

*Case report***A Case of Hypercalcemia after Thyroidectomy**Irimi Katsarou¹, Ourania Drakoulougona², Antonis Christopoulos³ and Goula Konstantina²¹Renal Unit, General Hospital Zakynthos, ²Renal Unit, St Andrews' General Hospital Patras, ³Doctor's Hospital Athens, Greece**Abstract**

Total thyroidectomy is complicated by hypoparathyroidism in 1-3% of patients. Hypoparathyroidism is treated with oral calcium and vitamin-D supplements. Everyday use of calcium and vitamin D can lead sometimes to hypercalcemia. Ingestion of large amounts of calcium and absorbable alkali that cause hypercalcemia, various degrees of renal failure, and metabolic alkalosis, can be associated with a diagnosis of calcium-alkali syndrome. This syndrome was first identified as milk-alkali syndrome, after treatment of peptic ulcer disease with milk and alkali which was widely adopted at the beginning of the 20th century. With the introduction of histamine-2 blockers and proton pump inhibitors, the occurrence of milk-alkali syndrome became rare; however, it has emerged recently as calcium-alkali syndrome because of the wide availability and increasing use of calcium carbonate, mostly for osteoporosis prevention. We present a female patient with hypoparathyroidism who presented with hypercalcemia and alkalosis as a result of treatment with calcium carbonate, vitamin D and thiazide diuretic. The patient was treated successfully by discontinuation of the above drugs, intravenous fluid administration and enhancement of calcium renal excretion. Hypercalcemia presenting as calcium-alkali syndrome is a diagnosis that requires a high index of suspicion in order to quickly identify the disorder and initiate appropriate therapy. It is important for clinicians to keep the syndrome on their list of differential diagnosis.

Keywords: hypercalcemia, hypoparathyroidism, calcium-alkali syndrome, vitamin D

Introduction

Total thyroidectomy is complicated by permanent hypoparathyroidism in a small percentage of patients. It's therapy consists of long-life treatment with calcium supplements (1.5-3 g/day) and active metabolite of vitamin D (0.5-2 µg/day).

Daily use of calcium with vitamin D can sometimes lead to hypercalcemia. Hypercalcemia is defined as an increase

in total serum calcium >10.5 mg/dl (>2.5 mmol/l) or ionized calcium >5.6 mg/dl (>1.4 mmol/l). An increase in total calcium over 14 mg/dl (3.5 mmol/l) is characterized as serious hypercalcemia-hypercalcemic crisis. Calcium-alkali syndrome consists of hypercalcemia, alkalosis and renal failure. Recently many patients present with this diagnosis and it is the third commonest cause of hypercalcemia [1,2].

We report a case of a female patient with total thyroidectomy and permanent hypoparathyroidism who presented with symptomatic hypercalcemia.

Case report

A 59-year-old female patient presented to the Emergency Department complaining on vomiting over the last 5 days, muscle ache and weakness. No fever or other symptoms were reported. From her past history the patient reported papillary thyroid cancer that was treated by thyroidectomy 20 years ago. She developed postoperative hypoparathyroidism and remained on life-long treatment with thyroxin 125 mg/day and calcium lactate gluconate and calcium carbonate. Although on calcium supplementation, the patient was frequently admitted to the Department of Internal Medicine of our Hospital because of tetanic crises. During her previous admission (one month ago), alphacalcidol (3g/24h) and hydrochlorothiazide 25 mg/24h were added to her drugs whereas the dose of calcium carbonate was also increased from 1 g to 3 g/24h.

On physical examination, arterial blood pressure was 110/70 mmHg and heart rate 75/min. No swelling or signs of dehydration were noted whereas the clinical examination of lungs, heart and abdomen showed no pathologic findings. No palpable lymph nodes were found. The ECG was normal.

Laboratory tests showed severe hypercalcemia [Ca: 18.4 mg/dl (normal range 8.5-10.1 mg/dl)], impaired renal function (serum creatinine: 2.8 mg/dl), hypokalemia (K: 2.8 mmol/l), normocytic anemia (Hb: 10.4 g/dl, Hct: 31.2%, MCV: 89), elevated CRP levels (7.3 mg/dl) and hyperuricemia (uric acid: 14.4 mg/dl). Sodium, chloride and proteins in blood were in normal range (Na: 135 mmol/l, Cl: 100 mmol/l, albumin: 4.2g/dl).

An ultrasound scan showed normal size and echogenicity of kidneys. A CT of the abdomen and lungs was also without any abnormality. PTH blood levels were low [PTH: 3 pg/ml (normal range 10-93)] whereas thyroid

hormone and alkaline phosphatase blood levels were within normal range.

After admission, the patient had polyuria (6800 ml/day) with a urine specific gravity of 1003-1004 and urine pH 7-7.5 (Table 1).

Table 1. Laboratory tests

Day	Na (mmol/L)	K (mmol/L)	Urea (mg/dL)	Cr (mg/dL)	Ca (mg/dL)	Uric acid (mg/dL)	Urine output ml
1	126	2.8	115.8	2.8	17.7	14.4	5400
2	135	3.4	108	2.9	18.4	10.4	6800
3	140	3.4	93.9	2.3	12.4	8.7	4200
5	141	3.0	82	2.2	10.3	7.1	3400
7	142	3.8	44.7	1.7	9.2	7.0	2500
8	143	3.8	45	1.7	7.8	6.8	2200

Hypercalcemia was managed with cessation of calcium and vitamin D supplements, administration of sodium chloride solutions and furosemide (20 mg/12hr intravenously). Hypokalemia was treated with potassium supplements. The patient was discharged 8 days after her admission in a good clinical condition with calcium levels of 7.8 mg/dl and improved renal function (serum creatinine: 1.7 mg/dl and GFR: 49.8 ml/min).

Discussion

Hypercalcemia is characterized by high calcium concentration in the blood which sometimes can lead to fatal complications. The manifestations of mild hypercalcemia are weakness and fatigue but as calcium levels increase further, symptoms become more serious. The level of calcium in the blood along with the rate of development of hypercalcemia are related with symptoms from central nervous system, gastrointestinal tract, heart and kidneys [3]. Stupor, weakness, confusion and coma represent serious symptoms from central nervous system whereas constipation, nausea, vomiting and lack of appetite are symptoms of hypercalcemia from the gastrointestinal tract. Moreover, patients with hypercalcemia can develop peptic ulcers and pancreatitis. Cardiac arrhythmias, hypotension and short QT interval in the ECG represent heart involvement whereas polyuria, dehydration and thirst along with presence of kidney stones and renal failure represent involvement of urinary tract.

In our patient, hypercalcemia was probably related to the administration of calcium sparing drugs alphacalcidol (3 mg/day), calcium carbonate (3000 mg) and diuretics (hydrochlorothiazide) in high doses. Calcium carbonate, which contains alkaline ions, and hydrochlorothiazide probably contributed to metabolic alkalosis whereas vomiting further exacerbated hypercalcemia and metabolic alkalosis by loss of hydrogen cations from gastrointestinal tract and contraction of intravascular volume. Diuretics represent the most common cause of drug-induced metabolic alkalosis. This is probably related to increased excretion of chloride in the urine that leads to intravascular volume depletion. The concentration of

bicarbonate increases because of reduced volume of distribution (contraction alkalosis) leading to mild metabolic alkalosis. Hypercalcemia due to thiazide diuretics is uncommon in patients without other comorbidities. It causes vasoconstriction of the afferent arteriole leading to decline of GFR as well as activation of calcium sensing receptor (CaSR) in the thick ascending limb of the loop of Henle leading to deactivation of Na-K-2Cl co-transporter that is deactivated with final result natriuresis and hypovolemia. Hypovolemia leads to increased bicarbonate reabsorption and alkalosis that further aggravates hypercalcemia (by activating a calcium channel in the distal convoluted tubule and in the colon resulting in increased calcium reabsorption) [4,5].

As our patient ingested a high dose of calcium and absorbable alkali (calcium carbonate), we thought that the patient could have calcium-alkali syndrome. This syndrome presented in the past as milk-alkali syndrome. Milk-alkali syndrome is characterized by hypercalcemia, renal failure and metabolic alkalosis [6]. Leo Hardt and Andrew Rivers in 1923 first reported the complications of Sippy diet treatment (Bertram W. Sippy 1866-1924) which consisted of great quantities of milk and calcium for peptic ulcer treatment. They correlated Sippy diet with renal failure and metabolic alkalosis [7,8]. Thirteen years later, Cuthbert Cope recognized also hypercalcemia as part of the syndrome, thus completing the classic triad [2]. After the introduction of H₂-antagonists and proton pump inhibitors for the treatment of peptic ulcer, the incidence of the syndrome declined and it became a rare cause of hypercalcemia [9,10]. Currently it has re-emerged as calcium-alkali syndrome that represents the third commonest cause of hypercalcemia, due to the wide use of calcium carbonate and vitamin D for prevention and treatment of osteoporosis [2,11].

In our case, we treated the patient's hypercalcemia by discontinuation of the responsible drugs fluid administration and furosemide in order to enhance renal excretion of calcium. Intravenous fluid and furosemide were enough for restoring calcium levels; however, renal function did not recover completely (creatinine clearance: 49.8 ml/min). Similarly to our patient, cases with

permanent functional and structural kidney damage have been described in the literature [12,13].

Conclusion

In conclusion, patients with predisposing factors for development of hypercalcemia such as renal failure and thiazide diuretic use should be closely monitored with frequent measurements of calcium blood levels when treated with calcium carbonate and vitamin D. Physicians should also consider the diagnosis of calcium-alkali syndrome for such patients, since it is a common cause of hypercalcemia.

Conflict of interest statement. None declared.

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