Hypercalcemia due to thyrotoxicosis; A case presentation

Vidhya Reddy, MD, Abhiram Javvaji, MD, Jaya Naran, DO, Muhammad Raza, MD

Endocrinology Department: Christopher W Barnes, DO and Ahmet Can, MD

Introduction:

Hypercalcemia is a commonly encountered electrolyte abnormality in the clinical practice, but the challenge exists due to its wide differential diagnosis and varied therapies. Here, we present a case of hypercalcemia, attributed to a rare etiology.

Case Presentation:

A 29-year-old male, recently diagnosed with Graves' disease, referred to our service for management. He had a 2-month history of neck enlargement, nausea, vomiting, hand tremor, fatigue, and episodic palpitations. Additionally, he had lost 100 pounds within an 8 month period, which was initially intentional but after 2 months became unintentional. His family history was unremarkable other than having an aunt and uncle with hypothyroidism. He also denied any bone pain, abdominal pain, muscle cramps, flank pain, or kidney stones.

A palpable thyroid gland was the only positive noted on physical exam.

Initial Labs: see Table 1.

Other pertinent labs showed normal BUN, creatinine, and liver function tests. Alkaline Phosphatase(ALP) was 106 (normal 38-126 U/L), and albumin was 3.5 (normal 3.5-5.0 g/dL). 24 hour urine calcium was 410.4 (normal 100-250 mg/24 hr) and 24 hour urine Creatinine was 1.5 (normal 0.8 -2.0 g/24 hr). SPEP and UPEP were within normal range.

Imaging:

- Ultrasound of thyroid gland: no discrete nodule(s) but reporte thyromegaly and increased vascularity.
- Iodine uptake and scan: an elevated both 4 hour uptake of 78.7% and a 24 hour uptake of 43.9%, congruent with Graves' Disease.

He was subsequently started on methimazole 30 mg daily and atenol 50 mg twice a day to control his sympathetic symptoms.

Labs and imaging were consistent with Graves' disease, but more concerning was the elevated serum calcium levels at 13.3 mg/dL. He was advised to go to the emergency room, where he received IV fluic with no other interventions to normalize his calcium levels.

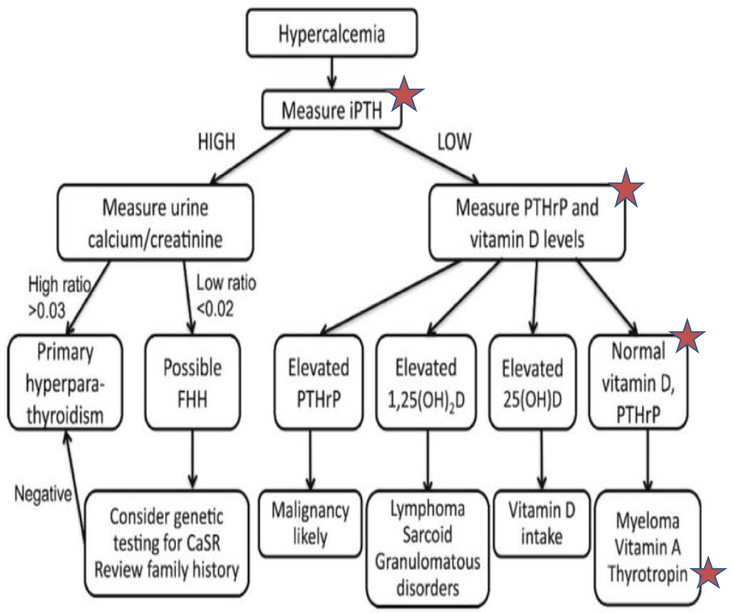
Table 1: Baseline thyroid function and calcium metabolism tests

Test	Results	Reference range
Free T_4 (*ng/dL*)	5.22	(0.58-1.64)
Total T_3 (*pg/dL*)	683	(87-178)
TSH (*μIU/mL*)	<0.01	(0.34-5.60)
AntiTPO (*IU/mL*)	1276.9	(<9.0)
AntiTg (*IU/mL*)	0.9	(<4.0)
TSI (%)	>500	(< 122)
Total Calcium (*mg/dl*)	13.3	(8.9 -10.3)
Ionized Calcium (*mg/dl*)	7.1	(4.5- 5.3)
Intact PTH (*pg/mL*)	1.3	(12.0- 88.0)
PTHrP (*pmol/L*)	< 2.0	(0.0-2.3)
25-OH vit D (*ng/dL*)	30.6	(30-100)
1,25- OH vit D (*pg/mL*)	7.5	(19.9-79.3)

TSH: Thyroid-stimulating hormone, AntiTPO: Anti- thyroid peroxidase, AntiTg: Anti- thyroglobulin, TSI: Thyroid-stimulating immunoglobulin, PTH: Parathyroid hormone, PTHrP: parathyroid hormone related protein

Figure 1: Diagnostic Algorithm of Hypercalcemia

- Flow of our patient is indicated with a red star



For additional information please contact:
Vidhya Reddy
vreddy@arnothealth.org

Follow- up Visit :

Patient followed-up with us 6 weeks later and reported a reduction of initial symptoms a few days after starting Methimazole.

Labs 6 weeks after initial visit noted:

- TSH <0.01 uIU/ML
- Free T4 improved from 5.22 ng/dL to 1.82 ng/dL
- Free T3 was reduced from 683 ng/dL to 450 ng/dL
- Serum calcium was reduced from 13.3 mg/dL to 10.5 mg /dL

Physical examination continued to show thyroid enlargement. Given the elevation of his free T4 and total T3, methimazole dose was adjusted from 30 mg to 40 mg per day. He was also advised to continue the atenolol.

Discussion:

We present a case of Graves' Disease with the rare sequela of hypercalcemia. Only 20% of patients with hyperthyroidism are reported to develop asymptomatic elevation of serum calcium levels. [1] Further etiologies of hypercalcemia such as Multiple Myeloma, Paget's Disease, and bone metastasis were excluded, as well as, drug related hypercalcemia. Figure 1. depicts the diagnostic approach for hypercalcemia.

The association between osteoporosis and hyperthyroidism was first established in 1891. The co-occurrence of this condition became infrequent once antithyroid medications were introduced in 1940s. [2] Pathophysiology of osteoporosis in the setting of Graves' Disease is thought to be due to elevated thyroid hormone levels stimulating bone resorption leading to increased serum calcium and urinary calcium excretion, which were both seen in our patient. Also, triiodothyronine (T3) increases the sensitivity of the bone to IL-6, causing increased osteoclastic activity. [1] It is thought that this elevated bone turnover would increase ALP, however in our case ALP was normal. A study reported that elevated serum ALP was only found in 50 % of patients with hyperthyroidism complicated by hypercalcemia. [3]

Conclusion:

The importance of treating hypercalcemia in a timely manner is well known, but in this case treatment of hyperthyroidism solved the underlying issue of thyrotoxicosis induced hypocalcemia.

References:

1. Korytnaya E, et al. An unusual case of hypercalcemia associated with graves' disease and vitamin d deficiency. Clin Med Insights Endocrinol Diabetes. 2011;4:25–28. doi:10.4137/CMED.S7116

2. Gorka J et al. Metabolic and Clinical Consequences of Hyperthyroidism on Bone Density. International Journal of Endocrinology. 2013 Jul. 2013:11.

3. Iqbal AA et al. Hypercalcemia in hyperthyroidism: patterns of serum calcium, parathyroid hormone, and 1,25-dihydroxyitamin d3 levels during management of thyrotoxicosis. Endocr Pract 2003 Nov-Dec; 9(6): 517-21.

4. Reagan P. et al. Approach to Diagnosis and Treatment of Hypercalcemia in a Patient With Malignancy. AJKD. 2014 Jan; 65(1): 141-147