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Case Report *Olgu Sunumu*

HYPERCALCEMIA DUE TO PRIMARY HYPERPARATHYROIDISM IN A PATIENT WITH GRAVES' DISEASE

Bir Graves Hastasında Primer Hiperparatiroidiye Bağlı Hiperkalsemi

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ABSTRACT

Hyperthyroidism is a hypermetabolic condition associated with excessive production of thyroid hormones by the thyroid gland. Thyroid hormones play an important role in bone and calcium metabolism. Mild to moderate hypercalcemia due to hyperthyroidism has been reported in approximately one in five patients. Hypercalcemia due to hyperthyroidism is associated with decreased or subnormal parathyroid hormone levels. The co-occurrence of hyperthyroidism and primary hyperparathyroidism is rare. However, in patients with hyperthyroidism, it is necessary to evaluate the parathyroid glands if hypercalcemia persists after an euthyroid state is reached.

Here, we report the case of a 30-year-old man with hypercalcemia who had Graves' disease and primary hyperparathyroidism and was successfully treated with combined thyroid and parathyroid surgery.

Keywords: *Hyperthyroidism, hyperparathyroidism, hypercalcemia, Graves' disease*

ÖZ

Hipertiroidizm, tiroid bezi tarafından aşırı tiroid hormonu üretimi ile olan ilişkili hipermetabolik bir durumdur. Tiroid hormonlarının kemik ve kalsiyum metabolizması üzerine önemli etkileri vardır. Yaklaşık beş hastadan birinde hipertiroidiye bağlı hafif ila orta derecede hiperkalsemi bildirilmiştir. Hipertiroidiye sekonder hiperkalsemiye azalmış ya da subnormal parathormon seviyeleri eşlik eder. Hipertiroidizm ile hiperparatiroidizm birlikteliği nadir olarak görülmektedir. Bununla birlikte, hipertiroidi hastalarında ötiroid duruma ulaştıktan sonra hiperkalseminin devam etmesi durumunda paratiroid bezlerinin ayrıntılı olarak değerlendirilmesi gerekir.

Burada, hiperkalsemisi olan, Graves hastalığı ve primer hiperparatiroidizm tanısı alan, kombine tiroid ve paratiroid cerrahisi ile başarılı bir şekilde tedavi edilen 30 yaşında bir erkek hasta olgusunu sunuyoruz.

Anahtar Kelimeler: *Hipertiroidizm, hiperparatiroidizm, hiperkalsemi, Graves hastalığı*

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INTRODUCTION

Thyroid hormones have effects on the regulation of bone metabolism. Mild to moderate hypercalcemia due to hyperthyroidism has been reported in approximately one in five patients (1). Although patients are usually asymptomatic, hypercalcemic crisis has been reported in the literature (1,2). The pathophysiology of hypercalcemia due to thyrotoxicosis is not fully understood. Increased calcium (Ca) mobilization from bone due to high bone turnover and a shortened bone remodeling cycle, as well as increased sensitivity of bone to parathyroid hormone (PTH) and increased catecholamine metabolism, have been demonstrated in hyperthyroidism (3-5). Hypercalcemia due to hyperthyroidism is associated with decreased or subnormal PTH levels (6). Thyroid disorders, such as thyroiditis, thyroid nodules, and thyroid carcinoma may coexist with parathyroid disorders (7-9). However the co-occurrence of hyperthyroidism and primary hyperparathyroidism (PHPT) is rare. Here, we report the case of a 30-year-old man who had Graves' disease (GD) and PHPT.

CASE REPORTS

The 30-year-old male patient was admitted to our hospital with palpitations, heat intolerance, weight loss, fatigue, tremor, and sweating. He had a blood pressure of 130/90 mmHg, a heart rate of 102 beats/minute, and a temperature of 36.6 °C. He had warm and moist skin. Blood test revealed thyroid stimulating hormone (TSH) <0.03 µU/L (0.27-4.2), free triiodothyronine (fT3): 14.34 pg/ml (2-4.4), and free thyroxine (fT4): 3.91 pg/ml (1-1.7), anti-thyroid peroxidase (anti-TPO): 229 IU/ml (0-34) and TSH receptor autoantibodies (TRAbs): 0.73 U/L (0-1.75). Serum total Ca corrected for albumin was 11.05 mg/dl, and inorganic phosphorus (P) was 3.61 mg/dl. His PTH level was slightly elevated at 85.9 pg/ml, and the 25-hydroxyvitamin D level was 31.8 ng/ml. The reference ranges in our hospital were 8.8-10.4 mg/dl for Ca, 2.5-4.5 mg/dl for P, 12-80 ng/l for PTH. Urine collected for 24 hours showed Ca excretion of 428 mg/day. The other laboratory parameters were within the normal range. Doppler ultrasonography revealed an enlarged thyroid gland with an inhomogeneous pattern and increased blood flow. Scintigraphy demonstrated enlarged thyroid gland. Because of the increased stimulation and function of the gland, activity was increased throughout the gland compared with background (Figure 1).

Figure 1: Technetium-99m (Tc-99m) pertechnetate thyroid scintigraphy (thyroid scan). Tc-99m shows an enlarged thyroid gland.

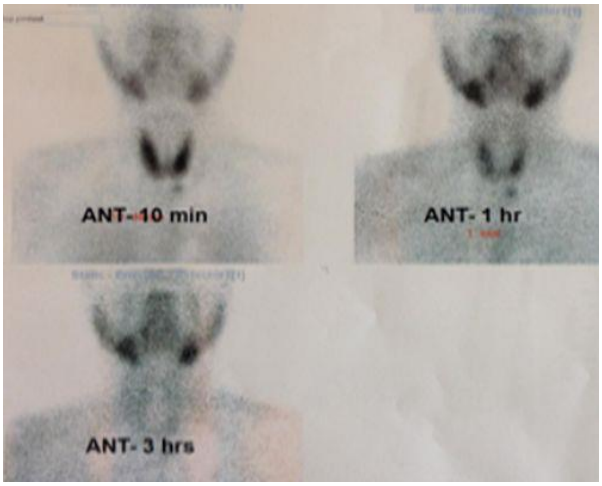

Figure 2: A lesion of the left lower parathyroid gland detected by 99mTc sestamibi scintigraphy.

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Members of her family did not have thyroid disease. Although TRAbs was negative, Graves' disease was diagnosed based on clinical, ultrasonographic, and scintigraphic findings, as well as anti-TPO positivity, lack of family history, and age at diagnosis. In our hospital, TRAbs measurement included any TSH receptor antibody measurement (blockers or stimulants). Therefore, the patient was classified as antibody-negative Graves' disease, although this is rare. The patient was treated with propylthiouracil 300 mg/day and propranolol 20 mg twice daily. The treatment successfully controlled palpitations, tremors, and sweating. His thyroid function normalized two months later. When he became euthyroid, serum Ca level decreased to 10.8 mg/dl and PTH increased to levels suggestive of hyperparathyroidism (108 pg/ml). Scintigraphy of the parathyroid glands was performed and revealed a parathyroid adenoma (Figure 2). Subtotal thyroidectomy and parathyroidectomy were performed. Follow-up examinations showed normalization of serum Ca and PTH.

DISCUSSION

The coexistence of hyperthyroidism and PHPT is rare (10-15). Arem et al. reported two patients with GD and PHPT (10). When the patients became euthyroid, their Ca levels decreased slightly and PTH levels increased. The patients were successfully treated by parathyroidectomy and subtotal thyroidectomy. Shuanzeng Wei et al. reported 21 patients with a history of GD, who developed parathyroid adenoma. The diagnosis was based on histology, intraoperative PTH monitoring, and other clinical features (11). In 11 patients, there was a history of radioactive iodine therapy GD. The authors emphasized that there may be an association between GD patients with a history of RAI and an increased risk of parathyroid adenoma. In the study by Abboud B et al, the prevalence of concurrent hyperparathyroidism in patients admitted for elective hyperthyroid surgery was 13.5% (12). Thirteen of 96 patients had hyperparathyroidism. None of the patients had clinical manifestations of hypercalcemia. Of these 13 patients, 11 had parathyroid adenoma and two had parathyroid hyperplasia. In this retrospective study, the authors suggested that this coexistence is not so rare and that the parathyroid glands should be examined before surgery in asymptomatic hypercalcemic patients with hyperthyroidism, especially in the elderly. Another case report reported hypercalcemia with a normal PTH level of 37 pg/mL (range, 15-65) in a patient with hyperthyroidism. After the patient was treated with methimazole and radioiodine and became euthyroid, serum Ca levels remained high and PTH increased to abnormal levels suggestive of hyperparathyroidism (13). Thalhammer M et al. reported a case of a 53-year-old woman with GD and hypercalcemia (14). The PTH level was within the normal range. A parathyroid adenoma was diagnosed by ultrasound-guided fine-needle aspiration biopsy. Under treatment with carbimazole, the patient became euthyroid, a decrease in serum Ca level was observed, but the PTH level remained within the normal range. Parathyroidectomy with almost total thyroidectomy was performed. In our case, PTH increased when the patient became euthyroid. Thyroid hormone could enhance the osteoclastic effect of PTH and exacerbate hypercalcemia, which then leads to relative suppression of PTH secretion by the abnormal parathyroid tissue (10). However, the initial normal PTH level is suggestive of PHPT, because the PTH level would likely be suppressed if the hypercalcemia were caused by hyperthyroidism alone (13). In our case, scintigraphy of the parathyroid glands revealed an adenoma. If parathyroid scintigraphy is normal, parathyroid adenomas can be localized preoperatively by ultrasound-guided fine-needle aspiration biopsy and immunochemical examination (14). The best treatment is combined resection of the thyroid and parathyroid

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glands in a single procedure when surgery is required (15).

In conclusion, hypercalcemia may occur in hyperthyroidism and may mask concomitant PHPT. Thus, if hypercalcemia persists after treatment of hyperthyroidism with high or unsuppressed PTH levels, this should indicate PHPT. To avoid repeated surgery and complications, it is necessary to evaluate parathyroid disease in hypercalcemic patients with GD.

Conflict of Interest: All authors declare that there is no conflict of interest

Researchers' Contribution Rate Statement: All authors made substantial contributions to the article. İdea-planning: IKS, ŞA; analysis-interpretation: IKS, RC; data acquisition: IKS, RC; manuscript preparation IKS, RC, ŞA and final manuscript approval IKS, ŞA.

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