Case Report

A Case of Hypercalcemic Crisis with Resistant Hypertension due to Hyperthyroidism

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A 50-year-old Japanese woman showed hypercalcemic crisis due to hyperthyroidism, accompanying with high blood pressure. High blood pressure, which did not decrease in spite of normalization of serum calcium and thyroid function, was only reduced after the administration of calcium channel blocker. It may suggest that her high blood pressure related with the vascular changes due to hypercalcemia and hyperthyroidism.

Key Words: Hyperthyroidism, Hypercalcemia, High blood pressure, Calcium channel blocker

In thyrotoxic patients, hypercalcemia has been reported to be relatively rare¹⁻³⁾. The occurrence of high blood pressure is seen both in patients with hypercalcemia⁴⁾ and in those with hyperthyroidism⁵⁾, however, concomitance of hypertension and hypercalcemia in patients with hyperthyroidism has received little attention in the literature. The patient described, who presented severe hypercalcemia and hyperthyroidism, continued to have high blood pressure after correction of high serum calcium level and thyroid function. Her blood pressure returned to normal only after the administration of nifedipine, a calcium channel blocker.

CASE REPORT

A 50-year-old woman with no family history of hypertension or endocrine diseases was referred to Keio University Hospital, on May 1980, because of marked general fatigue. She had been well until February 1980, when she first noticed palpitation on exertion. She consulted a physician, who informed her of her high blood pressure and advised her to take a low sodium diet. During the next 2 months, nausea and vomiting developed and she experienced even at rest. She consulted the physician again, who prescribed some medicines without benefit. Her general condition gradually became worse, and she was referred

to the hospital.

She appeared wasted and chronically ill. On physical examination at the time of admission, the temperature was 37.4°C, pulse 132 and respiration 19. The blood pressure was 174/98 mmHg. No ophthalmopathy was found. There was mild anemia and no jaundice. No cervical adenopathy was felt and no thyroid struma was palpated. A grade 2 systolic ejection murmur was heard at the apex. The lungs were normal. The liver, spleen and kidneys were not felt. No fine finger tremor was found. The extremities appeared normal and neurological examinations were negative. The urine was normal. The hematocrit was 33.6%: the white cell count was 4,300, with the normal differentials. The urea was 23.4 mg per 100 ml, the creatinine 1.3 mg, and protein 6.6 g per 100 ml. The sodium was 134 mEq per liter, the potassium 3.8 mEq, calcium 12 mg, and inorganic phosphate 4.8 mg. The results of endocrinological examinations are summarized in Table 1. An electrocardiogram showed sinus tachycardia at a rate of 136, with ST-segment changes. An X-ray survey of the bones revealed no abnormal lesion. The upper G.I. series were negative.

After admission, treatment of the hypercalcemia was begun with saline and furosemide as well as monitoring the central venous pressure.

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Table 1. The Endocrinological Examinations

	May 24, 1980	June 21, 1980	Normal range
Serum thyroid stimulating hormone	1.0	1.5	1.3-7.4 $\mu\text{g/ml}$
Serum thyroxine	38	12	15-25 $\mu\text{g/ml}$
Serum triiodothyronine	600	235	81-145 $\mu\text{g/ml}$
Serum parathyroid hormone	0.2	0.5	0.2-0.8 ng/ml
Plasma renin activity	0.1	0.2	1.2-2.1 ng/ml/hr
Plasma aldosterone concentration	29	25	30-100 pg/ml
Urinary catecholamines			
Norepinephrine	4.6	8.0	below 10 $\mu\text{g/day}$
Epinephrine	8.0	11.2	10-90 $\mu\text{g/day}$
Vanillylmandelic Acid	3.4	4.2	2-9 $\mu\text{g/day}$

The sinus tachycardia and high blood pressure continued despite normalization of the serum calcium. Propranolol (60 mg daily) and methimazole (15 mg daily) were started after the findings of elevated triiodothyronine (600 $\mu\text{g/ml}$). A combination of captopril (SQ 14225, 75 mg daily), furosemide (80 mg daily) and propranolol (60 mg daily) did not reduce the elevated blood pressure, but nifedipine (calcium channel blocker, 30 mg daily) decreased the blood pressure to the normal levels.

After the normalization of the blood pressure and thyroid function, exploration for parathyroid lesions was performed. Contrary to expectations, no marked adenoma or hyperplasia was found in the parathyroid. A week after the operation, the patient was discharged. Administration of nifedipine, propranolol and methimazole were continued for the next 2 months, and then the nifedipine was discontinued. The patient's blood pressure has remained in the normal range for more than 2 years.

DISCUSSION

It is well known that calcium has an important effect on blood pressure^{6, 7}. Rapid reduction of the serum calcium concentration is associated with a fall in blood pressure in man⁸. Moreover, more than one third of patients with primary hyperparathyroidism and elevated serum calcium levels are hypertensive^{9, 10}, and they often become normotensive after parathormone-producing tumors have been removed¹¹. Theoretically, calcium is considered to be able to induce elevation of blood pressure through peripheral vascular constriction¹² and through the release of pressor substances such as catecholamines and renin^{13, 14}.

In the patient described here, the blood pressure remained high after normalization of the serum calcium level. It seems unlikely, therefore, that calcium played any role in the elevation of blood pressure directly. Furthermore, since catecholamines were in the normal range, catecholamines did not appear to be responsible for the elevated blood pressure. The plasma renin activity was low and administration of angiotensin I converting enzyme inhibitor failed to decrease the blood pressure. These data do not suggest that the renin-angiotensin system could play a role in the cause of the hypertension of this patient. The normal renal function of the patient excluded the participation of renal insufficiency in elevating the blood pressure as in other patients with hypercalcemia¹¹. Also the elevated blood pressure of this patient was not reduced after normalization of thyroid function. It seems unlikely, therefore, that the increase in blood pressure in this patient was directly due to either hypercalcemia or hyperthyroidism. The more attracting explanation for the rapid and marked decrease of the blood pressure after the administration of calcium channel blocker is that, even after serum calcium level became normalized, the vascular tissue level of calcium still might be higher than expected. If it will take longer time to reduce the calcium level in the tissues compared to serum calcium level, calcium channel blocker may antagonize calcium in the tissue. This assumption may be supported by our findings that nifedipine exerts an effect on the intracellular calcium ion in dilating blood vessels¹⁵.

In summary, a rare case with hypercalcemia due to hyperthyroidism accompanying by high blood pressure was reported. The interesting point in this case is that high blood pressure was reduced only by calcium channel blocker.

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