



77-year-old woman with hypercalcemia

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Endorama

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History of Present Illness

- 77-year-old woman with metastatic small cell lung cancer and primary hyperparathyroidism was referred to the ED after having an outpatient calcium lab value of 14.
 - Started chemotherapy in November 2011 with progressive decline in function status.
 - In the past 1.5 weeks, she has essentially been bed-bound with waxing and waning mental status changes.
 - She has had extremely poor appetite.
 - Three days prior to presentation, she developed nausea, vomiting, and epigastric pain.
 - She followed up at Onc clinic on day of presentation.

Past Medical History

- Primary hyperparathyroidism:
 - Diagnosed in early 2008 with calcium of 10.5, PTH of 110.
 - Sestamibi scan revealed uptake in the left inferior pole of the thyroid.
 - 24 hour urinary calcium excretion of 178 mg (2L, Cr 960 mg).
 - Had osteoporosis, improving on Actonel.
 - No history of kidney stones.
 - Given high surgical risk (anticoagulation for recurrent DVTs) and improvement of BMD, surgery was deferred.
- Small cell lung cancer, status post lobectomy in 2008, etoposide in 2010, and radiation in 2011.
- Hypertension
- Hyperlipidemia
- GERD
- Osteoporosis
- Impaired glucose tolerance
- History of a left common femoral DVT, now off anticoagulation

Past Medical History continued

- Allergies:

- Penicillin
- Morphine

- Medications:

- Arformoterol and ipratropium nebulizers BID.
- Omeprazole 20 mg daily
- Prochlorperazine 5 mg q6 hrs prn
- Metoclopramide 5 mg q6 hrs prn
- Tylenol #3 q6 hrs prn

- Social History:

- Lives with her son.
- Dependent for all ADLs.
- Quit tobacco use in 2008.
- No current ETOH use.

- Family History:

- Sister with throat cancer.

- ROS:

- Back pain

Physical Exam

- Ht 160 cm (5' 3"), Wt 49.7 kg (109 lb 9.1 oz), BMI 19.41 kg/m²
- Temp 96.3 °F, BP 137/74, Pulse 84, Resp 18, SpO₂ 100% on 2L.
- Constitutional: Patient appears chronically ill, malnourished, lethargic.
- Eyes: Conjunctivae are not injected. Sclerae anicteric. Pupils are equal, round, and reactive to light.
- 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. Decreased breath sounds. No wheezes or crackles.
- Gastrointestinal/Abdomen: Normoactive bowel sounds. Soft, nontender, nondistended.
- Musculoskeletal/extremities: 1+ peripheral edema. Soft tissue mass on upper L side of back.
- Neurological: Alert and oriented to person, place, and month and year. Normal deep tendon reflexes.
- Skin: Skin is warm and dry. No acanthosis nigrans noted.
- Psychiatric: Lethargic.

Laboratory Data: History

Ca 10.5
PTH 110

9-11

11-12

11/4
Ca 12.1
Phos 1.4
Alb 4

11/18
Ca 10.6
Alb 3.7

12/21
Ca 14
Phos 1.9
Alb 4.2

2008

2009

2010

2011

2012

Laboratory Data: Admission

142	98	25		11.7
3.6	25	1.6	108	8.2
		(1.2)		36.1
				139

Ca 14.0, Phos 1.9, Mg 2.3

Total protein 7.5, albumin 4.2

Total bili 0.9, alk phos 72, AST 22, ALT 14

CT torso, 10/7/11

- Moderate to severe centrilobular emphysema.
- Scarring and traction bronchiectasis in the right apex compatible with previous surgery and radiation therapy.
- Interval decrease in subcarinal lymphadenopathy.
- Marked interval enlargement of distal paraesophageal lymph nodes.
- 18 mm soft tissue nodule in the subcutaneous fat of the left posterior chest wall markedly increased since previous, suspicious for a metastasis.
- No significant abnormality noted in bones.

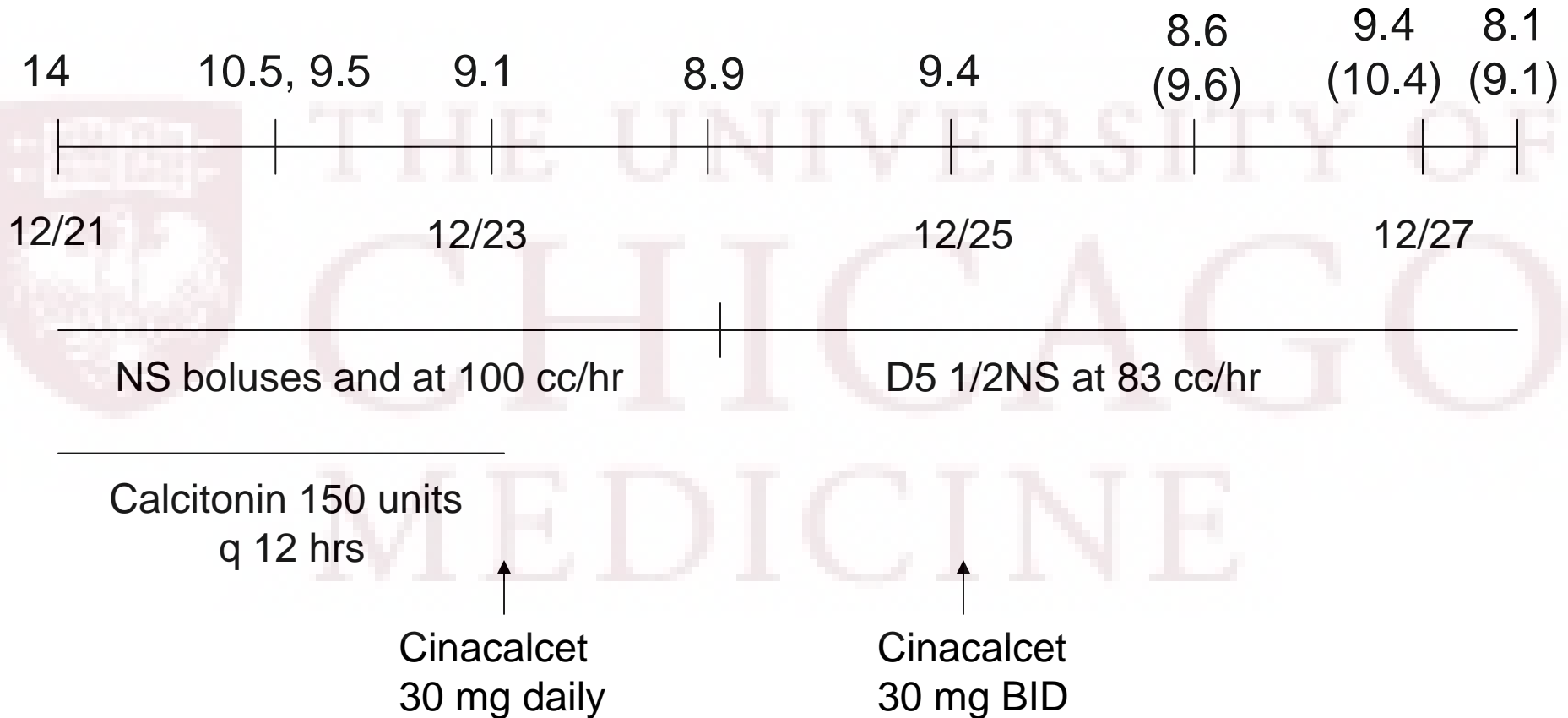
More labs

- PTH 262 pg/mL (15-75)
- PTHrp 0.5 pmol/L (>2)
- 25 OH vitamin D 20 ng/mL
- 1, 25 OH vitamin D 40 pg/mL (18-78)

Assessment:

- Gradually worsening primary hyperparathyroidism.
- Contributors of secondary hyperparathyroidism included low calcium diet, vitamin D insufficiency, and mild CKD.
- Acutely exacerbated by decreased mobilization, dehydration.

Calcium Trend



My Questions:

- What is the natural course of primary hyperparathyroidism?
- What is the data behind the use of cinacalcet?
- What other medical options are there?

Natural History of Primary Hyperparathyroidism

- Observational study of 116 patients.
- 49 asymptomatic patients were followed.
 - Biochemical changes:

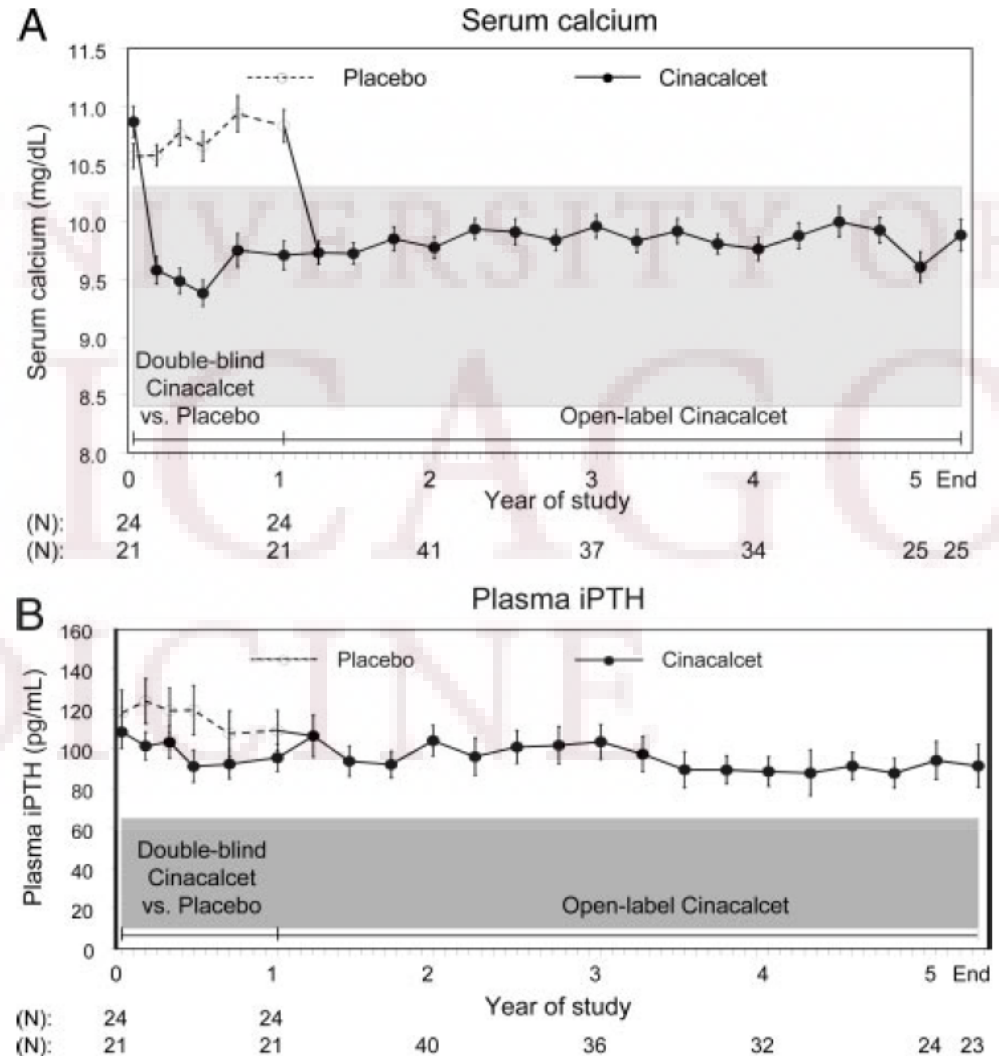
TABLE 2. Biochemical changes in asymptomatic patients followed up without parathyroidectomy (n = 49)

Variable	Baseline (n = 49)	Yr 5 (n = 25)	Yr 10 (n = 11)	Yr 13 (n = 9)	Yr 15 (n = 6)
Serum calcium (mg/dl)	10.5 ± 0.1	10.7 ± 0.1	10.8 ± 0.2	11.0 ± 0.2 ^a	11.1 ± 0.2 ^a
PTH (pg/ml)	122 ± 10	119 ± 12	123 ± 14	124 ± 16	121 ± 18
Serum creatinine (mg/dl)	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.2	0.8 ± 0.1
Urinary calcium (mg/dl)	238 ± 19	215 ± 23	185 ± 32	247 ± 36	202 ± 36
Serum 25-(OH) vitamin D (ng/ml)	21 ± 1	22 ± 2	22 ± 3	21 ± 3	19 ± 4
Serum 1,25-(OH) ₂ vitamin D (pg/ml)	56 ± 2	58 ± 3	54 ± 5	40 ± 5 ^a	48 ± 7

- BMD changes:
 - Lumbar spine was stable but femoral neck and distal radius had sig decline.
 - 37% showed disease progression.
- 8 symptomatic patients were followed (nephrolithiasis).
 - All showed progression: recurrent kidney stones, fracture, marked hypercalcemia.

Cinacalcet

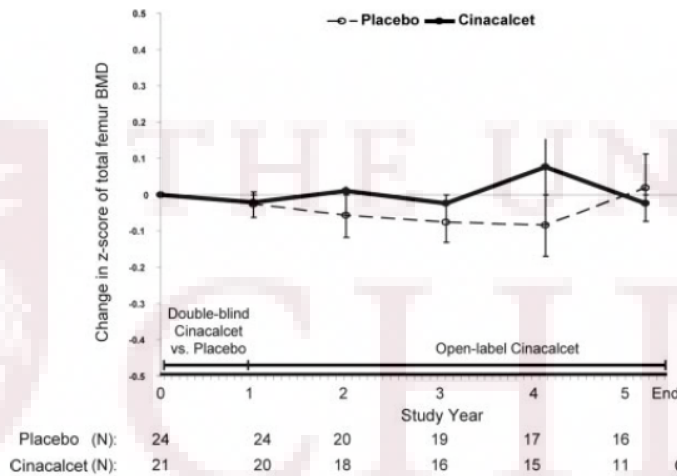
- 4.5 year open-label extension study
- 45 subjects with primary hyperparathyroidism
- Cinacalcet 30 mg BID, increased to 50 mg BID prn



Cinacalcet

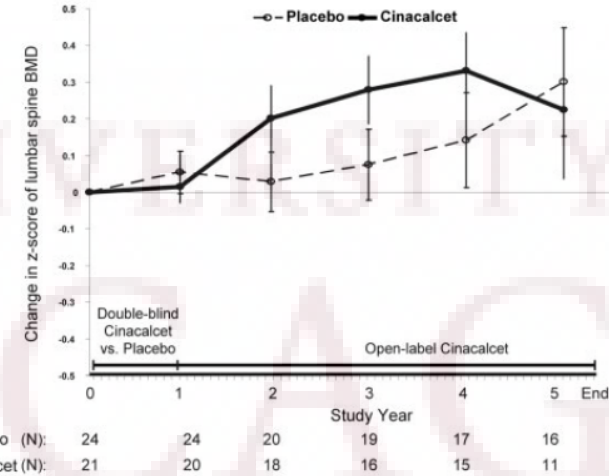
A

Mean (SE) change in total femur aBMD



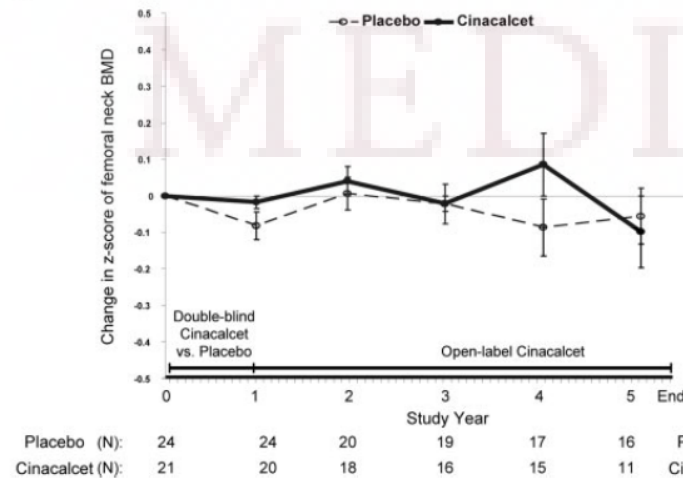
B

Mean (SE) change in lumbar spine aBMD



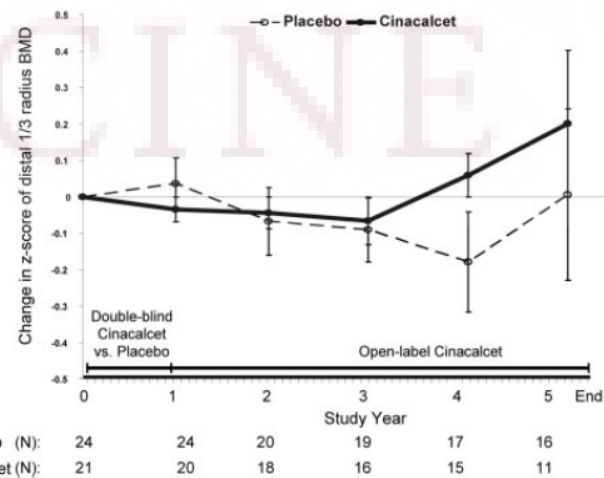
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Mean (SE) change in femoral neck aBMD



D

Mean (SE) change in distal 1/3 radius aBMD



Cinacalcet: adverse effects

TABLE 2. AE rate over the course of the parent trial and the open-label extension (no significant differences)

	Placebo (n = 24)	Cinacalcet
AE during initial 52-wk placebo-controlled trial (%)		
Headache	38	10
Arthralgia	25	14
Myalgia	25	24
Nausea	17	29
AE during the 4.5-yr, open-label extension study (%)		
Arthralgia		38
Myalgia		27
Diarrhea		22
Upper respiratory infection		20
Nausea		20

For the cinacalcet values, n = 21 for the initial trial and 45 for the extension study.

- Treatment-related AE:
 - Myalgias, 9%
 - Hypocalcemia, 4%
 - Nausea, 4%
 - Paresthesia, 4%
 - Renal stones, 4%
- Safety biochemistries including serum creatinine, liver function tests, and complete blood counts remained normal throughout the study.

Other Medical Treatment Options

- Estrogen:

- Increase BMD of 7.5% at lumbar spine, 7.4% at femoral neck and 7.0% at forearm.
- Slight decline in serum ionized calcium after 4 years and stabilization of PTH levels.
- Associated cardiovascular risks.

- Raloxifene:

- Statistically significant but small (0.5 mg/dL) reduction in the serum calcium and in the levels of markers of bone turnover.

- Alendronate:

- Increase BMD at lumbar spine and hip.
- Did not alter levels of serum calcium, PTH.

Orr-Walker et al. [Arch Intern Med.](#) 2000 Jul 24;160(14):2161-6.

Rubin et al. [J Clin Endocrinol Metab.](#) 2003 Mar;88(3):1174-8.

Khan et al. [J Clin Endocrinol Metab.](#) 2004 Jul;89(7):3319-25.

Take Home Points

- Asymptomatic primary hyperparathyroidism can be stable over 15 years.
 - However, these patients should be monitored.
- Cinacalcet improves biochemical indices but does not improve BMD and is a good option in non-surgical candidates.
 - Can be combined with alendronate.

References

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