



WELCOME TO UVM ECHO: CALCIUM DISORDERS AND BONE HEALTH

PARATHYROID VS NON-PARATHYROID MEDIATED DISORDERS

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June 16, 2021

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 - None



CALCIUM DISORDERS AND BONE HEALTH

PARATHYROID VS NON-PARATHYROID MEDIATED DISORDERS

UVM Project ECHO Series
Jeanne T. Gosselin, MD
June 16, 2021

OBJECTIVES

- Work-up and common causes of hypercalcemia
- Parathyroid hormone (PTH) vs. non-PTH mediated disorders
- Management
- Calcium homeostasis and bone health

CAUSES OF HYPERCALCEMIA

- Hyperparathyroidism (primary, secondary, tertiary) *
- Malignancy *
- Granulomatous diseases (e.g. sarcoidosis, TB, fungal infections, silicosis)
- Vitamin A and D toxicity
- Medications (e.g thiazide diuretics, lithium)
- Familial hyperparathyroidism (e.g familial hypocalciuric hypercalcemia)

* Primary hyperparathyroidism and malignancy account for 80-90% of hypercalcemia (Lafferty, J Bone Min., 1991)

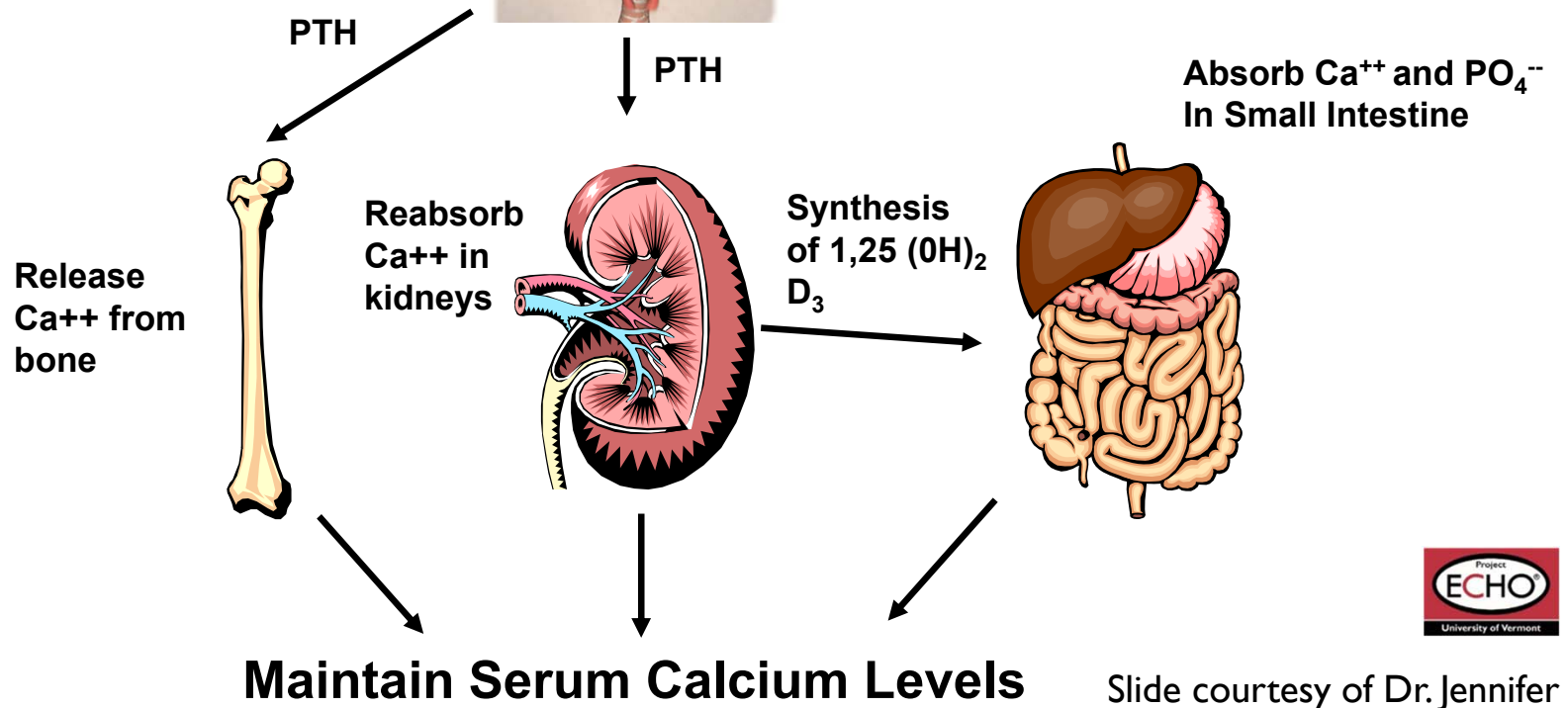
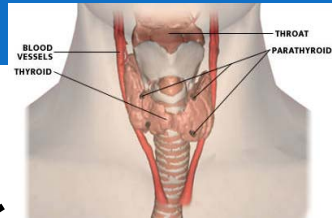
DEGREE OF HYPERCALCEMIA AND SYMPTOMS

- Mild: ULN to <12 mg/dL, usually asymptomatic (particularly if chronic) or have nonspecific fatigue, depression, constipation
- Moderate: 12-14 mg/dL, may present with polyuria, polydipsia, dehydration, anorexia, nausea, muscle weakness, confusion (particularly if rapid rise)
- Severe: >14 mg/dL progression of symptoms above, may lead to cardiac arrhythmias and coma

HYPERCALCEMIA: INITIAL WORK-UP

- Repeat serum calcium corrected for albumin, i.e. obtain ionized (free) calcium if available
- Compare prior calcium levels to determine a timeline of hypercalcemia
- Look at severity, duration, associated signs and symptoms (e.g. history of nephrolithiasis), family history to help narrow down a cause
- Examine patient for evidence of muscle weakness and dehydration, or an underlying process such as lymphoma or granulomatous disease
- Medication review (diuretic use, lithium, antacids, calcium, vitamin A and/or D supplementation)
- Laboratory work-up

CLASSICAL ACTIONS OF PTH



PTH-MEDIATED DISORDERS

- Primary hyperparathyroidism (PHPT) most common → frankly elevated PTH and hypercalcemia
 - Over-secretion of PTH by autonomous (not responsive to negative feedback) solitary adenoma (only 1-2% carcinomas)
 - Calcium may be only slightly elevated or even normal with concurrent vitamin D deficiency
 - Most common presentation is asymptomatic hypercalcemia detected on screening labs
 - Can occur at any age but increased risk > age 50-65
 - Female to male 2-3:1

PTH-MEDIATED DISORDERS

- Secondary hyper-PTH → appropriate elevation in PTH in response to reduced extracellular calcium, serum calcium low or normal
 - CKD with impaired 1,25(OH)D production, vit D deficiency, calcium malabsorption (Celiac, hx of gastric bypass)
- Tertiary hyper-PTH → persistently high PTH in ESRD, due to chronic hyperphosphatemia, 1,25(OH)D deficiency and hypocalcemia causing parathyroid hyperplasia
- Familial hyper-PTH: MEN type I, familial hypocalciuric hypercalcemia (FHH), and others (all rare)

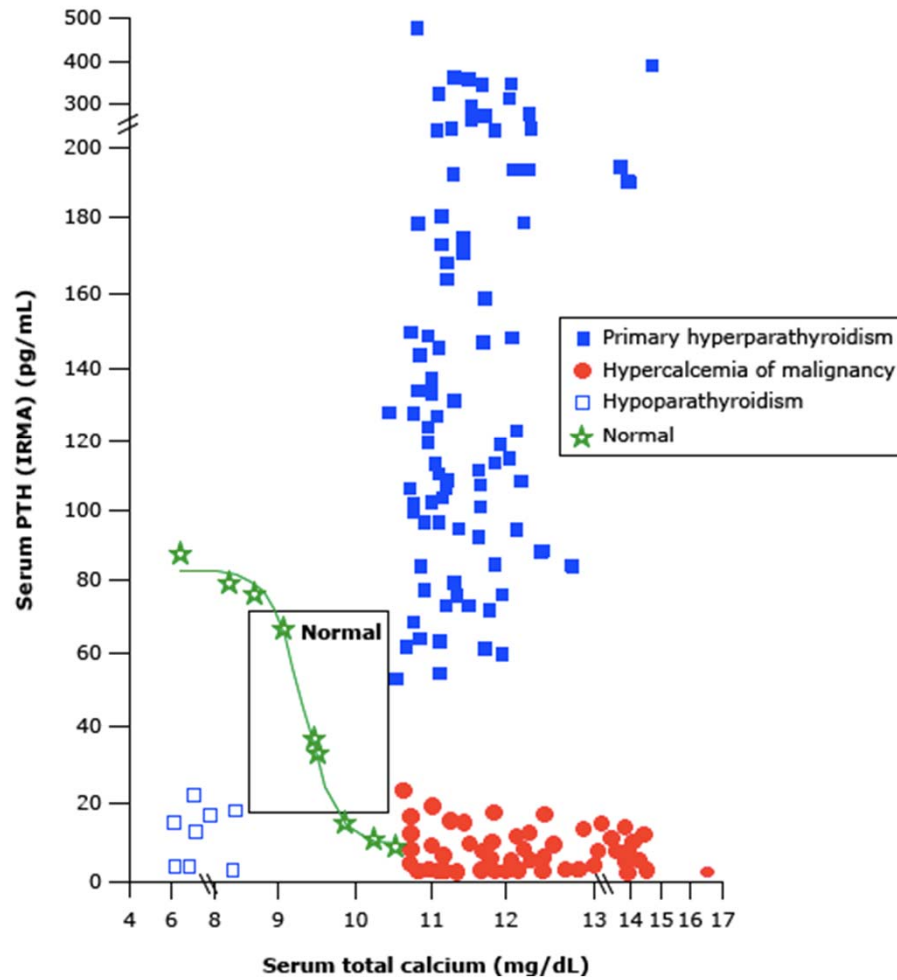
OTHER LABS/STUDIES

- Creatinine with eGFR, CBC, lytes, phosphorus, 25-OH vitamin D (calcidiol)
- When do I check 1,25-OH vitamin D (calcitriol)?
 - when PTH is low or low-normal
- ?24 hour urine calcium—yes, particularly if PTH normal or only minimally elevated
 - elevated → primary hyperparathyroidism (PHPT)
 - normal → likely PHPT with vit D deficiency or low calcium intake
 - Low → familial hypocalciuric hypercalcemia (FHH)
- DXA scan
- Consider imaging for nephrolithiasis (KUB, CT, US)

TREATMENT OF PRIMARY HYPERPARATHYROIDISM

- Depends on severity of hypercalcemia and symptoms
- Definitive treatment is surgical, reserve parathyroid sestamibi scan for surgical planning
- Asymptomatic patients with mild hypercalcemia can be monitored with repeat serum calcium and creatinine q 6-12 months, repeat DXA of L spine, hip and radius q 2 years
- Indications for surgery
 - increase in serum calcium level ≥ 1 mg/dL above ULN
 - CrCl < 60 mL/min
 - 24-hour urine calcium > 400 mg/day
 - presence of nephrolithiasis or nephrocalcinosis by imaging or increased stone risk by biochemical stone risk analysis
 - T-score on DXA of less than or equal to -2.5 (osteoporosis) at any site or evidence of vertebral fracture
 - age younger than 50 years

Serum parathyroid hormone (PTH) concentrations in hypercalcemia and hypocalcemia



Data from: Haden ST, Brown EM, Hurwitz S, et al. The effects of age and gender on parathyroid hormone dynamics. Clin Endocrinol 2000; 52:329.

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WORK-UP OF NON-PTH MEDIATED HYPERCALCEMIA

- PTH is low (appropriately suppressed)
- Severity and duration of hypercalcemia
- Always check 25(OH)D to rule out vitamin D toxicity
- Elevated PTHrP suggests humoral hypercalcemia of malignancy (solid tumors including head and neck, lung, breast, ovary)
- Normal PTHrP with elevated 1,25(OH)D suggests lymphoma or granulomatous disease
- Additional testing including SPEP, UPEP, CT torso may be indicated
- Further work-up by oncology, rheumatology, and/or ID may be necessary for non-PTH mediated hypercalcemia once vitamin D toxicity/medications have been ruled out as etiology

CALCIUM HOMEOSTASIS AND BONE HEALTH TAKEAWAYS

- Both hypo and hypercalcemia can cause metabolic bone disease
- In addition to the standard screening recommendations based on age and sex, patients with calcium disorders require evaluation of bone health with DXA scan
- A fragility (or other suspicious) fracture at any age should prompt basic metabolic bone work-up including calcium, vitamin D and PTH

QUESTIONS?



"I can cure your back problem, but there's a risk that you'll be left with nothing to talk about."

Thank you!



CASE PRESENTATION

RECORDING TO BE STOPPED FOR CASE PRESENTATION



CASES/HIPAA

- Names
- Address
- DOB
- Phone/Fax #
- Email address
- Social Security #
- Medical Record #



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