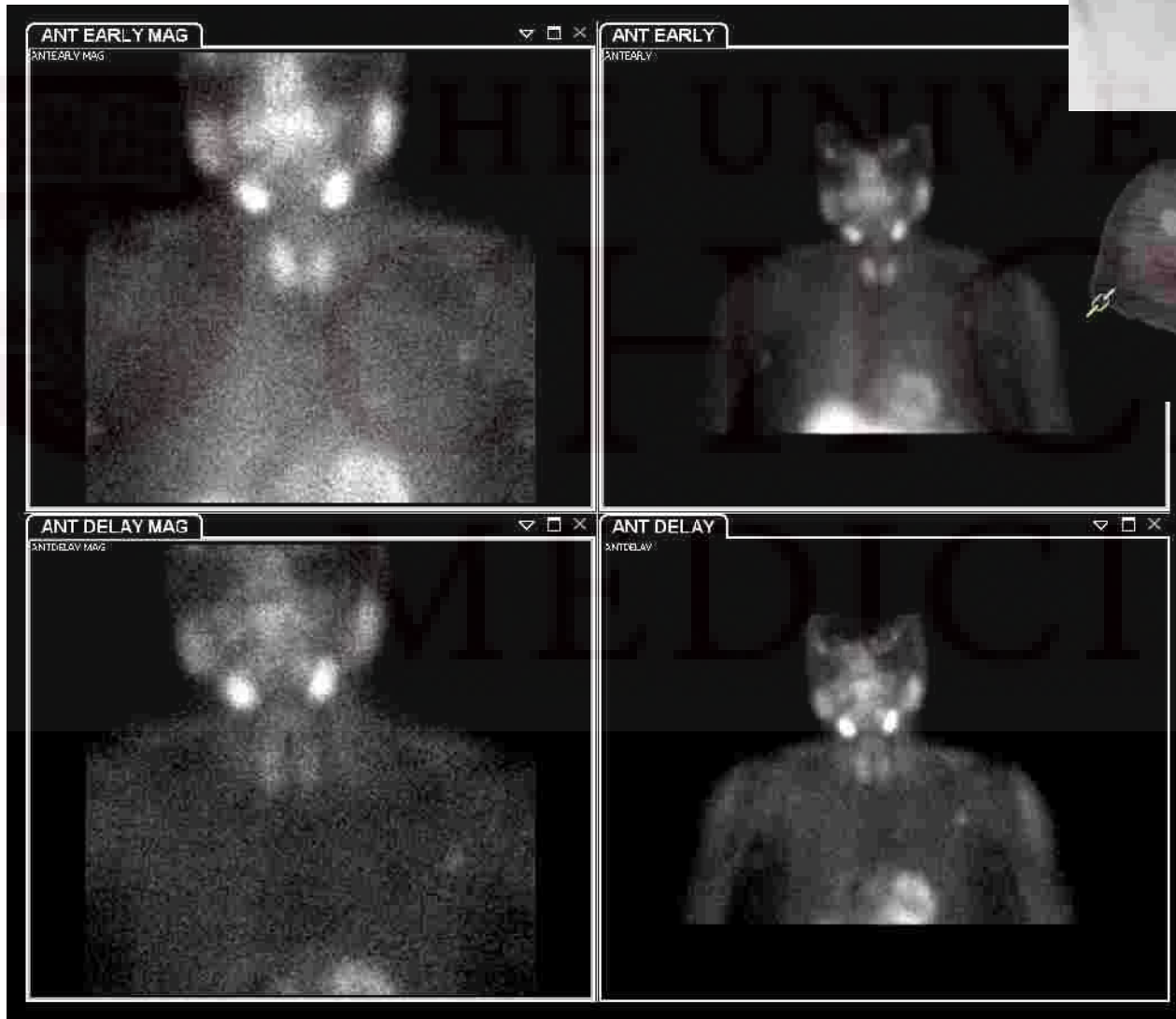
Post-hospitalization Follow Up

- | Primary care clinic: 1 month follow up
 - | Ca 10.6, phos 4.0, Cr 1.0
- | Endocrine clinic: 3 month follow up
 - | Ca 10.3, PTH 38, Cr 1.3
 - | Referred to Endocrine Surgery

Thyroid Ultrasound



Sestamibi Scan



Clinical questions:

- | How severe can hypercalcemia be from primary hyperparathyroidism?
- | Can thiazides be useful in patients with primary hyperparathyroidism?

Causes of Severe Hypercalcemia

Table 1. Characteristics of Hypercalcemic Patients Based on Calcium Level

	Mild (10.3–11.9 mg/dL)	Moderate (12.0–14.0 mg/dL)	Severe (Ca ≥ 14.0 mg/dL)
Patients, n (%)	221 (70.7)	72 (21.2)	28 (8.1%)
Age, years	59.0 ± 15.9	60.1 ± 14.4	60.3 ± 12.9
Male gender, n (%)	106/221 (48.0)	40/72 (55.6)	20/28 (71.4) ^a
Mortality, n (%)	37 (16.7)	25 (34.7)	12 (42.9%) ^b
Etiology, n (%)			
Malignancy	52 (24.9)	38 (52.8)	24 (85.7)
Uremia	87 (39.4)	16 (22.2)	1 (3.6)
Sepsis	19 (8.6)	1 (1.4)	0 (0)
Tuberculosis	8 (3.6)	7 (9.7)	2 (7.1)
Adrenal insufficiency	7 (3.2)	1 (1.4)	0 (0)
Primary hyperparathyroidism	0 (0)	2 (2.8)	1 (3.6)
Immobilization	6 (2.7)	0 (0)	0 (0)
Not identified	39 (17.6)	7 (9.7)	0 (0)

^a $P = 0.018$

^b $P < 0.001$

Yes, but how high?: a prospective study

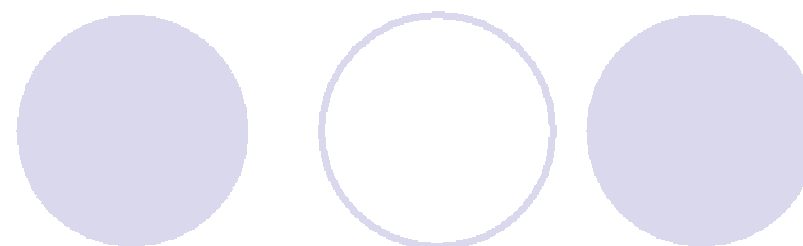


Table I Calcium levels in each category (mmol/l); individual levels given in groups with small numbers

	<i>n</i>	<i>Mean ± standard deviation (highest)</i>	
<i>Sustained hypercalcaemia (273)</i>			
Malignancy	122 (45%)	3.15 ± 0.52 (4.95)	19.8
Thiazide diuretic	59 (21%)	2.67 ± 0.05 (2.87)	11.48
Primary hyperparathyroidism	45 (17%)	2.88 ± 0.25 (3.69)	14.76
Renal	23 (8%)	2.92 ± 0.23 (3.56)	14.24
Rhabdomyolysis	4 (2%)	(3.43; 2.96; 2.77; 2.83)	13.72
Thyrotoxicosis	3 (1%)	(2.75; 2.68; 2.70)	11
Sarcoidosis	2 (1%)	(2.91; 2.73)	11.64
Lithium therapy	2 (1%)	(2.55; 2.73)	10.92
Obscure	13 (4%)		

And higher levels of calcium?: case reports

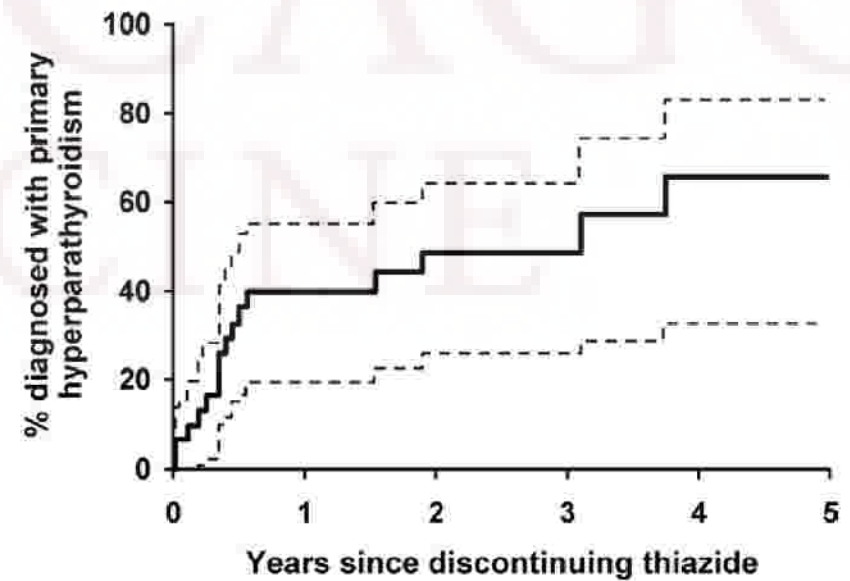
- | Case 1: 59 yo woman presented with 3 days of severe abdominal pain and progressive somnolence.
 - | Medications included HCTZ 50 mg and calcium citrate (400 mg) + D3 (100)
 - | Ca 19.8, ionized 9.7, phos 3.8, Cr 1.9
 - | “Normal PTH,” 25OH vit D, PTHrP, thyroid hormone, and cortisol
 - | Ultimately attributed to calcium citrate, vit D, and HCTZ.
 - | Desai et al. [Am J Ther](#). 2010 Nov-Dec;17(6):e234-6.
- | Case 2: 67 yo woman presented with 1 week of weakness, nausea, vomiting, and constipation.
 - | Ca 18.5 à 14.9 (PTH 1070) after discontinuation of hydrochlorothiazide
 - | Topsakal et al. [Jpn Heart J](#). 2003 Nov;44(6):1033-7.
- | Case 3: 61 yo man presented with weakness, confusion.
 - | Ca 18.1 (10.9 prior to start of HCTZ), phos 1.4; PTH 1040
 - | Strong et al. [West J Med](#). 1991 Mar;154(3):338-40.

TZD and Primary Hyperparathyroidism

Table 3 Clinical and Laboratory Spectrum of Thiazide-associated Hypercalcemia Among Olmsted County, Minn, Residents, 1992 to 2001, Overall and Subset Later Found to Have Primary Hyperparathyroidism

Characteristic	All Patients Mean $\pm$ SD, or n (%)	Primary Hyperparathyroidism Subset Mean $\pm$ SD, or n (%)
Female gender	68 (94.4)	19 (95.0)
Age at onset of hypercalcemia, y	63.9 $\pm$ 11.3	66.2 $\pm$ 11.2
Serum calcium before thiazide use, mg/dL	9.7 $\pm$ 0.4	9.7 $\pm$ 0.5
Maximum serum calcium on thiazides, mg/dL	10.7 $\pm$ 0.3	11.0 $\pm$ 0.4
Serum parathyroid hormone, pmol/L	4.8 $\pm$ 2.7	6.3 $\pm$ 4.4
Years from thiazide start to hypercalcemia	6.0 $\pm$ 7.2	7.3 $\pm$ 8.5
Reason for thiazide use		
Hypertension	68 (94.4)	20 (100)
Edema	2 (2.8)	0 (0)
Hypercalciuria/nephrolithiasis	2 (2.8)	0 (0)

SD = standard deviation.



Wermers et al. [Am J Med.](#) 2007 Oct;120(10):911.e9-15.

Interaction between TZD and Primary Hyperparathyroidism

6 patients with primary hyperparathyroidism on thiazide diuretics

Duration of treatment: 6 mo – 8 yrs

TABLE 2. The effects of thiazide administration and withdrawal. Mean values ($\pm$ s.e. mean)

Thiazide	Serum			24-hr urine			Creatinine clearance (ml/min)	Ca _E (μmol/l glomerular filtrate)	Index of phosphate excretion	
	Ca (mmol/l)	P (mmol/l)	iPTH (μg/l)	Ca (mmol)	Mg (mmol)	P (mmol)				
Present	2.8 (0.045)	11.2 (0.031)	0.85 (0.19)	1.05 (0.19)	5.96 (1.26)	239 (0.26)	3.36 (1.5)	21.85 (6.76)	67.3 (7.73)	53.5 (0.08)
Absent	2.68 (0.036)	10.7 (0.022)	0.78 (0.16)	1.04 (0.16)	8.33 (1.47)	334 (0.22)	2.70 (1.78)	21.87 (7.83)	75.1 (5.75)	57.5 (0.11)
P*	<0.01	n.s.	n.s.	<0.05	<0.01	n.s.	<0.05	n.s.	n.s.	n.s.

* = Paired *t* test; n.s. = not significant.

Take Home Points

- | Severe hypercalcemia can be caused by non-malignancy.
- | Thiazide use may unmask primary hyperparathyroidism and occasionally cause severe hypercalcemia.

ECG

