The key role of ^{99m}Tc-MIBI SPECT/CT in the diagnosis of parathyroid adenoma: a case report

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SUMMARY

The concomitant occurrence of primary hyperparathyroidism (PHPT) due to parathyroid adenoma and papillary thyroid carcinoma (PTC) is not common. The co-occurrence of parathyroid tumors and thyroid diseases can lead to misdiagnosis owing to mutual interference of imaging in the early period of disease. The most commonly used imaging techniques for the preoperative localization of parathyroid and thyroid adenomas are technetium-99m sestamibi (^{99m}Tc-MIBI) scintigraphy and ultrasonography of the neck. Recently, ^{99m}Tc-MIBI single-photon emission computed tomography associated with computed tomography scintigraphy (SPECT/CT) has been used to detect PHPT, and its diagnostic value is being evaluated. Herein, we report a patient with an unusual co-occurrence of parathyroid adenoma and multiple thyroid diseases, including papillary thyroid carcinoma, thyroid adenoma and lymphocytic thyroiditis, which were localized with ^{99m}Tc-MIBI SPECT/CT and confirmed surgically. We suggest that ^{99m}Tc-MIBI SPECT/CT can play an important role in the diagnosis of parathyroid and thyroid lesions. Arch Endocrinol Metab. 2015;59(3):265-9

INTRODUCTION

Primary hyperparathyroidism (PHPT) is a common asymptomatic endocrine disorder, and single-gland adenomas account for 75%-85% of all cases (1). Similarly, papillary thyroid carcinoma (PTC) is a common malignant tumor of the thyroid that accounts for approximately 70%-75% of all diagnosed thyroid carcinomas (2). Despite the high frequencies of these conditions, the concomitant occurrence of parathyroid adenoma resulting in PHPT and PTC is uncommon (3). Based on the incidence of PHPT and PTC (1,4), the incidence of the co-existence of PHPT and PTC can be roughly estimated to be 0.0023 per 100,000 persons per year (5).

The most commonly used imaging techniques for the preoperative localization of parathyroid and thyroid adenomas are technetium-99m sestamibi (^{99m}Tc-MIBI) scintigraphy and ultrasonography of the neck (6). In recent years, ^{99m}Tc-MIBI single-photon emission computed tomography and computed tomography scintigraphy (SPECT/CT) have been used to detect parathyroid adenomas, and the diagnostic value of these techniques has been validated (7,8). Herein, we report a patient with an unusual co-occurrence of a parathyroid adenoma and multiple thyroid diseases, including papillary thyroid carcinoma, thyroid adenoma and lymphocytic thyroiditis, which were localized with hybrid ^{99m}Tc-MIBI SPECT/CT and ultrasonography and confirmed operatively.

CASE REPORT

A 64-year-old woman with a 2-month history of symptoms of fatigue, low spirits, palpitation and weight loss presented to the endocrinology clinic in September 2012. The patient was 1.62 meters tall and weighed 58 kilograms and exhibited no trembling of her hands. Physical examinations revealed an enlarged thyroid with nodules exhibiting a tenacious quality and normal activity without tenderness. Examination of the patient's medical history revealed that she had suffered from hyperthyroidism in 1972, which was resolved with methimazole and propranolol treatment after 3 years. The patient experienced a recurrence of hyperthyroidism in 1992 that was resolved with the same treatment after 8 years. The patient reported no history of head or neck radiation exposure. Laboratory examinations revealed hyperthyroidism with elevated free triiodothyronine (12.7 pmol/L; normal range: 3.1-6.8 pmol/L) and free thyroxine (32.55 pmol/L; normal range: 12.0-22.0 pmol/L) and decreased thyroid stimulating hormone (< 0.001 mIU/L; normal range: 0.27-4.2 mIU/L). The patient's thyroglobulin level was slightly elevated at 94.9 ng/mL (normal range: 1.4-78.0 ng/mL), and her calcitonin level was normal at 3.92 ng/L (normal range: < 5 ng/L). Auto-antibody detections revealed a remarkably elevated thyroid peroxidase antibody concentration of > 1000 IU/mL, a normal thyroglobulin antibody concentration of 4.44 IU/mL (normal range: 0-115 IU/mL), and a normal thyrotropin receptor antibody concentration of 0.65 IU/mL (normal range: < 1 IU/mL). Her radioactive iodine uptake levels were 23% at 2 hours, 28% at 3 hours, and 60% at 24 hours. The patient was advised to adopt a low-iodine diet without medication. Thyroid function was reexamined and had nearly recovered to normal after 2 months with a free triiodothyronine level of 4.0 pmol/L, a free thyroxine level of 14.28 pmol/L, and a thyroid stimulating hormone level of 0.01 mIU/L. Thus, the patient was initially diagnosed with hyperthyroidism due to Hashitoxicosis. Incidentally, the patient was found to have an elevated serum calcium level of 2.7 mmol/L (normal range: 2.08-2.60 mmol/L), an elevated alkaline phosphatase level of 130 U/L (normal range: 15-112 U/L), and an elevated parathyroid hormone (PTH) level of 189.9 pg/mL (normal range: 15.0-65.0 pg/mL).

Thyroid ultrasonography revealed that the thyroid gland produced an uneven echo. A 0.6 × 0.5 cm low--echo lesion with obscure boundaries and weak blood flow signal in the isthmus was found and suspected to be thyroid cancer. Several low-echo lesions and cyst--solid mixed nodules with a maximum size of 1.0 × 0.6 cm were detected in the right lobe of the thyroid. A 2.0 × 1.4 cm cyst-solid mixed-echo area with some blood flow signal was detected in the lower pole of the left thyroid gland. Additionally, several accumulated 0.6 × 0.5 cm strong-echo areas with acoustic shadows in the rear were detected in the upper pole of the left thyroid gland. No significant lymph nodes in the neck were identified via ultrasonography (Figure 1). Fine-needle aspiration cytology was not performed in this subject. The patient was suspected to have thyroid cancer. A cervical CT scan revealed multiple low-density lesions with partial calcification. Dual-phase ^{99m}Tc-MIBI parathyroid scintigraphy revealed high radiotracer uptake at the lower pole of the left thyroid lobe in early and delayed imaging. Hybrid SPECT/CT scans revealed a nodule with high radiotracer uptake that was inferior and posterior to the left thyroid lobe and suggestive of a parathyroid adenoma (Figure 2).

The patient subsequently underwent parathyroidectomy. Four parathyroid glands were found posterior to the thyroid gland. Moreover, a mass measuring 1.5 × 1.0 cm with a clear boundary and medium texture was also found posterior and inferior to the left lobe of the thyroid gland. After performing a parathyroidectomy, this mass was confirmed to be a parathyroid adenoma. During the operation, a mass with a diameter of 0.5 cm, a hard texture, and a nearly clear boundary was palpable in the isthmus. The intraoperative frozen section revealed a papillary thyroid carcinoma. Additionally, a 2.0 × 1.5 cm mass exhibiting medium texture and a clear boundary was found in the lower pole of the left thyroid lobe. Next, isthmectomy and left thyroidectomy were performed, and pathological examinations confirmed the samples to be a papillary thyroid carcinoma and thyroid adenomas, respectively. PTH was normalized (16.73 ng/mL) 15 minutes after the operation. Histopathology and immunohistochemistry results revealed a parathyroid adenoma in the left parathyroid gland that was positive for PTH expression (Figure 3), a papillary thyroid carcinoma in thyroid isthmus that was positive for CK19 and G3 expression (Figure 4), and a thyroid adenoma with lymphocytic thyroiditis in the left thyroid lobe. At 2 weeks post-operation, the follow--up PTH level was 43.53 pg/ml, the serum calcium level was 2.41 mmol/L, the free thyroxine level was 12.85 pmol/L, and the thyroid stimulating hormone level was 1.08 mIU/L; all of these levels were within the acceptable ranges.

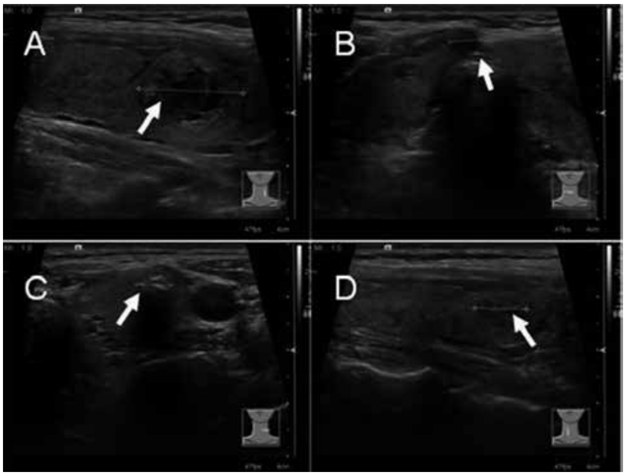

Figure 1. Thyroid ultrasonography of the patient. (**A**) A 2.0 × 1.4 cm cyst-solid mixed-echo area in the lower pole of the left thyroid gland. (**B**) A 0.6 × 0.5 cm low-echo lesion with obscure boundaries in the isthmus of the thyroid gland. (**C**) Accumulated 0.6 × 0.5 cm strong-echo areas in the upper pole of the left thyroid gland. (**D**) A 1.0 × 0.6 cm cyst-solid mixed-echo lesion in the right lobe of the thyroid gland.

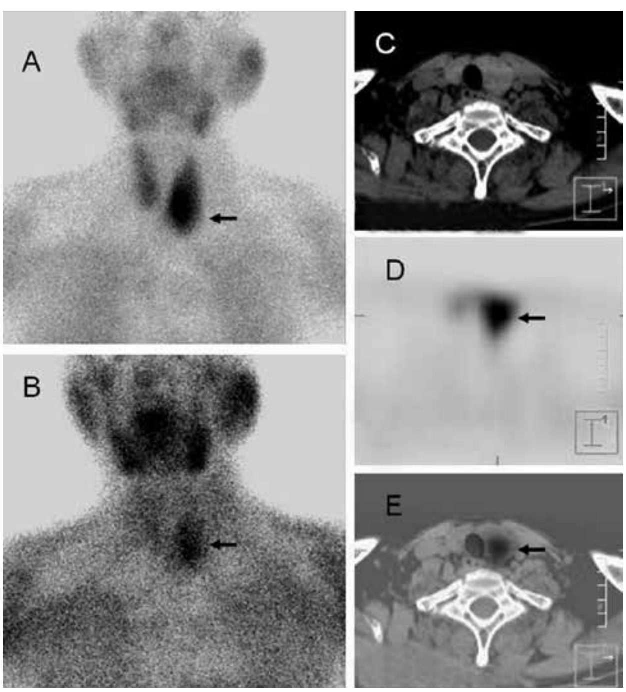

Figure 2. Dual-phase ^{99m}Tc-sestamibi parathyroid scintigraphy and SPECT/CT scans of the patient. (**A**) Early imaging of dual-phase ^{99m}Tc-sestamibi parathyroid scintigraphy. Thyroid gland was developed clearly, and high radiotracer uptake was revealed at the lower pole of the left thyroid lobe. (**B**) Delayed imaging of dual-phase ^{99m}Tc-sestamibi parathyroid scintigraphy. The radioactivity was decreased in the thyroid gland, and high radiotracer uptake was still revealed at the lower pole of the left thyroid lobe. (**C**, **D**, **E**) Hybrid SPECT/CT scans. High radiotracer uptake posterior to the left thyroid lobe coincided with a mass in parathyroid gland through CT scan. Hybrid SPECT/CT scans suggested a left parathyroid adenoma.

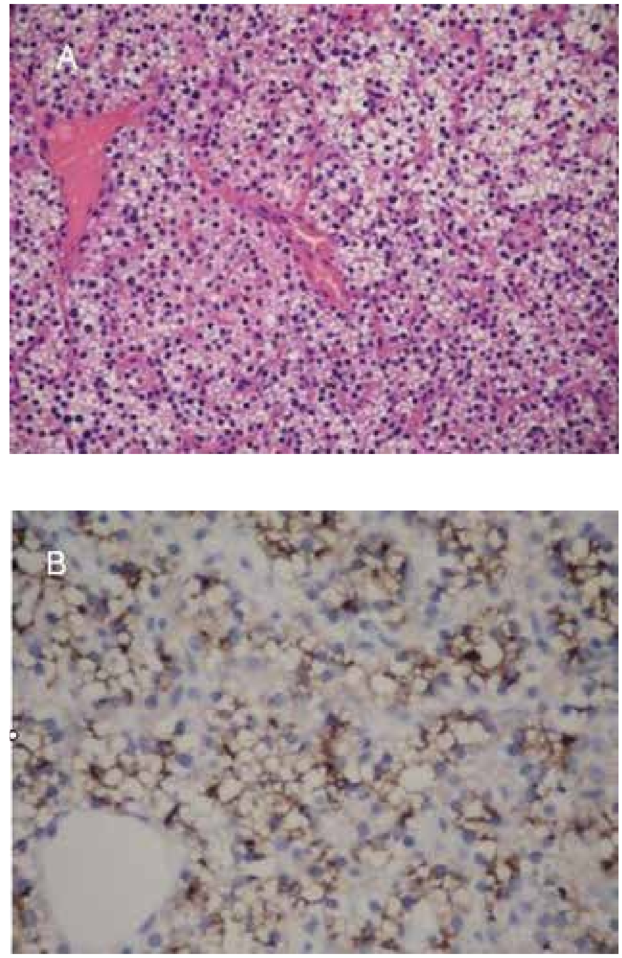

Figure 3. Pathological sections of parathyroid. (**A**) Histopathology section shown at higher magnification demonstrating typical features of a parathyroid adenoma (Hematoxylin-eosin; original magnification ×20). (**B**) Parathyroid hormone immunohistochemistry staining revealing positive PTH staining (Hematoxylin-eosin; original magnification ×20).

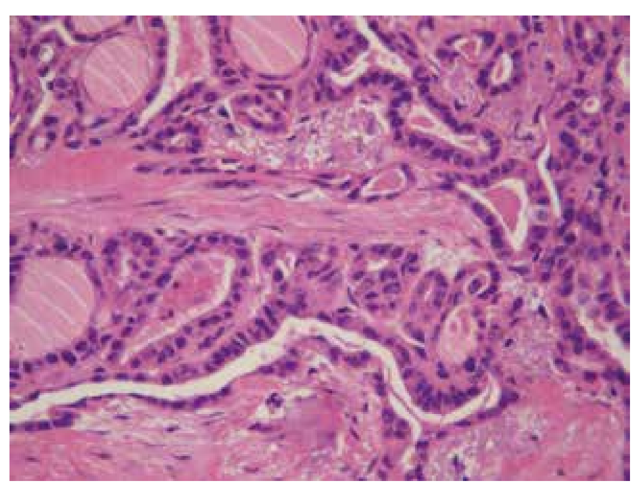

Figure 4. Higher-magnification image of papillary thyroid carcinoma (Hematoxylin-eosin; original magnification ×20).

DISCUSSION

Primary hyperparathyroidism is the third most common endocrine disease. The prevalence of this disease depends on the population studied and the diagnostic methods employed. Estimation of the true incidence of this disease is difficult, but the overall figures are consistent: between 27 and 30 per 100,000 person-years. The incidence of PHPT increases with age, and PHPT is more prevalent among women, particularly postmenopausal women (1). The crude incidence of thyroid cancer was 4.44 per 100,000 in a Chinese population from 2003 to 2007 (9). The relationship between concurrent thyroid and parathyroid disease was initially described in 1947. The frequency of the coexistence of primary hyperparathyroidism and thyroid carcinoma differs based on the study method employed. The frequency of thyroid disease in patients undergoing parathyroidectomy has been reported to range from 2.5 to 17.6%. However, the frequency of primary hyperparathyroidism among patients with thyroid disease has been reported to range from 0.3 to 8.7% (10). To date, the pathogenesis of the coexistence of primary hyperparathyroidism and thyroid carcinoma had not been established.

The coexistence of a parathyroid tumor and thyroid diseases is commonly misdiagnosed due to mutual interference during imaging in the early period of disease. The specificity and sensitivity of ultrasonography in the diagnosis of concurrent parathyroid tumor and thyroid nodules are low and are even lower than those of CT scans. ^{99m}Tc-MIBI is a radiotracer with lipophilic cationic properties that is distributed within the mitochondria, most prominently in normal cardiac and thyroid cells. Taillefer and cols. (11) developed a double-phase imaging procedure using ^{99m}Tc-MIBI for the detection and localization of parathyroid adenomas based on the fact that ^{99m}Tc-MIBI washes out more rapidly from the thyroid than from abnormal parathyroid tissue. ^{99m}Tc-MIBI scintigraphy images of parathyroid adenomas can be classified as intrathyroidal images and extrathyroidal images. Intrathyroidal images are characterized by increased uptakes of radioactivity in the thyroid gland during the early and delayed stages. Extrathyroidal images are characterized by an increased uptake of radioactivity superior or inferior to the thyroid gland at the early and delayed stages. One concern associated with intrathyroidal scintigraphy images is whether the origin of a concentrated lesion is an intrathyroidal adenoma (hyperplasia) or an extrathyroidal adenoma (hyperplasia) posterior to the thyroid gland. In our case, the patient presented to the hospital with symptoms of weight loss and fatigue. Although the serum calcium and parathyroid hormone levels were elevated, a cervical ultrasound and a CT scan revealed no signs of a parathyroid lesion. ^{99m}Tc-MIBI double-phase scintigraphy imaging produced an intrathyroidal image with a suspected intrathyroidal parathyroid adenoma. However, SPECT/CT found concentrated radioactivity inferior and posterior to the left thyroid lobe that was suspected to be an extrathyroidal parathyroid adenoma, which was confirmed during operation. Our case reconfirmed the value of ^{99m}Tc-sestamibi SPECT/CT in the localization of parathyroid adenomas.

The sensitivity of the dual-phase protocol for the diagnosis of parathyroid adenoma is 50%-86% (12). Despite its high sensitivity and specificity in the detection of parathyroid adenoma, SPECT alone is limited by its inability to provide anatomical details. Hybrid SPECT/CT systems allow for both functional and structural imaging to be performed in a single imaging session and result in improved image quality compared to functional imaging alone. Compared to SPECT alone, SPECT/CT can detect a greater number of abnormal lesions, particularly hyperplastic lesions. Sheng and cols. (13) found that ^{99m}Tc-MIBI SPECT/CT has significantly higher sensitivity in the detection of PHPT lesions than does ^{99m}Tc-MIBI dual-phase planar imaging (87.8% *vs.* 75.6%, $P < 0.05$). The sensitivity of ^{99m}Tc-MIBI SPECT/CT in the detection of parathyroid hyperplasic lesions was reported to be 50.0%, and no parathyroid hyperplasic lesions were detected with planar imaging in that study ($P < 0.05$). Additionally, ^{99m}Tc-MIBI scintigraphy imaging is susceptible to false positives and negatives, particularly in subjects with lesions smaller than 10 mm. In a study by Bural and cols., the correct detection and localization of hyperfunctioning parathyroid lesions with SPECT/CT (31 of 32 subjects) was superior to that of SPECT (22 of 32 subjects) alone. All of the lesions that were not detected with SPECT alone in 10 subjects were smaller than 10 mm (14). SPECT/CT also play an important role in the localization of parathyroid adenomas in patients with ectopic adenomas in locations that include the carotid sheath, anterior mediastinum, retropharynx, and intrathyroidal regions; these locations are typically overlooked by SPECT. Kaushal reported a case of a large intrathyroidal parathyroid adenoma that was diagnosed and accurately located preoperatively with

SPECT/CT (15). Kim and cols. (16) evaluated the efficacy of ^{99m}Tc-sestamibi SPECT/CT in minimally invasive parathyroidectomy by comparing the abilities of ^{99m}Tc-sestamib scintigraphy, SPECT and conventional imaging methods, including CT and ultrasonography, to identify the precise locations of parathyroid adenomas and hyperplasias and found that ^{99m}Tc-sestamibi SPECT/CT was helpful for minimally invasive parathyroidectomy.

Ultrasonography is effective in detecting lesions of the neck and can guide biopsy (12). High-frequency ultrasound can reveal the anatomical structure, hemodynamics, and microcirculatory perfusion of the thyroid gland when the gland features micronodules, which contributes to benign *vs.* malignant assessments. In the present case, a 0.6 × 0.5 cm low-echo lesion with an obscure boundary and weak blood flow signal in the isthmus was found and suspected to be thyroid cancer, which was confirmed operatively. However, investigation of the surrounding tissue, including the esophagus, trachea and lymph nodes, depended on computed tomography. Although fine-needle aspiration cytology is currently the best test for preoperative evaluations of thyroid nodules, it is not widely performed in China.

CONCLUSIONS

Although the co-occurrence of parathyroid adenoma, papillary thyroid carcinoma and thyroid adenoma with lymphocytic thyroiditis is rare, these conditions can and do coexist. Endocrinology physicians need to be aware of the possible simultaneous presence of thyroid and parathyroid lesions. The main diagnostic procedures for the preoperative localization of parathyroid and thyroid adenomas are ^{99m}Tc-MIBI scintigraphy and ultrasonography of the neck. Hybrid ^{99m}Tc-MIBI SPECT/CT imaging is superior to CT and ^{99m}Tc-MIBI scintigraphy alone in the preoperative localization of all pathologic glands in patients suffering from multiglandular disease with primary hyperparathyroidism. The final diagnosis of concurrent parathyroid adenoma with thyroid carcinoma can be established based on postoperative histopathologic examinations.

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