Hypercalcemia and the cardiovascular system

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Abstract

Hypercalcemia, acute and chronic, irrespective of the cause, is known to have effects on the heart and the vascular system that are potentially life-threatening. Some of these effects include accelerated atherosclerosis, uncontrolled hypertension, structural effects, and progressive cardiac dysfunction. This case report demonstrates the effects of hyperparathyroidism-induced hypercalcemia on the cardiovascular system and clinical management in a patient with hypertension that was difficult to control.

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Keywords: Hypercalcemia, hyperparathyroidism, hypertension, heart failure, complete heart block, renal failure

Case report

A 45-year-old woman was referred to the hypertension clinic by her general practitioner, for assessment of a persistently increased blood pressure (> 160/110 mm Hg) over a 2-month period. On routine blood tests, she was noted to have an increased calcium concentration (corrected calcium 3.52 mmol/L), and was then admitted to hospital for further evaluation and treatment. Further blood tests revealed increased parathyroid hormone concentrations (266 pg/ml). Her alkaline phosphatase and vitamin D concentrations were normal. She was previously fit and well, with no significant past medical history, and was commenced on atenolol 50 mg a few days before her admission to hospital for control of her high blood pressure. Further questioning revealed that she had been feeling tired and low in the recent past. The patient had never smoked, and consumed alcohol only occasionally. Her father and brother were known to have high blood pressure.

On assessment, her pulse was 60 beats/min and her blood pressure was 145/85 mm Hg. There were no cardiac murmurs, and her lung fields were clear. The initial management was aimed at achieving normocalcemia and the patient was treated with intravenous fluids and pamidronate. Further investigations were carried out, and a parathyroid iodine/methoxyl isobutyl isonitrile (I/MIBI) scan (*Figure 1*) revealed a parathyroid adenoma at the lower pole of the right thyroid gland. Her calcium concentrations were monitored throughout her treatment. Echocardiography revealed normal left ventricular function, with no left ventricular hypertrophy. The heart valves were normal, with no significant aortic valve or left ventricular outflow tract gradient. Blood pressure was monitored during her hospital stay and found to have decreased with treatment of her hypercalcemia (*Table I, Figure 2*).

The patient was subsequently referred to the surgeons and underwent a partial parathyroidectomy and resection of the adenoma. Her serum calcium concentration decreased during the postoperative period (2.69 mmol/L) and her blood pressure decreased to 110/60 mm Hg.

Four months later, the patient was reviewed in the hypertension clinic and found to be well and asymptomatic, with a blood pressure of 125/71 mm Hg, although her calcium concentrations (2.85 mmol/L) were increased again.

The calcium concentrations gradually increased over the next few months (*Table I, Figure 3*), with a

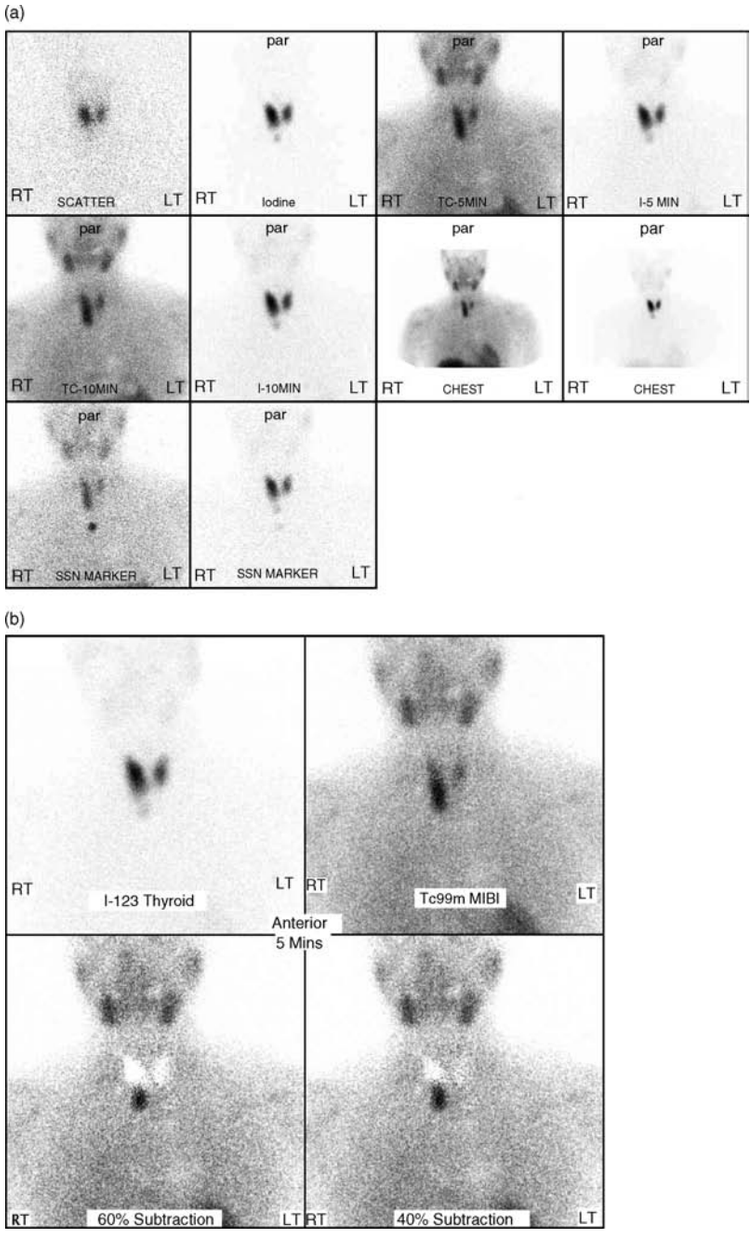

Figure 1. Parathyroid I/MIBI Scans at initial workup.

Table I. The patient's serum calcium and parathyroid hormone concentrations and blood pressure profile, from October 2004 to August 2005.

	Month and year								
	Oct 04	Oct 04	Nov 04	Dec 04	Feb 05	Mar 05	Apr 05	Jun 05	Aug 05
Serum calcium[a] (mmol/l)	3.52	2.69	2.81	3.25	3.02	2.92	2.84	3.03	2.85
Serum PTH (pg/ml)	266			126	156	124	117	116	76
Blood pressure (mm Hg)	147/87	110/70	110/66	153/92				142/95	125/71

[a]Corrected value. PTH, parathyroid hormone.

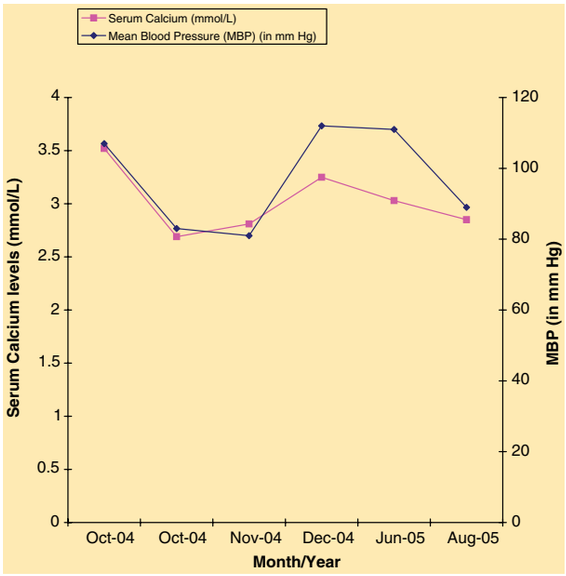

Figure 2. Serum Calcium vs Mean Blood Pressure.

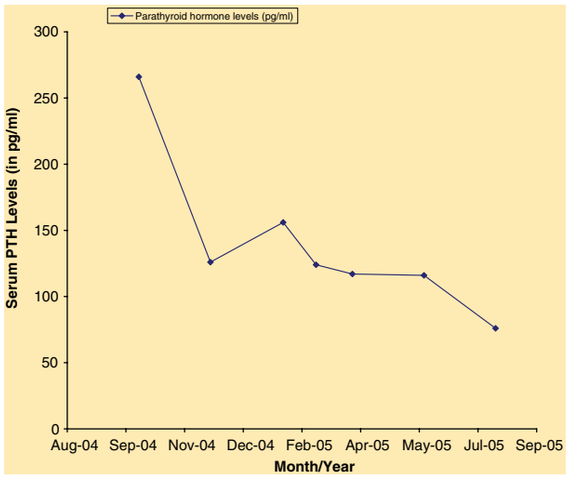

Figure 4. Trend in Serum Parathyroid hormone levels(PTH) (in pg/ml).

corresponding increase in parathyroid hormone concentrations (*Table I*, *Figure 4*). The patient also developed symptoms of polyuria and polydipsia. Repeat imaging of the neck was performed. A sonography of the neck (*Figure 5*) showed a single benign nodule in the lower pole of right lobe of the thyroid gland. However, an MRI scan (*Figure 6*) revealed a 10 × 10-mm focal area of high signal, seen in the inferior aspect of the right thyroid lobe, and a subsequent parathyroid I/MIBI scan (*Figure 7*) confirmed increased uptake in the inferior aspect of the right lobe of the thyroid, suggesting a recurrence of the adenoma. Her blood pressure increased to 142/95 mm Hg. She currently awaits a parathyroidectomy.

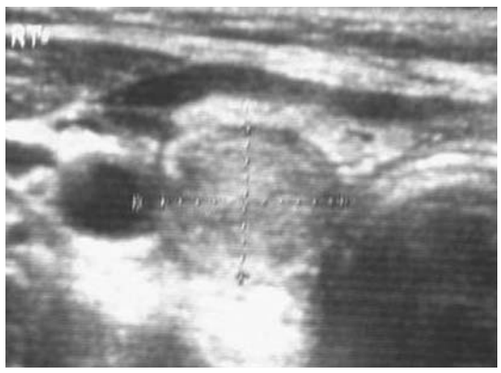

Figure 5. Sonography of the neck. Parathyroid Adenoma.

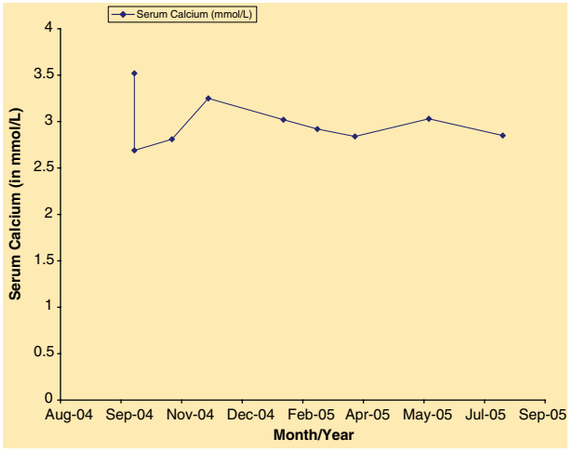

Figure 3. Trend in Serum Calcium levels (in mmol/L).

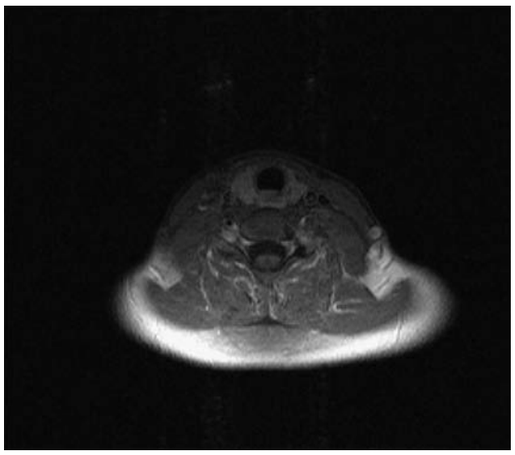

Figure 6. MRI Scan Neck.

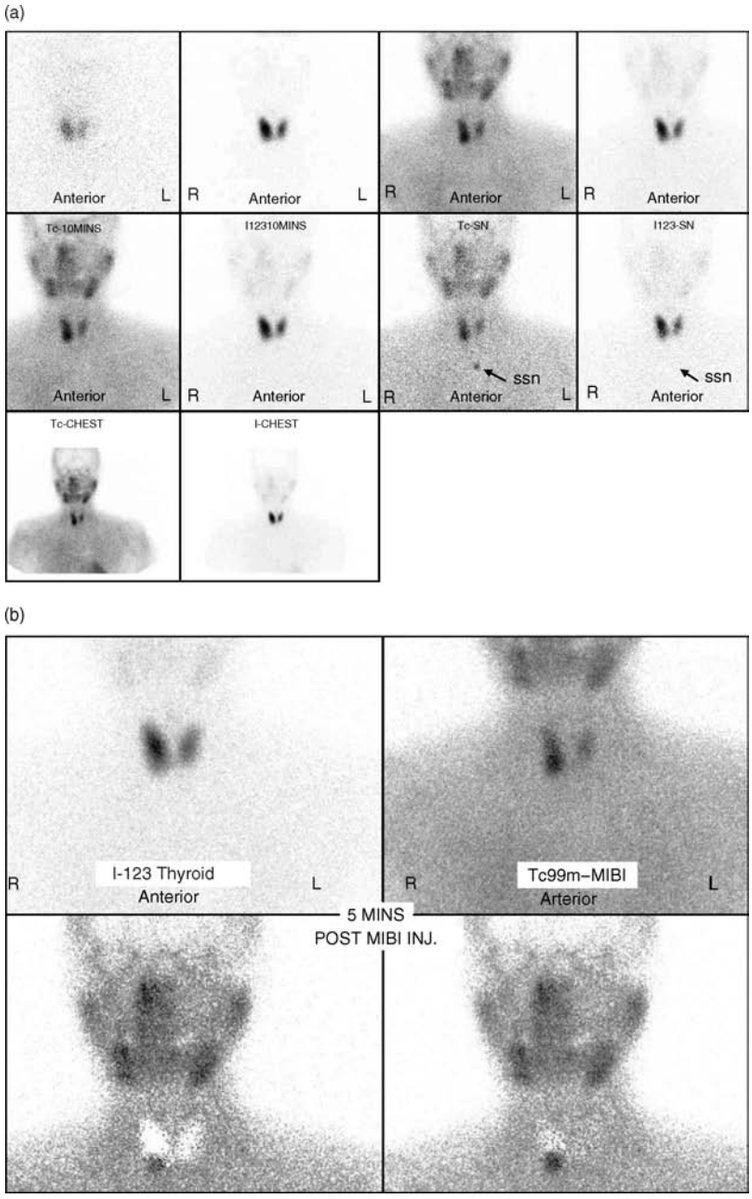

Figure 7. Repeat parathyroid I/MIBI Scan a few months later.

Discussion

Hyperparathyroidism is characterized by hypercalcemia resulting from excessive release of parathyroid hormone (PTH), most cases being discovered accidentally when hypercalcemia is noted during a routine serum chemistry profile. In most patients, symptoms are mild at the time of presentation and resolve with surgical correction of the disorder. In 85% of affected persons, primary hyperparathyroidism (PHPT) results from an adenoma in a single parathyroid gland. Hypertrophy of all parathyroid glands causes hyperparathyroidism in 15% of patients. Parathyroid malignancies account for a small number of cases of hyperparathyroidism. The parathyroid glands regulate calcium and phosphorus concentrations by releasing variable amounts of parathyroid hormone, which increases serum calcium concentrations while decreasing serum phosphorus. Under usual conditions, the rate of secretion of parathyroid hormone is inversely proportional to the serum calcium concentration.

Hyperparathyroidism, particularly PHPT, with changes in the serum calcium and PTH, is known to affect cardiovascular function. The cardiovascular effects of hypercalcemia include hypertension, left ventricular hypertrophy, arrhythmias, vascular calcification, and a shortened QT interval on the

electrocardiogram. Once a symptomatic disorder characterized by significant hypercalcemia, PHPT today is most commonly seen in asymptomatic individuals with serum calcium concentrations that are within 1 mg/dL of the upper limits of normal, with a consequent change in the cardiovascular manifestations [1]. It is hypothesized that calcium is related to the development of hypertension by its effect on smooth muscle vasoconstriction.

Of note, both acute and chronic hypercalcemia can cause hypertension. Acute hypercalcemic hypertension is postulated to be related to the effects of calcium on the vascular smooth muscle cells, with increased calcium ion influx through calcium channels and a direct effect on vascular smooth muscle cells and increased vascular resistance. In addition, increased catecholamines have been demonstrated in hypercalcemia-induced hypertension. Indeed, the release of catecholamine is dependent upon calcium ion activity, with calcium ions facilitating the release of epinephrine from the adrenal medulla and norepinephrine from sympathetic nerve ending. Catecholamines, via binding with α_2-adrenergic receptors, could induce vasoconstriction [2]. However, Maheswaran and Beevers [3] did not find a significant correlation between calcium concentrations and preoperative blood pressure in 115 patients with PHPT who subsequently underwent parathyroidectomy.

Increased PTH, with its direct positive chronotropic and mediated inotropic effects on the heart, has been associated with the development of left ventricular hypertrophy [1]. Although there have been suggestions of a role of increased PTH concentrations in the pathogenesis of hypertension, infusion of synthetic PTH has been reported to cause a decrease in the blood pressure [4].

Patients with PHPT were considered to be at high risk of death from cardiovascular disease [5–8]. A Swedish study that followed patients with hyperparathyroidism for more than 10 years showed that mortality from cardiovascular disease was greater in the study individuals with hyperparathyroidism than in the control population. Patients with hyperparathyroidism are also more likely than control individuals to have hypertension and congestive heart failure, and are more likely to exhibit changes on the electrocardiogram [9]. Hypertrophic cardiomyopathy and a decrease in function of the muscles of ventilation may account for some of this effect [10].

Summary

Hypercalcemia and PHPT are associated with the development of hypertension that may be difficult to control, with resulting end-organ effects such as left ventricular hypertrophy, heart failure, and renal damage. The evaluation and work-up of patients with hypertension that is uncontrolled or difficult to control should include a check of the patient's serum calcium concentrations to rule out hypercalcemia and PHPT, as treatment of the high serum calcium concentrations may improve blood pressure control and prevent end-organ damage. ■

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