

Case Report

Thyroid Cancer Presenting with Concomitant Metastatic Breast Cancer in the Thyroid

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Abstract.

The thyroid is an unusual site to find cancer metastasis. When it does occur, such cancer spread is often manifested in multiple metastases and generally suggests a poor prognosis. We presented here a 49-year-old woman recently diagnosed with thyroid cancer, who had been treated for stage IIA breast cancer 8 years ago. After radical right thyroidectomy and left subtotal thyroidectomy, her pathological report showed papillary thyroid carcinoma, right thyroid, with concomitant metastatic breast carcinoma. This is the first case of which we are aware involving coexisting thyroid cancer and metastatic breast cancer in the ipsilateral lobe. Moreover, the circumstances of this case show a very unique clinical course compared with previous studies. Given the unusual circumstances of our case, we further discuss the relationship between thyroid cancer and breast cancer.

Keywords : thyroid metastasis, thyroid cancer, breast cancer, ipsilateral

病例報告

甲狀腺癌以同時伴隨乳癌轉移至甲狀腺的形態呈現

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中文摘要

甲狀腺是一個不尋常的癌症轉移位置。甲狀腺被癌症轉移通常發生在已有他處轉移的情況下，而且一般預後不佳。我們舉出一位 49 歲的女性，曾在八年前罹患第二期乳癌並接受過手術與化學治療。她後來被診斷出罹患甲狀腺癌。經過右側甲狀腺根除術與左側次全甲狀腺切除術。病理報告顯示，右側乳突性甲狀腺癌，同時伴隨乳癌轉移至右側甲狀腺。這是第一例甲狀腺癌與轉移性乳癌並存在同一側甲狀腺的病例。而且與以前的文獻相較，它表現出非常獨特的臨床病程。我們也針對甲狀腺癌和乳癌的的關係進行了

討論。

關鍵字: 甲狀腺轉移、甲狀腺癌、乳癌、同側

INTRODUCTION

Although rich in vasculature, the thyroid gland is a rare site of metastatic diseases, accounting for only 2–3% of all malignant tumors of the thyroid [1]. Tumors of the breast, bronchi, gastrointestinal system and kidneys are the most common sites of origin [1]. Metastasis to the thyroid gland usually occurs with concomitant metastases elsewhere [2], and often implies poor prognosis for patients who usually die shortly after the appearance of thyroid metastasis [2,3]. Here we reported a case of thyroid cancer with concomitant breast cancer metastasis within the same lobe. After satisfactory treatment, the patient had survived disease-free, with no sign of either cancer for years.

CASE REPORT

A 49-year-old woman was diagnosed with and treated for breast cancer 8 years ago. She had undergone modified radical mastectomy to address left side breast cancer. Pathological report showed infiltrating duct carcinoma of the left breast, pT2N0M0, stage IIA, estrogen receptors (ER)-positive, progesterone receptor (PR)-positive, Her-2/Neu-negative. Then she received adjuvant chemotherapy with CMF (cyclophosphamide, methotrexate and fluorouracil) regimen and tamoxifen.

The patient had a past history of goiter and hypothyroidism when undergoing Eltroxin therapy. In 2007, an enlarged right neck mass was noted. Sonography revealed a 5 x 4 x 3 cm nodule with cyst formation in

the right lobe, and two small nodules with calcifications in the left lobe. Fine needle aspiration showed atypical cells. Thyroid cancer was suspected, and radical right thyroidectomy with lymph node dissection and left subtotal thyroidectomy were undertaken.

The histological sections showed coexisting papillary thyroid cancer tissue and some mucinous metastatic neoplasm (Figure 1A). Papillary tumor was mixed with follicular composition (Figure 1B), and its cytological features (papillary architecture, nuclear pseudo-inclusions, nuclear grooves, lack of nucleoli) are well-recognized (Figure 1C). One piece of histology-distinct tissue was identified among the papillary neoplastic area (Figure 2A) with prominent nucleoli (Figure 2B), which is impressed as a metastatic neoplasm. The TTF-1 stain showed positive in normal and neoplastic thyroid cells, but negative in the metastatic cells (Figure 3A). The metastatic tumors were positive for ER stain (Figure 3B) as well as the PR stain (Figure 3C). So the final pathological diagnosis was papillary thyroid carcinoma (pT3N0M0), right thyroid, with concomitant metastatic breast carcinoma, which most likely originated from the previous breast cancer diagnosed 8 years ago.

Imaging survey showed no evidence of metastasis elsewhere on the patient. She then received one course of Iodine-131 therapy. Leuprorelin acetate (Leuplin) was then prescribed for one year, then therapy was shifted to the aromatase inhibitor after menopause. She then received regular follow-up and examination in our hospital and is currently free of both cancers.

DISCUSSION

Thyroid is an unusual site of cancer metastasis. In an autopsy study, breast and lung carcinoma are the two most frequently observed primary sites metastasizing to thyroid [4]. However, in the clinical survey

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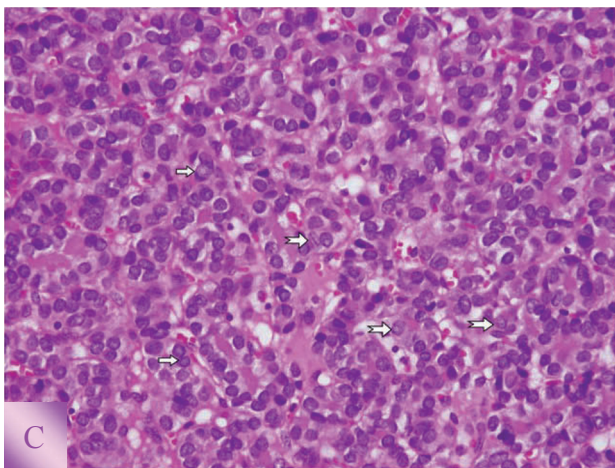
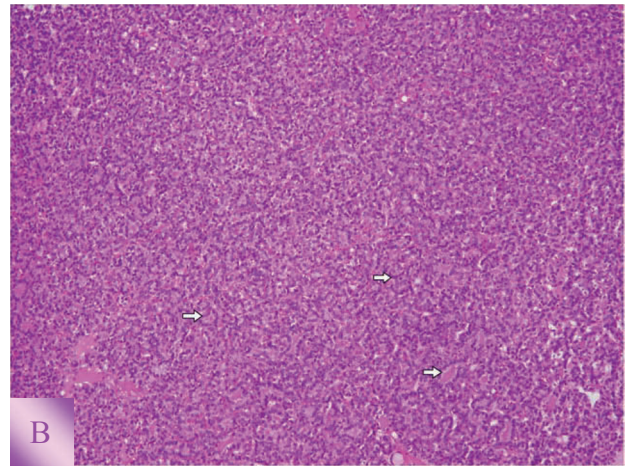
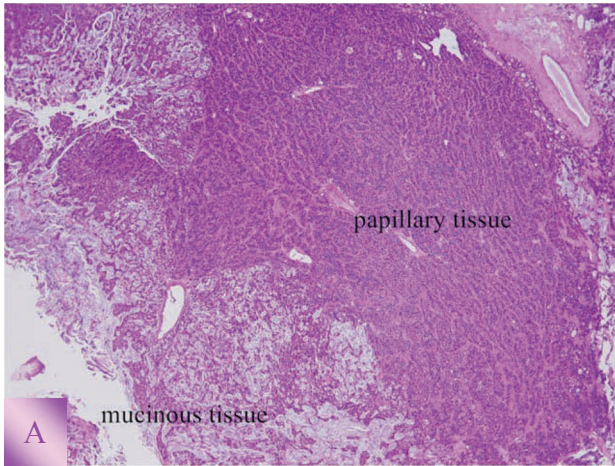


Figure 1. (A) Within the thyroid specimen, it shows coexisting papillary thyroid cancer tissues (right side) and mucinous metastatic neoplasm (left side) (100X). (B) Papillary thyroid cancer tissue is mixed with follicular composition (⇨), which is follicular variant (200X). (C) The cytological features of papillary thyroid cancer: nuclear pseudo-inclusions (⇨), nuclear grooves (⇨), lack of nucleoli (⇨) (800X)

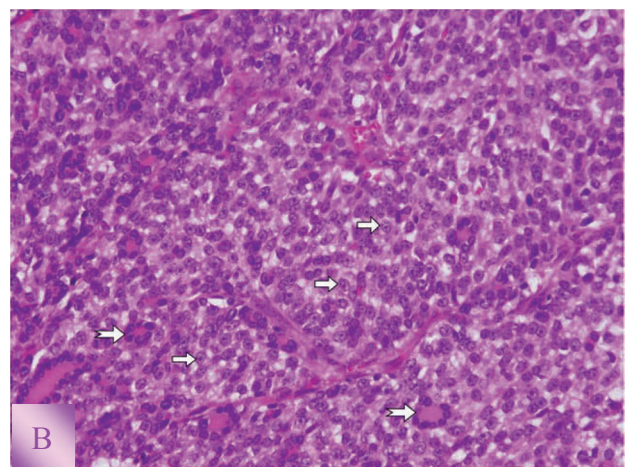
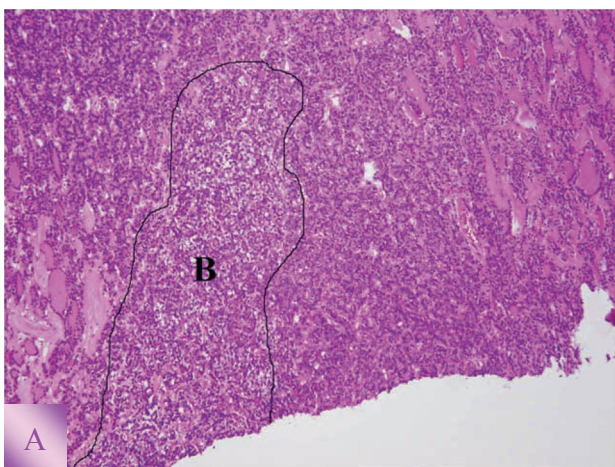


Figure 2. (A) One piece of histology-distinct tissue (labeled “B”) is identified among the papillary neoplastic area (100X). (B) Cells within this “B” area have nucleoli (⇨), which are lacking in thyroid cancer cells (⇨) (400X)

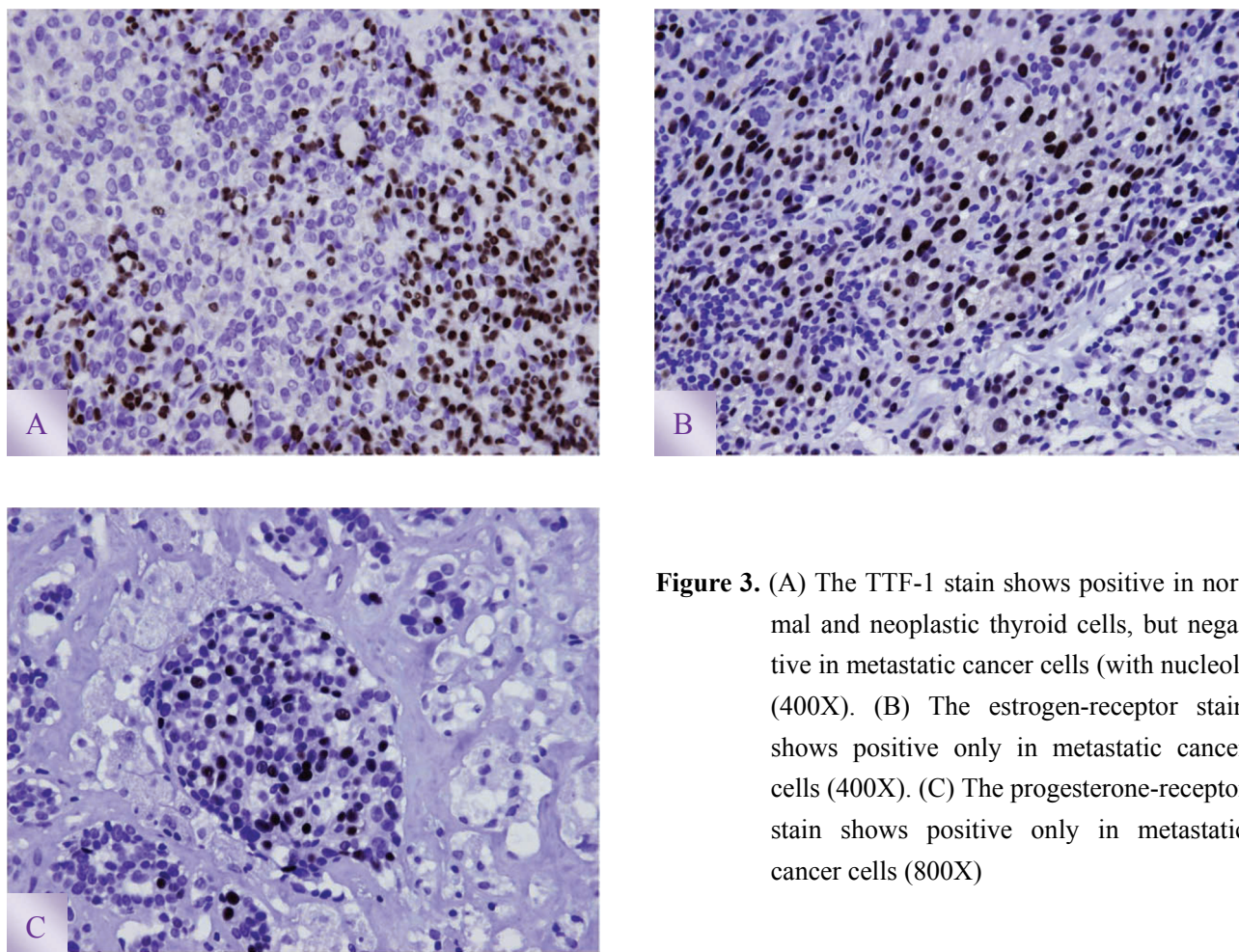


Figure 3. (A) The TTF-1 stain shows positive in normal and neoplastic thyroid cells, but negative in metastatic cancer cells (with nucleoli) (400X). (B) The estrogen-receptor stain shows positive only in metastatic cancer cells (400X). (C) The progesterone-receptor stain shows positive only in metastatic cancer cells (800X)

of thyroid metastasis, kidney was the most common primary tumor site (33%), followed by lung (16%), breast (16%), esophagus (9%), and uterus (7%) [5].

Metastasis to the thyroid gland usually occurs with concomitant metastases at other organs [2,6], and often implies poor prognosis of patients [2] with median survival time around 10 months [3]. Thyroid metastasis usually occurs late after diagnosis of primary tumor, with mean duration of 106 months for renal cell carcinoma, 131 months for breast cancer, and 132 months for uterine cancer [5]. In our case, it took 8 years after diagnosis of primary breast cancer to detect metastasis to the thyroid gland. However, there was no concomitant metastasis into other organs. Furthermore, the patient's chances of achieving long-term survival

and remaining disease-free could improve after therapy.

Patients with breast cancer may have an increased risk for thyroid cancer. In 1987, an epidemiological analysis by McTiernan revealed women with a history of breast cancer were almost 3 times more likely to develop thyroid cancer [7]. A retrospective study of 2786 newly diagnosed breast cancer patients in Japan also demonstrated a significantly increased risk of ovarian cancer, thyroid cancer and non-Hodgkin's lymphoma compared to the general population [8]. In a recent study, sonographic screening for thyroid cancer in females undergoing concomitant breast sonography showed a significantly higher incidence of thyroid cancer in the breast cancer group than those

without such cancer [9]. Sonographic screening of breast cancer patients in Korea also showed a high incidence (2.5 %) of thyroid cancer [10].

On the other hand, in a study done by the M.D. Anderson Cancer Center, an increased incidence of subsequent breast carcinoma was found in young adult women (40-49 y/o) who had a history of thyroid cancer [11]. According to the data from the Surveillance, Epidemiology and End Results (SEER), patients younger than 40 years of age at the time of diagnosis of thyroid cancer had a 39% increased risk of a second cancer of the breast, prostate, and kidney [12]. Another SEER analysis of 1,333,115 persons also demonstrated premenopausal women with thyroid carcinoma have a significantly increased risk of subsequent breast carcinoma [13]. So patients with thyroid cancer may also have elevated chances of developing breast cancer.

There are also studies regarding the correlation between breast cancer and non-malignant thyroid disease. In 1996, a prospective study by Giani et al. revealed that the overall prevalence of thyroid disease (including nontoxic goiter and Hashimoto's thyroiditis) in breast cancer patients was higher than in the control group [14]. The prevalence of the presence of thyroperoxidase antibody, an indicator of Hashimoto's thyroiditis, is higher in breast cancer patients than in controls (23.5% vs. 8%; $P < 0.005$) [15]. Previous studies have also shown that preexisting thyroid disease (i.e., multinodular goiter and thyroid nodules) may provide a nidus for metastases to the thyroid gland [4]. Our patient had a history of goiter with hypothyroidism, which may facilitate the metastasis of her breast cancer to the thyroid gland.

The presence of ERs in papillary thyroid carcinoma has been demonstrated by immunohistochemistry, indicating that estrogen may affect the proliferation of ER-positive papillary thyroid carcinoma [16]. Higher levels of ERs were also found in neoplastic than in normal thyroid tissues [17]. 17β -estradiol, a potent mitogen for benign and malignant thyroid tumor cells,

could exert a growth-promoting effect by activating mitogen-activated protein kinase pathway [18]. In addition, a rare genetic syndrome, Cowden's disease, had increased the risk of both breast and follicular thyroid cancers [19]. These studies provide possible explanations of the mechanism of sequential occurrence of these two cancers.

The patient here presented a case of occult metastases, which by definition are not detected on routine imaging examination. They are usually detected incidentally on pathology tissues obtained for other purposes [20]. For occult metastases, it takes a long time before the spreading cancer becomes clinically evident, and therefore shows better prognosis than frank metastases. For this patient, she received therapy immediately after diagnosis, which could explain her good prognosis in comparison with previous reports.

In conclusion, we presented a rare case with concomitant primary thyroid cancer and metastatic breast cancer within the same lobe of the thyroid. Unlike previous reports, our patient did not have disseminated disease and enjoyed long-term disease-free survival after therapy. Coexisting breast cancer and thyroid cancer, although rare, should be viewed as a diagnostic option requiring timely treatment in clinical practice when appropriate.

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