Sonographic Findings of Metastatic Disease to the Thyroid

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The goal of this study was to evaluate the ultrasonographic findings of thyroid metastases arising from non-thyroid primaries. The study over a 5-year period comprised nine patients who had histopathologically proven metastatic disease to the thyroid. Ultrasonography was available in all cases. Ultrasound-guided needle aspiration was performed on 10 suspected nodules as determined by ultrasound. The ultrasonographic findings were analyzed in two different ways. The first analysis included only those nodules biopsied, and the second analysis included all the nodules, biopsied and non-biopsied. The primary neoplasms were breast carcinoma (n=6), uterine leiomyosarcoma (n=1), cervical carcinoma (n=1), and nasopharyngeal carcinoma (n=1). Excluding 2 nodules, the 8 remaining metastatic nodules exhibited ill-defined hypoechoic character with heterogeneous texture. The other two nodules showed relatively circumscribed iso- or hypo-echoic character with cystic portion. From the analysis of ultrasonographic findings including all thyroid nodules irrespective of pathologic proof, 7 cases - excluding the 2 cases from the 9 cases - showed unilateral or bilateral multiple nodules suspected of metastasis. There was no evidence of microcalcification in any thyroid nodules. In conclusion, the sonographic findings of the thyroid metastatic nodules were not specific, but unilateral or bilateral multiple suspected thyroid nodules without evidence of microcalcification may be suggestive of metastatic nodules among patients with a known primary non-thyroidal tumor.

Key Words: Thyroid, neoplasms, thyroid, US thyroid, biopsy

INTRODUCTION

Despite the fact that the thyroid gland is one of the most vascular organs of the body, clinical and surgical series have reported an incidence of secondary malignancies in this gland of only 3%. Nevertheless, thyroid metastases are not an exceptional finding; at autopsy they are encountered in a variable percentage (2% to 24%) of patients affected by malignant neoplasms.

The thyroid nodules found in patients who have malignant disease, could be benign thyroid diseases, second primaries, or metastases from other organs. High-resolution ultrasonography, being highly sensitive in the detection even of those thyroid nodules not palpable in a clinical examination, plays a major role in guiding fine-needle aspiration (FNA) of such lesions.

We evaluated the sonographic findings of thyroid metastases arising from non-thyroidal primary.

MATERIALS AND METHODS

A retrospective review of our histopathologic records over the period January 1995 to April 2000 identified 9 cases of metastatic lesions to the thyroid gland. Lesions arising from the direct invasion from the head and neck were discarded from the study.

The patients' age and gender, the interval period of development of thyroid metastases since the primary lesion was diagnosed, primary cancer site, local tumor recurrence, clinical presentation, and metastasis in other organs were

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analyzed.

Following ultrasonography for all 9 patients, ultrasonography guided FNA was performed on 10 representative suspected thyroid nodules in the 9 patients. Follow-up ultrasonography was performed retrospectively in 2 patients at six-and-eight months after the initial diagnosis.

Ultrasonography was performed with HDI 3000 and UM-9 HDI scanner (Advanced Technology Laboratories, Bothell, Wash, U.S.A.) with broad bandwidth of 10-5 and 7-4 MHz. Aspirates were obtained using a pistol-grip syringe holder (MANAN Aspir-Gun, Medical device technologies Inc, Gainesville, Florida, U.S.A.), 20-ml plastic disposable syringe, and a 21-gauge needle. Any of the following were regarded as indicating the presence of malignant thyroid nodules; hypoecho-genicity relative to the normal thyroid paren-chyma, microcalcifications, poorly defined mar-gins, infiltration of structures around the thyroid, and cervical lymph node metastasis. Lymph nodes, of a rounded shape with no echogenic hilum which exceeded the size criteria for malignancy were regarded as indicative of malignant findings.

The ultrasonographic examinations of the thy-roid nodules, retrospectively reviewed by consen-sus reading of two experienced radiologists (S.Y.C, E.K.), were analyzed in two different ways. The first analysis included only those nodules biopsed and pathologically proven. The second analysis included all the nodules, biopsed and non-biopsed. Special attention was given to the echogenicity of the masses relative to that of the thyroid gland (hypoechoic, isoechoic, hypoecho-choic); the character of the margin (well defined or ill defined); the echogenic texture (homogeneous or heterogeneous); the presence or absence of any cystic portion or septation or calcification; the number of lesions (single or multiple); and the laterality of lesions (unilateral or bilateral). The results of CT were available in 2 cases.

Cytopathologic review was performed for all patients. Nine of the 10 nodules in the 9 patients were diagnosed as metastatic thyroid tumor on the basis of cytology. Cytologic findings of the aspiration biopsy specimens were identical to those of the primary tumors in 4 patients, for whom pathologic slides of the primary tumor were available. Total thyroidectomy was performed on 2 patients. One patient with breast cancer was initially diagnosed with a primary thyroid tumor (anaplastic carcinoma) according to the cy-tology report but was later proven to have metastasis by surgical pathology. The other patient with breast cancer underwent surgery with consent.

RESULTS

The average age of the 9 patients at the time of diagnosis of the thyroid metastases was 52 years (range: 41-61 years old). All patients were women. The thyroid metastases appeared on average 48 months (range: 1 year 10 months-8 years) after discovery of the primary tumor.

The 9 primary tumors confirmed as metastasis to the thyroid resulted from breast carcinoma (6 cases), uterine leiomyosarcoma (1 case), cervical carcinoma (1 case) and nasopharyngeal cancer (1 case). At the time of diagnosis of thyroid metastasis, local tumor recurrence at primary site was found in 4 cases, which were from breast cancer.

Of the 9 patients, 2 presented only with a single palpable thyroid mass while 1 had both palpable thyroid masses and cervical lymph nodes. In 2 patients, thyroid nodules due to metastatic disease were incidentally discovered during US due to palpable axillary masses and cervical lymph nodes. In the remaining 4 patients with past his-tories of breast cancer, metastatic thyroid nodules were incidentally discovered during postoperative follow-up ultrasonography. All patients had extensive metastases in other organs at the time of ultrasonographic examination (Table 1).

The ultrasonographic finding of thyroid metas-tatic nodules as proved by aspiration are presented in Table 2. Six cases showed enlarged cervical lymph nodes. Excluding only 2 from the 10 nodules, the other 8 metastatic nodules ex-hibited ill-defined hypoechoic character with hetero-geneous texture. The remaining 2 nodules dis-played relatively well-defined margins, but partly ill-defined margins. Two cases revealed some cystic portion within the nodules. One (case 1) of these two presented an isoechoic nodule with internal cystic portion. The other, from uterine leiomyosarcoma (case 7), manifested a hypoechoic...
Table 1. Patients with Metastatic Disease to the Thyroid

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Primary site</th>
<th>Period preceding thyroid mass (months)</th>
<th>Clinical presentation</th>
<th>Other metastases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Breast</td>
<td>49</td>
<td>No symptom</td>
<td>Lung, bone</td>
</tr>
<tr>
<td>2</td>
<td>Breast</td>
<td>61</td>
<td>No symptom</td>
<td>Lung</td>
</tr>
<tr>
<td>3</td>
<td>Breast</td>
<td>51</td>
<td>Palpable cervical node</td>
<td>Lung, bone, liver</td>
</tr>
<tr>
<td>4</td>
<td>Breast</td>
<td>32</td>
<td>No symptom</td>
<td>Lung, liver</td>
</tr>
<tr>
<td>5</td>
<td>Breast</td>
<td>22</td>
<td>No symptom</td>
<td>Bone, peritoneal carcinomatosis</td>
</tr>
<tr>
<td>6</td>
<td>Breast</td>
<td>33</td>
<td>Thyroid mass</td>
<td>Lung</td>
</tr>
<tr>
<td>7</td>
<td>Uterus</td>
<td>57</td>
<td>Thyroid mass</td>
<td>Lung</td>
</tr>
<tr>
<td>8</td>
<td>Nasopharynx</td>
<td>60</td>
<td>Axillary mass</td>
<td>Lung, bone, brain</td>
</tr>
<tr>
<td>9</td>
<td>Cervix</td>
<td>32</td>
<td>Thyroid mass</td>
<td>Lung</td>
</tr>
</tbody>
</table>

& palpable cervical node

Table 2. Ultrasonographic Finding of 10 Metastatic Nodules Confirmed with Fine Needle Aspiration

<table>
<thead>
<tr>
<th>Echogenicity</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperechoic</td>
<td>0</td>
</tr>
<tr>
<td>Isoechoic</td>
<td>1</td>
</tr>
<tr>
<td>Hypoechoic</td>
<td>9</td>
</tr>
<tr>
<td>Margin</td>
<td></td>
</tr>
<tr>
<td>Well-defined</td>
<td>2</td>
</tr>
<tr>
<td>Ill-defined</td>
<td>8</td>
</tr>
<tr>
<td>Echogenic texture</td>
<td></td>
</tr>
<tr>
<td>Homogeneous</td>
<td>1</td>
</tr>
<tr>
<td>Heterogeneous</td>
<td>9</td>
</tr>
<tr>
<td>Irregular septation</td>
<td>1</td>
</tr>
<tr>
<td>Cystic portion</td>
<td>2</td>
</tr>
</tbody>
</table>

Two cases (cases 3, and 8) registered a rapid increase in both nodule size and number on the 6 and 8 month follow-up ultrasonography, respectively, which is highly suggestive of metastatic nodules rather than primary malignancy or benignancy (Fig. 2). The results of CT scans, available in 2 cases (cases 3, and 6), showed a diffusely infiltrative hypodense lesion in both lobes of the thyroid, as well as bilateral cervical lymphadenopathy, observations that correlated well with the ultrasonographic findings (Fig. 3).

All ultrasonographic findings of thyroid nodules were also analyzed, irrespective of the cytopathologic proof (Table 3). Six cases with multiple unilateral or bilateral suspected nodules (cases 3, 4, 5, 6, 8, and 9) were also associated with a high possibility of metastasis. However, the exact diagnosis of case 1 with two suspected nodules and multiple benign looking nodules and cases 2 and 7 with only solitary suspected nodules could not be differentiated into either primary malignancy or metastatics nodule by ultrasonography (Fig. 4).

Fig. 1. Case 7. Thyroid metastasis arising from uterine leiomyosarcoma in a 61-year old woman. Transverse sonogram shows a relatively circumscribed cystic mass (large arrows) with irregular walls and septae (small arrows) located in the right lobe of the thyroid. This finding is similar to that of uterine leiomyosarcomas. (T, trachea.)
nodules (arrows) which have increased in number and size. C. Enhanced CT scan shows ill-defined hypodense nodules (arrows) in both lobes of the thyroid.

**Table 3. Analysis of ultrasonographic Finding in Metastatic Disease to the Thyroid**

<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral solitary suspected nodule (case 2, 7)</td>
<td>2</td>
</tr>
<tr>
<td>Unilateral multiple suspected nodules (case 5)</td>
<td>1</td>
</tr>
<tr>
<td>Bilateral multiple suspected nodules (case 3, 4, 6, 8, 9)</td>
<td>5</td>
</tr>
<tr>
<td>Bilateral two suspected and multiple benign looking nodules (case 1)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total cases</strong></td>
<td><strong>9</strong></td>
</tr>
</tbody>
</table>

**Fig. 2.** Case 8. Thyroid metastasis arising from nasopharyngeal carcinoma in a 60-year old woman. A. Transverse sonogram of the right lobe of the thyroid shows multiple masses with inhomogeneous hypo- and isoechoic texture. The mass reveals a small anechoic area, consistent with necrosis (arrows). (C, carotid artery; T, trachea.) B. Despite 7 months of radiation therapy, longitudinal sonogram of the right lobe of the thyroid shows ill-defined conglomerated masses (arrows) in both lobes of the thyroid.

**DISCUSSION**

Among patients with a history of a malignant neoplasm, metastatic spread to the thyroid gland is far more common than primary malignant tumors of thyroid origin; however, most metastases are discovered only at autopsy.\textsuperscript{9,11}

Primary tumors that most frequently metastasize to the thyroid gland are the ones that most often give rise to blood-borne metastases, such as malignant melanoma, renal, breast and lung carcinoma, and, less frequently, secondary lesions...
from pancreatic and gastrointestinal malignancies.10,12-14

Metastatic lesions usually do not present an important clinical problem because they are most often small and are generally associated with evidence of widespread malignant disease.15-18 However, some patients present with symptoms such as dysphagia, stridor, hoarseness, or a palpable neck mass.12,19-21 In this study, five of the 9 patients presented with clinical symptoms. And in the other 4 patients with a past history of breast cancer, metastatic thyroid nodules were incidentally discovered during ultrasonography. Because an association between breast cancer and thyroid

Fig. 3. Case 9. Thyroid metastasis arising from cervix carcinoma presents as a palpable thyroid mass and cervical lymph nodes in a 51-year-old woman. A. On transverse sonogram of the right lobe of the thyroid, the majority of the gland is hypoechoic and inhomogeneous. The remaining normal thyroid tissue is seen in peripheral portion. (C, carotid artery; T, trachea.) B. Enhanced CT scan shows a diffusely enlarged gland which appears hypodense, suggesting an infiltrative process.

Fig. 4. Case 2. Thyroid metastasis arising from breast carcinoma in a 61-year old woman. A. Transverse sonogram of the right lobe of the thyroid shows an ill-defined hypoechoic nodule (arrows). (C, carotid artery.) B. Longitudinal sonogram of the left lobe of the thyroid shows three nodules. The first one is a heterogeneous isoechoic nodule, with a partly ill-defined margin and cystic portion, which was regarded as a suspected nodule (arrowhead). And it was confirmed to be a metastatic nodule by aspiration. The second one (open arrowhead) is a circumscribed isoechoic nodule and the third one (closed arrow) shows eggshell calcification. Although not pathologically proven, these three nodules were regarded as benign nodules according to ultrasonographic findings.
disease has been suggested by some investigators and because thyroid nodules are more frequently found in women, we simultaneously examined the thyroid during breast ultrasonography. Consequently, the metastatic thyroid nodules found in the breast cancer patients did not reveal any symptoms and represented a large proportion of the metastatic nodules to the thyroid in our study.

Not all suspected thyroid nodules were aspirated on and FNA was performed only on representative suspected thyroid nodules. The remaining suspected thyroid nodules not proven by pathology may have been benign nodules, secondary primaries or metastases from a distant primary. However it is possible that some of the benign looking nodules were actually malignant. Although metastatic carcinoma of nonthyroidal origin may mimic primary thyroid neoplasm in imaging studies, the authors suggest that the ultrasonographic finding in the present study of 6 cases with multiple unilateral or bilateral suspected nodules indicates a high possibility of metastasis in patients with a known primary tumor. Each metastatic nodule of the thyroid was similar in appearance on ultrasonographic examination to primary thyroid neoplasms, but presented no evidence of the microcalcification typically found in papillary carcinoma.

Despite the relative specificity of the pathologic appearance of papillary and follicular carcinoma, some less common primary thyroid cancers, such as small cell, giant cell, spindle cell and clear cell carcinomas may appear histologically indistinguishable from metastases arising from distant sites. In this study, it was also occasionally difficult to differentiate between primary and metastatic carcinoma on cytology, necessitating the performance of bilateral thyroidectomy in these cases. However, in most cases, cytologic examination was useful for identifying the nonthyroidal origin in the following terms; deficient finding of papillary or follicular carcinoma, positive staining for estrogen and progesterone receptors in breast cancer patients, negative staining for both thyroglobulin and calcitonin, and same histological findings between the primary and metastatic tumors.

Metastases to the thyroid have been associated with a poor prognosis. In this study, the survival period could not be analyzed due to the absence of any long-term follow-up. However, because most of the patients had disseminated disease, a poor prognosis was expected. More recently, a study at the Mayo Clinic of 43 patients with metastatic disease to the thyroid over a 10-year period among patients who had prolonged disease-free intervals (10-26years) was reported. This study suggested that in a patient with a thyroid nodule and a history of cancer, metastatic disease should be definitively considered until proven otherwise.

Although there is no clear consensus regarding the role of surgery in metastatic disease of the thyroid, most investigators advocate thyroidec- tomy when there is no clinical evidence of other organ involvement, especially in the case of slow growing tumors, such as carcinoma of the kidney or breast. On the contrary, extensive surgical procedures for more aggressive tumors, such as carcinoma of the lung, do not seem to prolong survival.

In conclusion, the sonographic finding of thyroid metastasis is nonspecific and the differentiation between primary and metastatic tumor remains difficult. However, unilateral or bilateral multiple suspected thyroid nodules without evidence of microcalcification on ultrasonography may be suggestive of metastatic nodules among patients with a known primary tumor. Furthermore, ultrasonographic guided aspiration biopsy is helpful for the diagnosis of thyroid metastasis and may aid the surgeon in establishing a plan of treatment.

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