

# TUMOR-TO-TUMOR METASTASES TO FOLLICULAR ADENOMA OF THYROID: CASE REPORT AND REVIEW OF THE LITERATURE

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Metastasis to the thyroid gland is a rare occurrence, and metastasis to a pre-existing thyroid lesion is much rarer still. The most common sites of primary metastases are the lung, breast, kidney, skin and stomach. Usually the presence of a thyroid gland metastasis is discovered on post mortem examination, while clinically evident metastasis can be mistaken for primary thyroid carcinoma.

## Case Report

A 40-year-old female patient was diagnosed with breast infiltrating ductal carcinoma in 1994. The patient had segmental mastectomy and axillary clearance followed by six courses of chemotherapy. On her admission to receive the sixth course of chemotherapy in 1996, she was noticed to have left thyroid solitary nodule. Thyroid CT scan showed a single cold left thyroid nodule which was followed by left hemithyroidectomy. The histopathological examination of the specimen showed a thyroid adenoma containing foci of metastatic mammary carcinoma which was confirmed by immunohistochemical staining.

The patient's postoperative course was uneventful and further work-up for breast cancer failed to demonstrate any metastases. In the following months, the patient was doing fairly well except for a right upper arm edema. In 1997, follow-up CT scan of the abdomen and pelvis showed bony osteoblastic lesion in the pelvic bone. There was no evidence of secondary metastasis involving the liver, spleen or lung, neither was there any evidence of local or axillary recurrence. Thyroid CT scan showed no abnormalities. The patient continued to be free of distant metastasis for two years except for pelvic bone deposits which became multiple and larger in size. The patient was then lost to follow-up until she presented again to the clinic in February 2000, with abdominal distension and symptoms of gastroesophageal reflux disease, but with no evidence of local recurrence. CT scan of the abdomen and chest showed

died shortly afterwards. No postmortem examination was performed.

## Pathological Findings

Macroscopic examination revealed a dark brown left thyroid lobe moderately firm in consistency. Cut sections revealed the presence of a well-circumscribed nodule measuring 2.5x3 cm in diameter, with no evidence of hemorrhage or necrosis. The rest of the thyroid tissue was unremarkable.

Microscopic examination of the sections showed normal thyroid tissue containing follicular adenoma with a predominantly microfollicular pattern. The capsule was thin and completely surrounded the nodule with no evidence of capsular or vascular invasion.

The follicles were small, round, and contained colloid material. Scattered throughout the thyroid adenoma, but mainly centrally, were atypical mitotically active cellular nests. The cells had large pleomorphic nuclei, with prominent nucleoli (Figure 1). Some of the islands showed a background of fibrous tissue surrounding and intrapping individual and small clusters of cells, while others showed stromal myxoid degeneration and foci of necrosis (Figure 2). Lymphatic permeation was also seen. There was no evidence of vascular or capsular invasion. The morphological appearances were in keeping with metastatic mammary carcinoma.

For confirmation, immunohistochemical stains for the following markers were performed: cytokeratin (CK), epithelial membrane antigen (EMA), carcinoembryonic antigen (CEA), thyroglobulin, calcitonin, human milk fat globulins (HMFG 1&2), and estrogen receptors. The results were as follows:

EMA and CK: strong positivity in the poorly differentiated carcinoma

CEA: focal positivity of doubtful significance.

Thyroglobulin: positive in normal thyroid and the follicular adenoma, and negative in tumor cells (Figure 3)

HMFG1: focal positivity of doubtful significance

HMFG2: strong positivity in poorly differentiated carcinoma, and negative in normal and adenoma cells

FIGURE 1. Metastatic tumor cells showing nuclear pleomorphism, prominent nucleoli and mitotic activity (H&E, 10x20).

FIGURE 2. Tumor cells on a background of fibrous tissue (H&E, 10x10).

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Accepted for publication 16 April, 2002. Received 23 October 2001. small multiple lesions in the lung and the liver which were considered to be metastatic deposits. The patient's general health deteriorated and she developed pancytopenia and

FIGURE 3. Immunohistochemical stain for thyroglobulin showing positive follicular cells while the metastatic tumor cells are negative (H&E, 10x20).

FIGURE 4. Immunohistochemical stain for estrogen receptors showing positive metastatic tumor cells and negative follicular cells(H&E, 10x20).

Calcitonin: no staining within the poorly differentiated tumor .

Estrogen receptors: positive in poorly differentiated carcinoma (Figure 4). The positivity for human milk fatty globulin, although not absolutely specific for carcinoma of breast, was highly suggestive in the face of clinical settings, and were considered to be metastatic carcinoma of mammary origin.

### Discussion

The thyroid gland is one of uncommon sites of metastasis in the body, and it is usually discovered as an incidental finding at autopsy.<sup>1</sup> Despite this rarity, it can still be mistaken clinically and pathologically for a primary thyroid cancer. Thus continuous awareness is required with respect to clinical recognition and treatment.<sup>2</sup>

The primary sites of metastases usually are the lung, breast, kidneys, skin, stomach,<sup>1</sup> and also the oral cavity, esophagus, colon and pancreas.<sup>2</sup> However, lung and breast carcinomas are the most frequently identified primaries found at autopsy, while renal cell carcinoma comprises over 50% of secondary thyroid malignancies diagnosed clinically.<sup>3</sup> Very rarely, the primary tumor can be a soft tissue tumor such as malignant fibrous histiocytoma.<sup>3</sup>

Thyroid gland involvement by secondary malignancies can be part of multi-organ involvement,<sup>4</sup> or rarely can be a site of solitary metastasis as from renal cell carcinoma.<sup>5,6</sup> Metastasis to a primary thyroid neoplasm can also occur very rarely, as part of a tumor-to-tumor metastasis phenomenon.<sup>1,7,8</sup> In 1994, Ro et al. reported two cases of tumor-to-tumor metastasis in which the thyroid gland follicular adenoma was a recipient tumor in both cases of breast and prostatic carcinoma.<sup>1</sup> In 1999, Baloch and Li Volsi described another three cases of tumors metastasizing to follicular variant of papillary thyroid carcinoma. The donor tumors were small-cell carcinoma of the lung, neuroendocrine carcinoma of probable pancreatic origin, and clear-cell carcinoma of kidney.<sup>7</sup> In the year 2000, Kamaeyama et al. reported two autopsy cases of carcinomas that metastasized to a thyroid follicular adenoma. The first was from colonic carcinoma, while the second was from primary lung carcinoma.<sup>8</sup>

By definition, tumor-to-tumor metastasis implies that metastatic tumor must infiltrate the recipient neoplasm and not as vascular permeation or contiguous growth.<sup>1</sup> In a series of 46 previously reported cases, Sella and Ro<sup>9</sup> found that the most common host tumor was renal cell carcinoma, followed by sarcoma. This, according to many authors, is attributable to the rich vascular supply of the tumors, in

addition to the high lipid and glycogen content of renal-cell carcinomas which act as a rich "fertile" medium for acceptance of donor tumor cells.<sup>9</sup>

Thyroid gland, although a highly vascular organ, the incidence of secondaries is low, probably because it provides an "unfavorable soil" for tumor implantation and growth. However, benign and malignant thyroid tumors, perhaps by virtue of their increased vascularity and changes that might have taken place in the microenvironment of tumor cells, may provide a fertile soil for homing and growth of metastatic tumor cells.

In summary, one should keep in mind that metastasis to thyroid gland does occur rarely, and may simulate primary thyroid neoplasms. Thus, the possibility of metastasis in cases of thyroid nodules should be considered particularly in patients with other primary tumors as renal-cell carcinoma.

### References

1. Ro JY, Guevriero C, El Naggar AK, Ordonez NG, Sorge JG, Ayala AG. Carcinoma metastatic to follicular adenomas of the thyroid gland Report of 2 cases. Arch Pathol Lab Med 1994;118:551-6.
2. Rosen IB, Wafish PG, Bain J, Bedard YC. Secondary malignancy of the thyroid gland and its management. Ann Surg Oncol 1995;2:252-6.
3. Haugen BR, Nawaz S, Cohn A, Shroger K, Bunn PA, Liechty DR. Secondary malignancy of the thyroid gland: a case report and review of the literature. Thyroid 1994;4:297-300.
4. Koutkia P, Safran H, Kahn C. Metastatic carcinoma mimicking primary thyroid cancer. Med Health R I 2001;84:204-6.
5. Seki H, Ueda T, Shibata Y, Sato Y, Yagihashi N. Solitary thyroid metastasis of renal clear cell carcinoma: report of a case. Surg Today 2001;31:225-9.
6. Niiyama H, Yamaguchi K, Nagai E, Furukawa K, Torisu M, Tanaka M. Thyroid gland metastasis from renal cell carcinoma masquerading as nodular goiter. Aust N Z J Surg 1994;64:286-8.
7. Baloch ZW, Li Volsi A. Tumor to tumor metastasis to follicular variant of papillary carcinoma of thyroid. Arch Pathol Lab Med 1999;123:703-6.
8. Kameyama K, Kamic NI, Okita H, Hata J. Metastatic carcinoma in follicular adenoma of the thyroid gland Pathol Res Pract 2000;196:333-6; discussion, 337-8.
9. Sella A, Ro JY. Renal cell cancer: best recipient of tumor to tumor metastasis. Urology 1987;30:35-8.