Breast cancer metastatic to the bilateral thyroid: a case report and literature review

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Abstract
The thyroid gland is a relatively rare site for secondary malignancy. Here we describe the case of a 41-year-old woman with a history of bilateral breast cancer. She presented with elevated serum carbohydrate antigen 153 level. Ultrasonography revealed the bilateral thyroid lobes and isthmus diffuse distribution of point-like calcifications. No nodules were palpable, and total thyroidectomy was performed. A firm diagnosis of metastatic breast carcinoma to the bilateral thyroid was established. With this report, we could strengthen the argument that any patient with a thyroid lesion and a history of malignancy should be considered to have a metastasis until proven otherwise; further, we conclude that total thyroidectomy for the multifocality of metastases to the thyroid gland is feasible when metastatic cancer is limited to the thyroid. With a combination of comprehensive treatments, such as chemotherapy, radiotherapy and endocrine therapy, the survival of the patient can be prolonged.

Introduction
Secondary malignancy of the thyroid gland is relatively rare, although the thyroid gland is richly supplied with blood. In clinical papers, the incidence of secondary malignancy of the thyroid gland is low, according to various sources, constituting 2%–3% of all malignant tumours of the thyroid1; however, autopsy series on patients with cancer have yielded incidence rates ranging from 1.25% to as high as 24%2. Some reports show that the most common primary sites are the kidney, lung, breast and the gastrointestinal tract3,4. Here we describe a rare case of breast carcinoma metastatic to the bilateral thyroid after excision of the left breast in May 2003 and the right breast in July 2008.

Case presentation
The patient was a 41-year-old woman who underwent radical mastectomy for an invasive ductal carcinoma of the left breast in May 2003, followed by adjuvant chemotherapy, radiotherapy and endocrine therapy. All fifteen resected axillary nodes were positive for carcinoma at the time of the radical mastectomy. For a period of five years and two months, she was free of disease, and in July 2008, she developed right breast carcinoma with right axillary lymph node metastatic disease, for which she underwent neoadjuvant chemotherapy, modified radical mastectomy and adjuvant chemotherapy. Two resected axillary nodes were positive for carcinoma at the time of the modified radical mastectomy. Unfortunately, she presented with recurrent breast carcinoma on the right chest wall in November 2008. Second-line chemotherapy, radiotherapy and ovarian castration endocrine therapy followed. In November 2010, the patient was admitted for elevated serum carbohydrate antigen (CA) 153 level. Ultrasonography ‘accidently’ revealed the bilateral thyroid lobes and isthmus diffuse distribution of point-like calcifications, and colour Doppler flow imaging (CDFI) did not show abnormal blood flow (Figure 1). Physical examination revealed no palpable thyroid nodules and cervical lymph nodes. The patient had serum CA153 of 76.0 kU/L (normal, 0–25.0 kU/L), and a pre-operative thyroid function test showed slightly elevated level of serum thyroglobulin antibody (TgAb) (5.4 kU/L; normal, 0–4.0 kU/L), while serum levels of triiodothyronine (T3), thyroxine (T4), free T3 (FT3), free T4 (FT4), thyroid-stimulating hormone (TSH) and thyroid peroxidase antibody (TPOAb) were within the normal range.

The patient underwent total thyroidectomy after initial diagnosis, and histopathologic analysis revealed metastatic breast carcinoma to the bilateral thyroid (Figure 2a and b). The biopsied tissue was paraffin embedded, and the sections were stained with haematoxylin-eosin (HE). Immunohistochemical (IHC) staining showed that the thyroid carcinoma was negative for thyroid transcription factor-1 (TTF-1) (Figure 3a), cytokeratin (CK) 7 (Figure 3b), CK 20 (Figure 3c), human epidermal growth factor receptor 2 (HER2) (Figure 3d) and thyroglobulin (Figure 3e) but was positive for estrogen receptor (ER)
Case presentation (Cont.)

(Figure 3f) and progesterone receptor (PR) (Figure 3g). IHC staining also showed that Ki-67-positive cell population was >30% (Figure 3h). A conclusive diagnosis of metastatic breast carcinoma to the bilateral thyroid was made. The patient received second-line chemotherapy, cervical radiotherapy and endocrine therapy again after total thyroidectomy. Serum CA153 descended to a slightly high level of 35.9 kU/L (normal, 0–25.0 kU/L) in April 2011, and she then refused to undergo periodic second-line chemotherapy. The patient was followed up for 1 year and 8 months after her total thyroidectomy. She was found to have an elevated serum CA153 level of 304.9 kU/L (normal, 0–25.0 kU/L), but she showed no evidence of other regional metastatic breast carcinoma.

Figure 1: Ultrasonography ‘accidentally’ reveals the bilateral thyroid lobes and isthmus diffuse distribution of point-like calcifications and CDI does not show abnormal blood flow.

Figure 2: Breast cancer metastatic to the bilateral thyroid (HE stain): (a) original magnification ×100, (b) original magnification ×400.

Figure 3: IHC staining of the thyroid carcinoma was negative for (a) TTF-1, (b) CK 7, (c) CK 20, (d) HER2, (e) thyroglobulin, but it was positive for (f) ER and (g) PR. (h) IHC staining shows that Ki-67-positive cell population was >30%.

Discussion

The thyroid gland is a rare site for secondary metastatic lesion. Thyroid metastases could present long after the detection of a primary carcinoma, or the metastatic lesions could be discovered in the thyroid shortly after the detection of the primary carcinoma. The presently analyzed patient presented with left breast carcinoma in May 2003, right breast carcinoma in July 2008, recurrent breast carcinoma on the right chest wall in November 2008 and metastatic breast carcinoma to bilateral thyroid in November 2010. In autopsy studies, >24% of tumours have been found to metastasize to the thyroid in patients who have died of disseminated malignancy, but most of these thyroid metastases are clinically silent. Metastases are usually multiple or diffusely infiltrate thyroid tissues. In our patient, the ultrasonography revealed the bilateral thyroid lobes and isthmus diffuse distribution of point-like calcifications, which were similar to that presented in the literature. Metastatic disease involving the thyroid is usually observed in elderly individuals in their sixth and seventh decades of life. However, the presently analyzed female patient was only 41 years old. Metastatic tumours may present with scant symptoms and the absence of firm local manifestations and documented neoplastic disease in medical history may at first lead to an erroneous diagnosis. In our case, the history of the bilateral breast cancer was known at the time the patient was admitted, but whether it was a metastatic breast carcinoma to the thyroid or a primary tumour of the thyroid constituted a diagnostic dilemma for us. Therefore, an aggressive surgical approach was adopted by us, and total thyroidectomy was...
Discussion (Cont.)

performed intraoperatively. In the presented material, besides the medical history, a firm diagnosis of metastatic breast carcinoma to the bilateral thyroid could be established fundamentally based on the histology of paraffin-embedded sections and IHC. IHC was very useful in distinguishing metastatic breast carcinoma from primary thyroid carcinoma. In our case, the thyroid sample was negative for TTF-1, thyroglobulin, HER2, CK 7 and CK 20, but was positive for ER and PR. TTF-1 and thyroglobulin are sensitive and specific markers that should be positive in primary tumours of thyroid follicular epithelial origin. TTF-1 is usually expressed in thyroid medullary carcinoma and was negative in our patient. Thyroglobulin is negative in metastatic tumours and positive in most primary thyroid tumours. The expression of ER and PR identified the metastatic carcinoma from breast.

There has been no international consensus on the surgical approach to metastatic disease involving the thyroid gland. However, an aggressive surgical approach has been recommended by many authors, and most authors agree that surgical treatment is warranted in the absence of widespread metastatic disease or for palliation of local symptoms such as relieving dyspnea or dysphagia and facilitating a tracheostomy. Aggressive surgical treatment may be curative for solitary metastatic renal cell carcinoma. Nevertheless, if the primary tumour is not controlled, systemic metastasis or tumour cachexia may occur in advanced cancer patients; consequently, the aggressive surgical approach would not be generally preferred. Total thyroidectomy is recommended for patients with metastatic cancer limited to the thyroid because of the multifocality of metastases to the thyroid gland. Our patient underwent total thyroidectomy, and no significant neck lymph nodes were explored intraoperatively. The patient received second-line chemotherapy and radiotherapy after total thyroidectomy. This management policy also allowed for a safe postoperative levothyroxine substitution.

Metastatic disease of the thyroid is generally considered an ominous prognosis, and most affected patients cannot survive long enough because of extensive metastasis of tumour, in addition to clinical findings of the renal carcinoma metastases to the thyroid are often better biological behaviour. Our patient was followed up for 1 year and 8 months after her total thyroidectomy and found to have an elevated serum CA153 level of 304.9 kU/L (normal, 0–25.0 kU/L), but she presently shows no evidence of other regional metastatic breast carcinoma.

Conclusions

1. Clinicians should pay attention to the elevated CA153 levels after excision of the primary breast carcinoma.
2. We should increase the clinical awareness of metastatic disease to the thyroid, especially in patients with a history of malignancy.
3. We conclude that total thyroidectomy for the multifocality of metastases to the thyroid gland is feasible when metastatic cancer is limited to the thyroid. With a comprehensive treatment involving chemotherapy, radiotherapy and endocrine therapy, the survival of patients can be prolonged.

Abbreviations list

CA, carbohydrate antigen; CDFI, colour Doppler flow imaging; CK, ckytokinin; ER, estrogen receptor; FT₄, free T₄; FT₃, free T₃; HE, hematoxylin-eosin; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; PR, progesterone receptor; T₃, triiodothyronine; T₄, thyroxine; TgAb, thyroglobulin antibody; TPOAb, thyroid peroxidase antibody; TSH, thyroid-stimulating hormone; TTF-1, thyroid transcription factor-1.

Case report

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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References

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