Case Report

Thyroid Crisis Associated with Severe Hypocalcemia

Yasuyoshi YAMAJI**, Matsuhiko HAYASHI**, Yutaka SUZUKI,

Kumiko NOYA and Osami YAMAMOTO*

A 30-year-old woman with thyroid crisis and impaired renal function presented with severe hypocalcemia. She had already had hypocalcemia one yr previously when her serum creatinine level was normal. A normal level of serum amino terminal fragment of parathyroid hormone in spite of severe hypocalcemia suggested impairment of parathyroid function. Since her serum magnesium was normal and she had no history of neck surgery or radioiodine therapy, her hypoparathyroidism was considered to be idiopathic. This is the seventh case with co-existing Graves' disease and idiopathic hypoparathyroidism reported in the literature.

Key words: Graves' disease, Idiopathic hypoparathyroidism

Patients with hyperthyroidism frequently have hypercalcemia as well. Accelerated bone resorption is considered to be responsible for this hypercalcemia (1). On the other hand, hypocalcemia is an extremely rare association of uncomplicated hyperthyroidism. To our knowledge, only seven such cases have been reported (2–8). We report an additional case of hyperthyroidism with severe hypocalcemia. Idiopathic hypoparathyroidism is thought to be the underlying cause.

CASE REPORT

On June 13, 1987, a 30-year-old Japanese woman was admitted to our hospital for loss of consciousness. She had been diagnosed as hyperthyroid in 1982 but had not received any treatment. She had diarrhea and nausea for the past two wk. She was unable to eat for two days.

On examination, she was stuporous. She was thin but had no stature abnormalities, such as Albright's osteodystrophy. Her skin was dry. No rash was present. Body temperature was 38.5°C, blood pressure, 98/54 mmHg, and pulse was irregular at 200/min. Exophthalmos and diffuse goiter were

present. There was no lymphadenopathy. Chest and abdominal examinations were normal, except for the tachycardia. There was no edema. Neurological examination was positive for Trousseau's sign and Chvostek's sign.

Laboratory studies on admission showed normal urinalysis. White cells were 11,400/mm³, red cells 458 × 10⁴/mm³, and platelets 20 × 10⁴/mm³. Blood urea nitrogen was 88 mg/dl, serum creatinine 2.9 mg/dl, urate 17.4 mg/dl, sodium 140 mEq/l, potassium 4.4 mEq/l, chloride 112 mEq/l, calcium 3.9 mg/dl, phosphorus 11.1 mg/dl, magnesium 1.8 mg/dl, total protein 7.5 g/dl, albumin 3.5 g/dl, total bilirubin 0.5 mg/dl, glucose 91 mg/dl, aspartate aminotransferase 71 IU/l, alanine aminotransferase 51 IU/l, amylase 191 IU/l, alkaline phosphatase 765 IU/l (N: 81 IU/l – 224 IU/l), and lactate dehydrogenase 714 IU/l (N: 210 IU/l – 382 IU/l). Arterial blood gases while administering 4 l/min of nasal oxygen were PaO₂ 176 mmHg, PaCO₂ 21 mmHg, pH 7.22, bicarbonate 8.8 mEq/l, and base excess –16.9 mEq/l. Electrocardiogram (ECG) demonstrated atrial fibrillation with rapid ventricular response. Chest X-ray was normal. Renal ultrasound

From Department of Internal Medicine and *Department of Surgery, Social Insurance Saitama Chuo Hospital, Urawa

**Present address: Department of Internal Medicine, Keio University School of Medicine, Tokyo

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Reprint requests should be addressed to Yasuyoshi Yamaji, MD, Department of Internal Medicine, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160, Japan

was normal. Serum thyroxine (T₄), free T₄, triiodothyronine (T₃), and free T₃ exceeded 30 µg/dl, 8.0 ng/dl, 8 ng/ml, and 15 pg/ml, respectively. Serum thyroid stimulating hormone was under 0.1 U/ml. Antithyroglobulin antibody was $\times 6,400$ ($N < \times 100$), antimicrosomal antibody $\times 409,600$ ($N < \times 100$), and anti-TSH-receptor antibody 82.1% ($N < 15\%$). She also had exophthalmos and diffuse goiter as described previously, thus her thyrotoxicosis was considered to be due to Graves' disease.

On the second hospital day, when serum calcium was 3.6 mg/dl and serum creatinine was 4.2 mg/dl, serum immunoreactive parathyroid hormones (PTH) were determined (Special Reference Laboratory, Tokyo). Amino terminal fragment of PTH (N-PTH) was measured using a ¹²⁵I-radioimmunoassay system using human 1-34PTH. This assay system provides a detection limit of 0.015 ng/ml N-PTH per ml of serum and the normal range is under 0.12 ng/ml (9). Her serum N-PTH was not elevated (0.053 ng/ml) in spite of the severe hypocalcemia. Carboxy terminal fragment of PTH (C-PTH), determined using ¹²⁵I-radioimmunoassay kit for human C-PTH (EIKEN, Tokyo, Japan), was 2.4 ng/ml ($N < 0.5$ ng/ml).

Records were obtained from another hospital where she was admitted in June 1986 after a car accident. Although her serum creatinine and albumin were normal (0.8 mg/dl and 3.9 g/dl, respectively), her serum calcium was already depressed at 6.6 mg/dl.

She had untreated Graves' disease and an impairment of consciousness, with diarrhea, fever, and tachycardia. Thus, we treated her as thyroid crisis. Her impaired renal function was thought to be induced by renal hypoperfusion in this episode. Methimazole 120 mg p.o., Lugol's solution 10 drops p.o., hydrocortisone 500 mg i.v., and propranolol 2 mg i.v. were started. Intravenous fluid replacement was started.

Twelve h after admission, consciousness improved. Body temperature went down to 37°C. ECG showed a normal sinus rhythm of 100/min. Urine volume was 2,000 ml/24 h.

On the third hospital day, she developed respiratory failure. Her chest X-ray revealed left lung atelectasis. Tracheal intubation was performed and

mechanical ventilation was started. Her arterial PaO₂ remained above 60 mmHg for the subsequent 6 h. However, her systolic blood pressure dropped to 40 mmHg 7 h after intubation. She died soon after.

DISCUSSION

A case of thyroid crisis with hypocalcemia was reported. Hypocalcemia is an exceedingly rare complication of hyperthyroidism. Seven cases of Graves' disease with hypocalcemia have been reported in the literature (2–8). None of these patients had a history of neck surgery or radioiodine therapy. In six cases, idiopathic hypoparathyroidism was considered to be the cause of hypocalcemia (2–7). The cause was unknown in the remaining one patient (8). The etiology of hypocalcemia in the present case is also uncertain. Some speculation, however, is possible. Hypocalcemia was already present in June 1986. Her serum creatinine was normal at that time. It is most likely that hypocalcemia persisted until the fatal thyroid crisis. Impaired renal function, noted at the time of admission to our hospital, might have worsened her hypocalcemia. It is unlikely that renal failure alone was responsible. Furthermore, in spite of severe hypocalcemia, her serum N-PTH concentration was within the normal range. By most assay methods, even low-normal levels of PTH are diagnostically significant for hypoparathyroidism in the presence of hypocalcemia (10). It is also known that patients with pseudohypoparathyroidism have elevated levels of N-PTH (11, 12). These reports support our view that our patient had an inappropriately low level of N-PTH consistent with hypoparathyroidism. The increased level of C-PTH is most likely due to impaired function of the kidney, where C-PTH is metabolized (13). Her hypoparathyroidism is considered to be idiopathic since she had no history of neck surgery or radioiodine therapy, and her serum magnesium was normal. However, the Ellisworth-Howard test, which would have confirmed the diagnosis, was not performed.

The association of Graves' disease with idiopathic hypoparathyroidism may have been coincidental. However, it is interesting to note that Graves' disease and possibly idiopathic hypoparathyroidism have an autoimmune basis (14). In six case reports of Graves' disease with hypoparathyroidism, this possibility of

autoimmunity to both glands was suggested. Autoimmunity to the parathyroid gland, however, was not confirmed in the reports (2–7). The present case had autoantibodies against the thyroidal antigens, however, there was no evidence of autoimmunity to the parathyroid glands.

Hypoparathyroidism is known to accompany other autoimmune diseases such as Addison's disease (15), Hashimoto's disease (16), and pernicious anemia (17). Some endocrinopathies as well as nonendocrine disease induced by autoimmunity are noted to occur in the same individual. The term polyglandular autoimmune syndrome (PGA) has been applied to these disease groups. Currently, the classification of PGA proposed by Neufeld et al (18) is generally accepted (19). In this classification, type I PGA is present in patients who have at least two of the following: Addison's disease, hypoparathyroidism, chronic mucocutaneous candidiasis. Associated immune disorders may be present. Type II PGA is present in patients who have Addison's disease with autoimmune disease and/or insulin-dependent diabetes mellitus, but who do not have hypoparathyroidism or candidiasis. Coexistence of Graves' disease and idiopathic hypoparathyroidism may be related to PGA. Further studies, however, are most certainly required.

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