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Case Report

Late Onset of an Overlooked Follicular Thyroid Carcinoma Presenting as a Chest Wall Tumor 10 Years Following Thyroidectomy

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ABSTRACT

Objective: Metastatic chest wall tumors resulting from thyroid carcinomas are not unusual; however, the late onset of metastasis of a follicular thyroid carcinoma (FTC) is extremely rare. We aim to present a report of a case with chest wall metastasis of an FTC 10 years following thyroidectomy.
Methods: Among the studies performed were chest wall tumor imaging, serum thyroid stimulating hormone determination, and histopathology of the chest wall tumor and thyroid tissue examination.
Results: An asymptomatic 28-year-old woman was noted to have a left-sided chest wall mass on a chest X-ray performed for a job application. She had a history of right hemithyroidectomy 10 years prior to her admission, which had been reported as a thyroid follicular adenoma. Computed tomography showed a tumor measuring 75 × 50 mm in diameter localized at the left paravertebral region. The maximum standardized uptake value of the tumor was seven in positron emission tomography. Histopathologic finding of the trucut biopsy of the chest wall tumor revealed metastasis of a differentiated thyroid carcinoma. The patient underwent a completion left hemithyroidectomy with chest wall resection and reconstruction. Previous right hemithyroidectomy material was examined and diagnosed as minimally invasive FTC. Histopathologic finding of the resected chest wall tumor was consistent with metastasis of an FTC.
Conclusions: Although extremely rare, the late metastasis of a thyroid carcinoma should be considered in the differential diagnosis of patients with chest wall tumors who have a previous history of thyroidectomy even with a diagnosis of benign tumor.

Introduction

Chest wall tumors comprise a heterogeneous group of lesions that are challenging to diagnose and treat. These neoplasms account for <5% of thoracic malignancies, and they can arise from any soft tissue or bony structure around the thoracic cavity. They may occur as primary or metastatic tumors. Metastatic chest wall tumors most frequently occur with hematogenic, lymphogenic, or transdiaphragmatic spread.[1] In addition, a needle biopsy of an intrathoracic or intra-abdominal primary tumor may result in an implantation metastasis of the tumor to the chest wall.[2,3]

Follicular thyroid carcinoma (FTC) accounts for approximately 10% of all thyroid cancers. It has a tendency of hematogenous metastasis with a rate of 6% to 20% compared with papillary thyroid carcinoma.[4] However, metastases to the chest wall in a long-term follow-up after surgery are extremely rare.[1]

Metastatic chest wall tumors resulting from thyroid carcinomas have been reported.[1,5–8] Here, we present a 28-year-old woman with a chest wall metastasis from FTC, which was misdiagnosed as follicular adenoma 10 years before her admission. The patient underwent an aggressive chest wall resection and reconstruction with vertebral column instrumentation.

Case Report

The patient was an otherwise healthy 28-year-old woman who was noted to have a left-sided mass on her chest X-ray, which was performed for a job application. The patient had a right hemithyroidectomy 10 years ago, which was pathologically diagnosed as

Abbreviations: DTC, differentiated thyroid carcinoma; FTC, follicular thyroid carcinoma; RAI, radioactive iodine; TSH, thyroid stimulating hormone; Tg, thyroglobulin.

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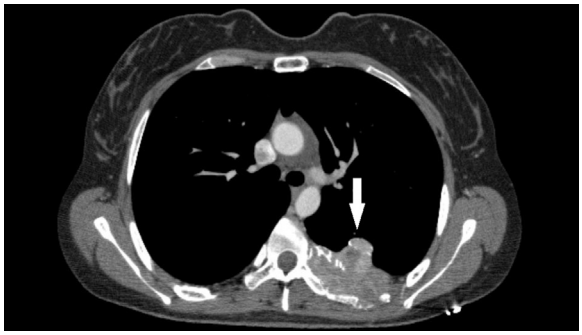

Fig. 1. Computed tomography showing a left-sided chest wall tumor localized at the paravertebral region.

a thyroid follicular adenoma. On physical examination, a Kocher incision of the previous thyroidectomy was visible on her neck. The thyroid gland was unremarkable without any nodule or lymphadenopathy. Laboratory examinations, including thyroid functions tests, were within the normal limits. Thyroid stimulating hormone (TSH) level was 1.08 (range, 0.27–4.2 mIU/L). Free triiodothyronine level was 4.64 (range, 3.1–6.8 pmol/L), and free thyroxine level was 15.17 (range, 12–22 pmol/L). Thyroglobulin (Tg) and antithyroglobulin levels were 22.42 (range, 3.5–77 ng/mL) and 12.44 (range, 0–115 mIU/L), respectively. Neck ultrasonography showed a left lobe and a residual right lobe with diameters of 11 × 17 × 52 mm and 6 × 7 × 24 mm, respectively, with bilateral and apparently benign lymph nodes.

Computed tomography of the thorax showed a rib destructing tumor, measuring 75 × 50 mm in diameter, which was localized at the left paravertebral region (Fig. 1). Trucut biopsy of the chest wall mass revealed a follicular-patterned lesion with luminal colloid-like material. Immunohistochemically, the follicular epithelium was positive for thyroid transcription factor-1 and Tg. No papillary-like nuclear features were observed. The tumor was located on the chest wall; thus, the possibility of an ectopic thyroid tissue was excluded, and it was reported as the metastasis of a differentiated thyroid carcinoma (DTC). The previous thyroidectomy material was obtained and examined in our pathology department. Hematoxylin and eosin-stained sections of the formalin-fixed paraffin-embedded tissue sections revealed an encapsulated follicular-patterned lesion. Papillary-like nuclear features were absent. Serial sections of the lesion revealed a focal capsular invasion, which

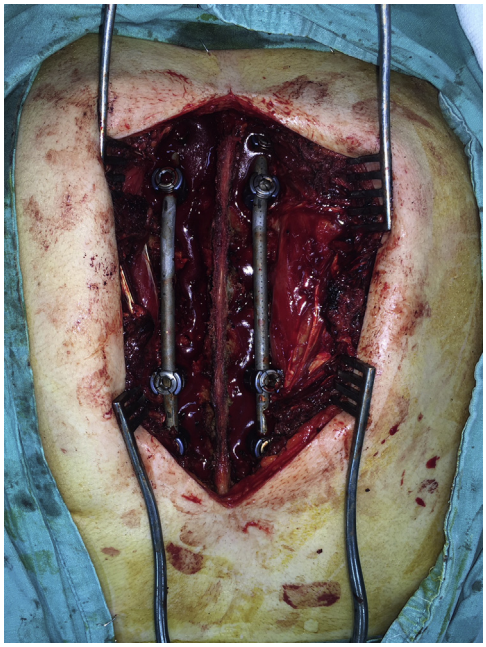

Fig. 3. Operative field following the fifth and sixth partial vertebrectomy with posterior instrumentation on the prone position.

was not present at the initial sections (Fig. 2), and the lesion was reported as minimally invasive FTC.

Positron emission tomography showed the mass with a maximum standardized uptake value of seven, with an increased uptake at the left adnexal location. Magnetic resonance of the brain and abdomen did not show any abnormality. The Gynecology department interpreted the left adnexal involvement as a lesion with a benign nature. On the other hand, magnetic resonance of the thorax showed tumor invasion to the pedicles and transverse processes of the fifth and sixth vertebrae.

The patient underwent a left total thyroidectomy and excision of the residual right thyroid lobe on supine position with Kocher incision. Later, she was placed on prone position for the fifth and sixth partial vertebrectomy with posterior instrumentation, which was performed with a posterior longitudinal incision (Fig. 3). Finally, we performed a chest wall resection including the fourth to seventh ribs on the right lateral decubitus position (Fig. 4) in

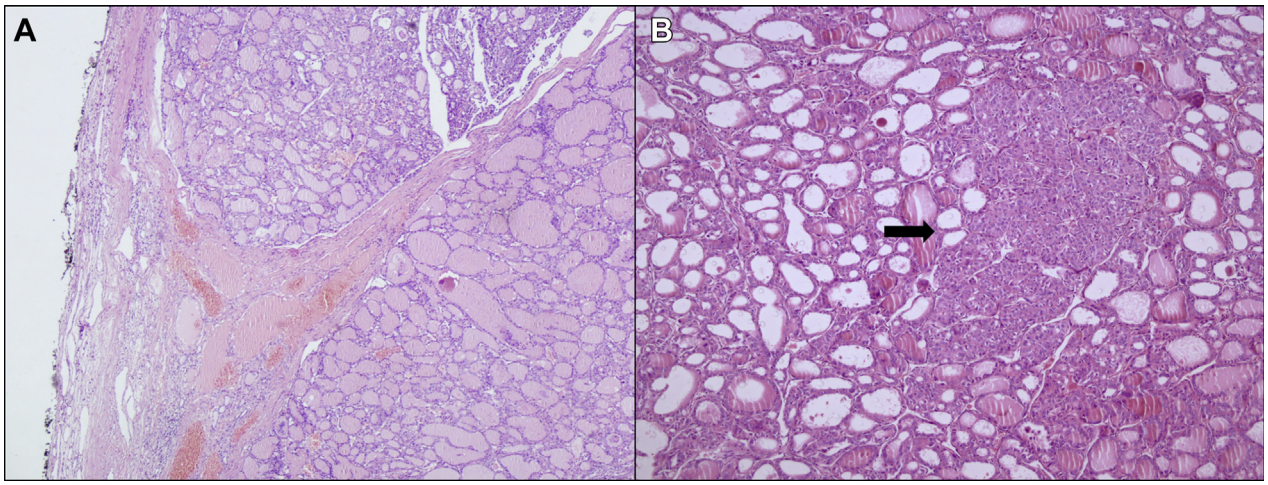

Fig. 2. Hematoxylin-eosin-stained sections of the thyroidectomy specimen that was performed in 2009. Follicular-patterned lesion with capsular invasion is seen (*A*, magnification: x4). Solid areas with oncocytoid features (arrow) are seen among the follicles without any obvious papillary-like nuclear features (*B*, magnification: x10).

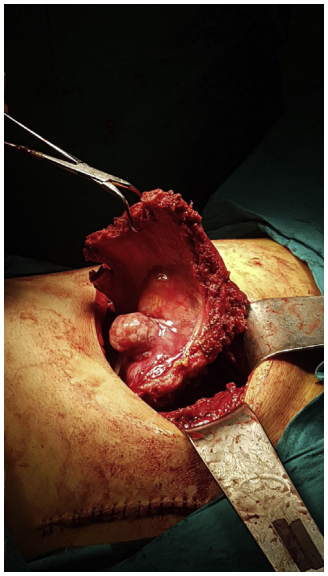

Fig. 4. En-bloc chest wall resection on the right lateral decubitus position.

addition to a sandwich graft reconstruction consisting of prolene mesh and methylmethacrylate. The postoperative course was uneventful, and she was discharged on postoperative day 7.

The histopathologic examination of the lesion revealed a follicular-patterned lesion with focal oncocytic differentiation, lacking papillary-like nuclear features. The morphology of the metastatic lesion was similar with the previous lesion of hemithyroidectomy specimen, which had been removed 10 years ago. The histologic diagnosis was metastasis of an FTC (Fig. 5). Interestingly, left thyroidectomy specimen revealed an area of 0.3 cm papillary microcarcinoma focus with classical architecture. The *KRAS, NRAS, BRAF,* and *TERT* promoter mutation profile of the primary tumor and the metastasis was investigated by reverse transcription polymerase chain reaction (for *KRAS, NRAS,* and *BRAF*); results of PCR-based direct sequencing (for *TERT*) were all negative in our patient.

TSH level was 63.16 (range, 0.27–4.2 mIU/L), and free thyroxine level was 3.43 (range, 12–22 pmol/L) at the first postoperative month. Tg and the anti-thyroglobulin levels were 0.373 (range, 3.5–77 ng/mL) and 19.59 (range, 0–115 mIU/L), respectively. The patient received 150 mCi of radioactive iodine (RAI) treatment at the first postoperative month. A whole-body I–131 scintigraphy after RAI revealed an increased uptake on the right side of the thyroidectomy site, possibly resulting from a remnant of the thyroid tissue. The patient was started with a treatment of gradually increasing doses of 75 mcg of levothyroxine sodium. On postoperative 6-month follow-up, free triiodothyronine level was 4.91 (range, 3.1–6.8 pmol/L), and free thyroxine level was 21.45 (range, 12–22 pmol/L). TSH and Tg levels were 0.007 (range, 0.27–4.2 mIU/L) and 0.04 (range, 3.5–77 ng/mL), respectively. The patient is doing well at 11 months postoperative and is receiving 150 mcg of levothyroxine sodium.

Discussion

Thyroid carcinomas are mostly papillary carcinomas, and the most common route of metastasis is lymphogenic spread; therefore, cervical lymphadenopathy is the most common presentation. On the other hand, FTC has a significantly less common prevalence of cervical lymph node metastases at diagnosis with a rate of 2% to 8% than papillary thyroid cancer. The prevalence increases up to 17% in a widely invasive FTC.[4] Although FTC is a relatively indolent differentiated thyroid cancer, distant metastasis may also occur in 5% to 19% of patients because it has a tendency to invade blood vessels and metastasize by hematogenous spread to distant sites as in our patient.[7] The most common locations of metastases are the bones and lungs, although other unusual sites, such as the parotid gland, skin, brain, ovary, adrenal gland, kidney, pancreas, breast, and eye, have also been reported.

Although synchronous metastasis of thyroid carcinoma to the chest wall is not uncommon,[1,7] we are aware of very few reports of FTC as a late onset of metastases to the chest wall.[5,8] Eroglu et al have reported a case of a woman who presented with a sternal tumor appearing 13 years after total thyroidectomy for an FTC.[5] Furthermore, Mssrouri et al have reported some cases with metachronous sternal metastasis at an average delay of 10 years after thyroidectomy.[8] Moreover, previous reports have emerged regarding the late onset metastasis of an occult FTC as a mass in the kidney[9] or in the ciliary body of the eye.[10] Matei et al have described a case of a patient with a renal mass who underwent a radical

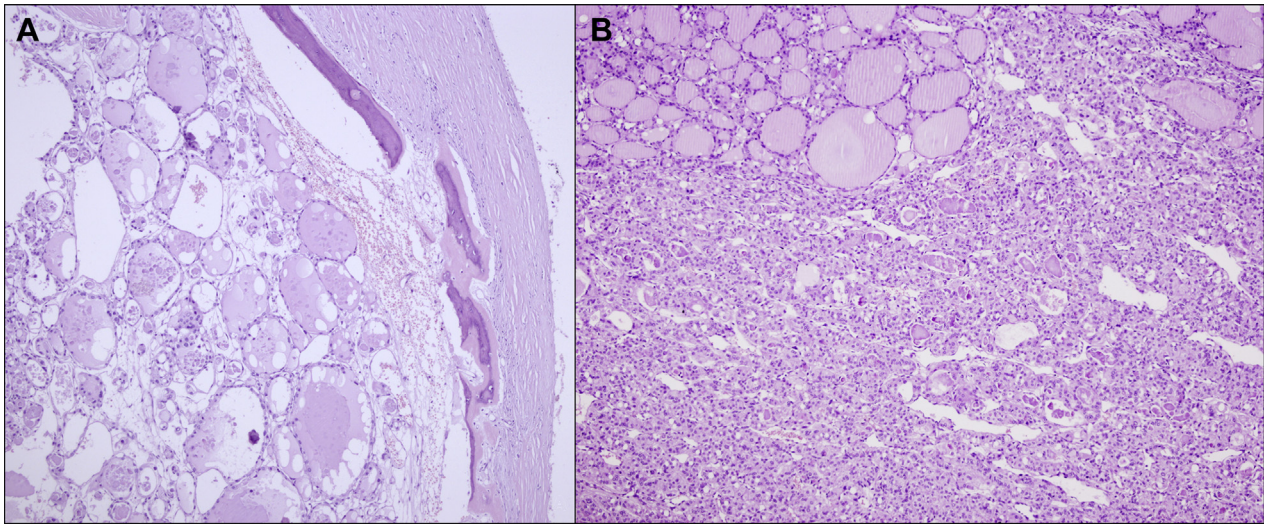

Fig. 5. Follicular-patterned lesion, lacking papillary-like nuclear features, is invading the soft tissue and bone (*A*, H&E, 10x magnification). Besides the follicular areas, more solid areas with oncocytoid features are seen (*B*, H&E, magnification: x10.) H&E = Hematoxylin-eosin–stain.

surgery with subsequent RAI treatment, revealing itself as a solitary metastasis from FTC, appearing 10 years after a total thyroidectomy.[9] Similarly, Lommatzsch et al has reported a case of a 20-year-old woman who was diagnosed to have a differentiated FTC following the excision of the ciliary body in her left eye. Iridocyclectomy was performed to excise the tumor, which was believed to be a melanoma. However, histologic examination showed metastasis of a well-differentiated FTC, which had been excised 16 years before the diagnosis. This patient was treated by total thyroidectomy and RAI.[10] The previous diagnosis in this patient was a benign thyroid adenoma, which was diagnosed as FTC after the reevaluation, as in our case.

Slutzky-Shraga et al presented a series of metastatic DTC who had been initially diagnosed with benign follicular lesion.[11] Similarly, metastatic bony tumors of thyroid cancer may even present without any histologically identifiable or detectable primary thyroid malignancy.[12,13] The proposed mechanisms to explain this issue include missed primary tumors due to occult location and regression of the primary tumors.[11,13] Our case was also diagnosed as follicular adenoma, and the chest wall mass was reported to be a metastasis of DTC. In this condition, reevaluation of the previous thyroidectomy specimen and residual thyroid tissue becomes mandatory. The accurate diagnosis of thyroid follicular tumors is challenging and controversial. Careful and intense histopathologic examination of the lesion is necessary for an accurate diagnosis. As in our case, serial sections could reveal capsular and/or vascular invasion, which were not seen at the primary sections. In addition, the actual resection specimen of the left thyroid lobe in our case showed an area of papillary microcarcinoma with classical architecture. The histomorphology of the chest wall mass was consistent with the metastasis of FTC.

On the other hand, Melo et al showed the significance of *TERT* promoter mutation as an indication for a clinically aggressive tumor with an unfavorable survival outcome and its independent prognostic value in a large series of DTCs.[14] Additionally, Malik et al reported that the differentiated thyroid cancers presenting with bone metastasis have a high prevalence of *TERT* mutations with frequently coexisting RAS mutations regardless of the tumor size. They proposed that these tumors with this molecular signature have a favorable response to RAI treatment.[15] However, the primary and metastatic tumors did not have any mutation, including *KRAS, NRAS, BRAF,* and *TERT,* as in our patient.

Thyroid carcinoma with distant metastasis has a 5-year mortality risk as high as 25%.[16,17] In addition, FTC has a comparably favorable 10-year survival rate of any tumor with bone metastasis with a rate of 13% to 21%, provided that it is an early diagnosis.[18] The most common site of bone metastasis in FTC is the vertebrae in 52.2% of cases, followed by the femur (20.4%), skull (16.0%), pelvis (16.0%), and clavicle (13.6%). The following have been proposed as the prognostic predictors in patients with bone metastasis: high serum calcium levels, aggressive tumor type, delayed diagnosis, male sex, age over 65 years, and multiple organ involvement.[19] Thyroid cancer is unique among malignancies because age is accepted as one of the staging variables. Younger age predicts an excellent prognosis and patients older than 40 or 50 years of age show unfavorable prognosis.[20] However, our patient developed a chest wall metastasis 10 years after surgery, although she had undergone thyroid surgery at the age of 18.

The metastasis of thyroid carcinoma requires additional surgical resection, external beam radiotherapy, endocrine therapy, or RAI treatment. Wu et al found that patients with bone metastases of differentiated thyroid cancer, those receiving RAI treatment with combined treatments, such as surgery, radiofrequency ablation, cryotherapy, arterial embolization, external beam radiation, Cyberknife, systemic targeted therapy, and anti-resorptive medication, had comparably more favorable survival rates than those who received RAI treatment alone. Moreover, initial RAI therapy within the postoperative 6 months resulted in a better median survival.[21] On the other hand, surgery appears as the optimal treatment for bone metastasis of thyroid carcinoma provided that the metastasis is solitary and feasible as in our case. Surgery may also be recommended for RAI-resistant bone metastases of thyroid carcinoma.[6] Moreover, the resection of multiple bone metastases can enhance the efficacy of RAI treatment for pulmonary metastases with resultant prolonged survival.[5] In addition, immunotherapy with pembrolizumab, external beam radiation, and bisphosphonate therapy might be helpful for patients who do not benefit from an initial adjuvant RAI treatment and metastasectomy.[18,22] Moreover, the Food and Drug Administration approved multiple kinase inhibitor drugs that act similar to anti-angiogenic multikinase inhibitors, such as vandetanib, cabozantinib, sorafenib, and lenvatinib, and are available for advanced thyroid cancer. Other drugs for this indication are mutation-specific dabrafenib/trametinib for BRAF-mutated anaplastic thyroid cancer and larotrectinib for NTRK-fusion thyroid cancer.[23]

Conclusion

Although extremely rare, a metastatic chest wall tumor from a thyroid carcinoma may occur in the long-term follow-up in patients who had undergone a thyroid resection even with a benign tumor diagnosis. The possibility of misdiagnosis should be kept in mind for an accurate patient management. Aggressive surgical resection might be one of the optimal choices of treatment for these patients who present with a solitary metastasis.

Disclosure

The authors have no multiplicity of interest to disclose.

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