Hypocalcaemia, a possible manifestation of thyrotoxicosis

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Summary

A severely thyrotoxic patient was found to have hypocalcaemia and tetany, which cleared when she became euthyroid.

Cessation of treatment with propranolol and propylthiouracil resulted in a recurrence of the thyrotoxicosis and the reappearance of hypocalcaemia. Reinstitution of treatment resulted in a second remission of the thyrotoxicosis and correction of the hypocalcaemia.

It is suggested that in this patient, the thyrotoxicosis was the cause of hypocalcaemia. The various pathogenetic mechanisms are discussed.

KEY WORDS: hypocalcaemia, thyrotoxicosis, osteoporosis, vitamin D.

Introduction

Hyperthyroidism seems to influence the metabolism of calcium. Enhanced osteoclastic activity with increased bone resorption (Follis, 1953), decreased intestinal absorption of calcium (Shafer and Gregory, 1972) and hypercalciuria are all described in hyperthyroidism and may induce changes in the serum calcium level. However, despite these abnormalities in calcium metabolism, most hyperthyroid patients are normocalcaemic. On occasions, mild hypercalcaemia, not severe enough to cause symptoms, has been noted (Mundy and Raisz, 1979). To our knowledge, there have been no reports of hypocalcaemia in thyrotoxicosis. A patient in whom severe hypocalcaemia was one of the presenting features of thyrotoxicosis is now reported.

Case report

A 55-year-old Jewish Caucasian woman was hos-

pitalized in April 1980 because of weakness and general deterioration of several weeks duration. Twenty years earlier, she underwent a craniotomy for resection of a meningioma. After the operation, she became blind and developed paralysis of her right arm. Since then, she had been confined to bed for most of the time. There was no history of bowel disturbance or medication.

On examination, the patient was weak and tremulous. Her blood pressure was 120/70 mmHg and her pulse rate was regular at 120/min. There was moderate diffuse enlargement of the thyroid gland. She had optic atrophy, a paralyzed arm of upper motor neurone type, and positive Chvostek and Trousseau signs.

Serum calcium levels ranged from 5.4 to 6 mg/dl (1.3-1.4 mmol/litre), serum phosphorus ranged between 3.6 to 4.5 mg/dl (1.18-1.42 mmol/litre) and the alkaline phosphatase was 127 u./litre (primarily from bone origin). The serum albumin was 40 g/litre. Twenty-four-hour urinary calcium excretion was 10 mg. Serum thyroxine was 20 µg/dl and radioactive iodine uptake 60% after 24 hr. The serum magnesium was 1.86 mg/100 ml (normal 2.1-3.0 mg/100 ml), the 25-hydroxy-vitamin D (Endelstein *et al.*, 1974) was low at 4.0 ng/ml (normal 12-35 ng/ml) and the serum parathyroid hormone normal at 0.75 ng/ml (normal <0.8 ng/ml). The 24-hr urinary cyclic AMP was raised at 4600 mmol (normal 2000-4000 mmol). Tests for malabsorption and other endocrine tests were normal, as were other routine blood tests. Roentgenologic evaluation showed severe osteoporosis. The electrocardiogram was consistent with hypocalcaemia.

Treatment was initiated with propranolol, 120

mg/day and propylthiouracil, 600 mg/day with supplementation of calcium (Sandoz), 500 mg/day. This treatment was continued for 4 weeks during which her condition improved and the Trousseau and Chvostek signs disappeared. Serum levels of thyroxine, calcium, alkaline phosphatase and the urinary calcium excretion returned to normal, and the patient was discharged.

The patient continued to take propylthiouracil and propranolol without calcium supplementations. Two months later, her serum levels of calcium, thyroxine and alkaline phosphatase were still normal. Six months later, she was found to be again thyrotoxic and hypocalcaemic and when closely questioned she reported that she had stopped the propylthiouracil 6 weeks previously. At that time, her serum calcium level was 7.6 mg/dl (1.82 mmol/litre) and serum thyroxine was 15.3 µg/dl.

Discussion

This patient suffered from symptomatic hypocalcaemia and thyrotoxicosis. Amelioration of the thyrotoxicosis induced normalization of her serum calcium, but the patient became hypocalcaemic when the thyrotoxicosis recurred. Except for the changes in her thyroid status, no other explanation could be found for the changes in her serum calcium. Her diet contained about 1000 mg calcium per day and she did not take any treatment that could influence calcium metabolism. Tests for malabsorption and endocrine or other metabolic disorders were negative. Although the patient had low levels of 25-hydroxy-vitamin D, these low levels did not change during the entire follow-up period and could not entirely explain the changes in the serum calcium levels. Thyrotoxicosis can cause low levels of vitamin D (Kaptein *et al.*, 1979; Valentzas *et al.*, 1977) and this low level can last for several months after correction of the endocrine abnormality. However, in contrast to our patient, no thyrotoxic patient with hypovitaminosis D has been reported to suffer from hypocalcaemia.

Hypoparathyroidism can be excluded as a cause for hypocalcaemia in this case since the patient had high 24 hr urinary excretion of cyclic AMP, very low urinary calcium excretion and a high serum level of alkaline phosphatase. Moreover, her serum parathyroid hormone level during the hypocalcaemic period was almost double that during the normocalcaemic period and decreased to baseline as her serum calcium normalized. All these findings point to the diagnosis of secondary hyperparathyroidism and rule out hypoparathyroidism.

Thyrotoxicosis can cause hypomagnesaemia (Rude and Singer, 1981). Hypomagnesaemia causes hypocalcaemia by causing secondary hypoparathyro-

idism (hypomagnesaemia decreases parathyroid hormone secretion and inhibits parathyroid hormone action on the renal tubules). However, since hypoparathyroidism can be excluded as the cause for the patient's hypocalcaemia, we do not believe that the mild hypomagnesaemia can be the explanation for the hypocalcaemia.

The negative correlation between the patient's serum thyroxine and calcium, without any other explanation for the changes in the serum calcium, points to thyrotoxicosis as the main cause of the hypocalcaemia (Fig. 1).

FIG. 1. The negative correlation between the serum thyroxine (T4) and calcium (Ca) levels in the patient. Normal serum level of thyroxine: 4.7–11.4 µg/dl; normal serum level of calcium: 9.0–11.0 mg/dl.

Alterations in calcium metabolism with negative calcium balance in thyrotoxic patients have been reported since the last century. The alterations of calcium metabolism during thyrotoxicosis are caused by changes in intestinal absorption, urinary excretion of calcium and by increased bone resorption. Thyrotoxicosis causes decreased intestinal calcium absorption, a decrease which reverses to normal with correction of the endocrine abnormality (Singhelakis, Alevizaki and Ikkos, 1974). The mechanism responsible for the decreased calcium absorption is not known. Rapid transition time of food in the intestine with malabsorption and diarrhoea were found in a small number only of thyrotoxic patients with low intestinal calcium absorption. Thyrotoxicosis can cause hypovitaminosis D, but it is suggested that this cannot be the entire explanation and thyrotoxic patients must have some other factor that decreases their calcium absorption in the distal part of the small intestine (Haldimann *et al.*, 1980).

Hyperthyroidism increases urinary calcium excretion (Aub *et al.*, 1929). This, together with the low

calcium absorption, tends to lower the serum levels. On the other hand, thyrotoxicosis, by direct and indirect effects, increases bone resorption and shifts calcium from the bone stores to the serum (Mundy *et al.*, 1976). This process is the main mechanism which counterbalances the hypocalcaemic effect caused by the effect of thyrotoxicosis on intestinal and urinary calcium metabolism. Most thyrotoxic patients are normocalcaemic and a few of them even show mild hypercalcaemia (Farnsworth and Dobyns, 1974) which is asymptomatic.

The patient described in this report was severely osteoporotic. It is possible that, because of the osteoporosis, the patient could not mobilise enough calcium from her decreased bone stores to counteract the effects of reduced intestinal calcium absorption and low serum vitamin D levels, caused by her thyrotoxicosis. It is also possible that other factors linked with hyperthyroidism contributed to this patient's hypocalcaemia. Correction of all these factors by normalizing the thyroid function increased the patient's serum calcium.

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(Accepted 4 November 1982)