

52 yo F w/a “cold foot”, found
to have hypercalcemia

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10/31/13

HPI

- Admitted for a “cold foot” x 3 days
- Weight loss of 50 lb in the last 6 months

CT Angio Aorta

- Found to have acute thrombosis of L ext iliac, distal SFA



- Acute thrombosis of L popliteal artery



Hospital course

- LLE thrombectomy... complicated by:
 - Melena post-op
 - Bradycardia and PEA arrest
 - Oliguria → CVVH from 7/30-8/1
- Consulted for abnormal TFTs

- PMH

HTN

CHF

Dyslipidemia

C-section x 2

Ectopic pregnancy

- Social History

1 PPD x years

No EtOH

- Family History

Mom- lung cancer

Sister- ovarian cancer

Brother- prostate cancer

- Medications

Aspirin 81 mg

Coreg 3.125 BID

Lasix 40 mg

Simvastatin 10 mg

Physical Exam

- Vitals: 36.3 , 114/86, 96, SpO₂ 97% , BMI 24.6,
- Gen: no apparent distress
- HEENT: no scleral icterus, no exophthalmos
- Neck: no thyromegaly, no palpable nodules
- CV: borderline tachycardia
- Pulm: crackles at bases
- GI: soft, non-tender, +ascites/abd distension
- Ext: LLE- wound vac
- Neuro: alert & oriented
- Psych: normal mood

Labs

137	107	17	110	8.7	14	124
4.4	22	0.9				
5.1	2.4		10.9			
2.8	77		1.7			
65	94		1.6			

TSH 0.24 (RR 0.3-4)
FT4 1.38 (RR 0.9-1.7)
TT3 69 (RR 80-195)
rT3 268 (RR 160-353)
TPO/Tg Ab neg

Differential Diagnosis Hypercalcemia

- Hyperparathyroidism
 - Primary HPT
 - Solitary adenoma
 - Parathyroid hyperplasia
 - Secondary/tertiary hyperparathyroidism
 - Lithium therapy
 - Familial benign hypocalciuric hypercalcemia
- Malignancy-associated hypercalcemia
 - PTHrP-mediated
 - Vit D mediated
 - Lytic bone metastasis
- Vitamin D related
 - Vitamin D intoxication
 - Sarcoidosis or other granulomatous diseases
- Endocrine disorders
 - Thyrotoxicosis
 - Addison's disease
- Miscellaneous
 - Immobilization
 - Thiazide diuretics
 - Vitamin A intoxication
 - Milk-alkali syndrome

Hypercalcemia

- Diagnosed with hypercalcemia 1 year ago
- Was on Sensipar 30 mg for a year
- 1 episode nephrolithiasis years ago
- No bone fractures
- Never evaluated for osteoporosis
- No history of sarcoid
- Not on medications causing this

More labs

- Ca 10.9→12.2
- Ionized Ca 5.9
- Mg 1.6
- Phos 1.7
- PTH 160 (RR 15-75)
- 25-OH vit D 6
- PTHrp 0.8 (RR <2)
- 1,25-OH vit D 15 (RR 18-78)

SPEP/UPEP

- Monoclonal IgG lambda
- 1 gm of proteinuria in 24 hr urine with a significant proportion of monoclonal free lambda light chains

Bone Marrow Biopsy

- Plasma cell dyscrasia involving a hypocellular bone marrow (25% cellular, 10% clonal plasma cells, lambda restricted) with concurrent amyloid deposition.

Skeletal Survey

- No discrete lesions of myeloma.

Transthoracic Echo

- Mild concentric LVH. LVEF 35.9%. RV systolic performance is mild-moderately reduced. LA severely dilated.

Cardiac MRI

- LVEF 35%. RV moderate systolic dysfunction RVEF 36%. Late GAD enhancement circumferentially, strongly suggestive of cardiac amyloidosis.

EGD

- Stomach: focally inflamed antral mucosa with amyloid deposition
- Duodenum: focal mildly active duodenitis with amyloid deposition and features suggestive of ischemia.

Colonoscopy

- Ascending colon: ischemic colitis with ulceration and amyloid deposition.

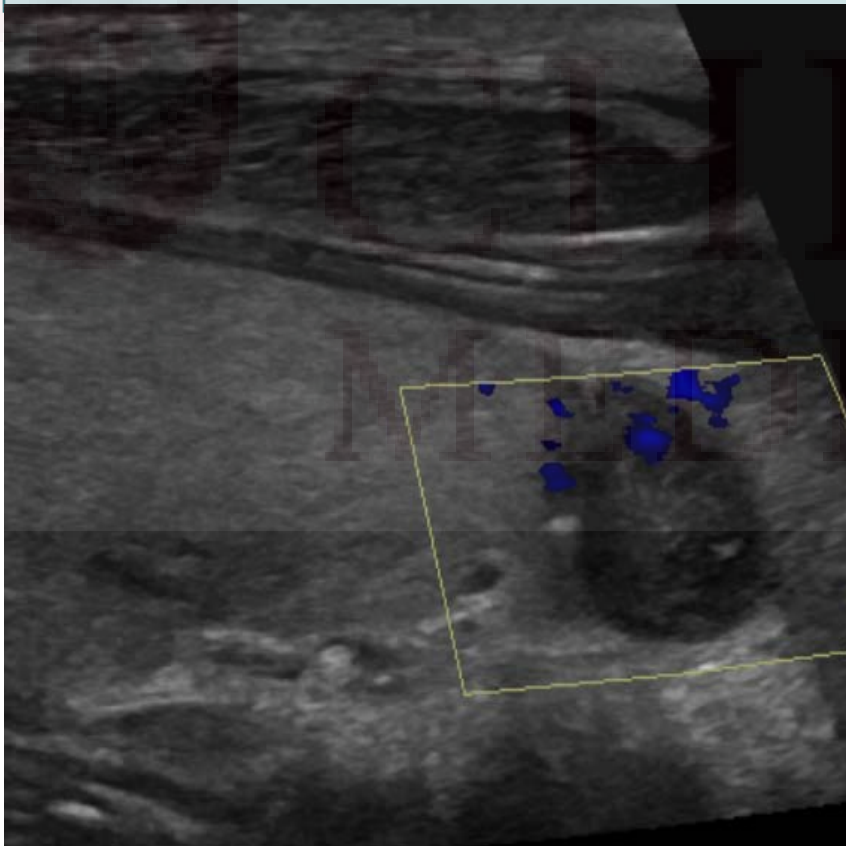
Thyroid US

R LOBE: 5.5x2.1x2.1 cm. L LOBE: 4.3x1.6x2.0 cm. ISTHMUS: 0.7 cm. Homogeneous parenchymal echogenicity bilaterally.

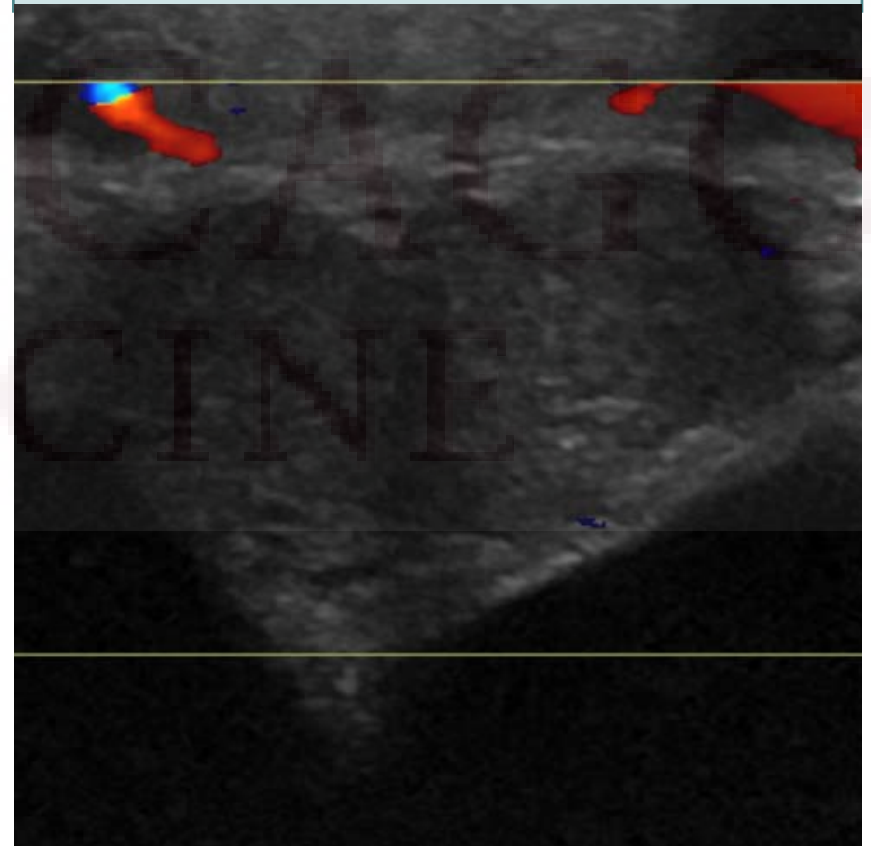
PARATHYROID GLANDS: Post/inf to R thyroid lobe → hypoechoic extrathyroidal nodule, represents hyperplastic parathyroid glands vs parathyroid adenomas. Inf to the L thyroid lobe → extrathyroidal, hypoechoic nodule represents a hyperplastic parathyroid gland or parathyroid adenoma.

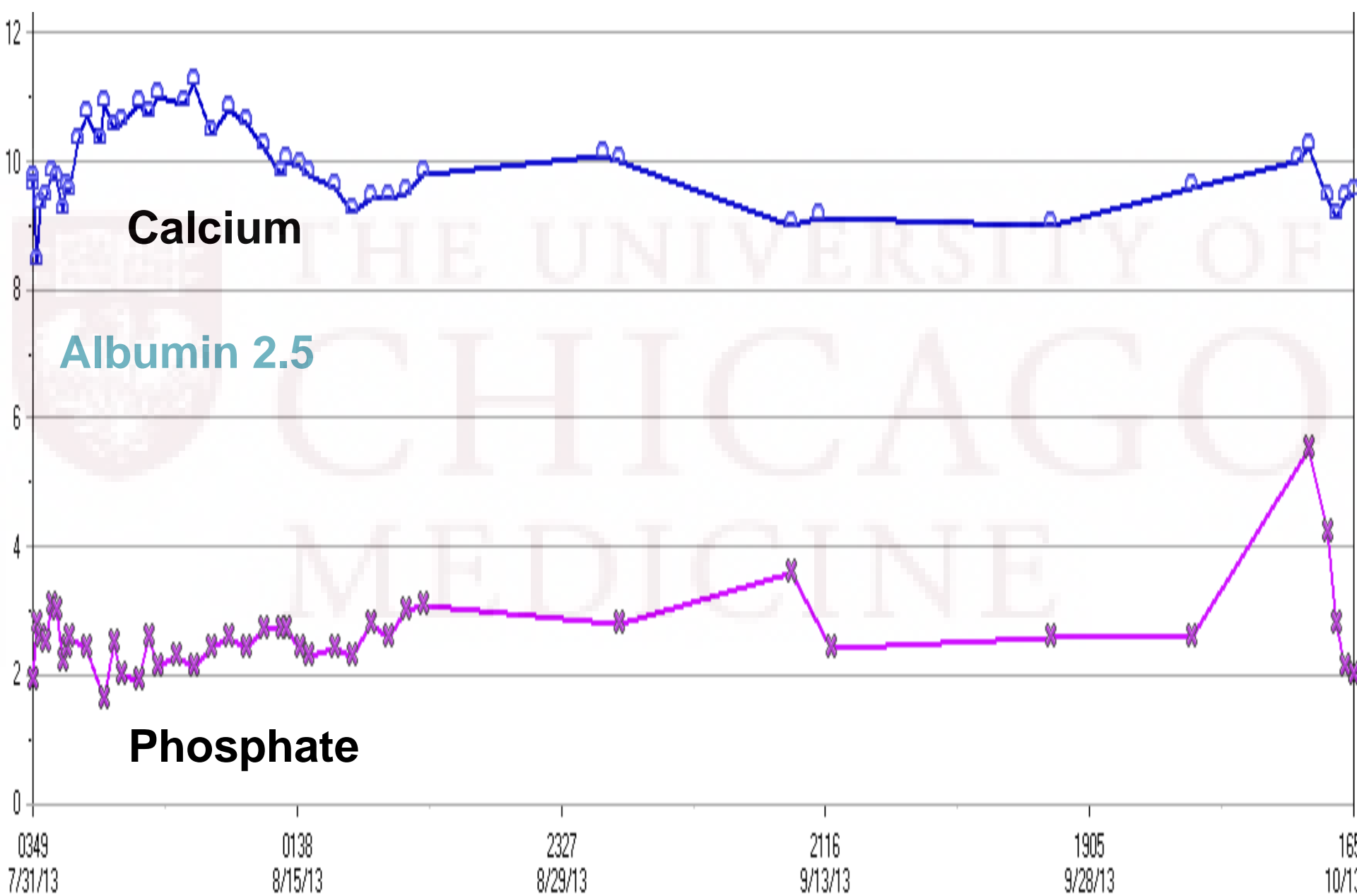
Thyroid Ultrasound

L lobe



R lobe





DXA scan

- L1-L4 spinal BMD = 0.802 g/cm² (T = -3.2)
- Total hip BMD = 0.752 g/cm² (T = -2.0)
- Forearm BMD = 0.740 g/cm² (T = -1.6)

Our Patient

- Diagnosis: Primary lambda- AL amyloidosis with cardiac, GI, bone marrow, possible endovascular and mild renal involvement, with 10% marrow monoclonal plasma cells
- Treated with Sensipar 60 mg daily
- Started chemotherapy with Bortezemib

Future tests

- 24h urine Ca/Cr
- Sestamibi scan → referral to endocrine surgery

Clinical Questions

- Association between PHPT and Monoclonal Gammopathy?
- Medical management PHPT
 - Cinacalcet
 - Severe vitamin D deficiency
- PTH as a biomarker in heart failure?

PHPT and Monoclonal Gammopathy

- Objective: to prospectively determine presence of monoclonal gammopathy in PHPT
- Cohort: 101 PHPT, 127 non-PHPT surg controls, 101 age/sex matched thyroid surg controls
- Results: monoclonal Ig was detected in 10% with PHPT compared with 2% of surgical controls ($p = 0.005$) and 3% of benign thyroid controls

Medical Management PHPT

- CI to parathyroidectomy or persistent PHPT have few non surgical options
- Cinacalcet is FDA approved for treating 2^o hyperparathyroidism in patients with CKD on HD and patients with parathyroid cancer.
 - Calcimimetic agent that levels by binding to CaSR on PTH cells → causes L-shift in CaSR set point
 - ↓PTH (neg feedback) → ↓Ca

Medical Management PHPT

- Objective: to establish efficacy of cinacalcet (up to 4.5 yrs) in \downarrow Ca in patients with PHPT
- Patients: 1) failed PTHx (n=29), 2) 1+ criteria for PTHx-no surgery (n=37), 3) mild asx PHPT (n = 15)
- Results: \downarrow Ca, \downarrow PTH, and \uparrow Phos were similar. No significant changes in BMD. Efficacy maintained for up to 4.5 yr of f/u
- Conclusions: cinacalcet is equally effective in the medical management of PHPT patients

Vitamin D Deficiency in PHPT

- Vitamin D inadequacy is more common in patients with PHPT
- Initiation of vitamin D therapy if 25-hydroxy vitamin D <20 ng/mL in PHPT
- Well-designed trials are needed to better define the safety and efficacy of vitamin D therapy in patients with concomitant vitamin D deficiency and PHPT

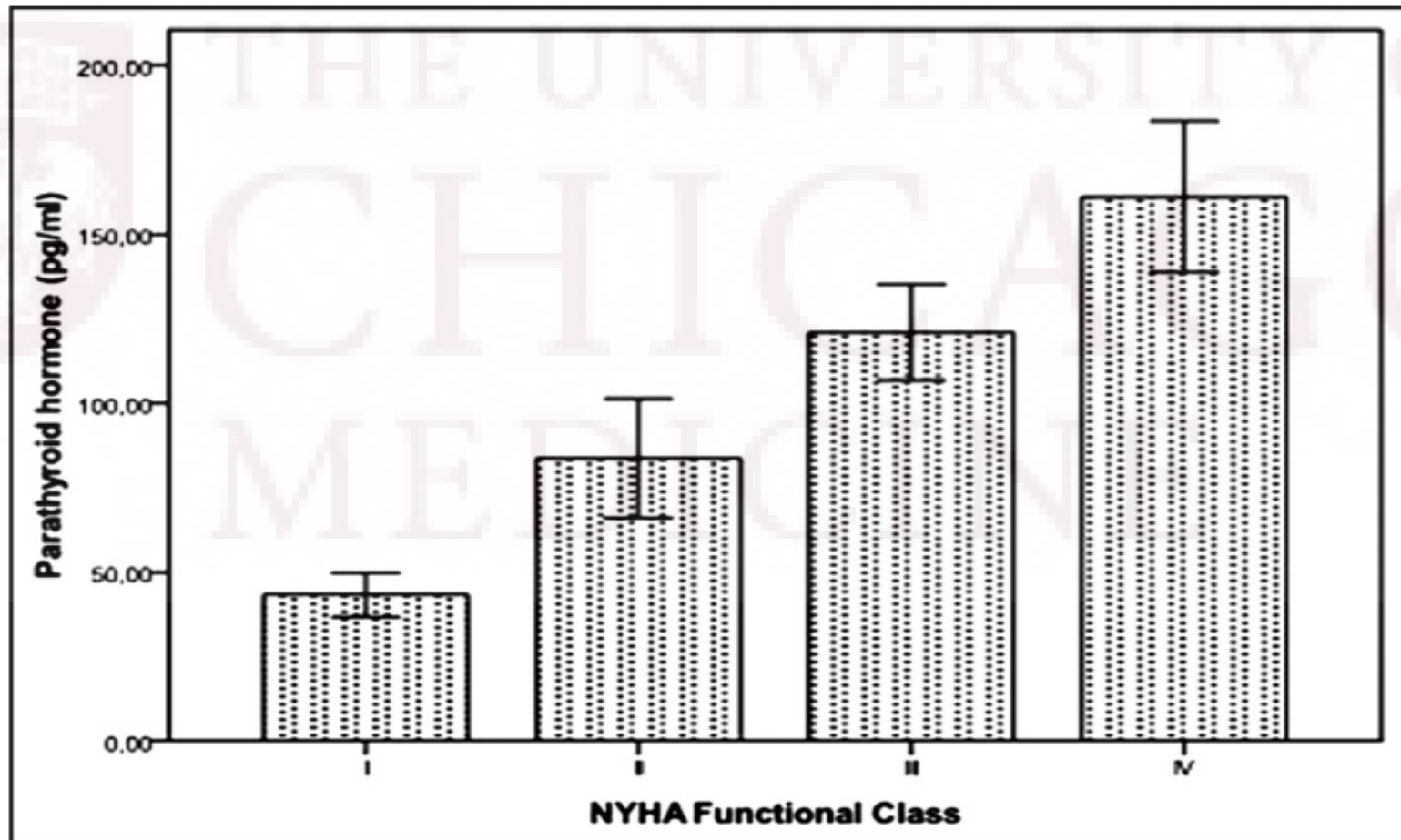
Vitamin D Deficiency in PHPT

- The causes of low circulating levels of 25-OHD in patients with PHPT are not totally understood.
 - Accelerated conversion 25-OH → 1,25-OH vitD?
 - Increased catabolism of 25-OH vit D?
 - Increased adiposity?

PTH as a biomarker in HF?

- Objective: to investigate whether PTH could identify patients with advanced HF
- Cohort: 150 outpatients w/systolic HF.
- Results: PTH = 43, 84, 121, and 161 pg/ml in NYHA functional classes I, II, III, and IV, respectively ($p < 0.001$). PTH levels were correlated with BNP level and LVEF ($p < 0.001$). Optimal cut-off value of PTH to predict advanced HF was > 96.4 pg/ml, with 93.3% Sn and 64.2 Sp.

PTH as a biomarker in HF?



Take Home Points

- Consider SPEP in patients with PHPT
- In patients with monoclonal gammopathy and hypercalcemia w/no other symptoms of progressive disease → check for PHPT
- Replete 25-OH vit D to >20 in PHPT
- PTH is being studied as a biomarker in HF

References

- Arnulf B et al. Prevalence of Monoclonal Gammopathy in Patients with Primary Hyperparathyroidism. *Arch Int Med* Feb 25 2002;162:464-467.
- Cetani, F et al. Cinacalcet efficacy in patients with moderately severe primary hyperparathyroidism according to the European Medicine Agency prescription labeling. *J Endocrinol Invest* Jul 2012;35(7):655-60.
- Peacock M et al. Cinacalcet HCl Reduces Hypercalcemia in Primary Hyperparathyroidism across a Wide Spectrum of Disease Severity. *J Clin Endocrinol Metab*, January 2011, 96(1):E9–E18.
- Nuti R et al. Vitamin D deficiency and primary hyperparathyroidism. *J Endocrinol Invest* Jul 2011;34(7 Suppl):45-9.
- Maharaj J et al. Primary Hyperparathyroidism and vitamin D in African Americans. *Endocrine Practice* 2012 Nov-Dec;18(6):947-53.
- Nasser M. Clinical Significance of Vitamin D Deficiency in PHPT, and Safety of Vitamin D Therapy. *South Med J* 2011;104(1):29-33.
- Khan AA. Medical Management of Primary Hyperparathyroidism. *Journal of Clinical Densitometry* 2013;16(1):60-63.