Metastasis to the Thyroid Gland; Unusual site of Metastasis.

A. Saber¹, S. Ramzy², I. Gouda³

¹Department of Clinical Oncology, Minia Medical School
² Department of Surgery, National Cancer Institute,
³ Department of Pathology, National Cancer Institute, Egypt

Abstract

The incidence of metastasis to the thyroid gland in autopsy series varies from 1.25% to 24%. Metastasis to the thyroid gland is usually considered as a terminal event, and the effectiveness of conventional treatment has been questioned.

Methods

Seven patients with metastasis to the thyroid gland were studied retrospectively. Primary tumor origin was identified in all of them. Metastasis to the thyroid gland was confirmed by fine needle aspiration cytology or histology. Data were analyzed for the type of malignant lesions, the clinical course of the disease, and the prognosis after thyroid involvement.

Results

Two patients had lung as a primary tumor site. Breast, iris, kidney, parotid and soft tissue sarcoma were the involved primary sites in the other cases. The time from the diagnosis of primary tumor to metastasis to the thyroid gland was considerable (ranged from 13-135 months, median 60 months). Fine needle aspiration cytology detected metastasis in five of seven patients. Treatment was surgery alone or surgery with adjuvant therapy. One patient didn’t receive any treatment.

Conclusions

In any patient with a previous history of malignancy, no matter how old that history is, a new thyroid mass should be considered as recurrence until proved otherwise. Although detection of metastasis to the thyroid gland often indicates poor prognosis, aggressive surgical and medical therapy may be effective in a small percentage of patients.

Key words

Malignancy, metastasis, thyroid gland.

Introduction

Metastasis to the thyroid gland is not as rare as previously believed. Its incidence have been shown, in autopsy series, to be more than the incidence of primary thyroid malignancy (1). The overall incidence, not surprisingly, varies from 1.25% in unselected autopsy series to 24% in autopsy of patients with widespread malignant neoplasms (2). As a result of the lack of awareness among clinicians of the above fact, clinical diagnosis of metastatic disease to the thyroid is expected to be less common than post-mortem findings. In both clinical and autopsy series, renal cell, breast and lung carcinomas are the most frequent sources of metastases to the thyroid (3,4). Therefore, in any patient with a previous history of malignancy, no matter how old that history is, a new thyroid swelling should be considered as recurrence until proved otherwise (5).

Although detection of metastasis to the thyroid gland often indicates poor prognosis, aggressive surgical and medical therapy may be effective in a small percentage of patients (6).

Patients & Methods

Reviewing the registries of National Cancer Institute (NCI), Cairo University & Minia Oncology Center, Ministry of Health, Egypt, during the period between 1989 to 2004, five
hundreds and thirty patients had primary thyroid malignancy. Only seven patients with the diagnosis of metastatic deposits to the thyroid gland were found. Diagnosis was confirmed histopathologically by a microscopic picture compatible with the primary disease as well as immunohistochemical negativity for thyroglobulin. The clinical data, treatment modality and response were evaluated.

**Results**

The current study included seven cases of pathologically confirmed metastatic disease to the thyroid treated at NCI, Cairo and Minia Oncology Center.

The clinical characteristics of the study group are listed in [Table 1].

In the current study, metastatic disease in the thyroid gland occurred at a median of 45 months (range 13-135 months) after diagnosis of the primary disease.

Thyroid deposit was the first site of distant metastasis in two cases (renal cell carcinoma and adenoid-cystic carcinoma of the parotid). It occurred after local recurrence and/or distant metastases in the other cases, [Table 2].

Metastatic thyroid deposits were found in the left lobe in four cases and in the right lobe in three cases. It was solitary in all cases but one (associated with multi-nodular goiter in one case of bronchial carcinoma). The size of the metastatic nodule ranged between 3-5 cm. Ipsilateral cervical lymph node involvement was documented in two cases (soft tissue sarcoma & malignant melanoma).

All patients included in the current study were having euothyroid status with no associated

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex</th>
<th>Age (yrs)</th>
<th>Diagnosis</th>
<th>Histology</th>
<th>Primary treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>45</td>
<td>Rt breast</td>
<td>IDC G II</td>
<td>S+ Cth+Rth</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>62</td>
<td>Rt Iris</td>
<td>amelanotic melanoma</td>
<td>S</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>68</td>
<td>soft tissue (Lt arm)</td>
<td>MFH</td>
<td>S+ Cth</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>62</td>
<td>Lt bronchial</td>
<td>adenocarcinoma</td>
<td>Cth</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>55</td>
<td>Rt bronchial</td>
<td>large cell carcinoma</td>
<td>Rth</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>39</td>
<td>Lt parotid</td>
<td>adenoid –cystic Ca</td>
<td>S+ Rth</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>36</td>
<td>Rt kidney</td>
<td>clear cell carcinoma</td>
<td>S</td>
</tr>
</tbody>
</table>

* One patient only had metastatic disease at presentation

S= surgery   Cth = chemotherapy   Rth = radiotherapy
MFH= malignant fibrous histiocytoma

**Table 1 Clinical characteristics of the study group**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Diagnosis</th>
<th>Local</th>
<th>Distant</th>
<th>Time between primary diagnosis and thyroid metastasis(months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Breast</td>
<td>No</td>
<td>Bone</td>
<td>63</td>
</tr>
<tr>
<td>2</td>
<td>Iris</td>
<td>Yes</td>
<td>Bone</td>
<td>45</td>
</tr>
<tr>
<td>3</td>
<td>Soft tissue</td>
<td>Yes</td>
<td>Pulmonary</td>
<td>135</td>
</tr>
<tr>
<td>4</td>
<td>Bronchial</td>
<td>No</td>
<td>Bone</td>
<td>13</td>
</tr>
<tr>
<td>5</td>
<td>Bronchial</td>
<td>Yes</td>
<td>Brain</td>
<td>14</td>
</tr>
<tr>
<td>6</td>
<td>Parotid</td>
<td>No</td>
<td>None</td>
<td>72</td>
</tr>
<tr>
<td>7</td>
<td>Kidney</td>
<td>No</td>
<td>None</td>
<td>34</td>
</tr>
</tbody>
</table>

**Table 2 : Pattern of treatment failure of the study group**
Fig. 1: Computed tomographic scan shows a 4x3-cm mass on the right lobe of the thyroid gland.

Fig. 2: Tc-99m Pertechnetate Thyroid scan showing a solitary cold (non-functioning) nodule in the right lobe with normal thyroid uptake.
Fig. 3 Malignant fibrous histiocytoma (case 3) infiltrating an area of colloid-containing thyroid acini (arrow). Haematoxylin and eosin stained; magnification x200.

Fig. 4: Photomicrograph of the same malignant fibrous histiocytoma showing storiform arrangement of fascicles of spindle and pleomorphic cells. Haematoxylin and eosin stained; magnification x200.

Fig. 5 Renal cell carcinoma (case 7) formed of clear cells forming trabeculae and acini, and infiltrating among thyroid tissue. Haematoxylin and eosin stained; magnification x200.
pathology in the thyroid gland except for the case of multinodular goiter.

Pre-operative investigations with thyroid scan and FNAB verified or strongly suggested metastatic disease in five out of seven patients. Five patients (except cases with metastatic bronchial carcinoma) were treated by hemi-thyroidectomy with lymph node sampling in two cases (soft tissue sarcoma & malignant melanoma).

Pathological examination of the thyroid tumor revealed a picture compatible with the primary tumor. The negative result of immunohistochemical staining for thyroglobulin also suggested the metastatic nature of the thyroid lesion.

Post-operatively, whole neck external beam irradiation aiming at 5000 cGy/25 fractions/5 weeks using 6Mv photons was given to two patients. One patient with malignant fibrous histiocytoma with thyroid capsular infiltration and the second patient with malignant melanoma with microscopic involvement of the cervical lymph nodes.

As for systemic therapy, the patient with breast carcinoma was controlled by hormonal therapy. Malignant fibrous histiocytoma was shifted to another line of systemic chemotherapy.

Table 3: Post-operative therapy received by the study group

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Diagnosis</th>
<th>Post-operative</th>
<th>Treatment</th>
<th>Follow-up(months)*</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Breast</td>
<td>No</td>
<td>Hormonal</td>
<td>37</td>
<td>AD</td>
</tr>
<tr>
<td>2</td>
<td>Iris (melanoma)</td>
<td>Yes</td>
<td>None</td>
<td>13</td>
<td>AD</td>
</tr>
<tr>
<td>3</td>
<td>Soft tissue</td>
<td>Yes</td>
<td>Chemotherapy</td>
<td>39</td>
<td>AD</td>
</tr>
<tr>
<td>4</td>
<td>Bronchial</td>
<td>No</td>
<td>Chemotherapy</td>
<td>4</td>
<td>DD</td>
</tr>
<tr>
<td>5</td>
<td>Bronchial</td>
<td>No</td>
<td>None</td>
<td>1</td>
<td>DD</td>
</tr>
<tr>
<td>6</td>
<td>Parotid</td>
<td>No</td>
<td>None</td>
<td>25</td>
<td>AF</td>
</tr>
<tr>
<td>7</td>
<td>Kidney</td>
<td>No</td>
<td>None</td>
<td>11</td>
<td>AF</td>
</tr>
</tbody>
</table>

* Follow up period started of date of thyroidectomy.

AD=alive with disease       AF= alive free of disease       DD=died diseased
NB: all patients had no evidence of disease in the neck.

Table 4: Frequency of Metastasis to the Thyroid Gland and Methods of diagnosis in Clinical Series (quoted from Nakhjavani et al.)
due to progression of pulmonary nodules.

The patient with renal cell carcinoma and parotid adenoid cystic carcinoma were kept under follow up, while one patient with bronchial carcinoma deteriorated rapidly on systemic chemotherapy and the other died rapidly without receiving any form of treatment. [Table 3]

Discussion

Metastasis to the thyroid gland is not unusual as previously believed. It has been shown in autopsy series to be more common than primary thyroid malignancy.

In most autopsy series, breast and lung carcinomas have been the two most frequent metastatic diseases to the thyroid gland. In contrast, renal cell carcinoma is usually the most frequent source in clinical series (6). In our study, it was difficult to conclude the incidence rate, as the number of the study group was small and no autopsy data is available.

But with increasing estimated new cancer cases all over the world, there is a potential for an increase in cases of metastasis to the thyroid gland.

Metastatic disease involving the thyroid gland may be a diagnostic problem. In the current study, all patients had an enlarging, firm or otherwise abnormal thyroid gland. Two patients had thyroid involvement clinically without any other metastasis identified. In addition, the long interval between the diagnosis of primary cancer and subsequent thyroid metastasis presented a diagnostic dilemma. In one of the cases of renal cell carcinoma of Mayo’s Clinic series, metastasis to the thyroid gland was noted 26 years after diagnosis of the primary tumor (range from 3 to 20 years in renal cell carcinoma) (6). In our study, more than 11 years elapsed before the diagnosis of thyroid metastasis in the case of malignant soft tissue sarcoma.

The appearance of metastatic disease in the thyroid gland often indicates poor prognosis. Metastasis to the thyroid gland from lung carcinoma represent preterminal events, and the average survival from diagnosis to death is 2-4 months (14). This was the case in our study, as the two patients with bronchial carcinoma died within four months after the evolution of thyroid metastasis.

FNA biopsy could confirm a clinical suspicion of metastasis to the thyroid gland accurately with low morbidity. It also might help avoiding unnecessary thyroidectomy in patients with a poor prognosis (15). On the other hand, some cases showed rapid progression of the thyroid masses causing significant airway compromise within one to two months of being clinically apparent. This behavior is similar to the aggressive picture of thyroid anaplastic carcinoma. Hence, thyroid metastatic deposits, merits serious consideration. Adequate surgical treatment may prove to be life prolonging or life saving. Shorter mean survival in patients who were treated non-surgically (25 months), compared to patients who underwent thyroidectomy alone or thyroidectomy with adjuvant therapy (34 months) was reported in one series (6).

Based on these data, six patients in our study were subjected to thyroidectomy in spite of having small metastatic thyroid nodule not causing respiratory compromise or dysphagia.

In conclusion, we recommend that in any patient with a known history of previous carcinoma, the appearance of a new thyroid mass should be regarded as potentially metastatic. Also, although therapy of metastatic malignancies is often considered to be palliative, aggressive surgical treatment in isolated cases may be curative and of survival benefit.

This highlights the importance of early recognition and management of thyroid metastasis which probably contributes to the prolonged survival in some patients and prevention of rapid onset of life threatening complications.

References

2. Haugen BR, Nawaz S, Cohn A, Shroyer


