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A case of hypercalcaemic crisis secondary to coexistence of primary hyperparathyroidism and Graves' disease

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A 46 year-old female patient presented to the hospital with ongoing and progressively increasing fatigue, severe nausea and vomiting, loss of appetite, constipation, palpitations and somnolence. Laboratory evaluation revealed a severe hypercalcaemia and overt hyperthyroidism. She was diagnosed with primary hyperparathyroidism accompanied by Graves' disease. The patient underwent total thyroidectomy and right inferior parathyroid gland adenoma excision on the 24th day of her admission to the hospital after calcium levels and free thyroid hormone levels were brought to normal ranges. We suggest that a possibility of simultaneous thyrotoxicosis and primary hyperparathyroidism in cases presenting with a hypercalcaemic crisis should be considered

Key words: hypercalcaemic crisis, primary hyperparathyroidism, Graves' disease

Hypercalcaemic crisis is a rarely seen condition characterized with severely elevated calcium and changes in the mental state. A case of hypercalcaemic crisis secondary to primary hyperparathyroidism and simultaneous Graves's disease is presented herein.

Subject and Results

A 46 year-old female patient presented to the hospital with ongoing and progressively increasing fatigue, severe nausea and vomiting, loss of appetite, constipation, palpitations and somnolence. She had no known chronic disease and was not on any drugs or herbal treatment. Upon physical examination, she was conscious, oriented and fully cooperated. Her blood pressure was measured as 134/92 mmHg, her pulse was 115 beats/min and was rhythmic with a body temperature of 36.8°C. Her thyroid gland was found to be diffusely enlarged, her skin turgor was decreased and oral mucosa was observed to be dry.

Laboratory evaluation revealed a severe hypercalcaemia and overt hyperthyroidism (Table 1). Ultrasonography of the thyroid gland disclosed a diffusely enlarged thyroid gland with increased vascularity and thyroid scintigraphy with Tc-99m pertechnetate revealed a diffusely increased activity in the thyroid gland (Figure 1). Ultrasonography of the neck revealed a hyperechoic solid lesion compatible with a parathyroid adenoma measuring 18 x 8 mm inferior to the right lobe of the thyroid gland (Figure 2). Retention of the radioactive material during Tc-99m MIBI scan was observed at the posterior side of the right lobe compatible with the observed area at neck

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Table 1
Laboratory variables during follow-up.

Parameter	Normal range	At admission	Operation day (24 days after admission)	Two months after operation
Calcium (mg/dl)	8.4–10.2	16.2	9.2	8.8
Phosphorus (mg/dl)	2.3–4.7	1.2	2.1	3.0
Magnesium (mg/dl)	1.6–2.6	1.48	1.56	1.89
Albumine (g/dl)	4.1–5.0	3.8	3.2	4.0
PTH (pg/ml)	12–65	497.7	450.2	32.2
Free T_3 (pg/ml)	2.3–4.2	9.27	2.66	2.25
Free T_4 (ng/dl)	0.89–1.70	6.38	1.12	1.18
TSH (IU/ml)	0.56–5.57	<0.005	–	4.54
Anti-TPO (IU/ml)	0–34	>600	–	–
25[OH] D (mg/dl)	30–150	<5	–	21.2
AST (IU/l)	0–34	76	11	14
ALT (IU/l)	0–55	64	20	18
ALP (IU/l)	40–150	160	108	96
GGT (IU/l)	7–24	65	50	54
BUN (mg/dl)	15–40	32.4	16.2	15.4
Creatinine (mg/dl)	0.7–1.2	1.0	0.92	0.87
UEC (mg/day)	100–300	502	–	140

PTH – parathormone; Anti-TPO – anti-thyroid peroxidase antibody; AST – asparate aminotransferase; ALT – alanine aminotransferase; ALP – alkaline phosphatase; GGT – gama glutamyl transferase; BUN – blood urea nitrogen; UEC – urinary excretion of calcium

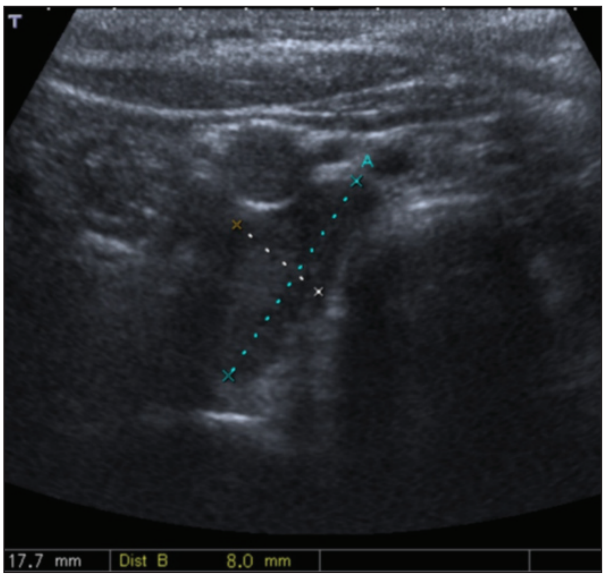

Figure 1. Hyperechoic solid lesion compatible with a parathyroid adenoma measuring 18 x 8 mm inferior to the right lobe of the thyroid gland.

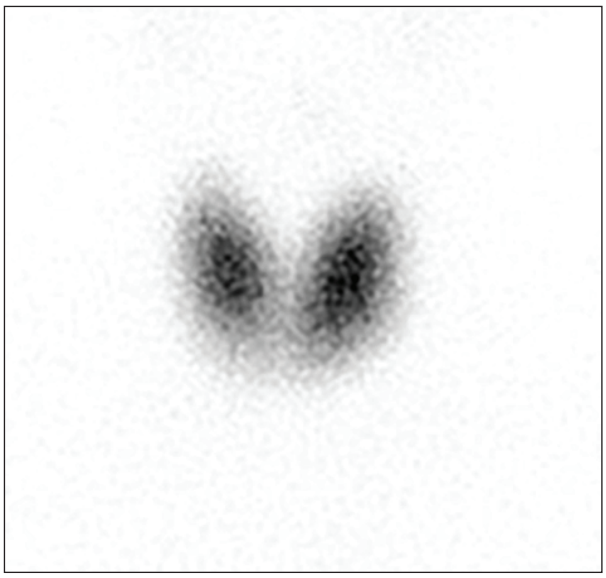

Figure 2. Planar thyroid scintigraphy with Tc-99m pertechnetate showed diffusely uptake of radiopharmaceutical in thyroid gland.

ultrasonography (Figure 3). Other anterior pituitary hormones, which were measured to exclude multiple endocrine neoplasia syndrome, fasting plasma insulin and gastrin levels and levels of 24-hour catecholamine degradation products, were in normal ranges. Computed tomography imaging of the abdomen revealed that pancreatic and adrenal glands were seen to be in normal. Magnetic resonance imaging of the pituitary disclosed no pathology.

Calcium levels and free thyroid hormone levels were brought to normal ranges following medical treatment (isotonic saline, intravenous furosemide, subcutaneous calcitonin, and intravenous zoledronic acid and methimazole tablet) that was started with the diagnoses of Graves' and primary hyperparathyroidism (Table 1). The patient underwent total thyroidectomy and right inferior parathyroid gland adenoma excision on the 24th day of her admission to the hospital. Parathormone (PTH) level was seen to drop down from 450 mg/dl to 15 mg/dl using intraoperative rapid parathormone test. Histopathological examination revealed findings compatible with a parathyroid adenoma and Graves' disease with no signs of malignancy of the parathyroid or thyroid glands. Treatment with calcitriol was started postoperatively, since the calcium level of the patient was slightly low and the patient was discharged on the 30th day of her admission to the hospital. The calcitriol treatment was ceased two months after her discharge from the hospital when she came for a follow-up visit (Table 1).

Discussion

Elevation of the thyroid hormones is considered to cause hypercalcaemia through an increase in osteoclastic bone resorption, although the full mechanism is unknown (Pantazi and Papapetrou 2000). However, hypercalcaemia secondary to the effect of increased thyroid hormones alone is seen in 15–20% of the cases with hyperthyroidism. In addition, the hypercalcaemia, seen in those cases, is generally asymptomatic and moderate not exceeding the level of 12 mg/dl (Baxter and Bondy 1996). The PTH level in hypercalcaemia due to thyrotoxicosis is suppressed or is in a low/normal range secondary to a negative feedback effect. In addition, thyrotoxicosis causes hyperphosphatemia by increasing tubular reabsorption of phosphate independent from the PTH levels. The most common cause of hypercalcaemia in patients with thyrotoxicosis is the presence of a simultaneous primary hyperparathyroidism and can be diagnosed easily by measurement of PTH level (Korytnaya et al. 2011). Hypercalcaemic crisis is a rare complication of primary hyperparathyroidism. Only 1.6–6% of the patients with primary hyperparathyroidism present with hypercalcaemic crisis and the hypercalcaemic crisis is produced generally secondary to other intervening co-morbidities such as pancreatitis, hyperemesis gravidarum and thyrotoxicosis (Yokomoto et al. 2015). Association of primary hyperparathyroidism and thyrotoxicosis may facilitate development of hypercalcaemia and this may result in the picture of hypercalcaemic crisis.

Association of primary hyperparathyroidism and thyrotoxicosis has been reported at a higher rate compared to the priorly recognized percentage in recent publications. Abboud et al. (2006), in their study including 96 patients planned to be operated on for hyperparathyroidism, reported simultaneous thyrotoxicosis in 13 patients (13.5%). On the other hand, Wagner et al. (1999), in their retrospective study including 13 387 patients, reported that primary hyperparathyroidism was present in patients who had a

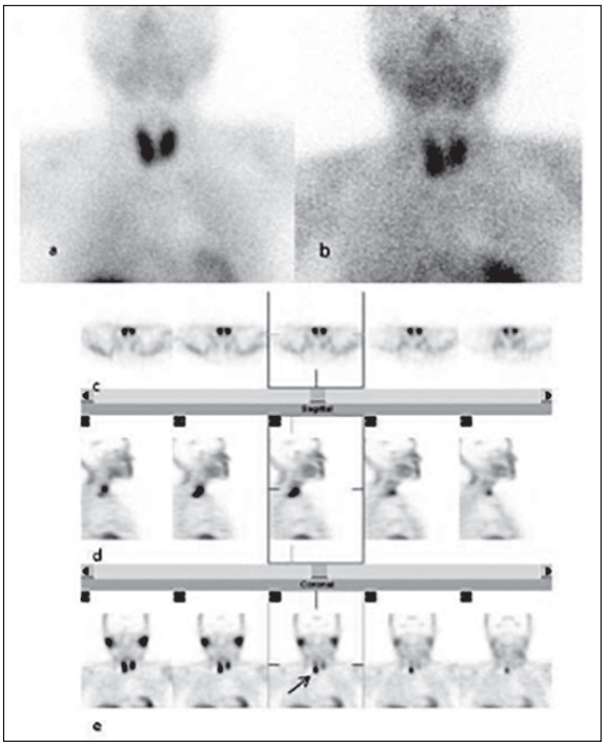

Figure 3. Tc-99m MIBI uptake in right and left thyroid lobes was depicted on early (a) and late (b) planar views of dual phase Tc-99m MIBI parathyroid scintigraphy. Transaxial (c), sagittal (d) and coronal (e) slices of SPECT study revealed a focus of increased activity in lower pole of right thyroid lobe (arrow, e) which was later confirmed as a parathyroid adenoma.

thyroid disease (0.29%) more frequently, compared to the ones without any thyroid disease (0.09%).

Development of a transient hyperthyroidism during parathyroid surgery has been reported in some publications. In the study by Lindblom et al. (1999), including 26 patients who had normal preoperative thyroid functions, a transient hyperthyroxinemia was detected in 12 patients in the early postoperative period and this was ameliorated in the 6th postoperative week. In that study, nine of the 12 patients with development of hyperthyroidism were symptomatic. In another study by Stang et al. (2005), in which 125 patients who had undergone parathyroid surgery were retrospectively analyzed, a newly developed hyperthyroidism was detected in 39 patients in the postoperative period. Among the patients, 12 were symptomatic; anti-thyroid treatment was used in five patients with development of overt hyperthyroidism and one patient needed to receive long-term anti-thyroid treatment. Essential mechanism in the hyperthyroidism developing following parathyroid surgery seems to be the manipulation of the thyroid gland during surgery. As seen in the studies stated above, parathyroid surgery is associated with a postoperative transient hyperthyroxinemia even in patients with normal thyroid functions. In this case, it can be proposed that the chances of development of a life-threatening complication, thyrotoxic crisis may be increased in a patient with untreated hyperthyroidism. Therefore, it is obvious that providing a euthyroid state preoperatively is critical for a safe surgical treatment. Besides, in a case of an hypercalcaemic crisis reported recently by Yokomoto et al. (2015), primary hyperparathyroidism and thyrotixicosis was simultaneously present and an operation performed following obtaining an euthyroid and normocalcaemic state resulted in success. In the case presented in this paper, the patient was sent for surgery after a euthyroid, normocalcaemic state was provided and successfully treated, and similar to the previously above-stated case.

In conclusion, we suggest that a possibility of a simultaneous thyrotoxicosis and primary hyperparathyroidism in cases presenting with a hypercalcaemic crisis should be considered. In addition, it is important to provide a euthyroid and normocalcemic preoperative state in order to achieve safety and success upon surgical treatment.

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