Papillary Thyroid Carcinoma with Primary Hyperparathyroidism: A Report of Two Cases and a Brief Literature Review

Primer Hiperparatiroidizme Eşlik Eden Papiller Tiroid Karsinomu Vakası: 2 Vaka ve Literatürün Kısa Derlemesi

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Abstract
Coexistence of medullary thyroid carcinoma and primary hyperparathyroidism (PHPT) is well described, however, the association of non-medullary thyroid cancer and PHPT is less recognized. Herein, we report two patients with PHPT and papillary thyroid carcinoma (PTC). Although no definitive data showing increased prevalence of non-medullary thyroid cancer in patients with parathyroid adenomas, possible coexistence of these two conditions should be borne in mind in preoperative evaluation. Turk Jem 2013; 17: 12-4

Key words: Primary hyperparathyroidism, thyroid carcinoma

Özet
Medüller tiroit kanseri ve primer hiperparatiroidi birlikteliği oldukça iyi bilinmesine rağmen, medüller dışı tiroit kanserleriyle birlikte hiperparatiroidizmin görülmesi daha az karşılaşılan ve tanınam bir durumdur. Biz burada primer hiperparatiroidi, ve papiller tiroit kanseri iki olgumuzu sunacağız. Paratiroid adenomlarında sahip hastalarda medüller dışı tiroit kanseri riskinin artığını gösteren bir bilgi olmasa da, bu iki hastalığın bir arada bulunabileceği akılda tutulmalıdır. Türk Jem 2013; 17: 12-4

Anahtar kelimeler: Primer hiperparatiroidism, tiroid kanseri

Introduction
Primary hyperparathyroidism (pHPT) is a common disease. The prevalence rate is about 1 to 4 per 1000, with a female: male ratio of 3:1 [1]. By far the most common lesion found in patients with pHPT is solitary parathyroid adenoma occurring in 75%-85% of cases [2]. The treatment of choice for pHPT is surgical removal of the adenoma. Papillary thyroid carcinoma (PTC) is the most common type of malignant thyroid tumor, constituting more than 70% of thyroid malignancies [3]. There has been an increasing incidence of PTC worldwide over the past few decades [4]. Fine needle aspiration biopsy (FNAB) is currently the most common method of examining solitary thyroid nodules. Coexistence of pHPT and PTC has been previously described in case reports and some surgical series. PTC has been reported in 2.1-4.2% of patients subjected to surgery for pHPT in large series [5-10]. Herein, we describe two cases of patients with pHPT and PTC.

Case 1
A 55-year-old Caucasian woman was referred to our clinic following determination of profound anemia (Hb: 6.4 g/dL) and hypercalcemia (Serum Ca: 11.4 mg/dL) in the internal medicine clinic where she originally presented with lethargy and fatigue. The
A 60-year-old Caucasian man was referred to our clinic following identification of hypercalcemia (serum Ca: 15.2 mg/dl) in the internal medicine clinic to which he had originally presented with back and lower back pain. The patient had no history of exposure to radiation. Laboratory findings confirmed the diagnosis of pHPT: serum Ca: 15.2 mg/dl, PTH: 1900 pg/mL, urinary calcium: 720 mg/day, serum creatinine: 2.1 mg/dl, and alkaline phosphatase: 2142 U/L. Thyroid function tests were normal. Neck USG revealed multinodular goiter. One of the 5 nodules, 23 x 19 mm in size, was hypoechoic and had a satellite nodule and calcification. There was a hypoechoic solid lesion measuring 18 x 17 mm compatible with a parathyroid adenoma on the right side. FNAB of the nodule was suspicious for PTC. Dual-phase 99mTc-sestamibi parathyroid scintigraphy was performed (Figure 1). Normal focal activity was observed in the thyroid gland and increased focal activity involvement in the inferior part of the thyroid lobe at images taken at 15 min. Involvement of the thyroid gland disappeared at images taken at 120 min and 4 hour, while increased activity involvement in the inferior part of the right thyroid persisted in a manner compatible with parathyroid adenoma. Isotonic saline at a rate of 4 L/day and 120 mg/day of furosemide were infused repeatedly to improve hypercalcemia during the preoperative period of hospitalization.

Then, total thyroidectomy, central lymph node dissection and parathyroidectomy were performed. The pathology report confirmed parathyroid adenoma (3.5 cm) and classic variant PTC (2 cm). Postoperative serum Ca fell to 8.2 mg/dl and PTH to 10 pg/mL. Calcium and calcitriol replacement was started. At examinations 6 weeks after surgery, no neck pathology was detected by USG and level of serum Ca was measured at 8.3 mg/dl under replacement therapy. The patient was given 100 mCi radioactive iodine treatment. At full body scintigraphy 1 week later, there was no involvement outside the thyroid bed. The patient was started on L-thyroxine therapy at 150 μg/day and placed under observation.

**Discussion**

Multinodular goiter was incidentally determined while investigating parathyroid adenoma in both cases. PTC was determined in one case following FNAB and in the other as a suspicious biopsy finding. We determined parathyroid adenoma as a result of surgery in both cases. We determined classic type papillary carcinoma, solitary in one case and multicentric in the other. Although the incidence of PTC associated with pHPT in small surgical series is around 9%-17.8% (11-13), in large series the level has been reported to be 2%-4.2% (5-10). The majority of PTCs in the great majority of these series were microcarcinoma (5,6,11). In the great majority of cases, the diagnosis was made through postoperative pathological examination. Additionally, the number of multicentric tumors metastasizing to the lymph nodes was relatively small (5,6,11). However, papillary carcinomas without microcarcinoma were more frequent in small series such as those of Kosem et al. (13) and Ogawa et al. (12). The cause of the association between thyroid disease and primary pHPT remains unclear. Although an association between osteosarcoma and pHPT has been shown in animal studies (14), no direct relationship was established between pHPT and cancer in human studies involving 1600 patients given human recombinant PTH (15-17). Some authors suggest a coincidence, however, most maintain that increased endogenous calcium, growth factors, epithelial growth factors, and goitrogenic factors may play a role (8,18). Head and neck radiotherapy, especially during childhood and adolescence, is another risk factor in the pathogenesis of HPTH and thyroid carcinoma (19,20). However, neither of our patients had any history of radiotherapy. The incidence of thyroid microcarcinoma in large autopsy series (5.3%-6.2%) (21,22) is similar to the PTC incidence cited in the large surgical series above (5-10). This also suggests that the occurrence of these two diseases together in single individuals is a matter of coincidence.
The reason for detecting the coincidence of thyroid papillary carcinoma and pHPT may be the use of common imaging techniques, such as USG of the neck, in the diagnosis of both diseases. In addition, when surgery to the same region is needed for pathologies of parathyroid, it can be performed in the same session. In such cases, greater attention will be paid to the thyroid. The diagnosis and timely treatment of associated thyroid abnormalities is desirable, because a delay in surgery may result in increased morbidity associated with a second neck exploration. It is, therefore, advisable to evaluate the thyroid gland prior to parathyroid gland operations.

Iakovou et al. (23) reported that a nodule containing papillary carcinoma still exhibited radioactivity in images 3 h later at dual phase 99mTc-sestamibi parathyroid scintigraphy. They suggested that dual phase 99mTc-sestamibi parathyroid scintigraphy might be useful in detecting thyroid malignancy preoperatively. Parathyroid scintigraphy was performed in our second case. While a sestamibi scan can be positive in different benign and malignant thyroid tumors (24), we observed no occlusion in the thyroid in images taken at the second and fourth hours.

In conclusion, although synchronous parathyroid and thyroid carcinomas are rare, they can and do coexist. Parathyroid adenomas and multinodular goiter were identified by preoperative USG of the neck in both of our patients. Preoperative FNAB of predominant thyroid nodules was useful in both cases, enabling surgery to be performed more aggressively and preventing a second operation that might increase morbidity and mortality. Although no definitive data showing that non medullary thyroid carcinoma incidence increases in patients with parathyroid adenomas, possible coexistence of both conditions should be borne in mind in preoperative evaluation.

Consent
Written informed consent was obtained from the patients for publication of these case reports.

References