Hypertension

Case Report

Development of Hypertension After Correction of Primary Hyperparathyroidism

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SUMMARY A statistical association between hypertension and hyperparathyroidism has been repeatedly reported, but the underlying pathogenetic mechanism has not been elucidated. A 51-year-old woman was hospitalized because of increasing motor disability caused by multiple bone and muscle aches with generalized weakness. She was found to have marked hypercalcemia and hypophosphatemia, increased parathyroid hormone secretion, but normal renal function and blood pressure level. After the identification and removal of a single parathyroid adenoma, the calcium/phosphate metabolism normalized in a relatively short time during which, however, hypertension developed in the absence of any other endocrine or renal dysfunction. A positive, highly significant relationship was observed between the progressive rise in blood pressure and the gradual increase in serum phosphate concentration occurring after the operation, suggesting that, in the hyperparathyroid phase, an underlying trend to hypertension could have been masked by the phosphate depletion, probably through its effects on cardiac and vascular smooth muscle function. (Hypertension 11: 285-287, 1988)

KEY WORDS • hypertension • hyperparathyroidism • hypophosphatemia

ARTERIAL hypertension is far more common in patients with primary hyperparathyroidism than in the general population. This association has been attributed to the combined effects of persistently high levels of serum ionized calcium and parathyroid hormone (PTH) or, alternatively, to a nephrolithiasis-induced or urolithiasis-induced renal damage. Two recent studies, moreover, showed that in many such patients the repair of hyperparathyroidism is not followed by stable normalization of blood pressure, even in patients without renal damage.

In this report we describe a patient in whom hypertension developed following surgical repair of primary hyperparathyroidism.

Case Presentation

A 51-year-old postmenopausal woman was hospitalized because of asthenia, severe bone and muscle aches, and increasing motor disability of unknown cause. Hereditary disorders were not elicited in the medical history. Two years before hospitalization, the patient had suffered renal colic alleviated by the passage of two stones.

The clinical examination disclosed a deformity of the dorsal segment of the spine and marked reduction of the muscular tone, particularly in the lower limbs. Blood pressure, measured every day between 0800 and 1000 by a well-trained observer using the same standard mercury sphygmomanometer, was always in the normal range (diastolic pressure, 74-88 mm Hg; systolic pressure, 110-134 mm Hg). The electrocardiogram showed no abnormality. Routine laboratory investigation indicated the presence of sustained hypercalcemia (serum total Ca, 2.97-3.65 mmol/L; normal value <2.8 mmol/L; serum ionized Ca, 1.35-1.62 mmol/L; normal value <1.25 mmol/L) as well as roentgenographic evidence of a widespread, severe reduction in bone density.

In addition, a marked increase in serum alkaline phosphatase was found (range, 769-1049 mU/mL; normal value <220 mU/mL) together with low serum phosphate levels (range, 0.45-0.71 mmol/L; normal value >0.80 mmol/L). In addition, a marked increase in serum alkaline phosphatase was found (range, 769-1049 mU/mL; normal value <220 mU/mL) as well as roentgenographic evidence of a widespread, severe reduction in bone density.

Serum concentrations of sodium, potassium, glucose, total protein, urea, and creatinine were within the normal range, as was the glomerular filtration rate (creatinine clearance corrected for body surface area = 2.02 ml/sec), while urinalysis showed calcium oxalate crystaluria. A reduced concentrating ability was suggested by intravenous pyelogram and rapid-sequence nephrogram. Urinary calcium output was en-
hanced both in 24-hour collections (range, 6.9–8.0 mmol/day; normal value < 6.25 mmol/day and in fasting specimens (range, 5.1–6.6 μmol/min; normal value < 3.0 μmol/min). Under fasting conditions, the tubular reabsorption rate of phosphate was reduced (0.056 mmol/dl of glomerular filtrate; normal value > 0.08 mmol/dl). Three distinct radioimmunological determinations of plasma PTH concentration gave consistently high values (range, 6.4–10.8 ng/ml; normal value < 0.8 ng/ml).

Preoperative noninvasive investigations (computed axial tomography, ultrasonography, radiothallium scanning) suggested the existence of three normal parathyroid glands and one abnormally enlarged gland located at the lower right pole of the thyroid gland. A surgical neck exploration confirmed this indirect evidence. Three parathyroid glands of normal dimension (< 5 mm) were identified, while close to the posterior surface of the lower right pole of the thyroid gland an isolated, encapsulated brown tumor (diameter > 1.5 cm) was found and removed. Histological examination showed that this tumor was a benign parathyroid adenoma consisting of small chief cells.

A dramatic fall of serum calcium occurred immediately after operation (serum total Ca, 1.51 mmol/L; treatment with calcium supplementation (Ca, 1.5 g/day p.o. for 15 days) returned serum calcium concentration to normal (serum total Ca, 2.18 mmol/L; serum ionized Ca, 1.03 mmol/L). Compared with the preoperative period, a slight increase in serum phosphate was observed (0.83 mmol/L) while plasma PTH fell into the normal range (0.3 ng/mL). Blood pressure at this time was still normal but slightly higher than previously observed (140/84 mm Hg).

After discharge from the hospital, the patient, observed for 1 month on an outpatient basis, consistently had normal serum concentration of total calcium (range, 2.10–2.31 mmol/L) and phosphate (range, 1.00–1.09 mmol/L), while alkaline phosphatase was almost reduced to normal values (300 μU/ml). During this period the patient experienced a progressive and rapid increase in blood pressure (first clinic visit, 162/98 mm Hg; second visit, 192/124 mm Hg) with no change in heart rate.

Therefore, the patient was rehospitalized. Body weight, serum sodium and potassium concentrations, hematocrit value, and plasma total protein level were comparable to those of the preoperative period. Renal function appeared to be slightly improved, as indicated by creatinine clearance determination (2.16 ml/sec) and normal urinalysis results. In addition, a new rapid-sequence nephrogram suggested improved renal concentrating ability compared with the previous observation. On a normal sodium diet (150 mmol/day), plasma renin activity (0.17 ng angiotensin I/L/sec) and serum aldosterone (198 pmol/L) were in the low-normal range of values for our laboratory, as was urinary free catecholamine excretion (201 nmol/day). Electrocardiogram and chest roentgenogram were unaltered. Serum total calcium (2.2 mmol/L), ionized calcium (1.05 mmol/L), phosphate (1.03 mmol/L), and PTH levels (0.1 ng/mL) were normal, as were the tubular reabsorption rate of phosphate (0.089 mmol/dl of glomerular filtrate) and the urinary calcium excretion (1.10 mmol/day).

Highly statistically significant direct correlations were observed when the values of serum phosphate concentration consecutively found during the first hospitalization, in the course of the postoperative outpatient follow-up, and during the second hospitalization were plotted against the corresponding values of systolic (n = 11, r = 0.86, p < 0.001), diastolic (r = 0.74, p < 0.01), or pulse pressure (r = 0.89, p < 0.001; Figure 1). No association was detected between the blood pressure increase and the corresponding values of serum calcium or PTH concentration.

**Discussion**

A recent retrospective study by Jones et al. reported that 20 of 44 hyperparathyroid patients who were initially normotensive were found to be hypertensive some time later after surgical repair of hyperparathyroidism. In our patient, hypertension developed soon after operation, a seemingly paradoxical finding in light of previous observations. A diagnosis of essential hypertension was made in our patient based on the absence of marked renal impairment, on the lack of any evidence of secondary hypertension, and on the satisfactory response to conventional antihypertensive treatment.

The rather sudden onset of high blood pressure following repair of parathyroid hyperfunction is impressive. It apparently was not related to any volume factor since postoperative body weight, hematocrit, and serum electrolyte and protein concentration were unchanged compared with the preoperative values. The patient did not report any major modifications of lifestyle or dietary habits that could in some way be related to the change in blood pressure. As menopause had occurred naturally 3 years before the first hospitalization, acute modifications of sex hormone production probably did not play a role in the blood pressure increase.
upsurge. Whatever the mechanism underlying the development of hypertension in this patient, it is reasonable to assume that such a mechanism was counteracted during the hyperparathyroid period by some other factor playing an antihypertensive role. This assumption would also account for the patient being in the low-normal range of blood pressure levels in that period, despite severe hypercalcemia.

Theoretically, the elevated preoperative PTH concentration itself may have exerted a protective effect because of the vasodilating and hypotensive properties of PTH; however, this possibility is definitely unlikely, as, in the presence of hypercalcemia, PTH has been shown to act as a prohypertensive factor, probably through a calcium ionophore effect on vascular smooth muscle cells.

In our opinion, a marked hypotensive effect during the hyperparathyroid phase may have been exerted by the severe phosphate depletion induced in our patient by her low renal capacity of phosphate reabsorption. This possibility is supported by the observation that the gradual increase in blood pressure observed after operation strongly paralleled the progressive correction of the hypophosphatemia (see Figure 1). There is convincing evidence that, both in animals and in humans, phosphate depletion may reversibly reduce blood pressure through a negative influence on cardiac performance and vascular sensitivity to vasoconstrictive agents.

This interpretation is in accordance with the existence of an association between hyperparathyroidism and hypertension and suggests that the strength of this association may be underestimated due to the common occurrence of marked hypophosphatemia in hyperparathyroid patients. In addition, this would provide an adequate explanation of the recent retrospective observation of hypertension developing in a large number of normotensive hyperparathyroid patients after surgical repair of hyperparathyroidism.

In conclusion, we suggest that, in future studies of the relation between the calcium/parathyroid axis and blood pressure regulation, the confounding effect of an altered phosphate metabolism should be carefully evaluated, based on the hypothesis that in many hyperparathyroid patients a negative phosphate balance can blunt the association of hyperparathyroidism with hypertension.

References
Development of hypertension after correction of primary hyperparathyroidism.
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