CASE REPORTS

FOLLICULAR CARCINOMA OF THE THYROID WITH METASTASIS TO THE BREAST

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A 75-year-old woman with two previous neck operations for follicular carcinoma of the thyroid presented with a breast mass nine years after diagnosis. The mass recurred one month after excisional biopsy. Pathological examination revealed metastatic follicular carcinoma. The breast tumor was weakly positive for estrogen receptor and positive for progesterone receptor. Recurrences in the neck and breast were resected. Residual disease in the neck and metastasis to the lungs were resolved by ^{131}I ablative therapy. Previous reports of thyroid metastasis to the breast were described as papillary carcinoma. This report describes a rare site of metastasis and briefly reviews the pathology, diagnosis, and management of thyroid carcinoma.

Carcinoma of the thyroid is a rare disease with a good prognosis and long patient survival. Nine thousand new cases in the United States are estimated for 1980 and approximately 1,000 deaths.[1] In England, the incidence of thyroid cancer is estimated to be about 0.7 percent of all cancers in women and 0.2 percent in men.[2] Age-specific rates increase with age and the tumor is more common in women than men. The incidence is less in blacks than in whites.[3] Regional lymph nodes are the most common site of metastasis. Other common sites are bone, liver, kidneys, and brain.[4] Most thyroid cancers grow slowly. Recurrences or metastasis may take several years or even decades to develop.

Reports in the literature of metastasis of thyroid carcinoma to the breast are sparse.[4,5] The case presented here relates the clinical course of a patient with follicular carcinoma of the thyroid, who developed metastasis to the breast seven years after resection of the thyroid tumor. To the authors' knowledge this is the first detailed documentation of metastatic follicular carcinoma of the thyroid to the breast.

CASE REPORT

A 75-year-old black woman was admitted to Howard University Hospital in June 1979 with a large mass in the right breast. A 4 × 5 cm mass in the upper inner quadrant of the right breast was first detected during a clinic visit in May 1979. An excisional biopsy at that time revealed metastatic follicular carcinoma. The tumor mass recurred one month after excision.

The patient's past history revealed that she had a subtotal thyroidectomy for a thyroid mass nine years previously in July 1970. The diagnosis was follicular adenoma of borderline malignancy. A mass in the right lobe of the thyroid, and two palpable adjacent right anterior cervical lymph nodes were detected in December 1976. A near total thyroidectomy with modified right radical neck dissection was performed. A diagnosis of follicular

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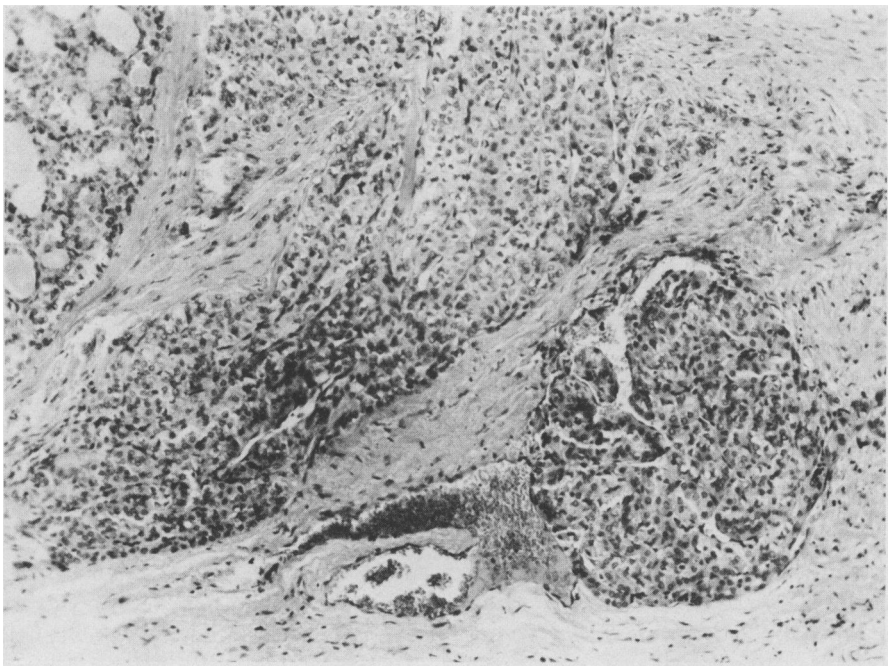

Figure 1. Oxyphilic type of follicular carcinoma of thyroid with capsular and vascular invasion

carcinoma was made (Figure 1). Six lymph nodes were found and all were negative for tumor metastasis. Radiotherapy, radioactive iodine therapy, and thyroid replacement or suppressive therapy were not employed.

On admission to the hospital in June 1979, the patient complained of hoarseness, productive cough of whitish sputum, dysphagia, and progressive weight loss. Significant findings on physical examination included a 1.5 × 2 cm node in the area of the left lobe of the thyroid and several nodules in the left anterior cervical lymph chain. There was coarse nodularity over the scar from previous thyroid surgery. A firm mass, partially fixed to the chest wall, occupied the entire right breast. No axillary nodes were palpated. Examination of the lungs and heart were unremarkable. The remainder of the physical examination was essentially normal. The white blood cell count was 10,000 mm^3, Hb 9.8 gm/100 ml, Hct 28%. The anemia was normochromic normocytic. Thyroid function and liver function studies were normal. Chest x-ray showed no evidence of metastasis. Xeromammogram of the opposite breast demonstrated no abnormalities. Resection of the thyroid mass, a modified left neck dissection and a simple mastectomy were done. Pathologic examination revealed a recurrent follicular carcinoma of the thyroid, involving skeletal muscle and skin, and metastatic follicular carcinoma in the breast (Figure 2). Estrogen receptor assay on the breast tumor was weakly positive (7.5 femto-moles/mg protein) and progesterone receptor assay was positive (42 femto-moles/mg protein). One month later, after three days of exogenous thyroid stimulating hormone (TSH), 10 units intramuscularly daily, a ^{131}I total body scan revealed residual uptake in the neck and significant uptake over both lung fields. A therapeutic dose of radioactive iodine, 100 mCi ^{131}I, was administered. Replacement therapy consisted of 0.1 to 0.2 mg of levothyroxine (Synthyroid).

Six months later, repeat ^{131}I total body scan showed disappearance of all activity over the lung fields indicating a response of the metastasis to the

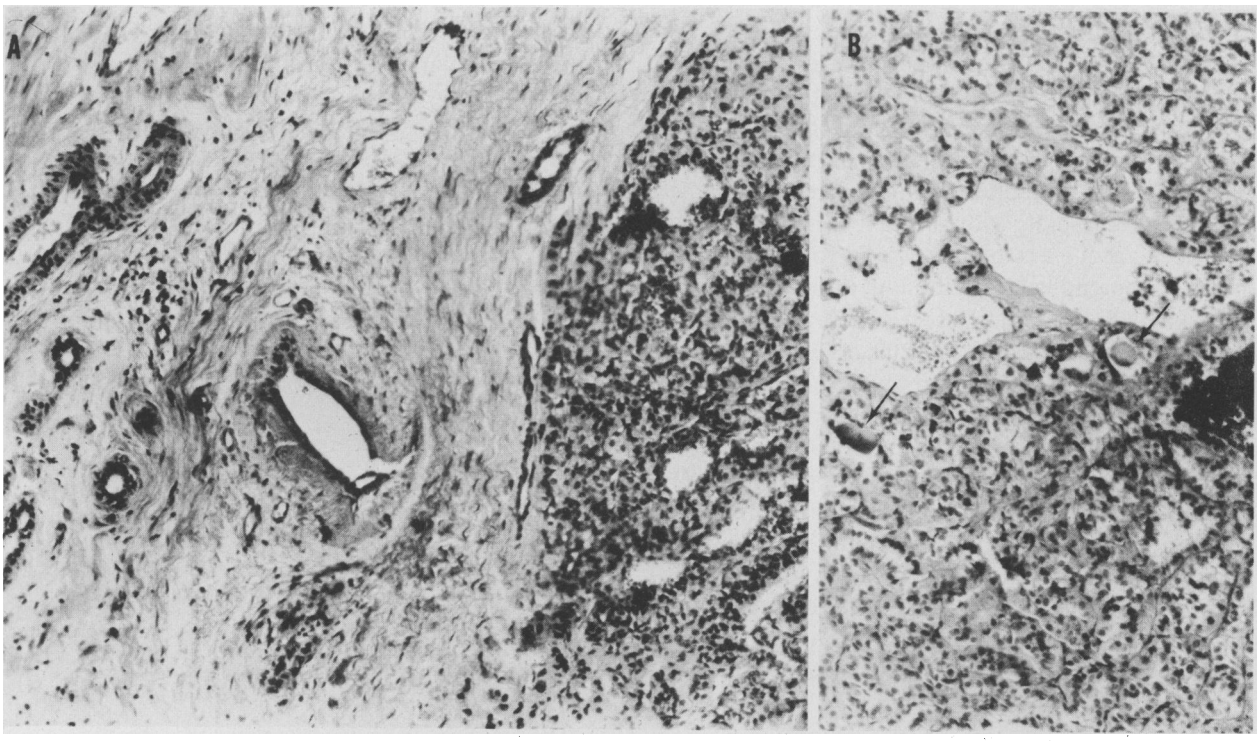

Figure 2. Metastatic follicular carcinoma involving the breast. (A) Atrophic mammary lobule and a dilated duct are shown on the left. (B) Different area of the breast tumor depicting follicles containing colloid (arrows)

radioactive iodine therapy. The patient continues to improve without significant signs of recurrence of metastasis.

DISCUSSION

The major histologic types of thyroid carcinoma are of papillary, follicular, mixed papillary-follicular, medullary, and undifferentiated carcinoma. The miscellaneous group includes squamous cell, malignant lymphoma, plasmacytoma, and sarcoma. Pure papillary or follicular carcinomas are rare.[4] Most of these tumors are mixed, with one predominant histologic type making up most of the tumor. Prognosis in thyroid carcinoma is related to the age of the patient, the histologic type of tumor, and, in most tumors, the size and extent of the lesion. In general, patients under age 35 have a better prognosis. Patients with papillary carcinoma have a good prognosis.

Follicular carcinoma accounts for about 15 percent of all thyroid cancers. The tumor tends to be encapsulated and spread by vascular invasion. The most common sites of metastasis are the lungs and the bones. Unlike papillary carcinoma this tumor rarely spreads to lymph nodes. Metastasis to lymph nodes have been reported to vary from 2 to 10 percent in follicular carcinoma and from 40 to 70 percent in papillary carcinoma.[4,6] In contrast to papillary carcinoma, the size of the primary lesion does not influence prognosis.[6] The tumor concentrates ^{131}I avidly. Soft tissue lesions respond better than bone metastasis. Metastases which concentrate ^{131}I respond well to ablative doses of radioactive iodine.

At present, the recommended treatment for follicular carcinoma of the thyroid is total thyroidec-

tomy, or near-total thyroidectomy, which consists of total lobectomy on the side of the cancer and partial lobectomy, leaving the posterior capsule intact, on the contralateral side.[7] Retention of the posterior capsule preserves viable thyroid tissue and avoids the risk of recurrent nerve injury. Lymph node dissection is only attempted when nodes are clinically palpable. Residual disease in the neck, recurrent or metastatic follicular carcinoma, is diagnosed by obtaining a total body scan utilizing 2-5 mCi ^{131}I. Detected disease is treated with ablative doses of 100-200 mCi ^{131}I.[8,9] However, distant metastasis can only be treated effectively if all normal tissue has been ablated. After ablation, the patient is placed on adequate replacement therapy, which also suppresses TSH, an important growth factor for thyroid follicular cells in most cases of differentiated follicular and papillary carcinoma. Chemotherapy and radiotherapy are usually reserved for disease refractory to radioiodine or thyroid hormone therapy. Adriamycin appears to be an active agent for progressive metastasis.[10]

Most target tissues in the endocrine system have hormone receptors. Hormone receptors are proteins which contain sites to which hormones can bind. The binding alters the receptors which subsequently mediate various cellular actions. Three types of hormone receptors have been described.[11] One type has specific receptors on plasma membrane surfaces, for peptide hormones and releasing factors. The receptors for steroid hormones are found in the cytoplasm. The third type is exemplified by thyroid hormones which have intracellular binding sites found in the nuclear chromatin of target cells. TSH interacts with specific TSH receptors and the cell membrane of the thyroid[12] activates adenylate cyclase and increases cyclic adenosine monophosphate (AMP) formation. TSH also stimulates functioning metastatic thyroid lesions. In this patient, estrogen receptor assay was weakly positive and progesterone receptor definitely positive. The role of estrogen and progesterone receptors in functioning thyroid metastasis is not known. The use of non-thyroid hormone therapy in estrogen positive receptor metastatic thyroid lesions has not been documented in the literature.

Breast[5] and skin are sites rare for thyroid metastasis. Metastatic lesions to the thyroid are more common and most frequently arise from breast and kidney.[4] Reports in the literature of thyroid metastasis to the breast have all been described as papillary carcinoma. To the authors' knowledge there are no reports of follicular carcinoma of the thyroid metastasizing to the breast. The rare site described here should alert the physician to include this in the differential diagnosis, especially in an elderly patient with a breast mass and a previous history of follicular carcinoma of the thyroid.

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