A Case of Papillary Carcinoma of the Thyroid Associated with Parathyroid Adenoma without Hyperparathyroidism

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A rare occurrence of the association of parathyroid adenoma in a case of thyroid papillary carcinoma is described. The patient was incidentally found to have parathyroid adenoma which was preoperatively diagnosed to be a metastatic lymph node. Analysis of her serum obtained before operation showed an elevation of serum parathyroid hormone (PTH) concentration without hypercalcemia. Since the association of hyperparathyroidism is high in patients with thyroid diseases, examination of not only serum levels of calcium and PTH but also careful interpretation of computed tomography (CT) and/or nuclear magnetic imaging (MRI) is necessary in the diagnosis of co-existing asymptomatic hyperparathyroidism.

(Key words: serum PTH, normal serum calcium, computed tomography (CT), nuclear magnetic imaging (MRI))

Introduction

It has been reported that thyroid disease is common in patients with hyperparathyroidism, and vice versa (1). Parathyroid adenoma is clinically recognized in patients presenting with either hypercalcemia or it may be a part of multiple endocrine neoplasia (MEN) type I and type IIa (2). There have also been sporadic reports of the coexistence of hyperparathyroidism and nonmedullary thyroid carcinoma (3–8). Thus, the presence of hyperparathyroidism has to be kept in mind in patients with thyroid carcinoma. In such cases, hypercalcemia is a virtually inevitable laboratory finding and therefore, is an important laboratory finding in the diagnosis of hyperparathyroidism. Except for such conditions, it is very rare to find parathyroid adenoma.

We have recently encountered a case of nonmedullary thyroid carcinoma (papillary carcinoma) associated with parathyroid adenoma which was initially diagnosed to be a metastatic lymph node of thyroid malignancy. She had neither radiologic abnormalities such as subperiosteal bone resorption nor symptoms associated with hyperparathyroidism. Since the elevated concentration of PTH normalized after operation, we speculate that the patient had asymptomatic hyperparathyroidism, namely parathyroid adenoma with the preclinical stage of hyperparathyroidism.

Materials and Methods

Serum concentrations of free T\textsubscript{3} (FT\textsubscript{3}) and free T\textsubscript{4} (FT\textsubscript{4}) were measured by analog method radioimmunoassay (RIA) kits (Amerlex FT\textsubscript{3} and FT\textsubscript{4}, Amersham International, Tokyo, normal range of FT\textsubscript{3} and FT\textsubscript{4} are 2.3–5.7 pg/ml and 0.80–2.10 ng/dl, respectively. Serum TSH levels were measured by an immunoradiometric assay (IRMA) kit (Spac TSH, Daiichi Isotope Lab, Tokyo, with normal range of 0.1–5.0 U/ml). Titers of anti-thyroglobulin (Tg) and anti-microsomal antibodies were measured by hemagglutination kits (Serodia-ATG, Serodia-AMC, Fujirebio Inc., Tokyo). Titers of serum anti-TSH receptor antibodies (TRAb) were measured using a commercially available radioreceptor assay kit (Baxter, Tokyo, normal range less than 10%). Serum calcitonin was measured by a double antibody RIA kit (Calcitonin kit Daiichi, Daiichi Isotope Lab, Tokyo, normal range, less than 100 pg/ml) and an IRMA kit ELSA-hCT, CSI diagnostic, Osaka, normal range, less...
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Serum concentration of parathyroid hormone (PTH), glucagon and gastrin were measured by RIA kits (PTH; Yamasa Syoyu, Tokyo, normal range 130–490 pg/ml, glucagon; Daiichi isotope Lab, Tokyo, normal range, 10.1–145.3 pg/ml, gastrin; Dainabott, Tokyo, normal range, 40–120 pg/ml). Urinary catecholamine, vanillylmandelic acid (VMA) and homovanillic acid (HVA) were measured by high performance liquid chromatography (HPLC, normal range for urinary noradrenaline, adrenaline, dopamine, VMA, and HVA were 10–90 μg/day, less than 12 μg/day, 100–700 μg/day, 2.6–9.2 mg/day, and 1.5–6.6 mg/day, respectively).

Case Report

A 46-year-old woman consulted our hospital with the chief complaint of an enlarged thyroid gland. Her past history was unremarkable except for hypertension of three years which had been treated with anti-hypertensive drugs. There was no history of neck irradiation. She denied past history of urolithiasis, peptic ulcer and pancreatitis. Family history disclosed that her mother and father had brain tumor and gastric cancer, respectively.

On physical examination, her height was 154 cm, weight 58.5 kg, blood pressure 166/90 mmHg and pulse 96/min and regular. She had a rubbery hard, smooth surfaced nodule (20 × 20 mm) on her right thyroid gland which was solid by CT and MRI imagings. Superficial lymph nodes were not palpable. Chest, heart and abdomen were unremarkable. Patellar and Achilles' jerks were normal. There was no edema in her legs.

Routine laboratory tests including serum albumin (4.1 g/dl) were unremarkable. Serum calcium and phosphorus concentrations were normal, being 4.6 mEq/l and 3.0 mg/dl, respectively. Urinalysis was normal. On thyroid function test, she had normal serum free thyroid hormones (FT3; 3.4 pg/ml, FT4; 0.94 ng/dl, with high normal basal TSH level (4.7 μU/ml). Anti-Tg and antimicrosomal antibodies were negative. Serum concentration of calcitonin measured by a double antibody RIA was high, being 240 pg/ml. However, measurement of the same sample with IRMA was normal, being

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Fig. 1. A) 99mTc-Tc-Technetium image showing the cold nodule in the right thyroid gland and lower pole of the right lobe. Arrows ① and ② indicate thyroid papillary carcinoma and parathyroid adenoma, respectively.

B) 201-Thallium image showing the hot thyroid nodule in the right thyroid gland. Arrow ① indicates papillary carcinoma of the thyroid.

Fig. 2. CT scan showing the localization of papillary carcinoma (arrow ①) and parathyroid adenoma (arrow ②).
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7.1 pg/ml. Discrepancy of serum calcitonin values obtained by double antibody RIA and IRMA is difficult to interpret at present. 99mTc Technetium scintigraphy revealed a cold area in the right lobe of the thyroid (Fig. 1A) and 201Tl Thallium scintigraphy showed an accumulation of radioactivity in the same area (Fig. 1B). Computed tomography (CT) and nuclear magnetic imaging (MRI) of the thyroid gland disclosed a solid tumor in the right lobe and an enlarged lymph node in its lower pole (Figs. 2 and 3).

Since aspiration biopsy and cytology (ABC) of the thyroid gland appeared suspicious of malignancy (class III) and the possible presence of metastatic lymph node was found based on CT and MRI findings, she underwent subtotal thyroidectomy in November 1988. During the operation several small tumors which were found in the lower pole of right thyroid lobe were removed. Histopathologic examination of removed specimen showed lymph nodes with metastatic lesion of thyroid papillary carcinoma. However, the histopathology of the biggest node revealed it to be a parathyroid adenoma. Since such a diagnosis was made, PTH concentration of serum which had been obtained before operation and kept frozen was measured retrospectively. It was shown that serum PTH was elevated (590 pg/ml). The level was normalized at two weeks and of 9 months after operation, being 320 pg/ml, and 330 pg/ml, respectively. Since two measurements of serum PTH concentration using the same serum obtained prior to operation resulted in the same level, the diagnosis of hyperparathyroidism was confirmed. Immediate postoperative concentrations of serum albumin, calcium and phosphate were 4.1 g/dl, 4.4 mEq/l and 3.0 mg/dl, respectively, which were within the normal range. Serum calcium ion concentration two weeks after operation was 2.48 mEq/l which was also within the normal range (normal range, 2.24–2.58 mEq/l). From these results it was concluded that the tumor in the lower pole of the right lobe of the thyroid gland as shown by CT and MRI was in fact a parathyroid adenoma. Since she had a past history of hypertension, the possibility of the presence of other endocrine abnormalities were examined postoperatively. It was shown that serum concentrations of glucagon and gastrin were normal, being 64 pg/ml and 120 pg/ml, respectively. Urinary noradrenaline, adrenaline, dopamine, VMA, and HVA were 76.7 μg/day, 7.2 μg/day, 422 μg/day, 5.9 mg/day, and 2.9 mg/day, respectively, which were also within the normal range. Thus, the presence of other endocrine adenomas such as multiple endocrine neoplasia (MEN) type I and IIa was ruled out.

Discussion

The present patient underwent subtotal thyroidectomy for possible thyroid malignancy. During the operation several small tumors were found in the lower pole of the right lobe of the thyroid gland which were preoperatively thought to be metastatic lymph nodes. Pathological examination however, disclosed that the biggest node removed was parathyroid adenoma. Thus, together with the elevated concentration of PTH, a diagnosis of thyroid papillary carcinoma associated with parathyroid adenoma was made.

It has been reported that the apparent frequency of thyroid diseases in patients with hyperparathyroidism is high. The genetic association of hyperparathyroidism and medullary thyroid carcinoma has been well recognized in the context of the multiple endocrine neoplasia, type II (2). There have also been reports concerning the coexistence of hyperparathyroidism and nonmedullary
thyroid cancer (3–8). A unique clinical feature of the patient is that despite an increased concentration of serum PTH before operation, she had neither clinical symptoms of hyperparathyroidism such as urolithiasis and gastric ulcer, nor laboratory data of hypercalcemia. Since it has been well known that in early or mild cases of hyperparathyroidism, serial analyses may show fluctuations of serum calcium within the normal range, her normal serum calcium concentration could have been in around the nadir of such fluctuation (2) and she might have had hypercalcemia on other occasions. Since the present patient showed an increased concentration of PTH without hypercalcemia, it was thought that the patient was in a very early asymptomatic stage of hyperparathyroidism (9).

There is a growing recognition that primary hyperparathyroidism is not a rare disease. One report stated that the annual incidence of hyperparathyroidism after introduction of routine measurement of serum calcium is 51.1 ± 9.6 cases per 100,000 (0.051%) (10). Other studies state that the prevalence among the adult population in the United States is one case among 834–1,000 adults, for a prevalence of 0.12–0.10% (11, 12). However, it is extremely difficult to make a diagnosis of asymptomatic hyperparathyroidism without measurement of the serum calcium concentration. In addition, it has been reported that hyperparathyroidism can be benign with only slight changes in bone density, function of other organs, or PTH or blood calcium levels (13). Since the association of hyperparathyroidism is high in patients with thyroid disease, it is very important not only to analyze the serum calcium levels but also to interpret carefully CT scan or MRI imagings in order to diagnose a slow progressive asymptomatic hyperparathyroidism before operation of benign and/or malignant tumor is performed.

References