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Case Report

HYPERCALCEMIC CRISIS AS A RARE PRESENTATION OF HYPERTHYROIDISM: A CASE REPORT

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A B S T R A C T

Hyperthyroidism is a well known cause of hypercalcemia but hypercalcemic crisis is very rare. The underlying mechanisms are still not clear. Thyroid hormone may have a role in stimulating bone turnover. A 63 year old lady presented with decreased level of consciousness with background history of vomiting, loss of apetite and weight loss. Her blood investigations revealed severe hypercalcemia with raised T3, T4 and low TSH. A final diagnosis of Graves' disease was made and patient was treated conservatively for correction of calcium with diuretics and intravenous fluids; and antithyroid treatment was started. She improved and was discharged.

INTRODUCTION

Hyperthyroidism is a disease characterized by increased level of thyroid hormone in the body, leading to symptoms and signs including palpitation, tremor, weight loss in spite of having good appetite, and complications related to the increased metabolic rate. Thyroid hormone also regulate bone metabolism. Hyperthyroidism has been associated with mild to moderate hypercalcemia in approximately 20% of total patients.[1]

A mild to moderate range of calcium rise is often seen but it rarely exceeds 3.0mmol/L in hyperthyroidism.[2,3] Hypercalcemia is defined as a calcium level exceeding 3.5mmol/L and patient often has symptoms including multiple kidney stones, constipation, and muscle weakness.[4] Severe hypercalcemia or hypercalcemic crisis is very rare.[5] . Only a few cases of hyperthyroidism associated hypercalcemic crisis have been reported.[6–8]. It was thought that thyroid hormone can directly stimulate bone turnover, elevate serum calcium, as well as urinary and fecal calcium excretion.[2,9,10]

We are presenting a case of hyperthyroidism associated hypercalcemic crisis and the effect of thyroid hormone on metabolism of calcium, phosphate, parathyroid hormone (PTH), and 1,25-OH2-D3 is being reviewed.

Case report-A 63 year female admitted to our hospital with complaints of low backache for 4 months, decreased appetite and weight loss of approximately 5-6 kg for 1 month, recurrent episode of nausea and vomiting for 20 days and decreased level of consciousness for 5 days. There was no history suggestive of fever, seizure episodes, recurrent episodes of diarrhoea/constipation, chronic cough with expectoration, headache, ear discharge, fall, trauma, visual disturbances, burning urination, and increased frequency of urine or decreased urine output. There were no similar episode in past. Patient was on NSAIDs (on & off) for backache for 4 months. Past history for diabetes, hypertension and anti tubercular treatment were negative.

On general examination, patient was thin built, lying on bed with GCS of E3V2M5, pulse was 106/min regular , rhythmic, normo-volumic and all peripheral pulses were palpable. Her blood pressure was 122/76 mmHg and respiratory rate was 14 /min. Patient was afebrile. No obvious neck swelling noted. Her breast examination was normal. Respiratory, cardiovascular and abdominal examinations were within normal limit. On nervous system examination, patient was in altered sensorium with GCS of E3V2M5. Neck rigidity and Kerning sign were absent. Sensory and motor examination could not be done.

Her arterial blood gas (ABG) analysis showed ionized calcium 1.860 mmol/L(normal range1.150-1.330 mmol/L) and other electrolytes were normal. Serum calcium was raised significantly to 12.6 mg/dl (corrected calcium with total albumin was 14mg/dl); whereas serum sodium, potassium and magnesium values were normal. Her serum creatinine was 1.7mg/dl (normal range 0.5-1.4mg/dl), blood urea 101mg/dl (normal range 15-45mg/dl), total protein 6.5gm/dl (normal range 6-8.5gm/dl), albumin 2.5gm/dl (normal range 3.2-5.5gm/dl) and alkaline phosphate 257 U/L (normal range 53-141 U/L). Her urine and stool examinations were normal. NCCT head and CSF analysis was normal. Thyroid profile showed T3-3.20 (normal 0.60-1.81 ng/ml) T4-19(5.01-12.45

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ng/ml) and TSH <0.01(normal-0.35-5.50 IU/ml). Antithyroid peroxidase antibody (anti TPO) was raised 34 IU/ml (normal range 0-20 IU/ml).

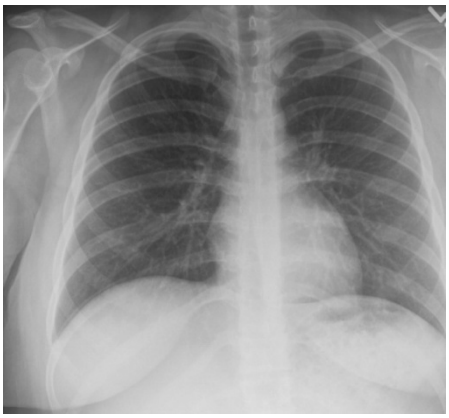
Serum phosphate level was 4.3 mg/dl (normal range 3.5-6.5 mg/dl). Her parathyroid hormone (PTH) level was 15pg/ml (normal range 14-72 pg/ml). Urinary Bence-Jones protein was negative. No 'M' peak was seen on serum electrophoresis. Vitamin D and alkaline phosphatase level were 232 nmol/L(normal-75-250 nmol/L) and 257 U/L (normal range 53-141 U/L) respectively.

Her electrocardiogram showed normal sinus rhythm with slightly increased QT interval. X ray chest, Lumbosacral spine, skull and hip were normal (Figure 1). Ultrasonography of bilateral thyroid lobe showed mildly increased blood-flow and vascularity without any nodules or irregular margins. Ultrasonography of abdomen and pelvis was normal. Dual energy X-ray absorptiometry showed T score of -1.5 at all lumbar spine and mild osteoporosis noted at neck of femur with T score of -2.5.

To look for cause of hypercalcemia, history was reviewed in order to find out any intake of oral medication (in the form of oral calcium supplement). To look for any evidence of malignancy, CECT abdomen and thorax was done, which was normal. Her tumor markers CA 125, CA 19-9, cancer embryo antigen(CEA) and alpha feto protein (AFP) was normal.

Based on these findings of low TSH with raised anti TPO and low bone marrow density on DEXA scan, a diagnosis of Grave's disease associated hypercalcemia was made. Patient was managed conservatively with IV fluids (5000 ml over 24 hour) and diuretics (furosemide) 20mg IV 8 hourly to control hypercalcemia. She was started on Tab. carbimazole 10mg, 1tab TDS with long acting beta-blocker, propranolol 40 mg OD. Her serum calcium and ionized calcium lowered down in 24 hour and normalized by 5th day. Patient regained consciousness as her serum calcium normalizes. Her renal function returned to normal level by day 5 (creatinine 0.7 mg/dl and urea 22 mg/dl). Patient was discharged on day 8 with serum calcium of 9.8mg/dl. She was advised to take Tab. carbimazole 10 mg, 1tab TDS along with plenty of fluids.

After 1 month her serum calcium was 9.2mg/dl, phosphate 3.8mg/dl with T3-1.51 (normal-0.60-1.81 ng/ml) T4-11.05 (5.01-12.45 ug/ml) and TSH 0.23 (normal-0.35-5.50 IU/ml). After 6 months her serum calcium was 9.6mg/dl, phosphate was 4.10 mg/dl and thyroid profile was T3-1.10 ng/ml, T4-7.80ng/ml and TSH 1.16 IU/ml.



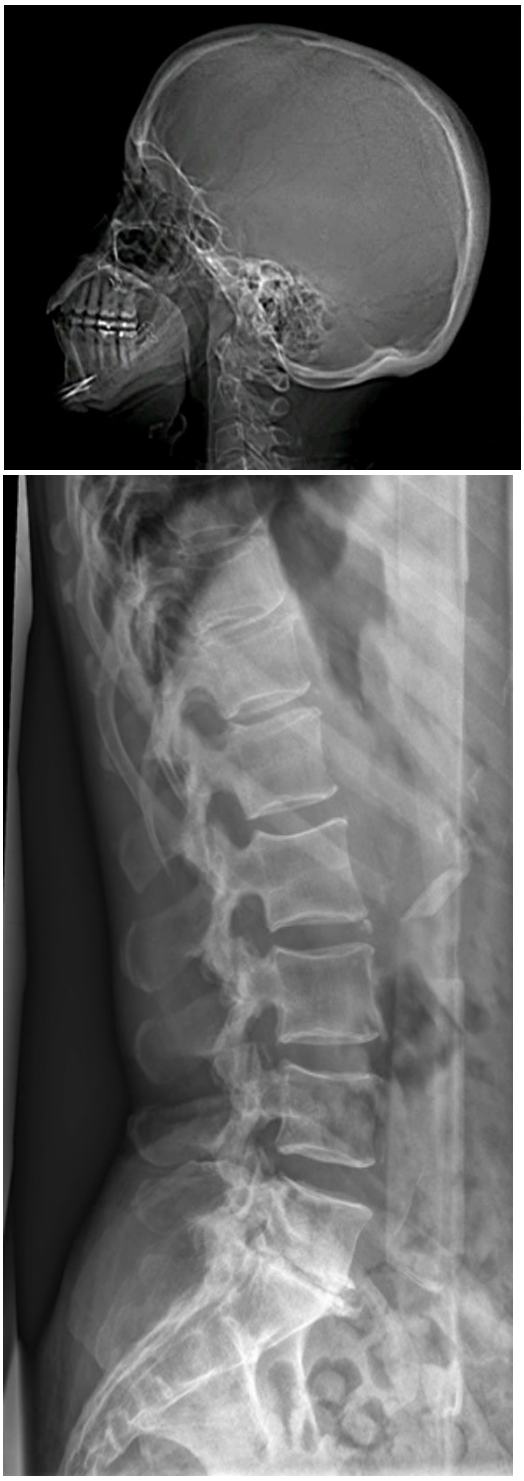


Figure 1 X ray chest, skull and Lumbosacral spine.

Discussion-Normal calcium level in body is well regulated by parathyroid hormone, vitamin D and calcitonin from bone, gut and kidney. Normal level of calcium is 8.8 to 10.7 mg/dl, mild hypercalcemia is 10.8 to 12 mg/dl, moderate is 12 to 14 mg/dl and severe hypercalcemia is >14 mg/dl.[11] A hypercalcemic crisis is an emergency situation with a severe hypercalcemia, generally above 14 mg/dL (or 3.5 mmol/l)[12]. The main symptoms of a hypercalcemic crisis are hypercalcemia with altered sensorium, abdominal pain, and constipation. 90% cases of hypercalcemia in elderly are due to hyperparathyroidism and malignancy.[13]

Pathophysiology of hypercalcemia in hyperthyroidism is poorly understood. It is thought that thyroid stimulating hormone (TSH) itself had a bone protective effect suggesting that suppressed TSH levels also play a role in hypercalcemia. TSH have osteoblastic and T3 have osteoclastic activity.[10]. The molecular mechanisms by which a hyperthyroid state effects bone includes increased sensitivity of β adrenergic receptors to catecholamines as well as increased sensitivity of bone to PTH.[14,15] Another clinical study demonstrated increased cortical porosity and resorption in hyperthyroid patients as compared to healthy controls.[16] Serum IL-6 and its soluble receptor positively correlate with thyroid hormone level in hyperthyroid patients. Thyroid hormone directly increases the sensitivity of bones to IL-6, which promotes osteoclastic differentiation via increasing the expression of the receptor activator of nuclear factor kB ligand (RANKL).[2,17] Adrenaline and glucocorticoid hormones are also dysregulated contributing to a hypercalcemic state.[6,18]

Primary hyperparathyroidism and malignancy were ruled out in our case by normal PTH and normal Ultrasonography of Neck, CECT Abdomen and Thorax and normal tumor markers. Osteolytic bone diseases such as multiple myeloma, Paget disease, or bone metastases were excluded based on normal ALP, PTH and urinary Bence-Jones protein and absence of 'M' peak on serum electrophoresis. Medication related hypercalcemia was ruled out as there was no suggestive history of intake of vitamin D and calcium in any form and her vitamin D level was also normal. Hence the final diagnosis of hyperthyroidism causing hypercalcemia was made. Rapid correction of calcium after rehydration and diuretic therapy resulted in immediate regain of consciousness and her calcium levels were maintained within normal limits with anti-thyroid treatment.

The primary treatment for hyperthyroidism-associated hypercalcemia is to control the hyperthyroid status. The rapid improvement in the symptoms is due to quick rehydration; however, antithyroid therapy improves the hyperthyroid symptoms and maintains the blood calcium level.[19] In this patient, FT3 and FT4 were normalized after 2 months. Although hypercalcemia often leads to decreased serum phosphate levels,[20] low PTH levels may cause increased reabsorption of phosphate in the kidney tubules. Previous studies have shown that hypercalcemic patients can have low to normal serum phosphate levels.[21)]

CONCLUSION

Hyperthyroidism-associated hypercalcemia crisisis a rare complication in hyperthyroid patients; however, this cause should not be ignored after excluding other causes of hypercalcemia. Timely treatment of hypercalcemia is a critical step for rapid control of symptoms and saving the life of the patients. Nevertheless, the treatment of hyperthyroidism is required to maintain the blood calcium level.

References

1. Baxter JD, Bondy PK. Hypercalcemia of thyrotoxicosis. *Ann Intern Med* 1966;65:429-42.
2. Iqbal AA, Burgess EH, Gallina DL, *et al*. Hypercalcemia in hyperthyroidism: patterns of serum calcium, parathyroid hormone, and 1,25-dihydroxyvitamin D3 levels during management of thyrotoxicosis. *Endocr Pract* 2003;9:517-21.
3. Alikhan Z, Singh A. Hyperthyroidism manifested as hypercalcemia. *South Med J* 1996;89:997-8.
4. Carroll MF, Schade DS. A practical approach to hypercalcemia. *Am FamPhysician* 2003;67:1959-66.
5. Korytnaya E, Rao NG, Mayrin JV. An unusual case of hypercalcemia associated with Graves' disease and vitamin D deficiency. *Clin Med Insights Endocrinol Diabetes* 2011;4:25-8.
6. Yokomoto M, Minamoto M, Utsunomiya D, *et al*. Hypercalcemic crisis due to primary hyperparathyroidism occurring concomitantly with Graves' disease. *Intern Med* 2015;54:813-8.
7. Suzuki H, Kondo K, Saruta T. A case of hypercalcemic crisis with resistant hypertension due to hyperthyroidism. *Jpn J Med* 1983;22:137-9.
8. Endo A, Shigemasa C, Kouchi T, *et al*. Development of hypercalcemic crisis in a Graves' hyperthyroid patient associated with central diabetes insipidus. *Intern Med* 1995;34:924-8.
9. Barut I, Tarhan OR, Cerci C, *et al*. Hypercalcemia syndrome. Coexisting hyperthyroidism, primary hyperparathyroidism and cancer of the gallbladder. *Saudi Med J* 2005;26:1119-21.
10. Bassett JH, Williams GR. The molecular actions of thyroid hormone in bone. *Trends Endocrinol Metab*. 2003;14:356-364.
11. Khosla S. Hypercalcemia and hypocalcemia. Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, eds. Harrison's Principle of Internal medicine. 18th ed. New York, NY: McGraw-Hill; 2012. Chapter 46.
12. Hypercalcemiain Emergency MedicineArchived 2011-04-25 at the Wayback Machine. at Medscape. Author: Robin R Hemphill. Chief Editor: Erik D Schraga. Retrieved April 2011.
13. Ahmad S, Kuraganti G, Steenkamp D. Hypercalcemic crisis: a clinicalreview. *Am J Med* 2015;128:239-45.
14. Cardoso LF, Maciel LM, Paula FJ. The multiple effects of thyroiddisorders on bone and mineral metabolism. *Arq Bras Endocrinol Metabol* 2014;58:452-63.
15. Dhanwal DK. Thyroid disorders and bone mineral metabolism. *Indian J Endocrinol Metab* 2011;15:S107-12.
16. Mosekilde L, Melsen F, Bagger JP, *et al*. Bone changes in hyperthyroidism: interrelationships between bone morphometry, thyroid function and calcium phosphorus metabolism. *Acta Endocrinol* (Copenh) 1977; 85:515-25.
17. Maxon HR, Apple DJ, Goldsmith RE. Hypercalcemia in thyrotoxicosis. *Surg Gynecol Obstet* 1978; 147:694-6.
18. Mallette LE, Rubenfeld S, Silverman V. A controlled study of the effects of thyrotoxicosis ad propranolol treatment on mineral metabolism and parathyroid hormone immunoreactivity. *Metabolism*. 1985; 34:999-1006.
19. Giovanella L, Suriano S, Ceriani L. Graves' disease, thymus enlargement, and hypercalcemia. *N Engl J Med* 2008; 358:1078-9.
20. Mosekilde L, Eriksen EF,Charles P. Effects of thyroid hormones on bone and mineral metabolism. *Endocrinol Metab Clin North Am* 1990; 19:35-63.
21. Gorka J, Taylor-Gjevre RM, Arnason T. Metabolic and clinical consequences of hyperthyroidism on bone density. *Int J Endocrinol* 2013;2013:638727. doi: 10.1155/2013/638727.