Metastatic Follicular Thyroid Carcinoma to the Thymus in a 35-year-old Woman

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Clinically detectable metastatic follicular thyroid carcinoma to the thymus is very rare in the literature and sometimes confused with false positive uptake of Iodine[131] (I^{131}) in the normal thymus or hilar lymph node. The authors report a 35-year-old woman with metastatic follicular carcinoma to the thymus. She underwent total thyroidectomy and I^{131} ablation with 200 mCi. Six months later, a follow-up I^{131} whole body scan showed continued radioactive iodine uptake in the retrosternal area and the serum thyroglobulin level remained continuously elevated with levothyroxine suppression therapy (22.3 and 36.4 ng/ml, 6 and 10 months after total thyroidectomy, respectively). CT scan of the chest revealed several aggregated cystic lesions in the retrosternal mediastinum, suspected to represent mediastinal metastasis. The surgically resected retrosternal mass was confirmed as a metastatic follicular carcinoma to the thymus. After surgical excision, the serum thyroglobulin level was below 1.0 ng/ml and I^{131} whole body scan showed no radioactive iodine uptake in the mediastinum. The patient showed no evidence of recurrence after excision of thymic metastasis during one year of 0.2 mg levothyroxine suppression therapy. We report a case of metastatic follicular thyroid carcinoma to the thymus without bone or pulmonary involvement.

Key Words: Follicular thyroid carcinoma, metastasis, thymus, iodine[131] therapy, resection

INTRODUCTION

Almost 10% of patients with papillary carcinoma and up to 25% of those with follicular

carcinoma have distant metastasis[1]; half of them have metastases at the time of diagnosis. Follicular carcinoma is known to have frequent vascular invasion with the most common metastasis being to the lung, bone, and lymph nodes.[2-5] In contrast the kidney, brain, and other soft tissues have rarely been reported as distant metastatic sites.[6,7] Mainly the patients' age, the tumor's metastatic sites, the ability to concentrate radioactive Iodine[131] (I^{131}), and morphology on chest X-ray[2,8,9] influence the outcome in patients with distant metastases. Complete surgical excision of distant metastasis in differentiated thyroid carcinoma has been reported to offer the best chance of prolonged survival.[8]

There is no report of metastatic follicular thyroid carcinoma to the thymus without pulmonary metastasis. However, the thymic accumulation of I^{131} after therapeutic dose for differentiated thyroid carcinoma does not always represent metastasis. Non-metastatic mediastinal uptake was considered to represent either ectopic thyroid tissue or secretions in the tracheobronchial tree.[10-13]

This report describes a 35-year-old woman with thymic metastasis of follicular carcinoma. This patient was asymptomatic and had no evidence of recurrence after total thyroidectomy, I^{131} ablation, excision of thymic metastasis and thyroid suppression therapy with 0.2 mg levothyroxine.

CASE REPORT

A 35-year-old woman was seen in November

1999 because of a growing anterior neck mass (about 5 cm) on the right side for 3 months. Other physical examinations were normal. She had undergone excision of a left neck mass, unconfirmed as a benign thyroid tumor 9 years previously.

Repeated fine needle aspiration of the right neck mass showed follicular patterned neoplasm with cellular atypia, suggestive of follicular carcinoma. CT scan of the neck revealed a large, ill-defined, heterogeneous, soft mass with no enlarged lymph nodes, and plain X-ray of the chest was normal. She underwent right lobectomy. Pathologic evaluation showed a 3.8 × 2.6 cm sized, minimally invasive, follicular carcinoma with clear resection margin (Fig. 1). One month later, whole body scanning using I^{131} revealed abnormal uptake in the thyroid remnant, regional lymph nodes and mediastinum. The serum thyroglobulin level 2 months after operation was 1750 ng/ml. She received 200 mCi I^{131} for ablation therapy and was started on thyroid replacement therapy with levothyroxine. Six months later, whole body scanning using I^{131} showed no thyroid uptake, but positive functional metastasis in the mediastinum (Fig. 2). The serum thyroglobulin value with levothyroxine suppression was 22.3 ng/ml 6 months after, and 36.4 ng/ml 10 months after, I^{131} ablation. But the serum thyroglobulin level without levothyroxine suppression was 110 ng/ml with TSH 93.9 mU/L for I^{131} whole body scan. CT scan of the chest revealed several aggregated cystic lesions in the retrosternal area, suspected to represent mediastinal lymph node metastasis (Fig. 3). She underwent resection of the retrosternal mass 1 year after ablation therapy. The resected mediastinal mass measured 3.5 × 2.0 × 2.0 cm. The microscopic findings of the lesion revealed diffusely scattered, variable sized follicles composed of highly atypical follicular cells, associated with dense fibrosis. The lesion was surrounded by the involuted thymus (Fig. 4). On immunohistochemical staining, the follicular cells revealed diffuse strong positivity for cytokeratin 19 and p53 (Fig. 5a and 5b). No area consisting of bland-looking follicles was found. The pathologic diagnosis was metastatic follicular thyroid carcinoma to the thymus. Two months later, the serum thyroglobulin level was below 1.0 ng/ml

and whole body scanning using I^{131} showed no abnormal uptake.

DISCUSSION

The overall ten-year survival rate for middle-aged adults is 90% for follicular carcinoma, while 30% of patients experience recurrences over several decades, depending on the initial therapy.[14] Seventy-five percent of patients with distant metastases from differentiated thyroid carcinomas die within five years of diagnosis. The decision to treat a patient with differentiated thyroid carcinoma is based on a variety of factors, but will typically depend on the nature and size of the primary tumor, evidence of local or distant spread, and the age of the patient. I^{131} whole body scan and determination of serum thyroglobulin level are the two most useful tools for the detection of functioning metastases in patients with differentiated thyroid carcinoma. An elevated serum thyroglobulin level indicates the presence of functioning thyroid tissue and should indicate therapy with radioactive iodine if there is no specific contraindication. In our case, the serum thyroglobulin level 2 months after total removal of thyroid was 1750 ng/ml and I^{131} whole body scanning revealed abnormal uptake in the thyroid remnant, regional lymph nodes and mediastinum.

The best therapy in cases of metastases of well-differentiated thyroid carcinoma includes complete excision of the thyroid gland and removal of as much of the metastatic foci as possible. Complete surgical excision of distant metastases in differentiated thyroid carcinoma has been reported to offer the best chance of prolonged survival.[8] When excision of such foci is not possible, treatment with I^{131} ablation and maintenance therapy with thyroxine to suppress TSH (thyroid stimulating hormone) is the best choice.[15] Our patient received ablation therapy and suppression therapy with levothyroxine. Six months later, positive uptake in the mediastinum and the serum thyroglobulin level was elevated continuously (22.30 ng/ml 6 months after, and 36.4 ng/ml 10 months after, I^{131} ablation) with levothyroxine suppression. CT scan of the chest revealed several aggregated cystic lesions in the retroster-
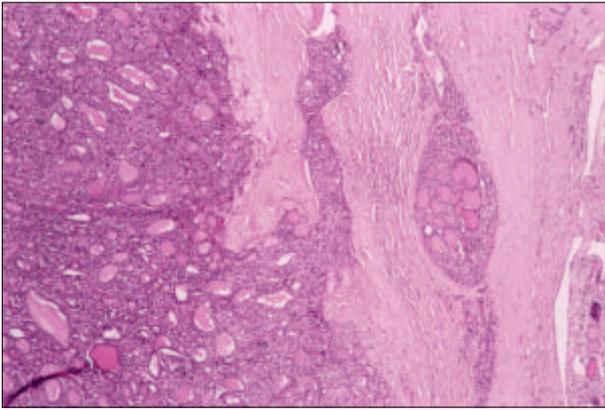
Fig. 1. Light microscopy. Peripheral portion of tumor showing penetration of the thick capsule by neoplastic follicles (H&E stain, × 40).
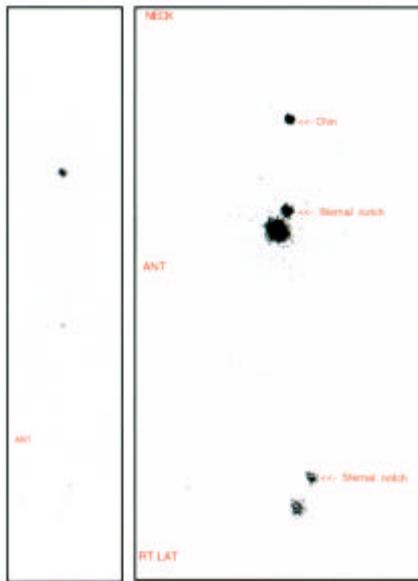

Fig. 2. I^{131} whole body scan 6 months after 200 mCi I^{131} ablation. No thyroid remnant uptake, but positive retrosternal uptake in the mediastinum is observed.

Fig. 3. CT scan of the chest demonstrates several aggregated cystic lesions in the retrosternal area, suspected to represent mediastinal metastasis.
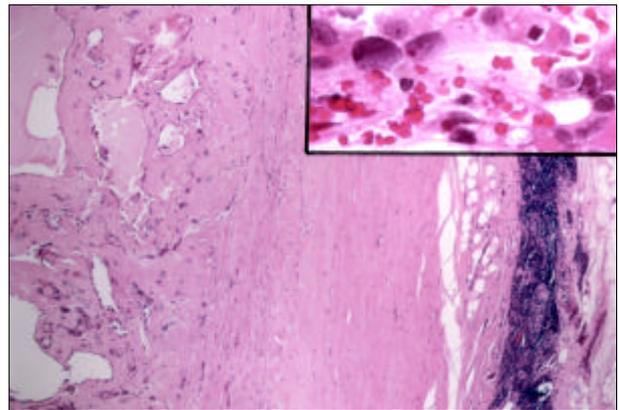

Fig. 4. Pathologic evaluation of the anterior mediastinal mass showing diffusely scattered, variable sized follicles associated with dense fibrosis. The lesion is surrounded by the involuted thymus (H&E stain, × 40). Insert shows atypical follicular cells having pleomorphic nuclei, coarse chromatin pattern and prominent nucleoli (H&E stain, × 400).
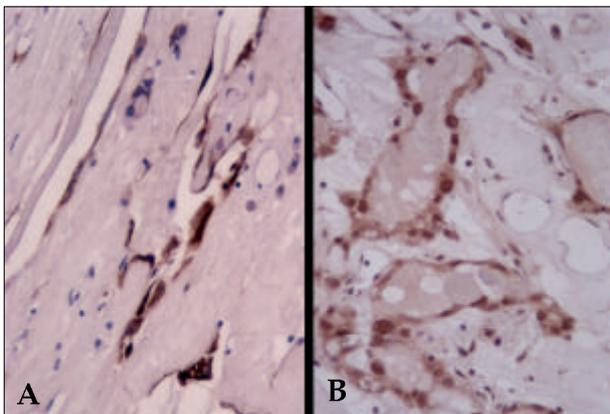

Fig. 5. On immunohistochemical staining, the follicular cells reveal diffuse, strong positivity for cytokeratin 19 (A) and p53 (B) (× 200).

nal area, suspected to represent mediastinal metastasis. We decided to resect the mass of retrosternal mediastinum and pathologic evaluation showed metastatic follicular thyroid carcinoma to the thymus.

Anterior mediastinal I^{131} uptake in patients with differentiated thyroid carcinoma does not always represent metastases. There are false positive radioiodine uptakes of anterior mediastinum such as hiatal hernia,[16] abnormal esophagus,[17] ectopic foci of thyroid tissue[18] and inflammation as well as non-thyroidal neoplasm.[19] Jackson et al.[20] showed that normal thymic cells can accumulate radioiodine. Michigishi et al.[21] reported two cases of differentiated thyroid carcinoma with intense anterior mediastinal uptake caused by hyperplasia of the thymus. Histologically the resected thymus gland showed hyperplasia and contained neither thyroid tissue nor metastatic foci of thyroid carcinoma. Salvatori et al.[13] reported one case of papillary thyroid carcinoma with thymic hyperplasia. Wilson et al.[22] reported 10 cases of differentiated thyroid carcinoma with thymic uptake of radioiodine and two cases of papillary thyroid carcinoma with thymic and pulmonary metastasis.

Salvatori et al.[13] and Michigishi et al.[21] suggested that patients with mediastinal radioiodine uptake can be separated into benign and malignant causes, with the former exhibiting the following characteristics: young age, mediastinal uptake evident only after high radioiodine doses, detection of a diffusely enlarged thymus with no other abnormal appearances on CT scans, and undetectable serum thyroglobulin levels after discontinuation of levothyroxine. In contrast, in patients with papillary thyroid carcinoma and metastatic mediastinal involvement, they always found intense I^{131} uptake after diagnostic and therapeutic doses, elevated thyroglobulin values, lymph node enlargement on CT scans, and pulmonary metastasis. In two cases (27- and 85-year-old) of Wilson et al.[22], papillary thyroid carcinoma with thymic metastasis presented abnormal thymic appearance on CT scans, persistent I^{131} uptake in the lung, and continuously raised thyroglobulin values (>1.0 ng/ml) after surgery and ablation.

In our case (35-year-old), the evidences suggesting thymic metastasis were intense I^{131} thymic

uptake after diagnostic and therapeutic doses, continuously elevated serum thyroglobulin values (22.30 and 36.4 ng/ml, 6 and 10 months after ablation, respectively), higher thyroglobulin level after discontinuation of levothyroxine therapy (110 ng/ml), and aggregated cystic lesions suspected to represent mediastinal metastasis on chest CT. Preoperative chest CT scan showed no concomitant pulmonary metastases, but other evidence raised the suspicion of mediastinal metastases. The patient underwent resection of the retrosternal mass and pathologic evaluation showed metastatic follicular thyroid carcinoma to the thymus. The two most important differential diagnoses are ectopic thyroid tissue in the thymus and primary follicular carcinoma arising in ectopic thyroid tissue in the thymus.[23,24] The possibility of the former was excluded by the diffuse cytologic atypia of the follicles and the diffuse strong immunoreactivity for cytokeratin 19 and p53 of this lesion.[25,26] The latter was extremely rare and there was no area of remaining bland-looking follicles in this thymic lesion. Therefore, we concluded that this was a case of true thymic metastasis of follicular thyroid carcinoma and the I^{131} positive thymic mass was successfully removed with surgical resection. I^{131} whole body scanning after resection revealed no evidence of abnormal thymic uptake and the serum thyroglobulin level dropped to below 1.0 ng/ml.

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