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Sonographic Presentation of Metastases to the Thyroid Gland: A Case Series

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Incidental sonographic discovery of thyroid nodules is an increasingly common event. The vast majority is benign, and those that are malignant, are generally associated with an indolent course and low mortality. Sonographic scoring systems have been developed to help clinicians identify nodules that warrant prompt fine-needle aspiration cytology (FNAC), but they are based largely on experience with papillary thyroid cancers. We analyzed the performance of four scoring systems widely used for this purpose (American Thyroid Association Guidelines, American Association of Clinical Endocrinologists/American College of Endocrinology/Associazione Medici Endocrinologi Guidelines, European Thyroid Imaging Reporting and Data System, and Korean Thyroid Imaging Reporting and Data System) in patients whose nodules proved to be metastases from other solid cancers. Such nodules reportedly account for 0.2% to 3% of all thyroid malignancies. Each scoring system was used to assess retrospectively the malignancy risk and indications for FNAC of five patients' thyroid nodules that were ultimately diagnosed as metastases (from renal cell carcinoma, breast cancer, and lung cancer in two cases and esophageal cancer). The primaries identified in these cases are those most commonly reported to metastasize to the thyroid. In two cases, the thyroid metastases were the first sign of undetected neoplastic disease. Although sonography alone cannot distinguish thyroid metastases from primary thyroid malignancies, all four scoring systems classified the metastatic nodules as suspicious enough to require FNAC. The five cases accounted for 0.2% of those cytologically examined in our center. In most cases, cytology provided useful guidance for the subsequent management of these lesions, which differs from that of primary thyroid cancers and requires multidisciplinary input.

Freeform/Key Words: cytology, diagnosis, fine-needle aspiration, metastasis, thyroid nodule, TIRADS

Detection of asymptomatic thyroid nodules during ultrasound screening programs or imaging performed for other indications is increasingly common, and the clinical management of these lesions is a challenge. Because most nodules are benign, it is important to avoid overdiagnosis and overtreatment. Clinical practice guidelines recommend restriction of fine-needle aspiration cytology (FNAC) to selected lesions whose ultrasonographic features are associated with malignancy. Several scoring systems have been developed for this purpose [1–4]. The "suspicious" features considered vary from system to system, but most (*e.g.*, marked hypoechogenicity, irregular margins, microcalcifications) have been selected on the

Abbreviations: CK, cytokeratin; FDG, fluorodeoxyglucose; FNAC, fine-needle aspiration cytology; ICTC, Italian Consensus for Thyroid Cytopathology.

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basis of studies of papillary thyroid cancers. Some of the systems have also been found to perform well in the detection of medullary thyroid cancer [5], but they are less accurate in patients with follicular thyroid cancers [6].

What about the 0.2% to 3.0% of thyroid malignancies that ultimately prove to be metastases from other solid tumors [7, 8]? Thyroid metastases have been reported in several types of cancer, the most common being renal-cell, lung, breast [9], and colon carcinomas [10]. Despite their rarity, these entities must be considered during the workup of new thyroid nodules. No data are available on the performance of ultrasound risk-assessment systems in patients whose thyroid nodules are metastatic. To address this gap, we reanalyzed five cases of thyroid metastases that were referred to our unit for assessment of thyroid nodules, retrospectively calculating the indication for FNAC using four of the ultrasound-based systems most widely used for this purpose (Table 1).

1. Cases

Patient 1 was a 57-year-old woman being followed for three small, apparently benign, thyroid nodules detected in 2005. The patient had a right nephrectomy with adrenalectomy in 2003 for clear-cell renal carcinoma (American Joint Committee on Cancer tumor-lymph nodes-metastasis stage pT1b), but regular oncologic follow-up assessments had been negative. Neck ultrasound performed in November 2012 revealed growth of one of the three nodules [Fig. 1(A)]. Given its ultrasound features (Table 1), this nodule was subjected to FNAC, which yielded indeterminate results [Bethesda class III, Italian Consensus for Thyroid Cytopathology (ICTC) TIR3B]. Total thyroidectomy was performed, and the nodule was histologically diagnosed as metastatic renal-cell carcinoma; the patient's other two nodules were benign.

Patient 2 was a 69-year-old man with lung adenocarcinoma (American Joint Committee on Cancer tumor-lymph nodes-metastasis stage pT2, pN0), who had undergone right pulmonary

Table 1. Features of the Metastatic Thyroid Nodules and Their Sonographically Estimated Risks of Malignancy

Case/Source of the Metastasis	Sonographic Features	Estimated Risk of Malignancy
Patient 1—Renal cell carcinoma [Fig. 1(A)]	Solid, inhomogeneous (central hypoechogenicity), smooth margins Dimensions: 9.5 × 8.7 × 17.5 mm	AACE: intermediate ATA: intermediate EU-TIRADS: 4 K-TIRADS: 4
Patient 2—Lung adenocarcinoma [Fig. 1(B)]	Solid, hypoechoic, irregular margins Dimensions: 13.3 × 17.6 × 20.4 mm	AACE: high ATA: high EU-TIRADS: 5 K-TIRADS: 5
Patient 3—Breast cancer [Fig. 1(C) and 1(D)]	Solid, hypoechoic, irregular margins Dimensions: 20.3 × 16.9 × 25.9 mm One suspicious lymph node (ipsilateral)	AACE: high ATA: high EU-TIRADS: 5 K-TIRADS: 5
Patient 4—Esophageal cancer [Fig. 1(E)]	Solid, markedly hypoechoic, irregular margins Dimensions: 20.7 × 20.8 × 32.3 mm Suspicious lymph nodes (bilateral)	AACE: high ATA: high EU-TIRADS: 5 K-TIRADS: 5
Patient 5—Lung cancer [Fig. 1(F)]	Solid, hypoechoic with focal marked hypoechogenicity, irregular margins Dimensions: 23 × 22 mm Suspicious lymph nodes (bilateral)	AACE: high ATA: high EU-TIRADS: 5 K-TIRADS: 5

TIRADS 4 and 5 indicate nodules with intermediate and high suspicion of malignancy, respectively.
Abbreviations: AACE, American Association of Clinical Endocrinologists; ATA, American Thyroid Association; EU-TIRADS, European Thyroid Imaging Reporting and Data System; K-TIRADS, Korean Thyroid Imaging Reporting and Data System.

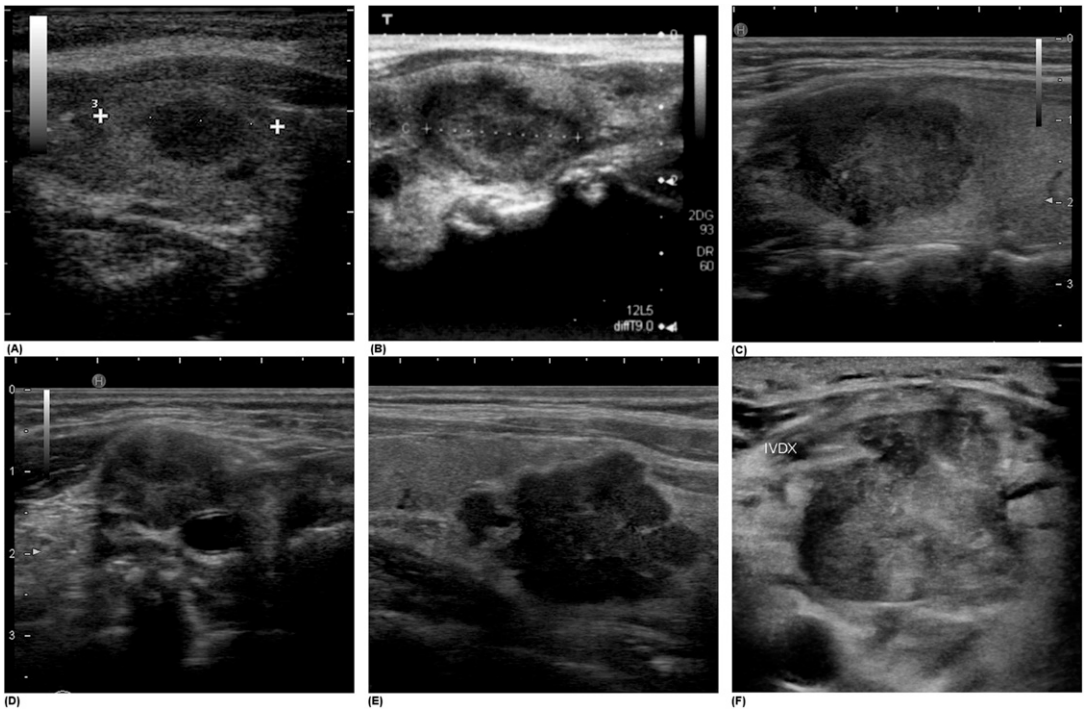

Figure 1. Ultrasonographic images of the metastatic lesions (A) renal cell carcinoma metastasis to the thyroid; (B) thyroid metastasis from lung adenocarcinoma; (C) thyroid metastasis and (D) level 2 cervical lymph node metastasis from breast cancer; (E) thyroid metastasis from esophageal cancer; and (F) thyroid metastasis from lung cancer. Detailed descriptions and US classifications are provided in Table 1.

lobectomy in March 2013. Follow-up imaging studies [full-body CT and 18-fluorodeoxyglucose (FDG)-positron emission tomography-CT] were unremarkable until April 2015, when focal FDG uptake was noted in the left thyroid lobe. In 2005, the patient had undergone radioiodine treatment of a hyperfunctioning thyroid nodule and had remained euthyroid since then. He was referred to our unit for assessment of the new nodule. Given its size and sonographic appearance [Table 1 and Fig. 1(B)], FNAC was performed. The lesion, unequivocally malignant (Bethesda class VI; ICTC TIR5), was composed of epithelial cells compatible with lung cancer. Total thyroidectomy was performed, and the lesion was histologically confirmed to be metastatic lung adenocarcinoma.

Patient 3 was a 47-year-old woman with metastatic ductal breast carcinoma (estrogen- and progesterone-receptor positive). In 2005, she had had a right mastectomy with homolateral lymph node dissection, followed by adjuvant chemotherapy. Reconstructive surgery performed in 2010 revealed other metastatic nodes in the right axilla, and bone metastases were discovered shortly thereafter. These metastases were treated with several courses of chemotherapy. In 2014, routine ultrasonography by her oncologist revealed a single, nonsuspicious nodule in the thyroid isthmus, which was being managed with sonographic surveillance alone. A repeat sonogram obtained in November 2017, because of a palpable neck mass, disclosed three additional thyroid nodules (one in the right lobe; two in the left) and a suspicious lymph node in the right lateral neck [Table 1 and Fig. 1(C) and 1(D)]. FNAC of the lymph node and the right lobe thyroid nodule revealed epithelial cells suggestive of metastatic breast carcinoma (Bethesda class VI; ICTC TIR5). Surgery—performed mainly for diagnostic purposes (lymph node biopsy, thyroid lobectomy)—confirmed the cytological findings, showing diffuse infiltration by ductal breast cancer.

Patient 4, a 39-year-old man, was referred to our unit by his otolaryngologist in November 2017 for assessment of recent-onset dysphagia and a palpable mass in the left lateral neck. Neck ultrasonography revealed a highly suspicious nodule in the left thyroid lobe [Fig. 1(E)],

along with other smaller nodules, and a suspicious lymph node in the right lateral neck (level III). FNAC of the left lobe thyroid nodule and contralateral lymph node revealed neoplastic epithelial cells suggestive of a nonthyroidal primary malignancy. In light of these findings, thyroid surgery was deferred and an 18-FDG-positron emission tomography-CT scan ordered. Focal uptake was seen in the esophageal wall, and the presence of esophageal adenocarcinoma was confirmed by endoscopic biopsy.

Patient 5 was a 69-year-old man undergoing followup in the hematology outpatient clinic for a cutaneous marginal zone lymphoma. In February 2018, a palpable lymph node was noted in the lateral neck. The sonographic examination by the hematology staff revealed an enlarged thyroid with hypoechoic nodules in each lobe. Multiple suspicious lymph nodes were seen bilaterally. Surgical biopsy of the most suspicious lymph node revealed connective and muscle tissues infiltrated by malignant epithelial cells, extensive necrosis, and no lymphoid tissue. Immunohistochemical findings [positivity for cytokeratin (CK)AE1/AE3, CK8/18, CK19, CK7, and thyroid transcription factor-1; negativity for CK20, napsin A, chromogranin A, thyroglobulin, melan-A, prostate-specific antigen, prostatic-specific acid phosphatase, neural cell adhesion molecule, p63, p40, and synaptophysin] were considered compatible with metastasis from a pulmonary or possibly thyroid malignancy. FNAC of the left lobe thyroid nodule [Table 1 and Fig. 1(F)], performed by our staff, revealed malignancy (Bethesda class VI; ICTC TIR5) with poorly differentiated epithelial cells. Full-body CT confirmed the presence of multiple solid nodules in both lungs, the largest (33 × 24 mm) located at the apex of the left lung.

2. Conclusions

Solid tumor metastases to the thyroid gland are rare: the lesions reported previously represented 0.2% of the thyroid nodules subjected to FNAC in our unit. The origins of the metastases in these five cases were those most commonly reported in the literature (*i.e.*, kidney, lung, breast, gastrointestinal tract) [7, 8]. The possibility of metastasis must be considered in the differential diagnosis of any new thyroid nodule. This is especially true in patients with histories of cancer, regardless of how long ago it was diagnosed and the current status of the disease. However, as illustrated by cases 4 and 5, thyroid metastases can also be the first sign of unsuspected cancer.

Systems currently used to assess sonographically the likelihood of malignancy in patients with thyroid nodules are helpful [1–4], but sonographic features alone cannot distinguish primary and metastatic malignancies of the thyroid. However, all four of the systems we tested consistently classified our patients' metastatic lesions among those few that were suspicious enough to warrant cytological evaluation, and in most cases, cytological findings provided useful guidance for subsequent management, highlighting the need for additional diagnostic procedures rather than immediate thyroidectomy (the option chosen in case 1, where the FNAC was indeterminate). Treatment decisions in these cases require multidisciplinary input. Thyroid surgery can be palliative when metastases are causing compressive symptoms, but it has traditionally been regarded as futile in the presence of diffuse metastatic involvement, which is generally associated with a poor prognosis. However, a recent meta-analysis [8] showed that total thyroidectomy increases both disease-free and overall survival in patients with thyroid metastases, even when accompanied by disseminated disease.

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