

Thyroid Dysfunction Induced by Metastatic Thyroid Cancer: Report of Two Cases

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Metastases to the thyroid gland are not frequently observed in clinical practice, although an overall incidence of secondary thyroid malignant tumors has been reported to range from 1.25% to 24% in autopsy series. Generally, patients with metastatic thyroid cancer present with euthyroidism and they do not develop thyroid dysfunction. Thyroid dysfunctions, including hypothyroidism and hyperthyroidism, rarely occur in patients with metastatic thyroid cancer. We describe here a case of hypothyroidism induced by thyroid metastasis from cancer of an unknown primary site in a 53-year-old man and another case of thyrotoxicosis induced by thyroid metastasis from lung cancer in a 65-year-old man. (*Endocrinol Metab* 25:370-373, 2010)

Key Words: Hypothyroidism, Thyroid neoplasms, Thyrotoxicosis

INTRODUCTION

Although an overall incidence of secondary thyroid malignant tumors ranging from 1.25% to 24% has been reported in autopsy series, metastases to the thyroid gland are not frequently observed in clinical practice [1-3]. Metastatic thyroid cancer is uncommon, but it must be distinguished from primary thyroid cancer because of the differences in management and prognosis. Generally, patients with metastatic thyroid cancer present with euthyroidism. There have been only a few cases characterized by transient thyrotoxicosis due to metastasis of an extrathyroid tumor [14]. The primary thyroid cancer is more aggressive and more infiltrative in patients with metastatic thyroid cancer accompanied by thyroid dysfunction than in those accompanied by euthyroidism. This suggests poorer prognoses in patients with metastatic thyroid cancer accompanied by thyroid dysfunction.

We report 2 cases of thyroid dysfunctions induced by thyroid metastases of primary cancer.

CASE REPORT

Case 1

A 65-year-old man was admitted to the hospital with neck swelling for 2 weeks. The patient had no notable past medical history. The neck mass increased in size about twice for the last 2 weeks, and he had restlessness and intermittent palpitation. He showed a weight loss of 3 kg during the last month. His vital signs were stable. Physical examination revealed bilateral cervical lymphadenopathy and diffuse goiter. The goiter was generally firm, about 7 cm in diameter and there were no palpable nodules in it.

The results of the thyroid function test were as follows: the free thyroxine (fT4) level, 5.75 ng/dL (normal range, 0.8-2.1 ng/dL); the total triiodothyronine (T3) level, 238 ng/dL (normal range, 80-170 ng/dL); the serum thyrotropin (TSH) level, nondetectable (normal range, 0.3-5.0 uIU/mL); the anti-thyroglobulin (anti-Tg) level, 7.30 U/mL (normal range, 0-60 U/mL); the anti-thyroperoxidase antibody (anti-TPO Ab) level, 7.66 U/mL (normal range, 0-60 U/mL); the TSH receptor Ab level, 2 U/mL (normal range 0-9 U/mL); and the serum Tg level, 468.4 ng/mL (normal range 0-50 ng/mL).

Ultrasonography of the thyroid gland demonstrated enlarged lobes with heterogeneous echogenicity and scattered hypoechoic areas (Fig. 1A). Color Doppler examination revealed mildly de-

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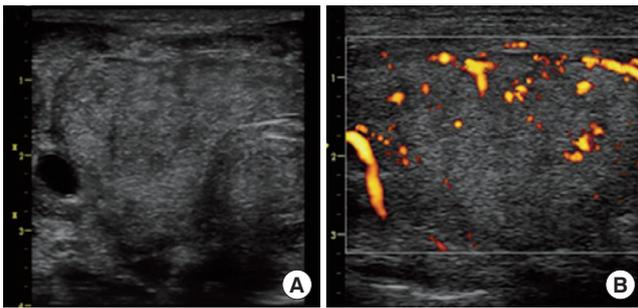


Fig. 1. (A) Ultrasonographic findings. Both lobes of the thyroid gland are enlarged with the heterogeneous echogenicity of the parenchyma and scattered hypoechoic areas. (B) Color Doppler shows that blood flow is slightly decreased in the parenchyma of both glands.

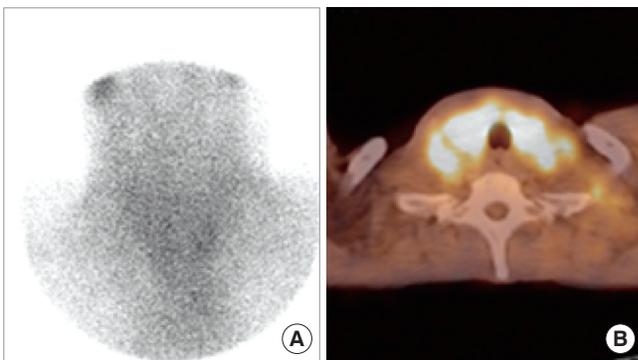


Fig. 2. (A) TcO₄-99m thyroid scan. The thyroid gland is poorly visualized. (B) F(18)-FDG PET/CT image demonstrates increased FDG uptake (maxSUV: right, 5.4; left, 5.1) in the thyroid gland and paratracheal LN (maxSUV: 4.7).

creased blood flow in both lobes of the thyroid gland (Fig. 1B). TcO₄-99m thyroid scan showed that the thyroid gland was poorly visualized and that the thyroid uptake rate was 2.6% (normal range, 1.4-5%) (Fig. 2A). Positron emission tomography-computed tomography (PET-CT) of the thyroid gland showed diffuse increased FDG uptake (maxSUV: right, 5.4; left, 5.1) (Fig. 2B). Cytologic examination of fine needle aspirates obtained from the thyroid gland showed adenocarcinoma, most likely metastatic, with frequent papillary growth (Fig. 3A).

Chest X-ray showed a 6-cm mass in the left lower lobe and CT was checked. Chest CT revealed a 6.2-cm mass in the left lower lobe. Bronchoscopic biopsy of the lung mass was performed and revealed a moderately to poorly differentiated adenocarcinoma suggestive of primary site in the lungs. The patient had metastases to the adrenal glands, brain and hilar/mediastinal/supraclavicular lymph nodes on both sides.

The patient received propranolol and underwent radiotherapy for brain metastasis. However, his general condition became aggravated, and thus the patient stopped radiotherapy. Four weeks

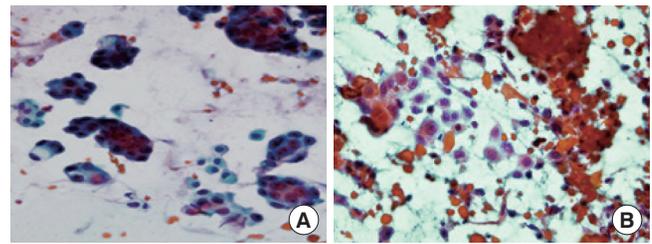


Fig. 3. Histologic findings. (A) Cytologic examination of fine needle aspirates from the thyroid gland reveals adenocarcinoma, most likely metastatic, with frequent papillary growth (H&E, × 200). (B) Cytologic examination of fine needle aspirates from the thyroid gland exhibits squamous cell carcinoma (H&E, × 400).

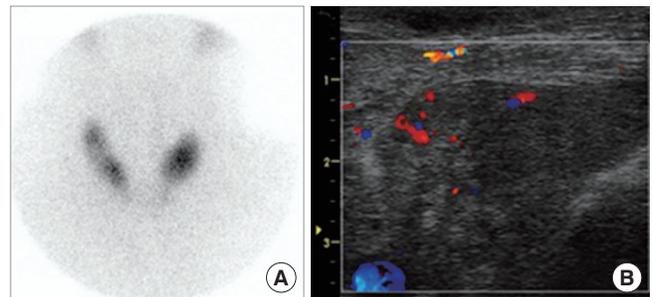


Fig. 4. (A) TcO₄-99m thyroid scan. Both lobes of the thyroid gland have a cold space occupying lesion (SOL). (B) Ultrasonographic findings. Diffuse and focal hypoechoicities are seen on both lobes.

after initial diagnosis, he died of lung cancer.

Case 2

A 53-year-old man visited to our hospital with a right neck mass that persisted for several weeks. The patient had no remarkable past medical history. He complained of fatigue and lethargy for 1 year and had loss of appetite. Physical examination revealed right neck swelling. The swelling in the submandibular area was a mass-like lesion that was mobile, hard and 2 cm in diameter.

Neck CT revealed multiple enlarged lymph nodes and heterogeneous low-density attenuation from right levels I, II, and IV. The right thyroid gland revealed a diffuse enlargement with internal heterogeneous low-density attenuation. Chest CT revealed multiple conglomerated metastatic lymph nodes in the supraclavicular and axillary areas, multiple metastatic lymph nodes in bilateral hilar, mediastinal and subcardinal areas, and pericardial/bilateral pleural effusions. Bone scans exhibited no bone metastasis.

The thyroid function test results were as follows: the fT₄ level, 0.77 ng/dL; the T₃ level, 50.7 ng/dL; the TSH level, 25.1 μIU/mL. Ultrasound-guided neck lymph node biopsy showed metastatic squamous cell carcinoma, with lymphovascular tumor emboli. On

ultrasonograms, the right lobe of the thyroid gland showed enlargement with diffuse hypoechogenicity and the left lobe showed enlargement with focal hypoechogenicity (Fig. 4A). TcO₄-99m thyroid scan showed that both lobes of the thyroid gland had cold space-occupying lesion (SOL) and the thyroid uptake rate was 2.6% (Fig. 4B). Blunt ultrasound-guided fine needle aspiration was carried out from the hypoechoic area of the right lobe, which established a definitive diagnose of squamous cell carcinoma (Fig. 3B). Thoracentesis was performed, and pleural fluid cytology showed poorly differentiated metastatic carcinoma. The patient received synthroid 100 µg per day and 2 sessions of taxotere-cisplatin-based systemic chemotherapy. Follow-up chest CT scans taken 3 months later revealed an increase in size of metastatic lymph nodes, and the chemotherapy regimen was changed to Xeloda-cisplatin. The patient received 3 sessions of Xeloda-cisplatin-based chemotherapy and died of cancer of unknown primary site 3 months after initial diagnosis.

DISCUSSION

If a malignant disease is associated with a goiter, a possibility of a metastatic tumor involving the thyroid gland is suggested. Metastatic thyroid cancer and thyroid dysfunction are probably infrequent, but diagnosis is important in the institution of appropriate therapy [15].

Involvement by non-thyroid malignancies may arise through direct spread from adjacent structures, retrograde lymphatic spread and hematogenous spread. A variety of presentations have been reported: from neck masses felt by the patient to nodular goiters discovered on physical examination and to lesions discovered on imaging studies [4-6]. Most clinical series have shown that renal cell carcinoma is the most common primary tumor related to symptomatic thyroid metastases, closely followed by breast and lung cancers [7-9]. Although it is difficult to clinically differentiate primary thyroid carcinoma from metastatic lesions, metastasis must be included in the list of the differential diagnoses for treatment and prognosis because it is not a rare cause of thyroid nodules. McCabe et al. [10] suggest that in patients with thyroid nodules who had a history of a malignant tumor in other organs and underwent resection previously, the diagnosis should be made initially with the suspicion of metastasis before it is completely ruled out.

Although hypothyroidism and hyperthyroidism represent un-

common events in patients with metastatic thyroid involvement, both thyroid dysfunctions have been documented in such patients [3,11,12].

A case of severe hypothyroidism induced by thyroid metastasis of cholangiocarcinoma has been reported in the literature [14]. This case showed that tumor cells that metastasized to the thyroid gland from cholangiocarcinoma destroyed the thyroid follicles, leading to severe hypothyroidism. Thyroid metastasis-related hypothyroidism is caused by massive infiltration of the thyroid gland by malignant tumor [3]; however, neoplastic embolization to the thyroid gland results in thyrotoxicosis when gland destruction occurs with leakage of stored hormones into the peripheral blood [11, 12].

In cases of thyroid metastases, there exists the possibility of thyroid dysfunction due to thyroid involvement. Most cases have been characterized by transient thyrotoxicosis due to massive metastasis of extrathyroid tumors. Miyakawa et al. [15] reported severe thyrotoxicosis induced by thyroid metastasis of lung adenocarcinoma. They speculate that aggressive invasion of tumor cells into the thyroid gland resulted in highly destructive thyrotoxicosis. Papi et al. [13] reported that all thyroid metastasis patients but one (n = 36), with thyrotoxicosis, were euthyroid at presentation and did not develop thyroid dysfunction during the follow-up.

Our 2 patients had dysfunctions of the thyroid gland due to the metastasis of the primary tumors. The first had destruction of the thyroid gland due to neoplastic embolization of the extrathyroidal tumors which induced thyrotoxicosis through the hormonal leakage of stored thyroid hormone. The second one showed hypothyroidism due to the massive infiltration of extrathyroidal tumor cells into the thyroid gland. It is conceivable that a progressive destructive process in the thyroid gland led to a short episode of thyrotoxicosis, which might have otherwise remained unrecognized [14]. In other words, aggressive invasion of tumor cells into the thyroid gland resulted in highly destructive thyrotoxicosis through neoplastic embolization, and the massive infiltration of primary cancer cells into the thyroid gland caused hypothyroidism. Therefore, we believe that neoplastic embolization occurs earlier due to aggressive tumor invasion in metastatic thyroid cancer with thyroid dysfunction than with euthyroidism. Then, as the massive infiltration of primary cancer cells into the thyroid gland progresses, hypothyroidism develops. This result suggests that prognosis may be poorer in metastatic thyroid cancer with thyroid dysfunction than with euthyroid due to such invasion and infiltration.

We reported 2 cases of metastatic thyroid cancer with thyroid

dysfunction. In patients with malignant disease and goiter, the possibility of metastatic cancer to the thyroid gland should be considered. In addition, primary cancers may be more aggressive and infiltrative in metastatic thyroid cancers with thyroid dysfunction than with euthyroidism, which may suggest poor prognosis in the former. It is believed that the accurate diagnosis of thyroid dysfunction is necessary to predict clinical outcomes in patients with metastatic thyroid cancer.

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