Medullary Carcinoma of the Thyroid with Bone Metastasis

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A woman with medullary carcinoma of the thyroid and a past history of breast cancer was found to have metastatic bone lesions. It was initially assumed that this was due to recurrent breast carcinoma, but bone biopsy revealed medullary carcinoma of thyroid origin. Although clinical bone metastasis is a rare event in patients with medullary carcinoma, quite clearly such an occurrence is possible. Medullary carcinoma should be considered in the differential diagnosis of patients with metastatic bone lesions.

We recently studied a woman with medullary carcinoma of the thyroid and a past history of breast carcinoma. When this patient was discovered to have metastatic bone lesions, it was assumed that this was due to recurrent breast carcinoma. To our surprise, bone biopsy revealed medullary carcinoma of thyroid origin.

**Case Report**

A 71-year-old woman was referred because of a 0.5 cm "thyroid" nodule in the left side of the neck. This patient had a subtotal thyroidectomy 30 years before for a "benign goiter." Postoperatively, she was not treated with thyroid hormone. Nine years before she had had a right modified radical mastectomy for breast carcinoma. The lymph nodes removed at that operation were free of metastases.

The thyroid scan (\[^{99m}\text{Tc}\]) revealed an asymmetrical distribution of the tracer with a normal appearing right lobe and only a small amount of tracer in the area of the left lobe. The nodule was so small that it could not be localized while the patient was under the scanner, and fine needle aspiration was likewise impossible. The serum free thyroxine index (FTI) was 1.8 (normal range: 1.4-4.0) and the serum thyroid-stimulating hormone (TSH) was 10.0 μU (normal range <8.0 μU). Because this nodule was so firm in consistency, surgical excision was advised. The nodule and thyroid isthmus were removed under local anesthesia because of coronary artery disease. Histologic evaluation revealed that this lesion was a lymph node extensively invaded by medullary carcinoma. Postoperative provocative pentagastrin testing (0.5 mcg/kg administered intravenously over a period of five seconds) revealed the following calcitonin values:

- baseline, 0.33 ng/ml, 2 min, 0.19 ng/ml, 5 min, 0.45 ng/ml, 15 min, 0.17 ng/ml, 30 min, 0.14 ng/ml, and 60 min, 0.13 ng/ml (normal baseline <0.45 ng/ml; normal rise <0.11 ng/ml) (1). Despite the borderline five-minute value, this test was interpreted as "probably" normal. Additional testing was not done at that time. The patient was placed on levothyroxine 0.1 mg daily.

Two years later the patient was found to have a 3.0 cm mass in the left side of the neck. Fine needle aspiration revealed recurrent medullary carcinoma. The serum calcitonin was 6.32 ng/ml (normal <0.135 ng/ml). The serum FTI was 3.5 and the serum TSH 4.0 μU. The serum calcium was found to be slightly elevated at 10.4 mg/dl (normal 8.8-10.0 mg/dl). The serum C-terminal parathyroid hormone (PTH) was 310 pg/ml (normal <150-375), and the intact PTH level was 464 pg/ml (normal, 163-347 pg/ml). Metabolic bone survey and bone scan (\[^{99m}\text{Tc}\] medronate [Osteolite]) revealed extensive metastases involving the skull, vertebrae, ribs, and femur (Fig. 1). The most likely cause of this bone metastasis was thought to be recurrent breast carcinoma. The neck was partially excised under local anesthesia. The tumor had the same appearance as the lesion excised two years before and was classified as secondary medullary carcinoma of the thyroid.

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Oncology consultation was obtained, and the patient was started on tamoxifen citrate with the presumptive diagnosis of coexisting metastatic breast carcinoma. Because of the extensive metastases to the right femur, it was decided that an intramedullary nail was necessary to avoid a pathologic fracture. Bone biopsy obtained at the time of operation revealed metastatic medullary carcinoma.

**Pathologic findings**

The excised left cervical lymph node had been almost completely replaced by metastatic tumor in which the cells were round, oval, or polygonal. The cytoplasm was eosinophilic and granular. The nuclei were round, somewhat hyperchromatic; a few were in mitosis. These cells were organized in islands separated by a fibrovascular stroma that contained no amyloid (Fig. 2). The tissue examined by electron microscopy was recovered from the paraffin block. The organelles were, as expected, poorly preserved; nuclei, cell borders, and interstitial tissues were clearly seen. There were intracytoplasmic, electron dense, round granules, conforming in all respects to neurocrine granules. The bone biopsy of the right femur had metastatic tumor identical to that seen in the cervical node (Fig. 3).

**Discussion**

It is not surprising that metastatic medullary carcinoma to bone was not seriously considered before the bone biopsy was performed, since only two such clinical reports could be found in the literature (2,3). The titles of these articles did not mention the unusual presence of
bone metastases, and one of the cases (2) was not substantiated by bone biopsy. A large retrospective clinical study (4) and 249 cases of medullary carcinoma did not contain a single case of bone metastasis. However, a careful post mortem study of 20 patients (5) revealed metastatic medullary carcinoma in four cases.

Although clinical bone metastasis is a rare event in patients with medullary carcinoma, quite clearly such an occurrence is possible. Medullary carcinoma should be considered in the differential diagnosis of patients with metastatic bone lesions.

References