Bronchogenic Carcinoma Mimicking Metastatic Thyroid Carcinoma

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We present a case of a false-positive ^{131}I scan in the follow-up of a patient with papillary thyroid carcinoma, which developed 24 yr after radiation therapy for Hodgkin's disease. In the primary evaluation of a neck mass, histology was typical for a papillary thyroid carcinoma and thyroglobulin staining was positive. After total thyroidectomy, ^{131}I uptake was seen in the hilum and right lung. The initial interpretation of these foci as metastatic disease was not supported by the progressive clinical course despite radioiodine treatment. Hence, repeated bronchial brushings and cytology of the pleural effusion were obtained. These specimens were negative in thyroglobulin staining and positive for synoptophysin, a marker for small-cell bronchial carcinoma. Thereby a small to medium cell undifferentiated bronchial carcinoma was demonstrated, which apparently was actively taking up iodine. In conclusion, an atypical clinical course of a suspected metastatic thyroid carcinoma should lead to a reevaluation of the initial diagnosis to prevent an inappropriate therapeutic regimen.

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Accumulation of iodine is typical in metastases of papillary and follicular thyroid carcinoma, particularly of ^{131}I after a complete thyroidectomy (*1*). Follow-up of the disease to detect residual or recurrent tumor includes the determination of thyroglobulin level, which is a sensitive (94%) and highly specific (96%) tumor marker (*2*). Reports of false-positive ^{131}I scans are rare. Since 1973, twelve cases have been reported in the literature (*3–14*), with only five of them being caused by malignant tumors (*3,8,10,12,13*) and two by bronchogenic carcinomas (*10,13*). We report a case of a false-positive ^{131}I scan in a patient with papillary thyroid carcinoma 24 yr after radiation therapy for Hodgkin's disease. Additionally, a small to medium cell lung cancer arose at the same time, which surprisingly showed exceptional uptake of iodine and therefore led to the erroneous staging of thyroid carcinoma and to an initially false therapeutic regimen.

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CASE REPORT

Hodgkin's disease was diagnosed in our patient in 1953. Radiation therapy of the supra- and infradiaphragmatic lymph nodes was continued until 1966 because of recurrent disease. In February 1990, an x-ray of the lungs showed a tumor of the right hilum. Supraclavicular lymph nodes on the right were palpable. Biopsy of the cervical lymph nodes revealed a papillary thyroid carcinoma. The specimen, stained for thyroglobulin, showed typical results of a brownish color (Fig. 1). Total thyroidectomy, including cervical lymph node removal, was performed and a papillary carcinoma pT2 was found. It was thought to be a secondary neoplasm that developed 24 yr after cervical radiation therapy. To evaluate the nature of the right hilum tumor, a diagnostic dose of 20 mCi ^{131}I was given prior to removal of the thyroid remnant. Scintigraphy 3 and 7 days later showed a prominent accumulation of radioiodine in the right hilum, the right upper lobe of the lung, the mediastinum and in a thyroid remnant (Fig. 2). The thyroglobulin level was elevated to 42 μg/liter (normal value <1 μg/liter) and the accumulations were assumed to represent additional lymph nodes and lung metastases. The patient was thus staged as pT2, N1b, M1 (UICC 1987). A therapeutic dose of ^{131}I (200 mCi) was given.

In April 1990, the patient presented with symptoms of thoracic outlet syndrome because of progression of the hilar tumor and mediastinal lymph nodes. A malignant pleural effusion also occurred. Bronchial brushing from the right bronchus intermedius revealed small, naked cells lying in groups, mostly without cytoplasm, with slightly polymorphic nuclei and a coarse-grained chromatin. Thyroglobulin staining was negative, but incubation of the specimen with synoptophysin, a marker of neuroendocrine tumors and of small-cell bronchial carcinoma, was positive (Fig. 3). Cytology of the pleural effusion revealed the same type of cells compatible with undifferentiated primary small-cell bronchial carcinoma. All specimens were reviewed by three independent pathologists from different institutions who concurred in their diagnoses.

From July to December 1990, chemotherapy (Cisplatinum and Etoposid) first led to a regression of the tumor, but the patient quickly relapsed despite treatment. In April 1991, brain metastases occurred. Despite high doses of prednisone and radiation therapy of the brain, the patient died 4 wk later. No autopsy was performed.

DISCUSSION

Iodine-131 is typical in metastases of differentiated thyroid carcinoma after complete removal of thyroid remnants. Sensitivity of the ^{131}I body scan is approximately

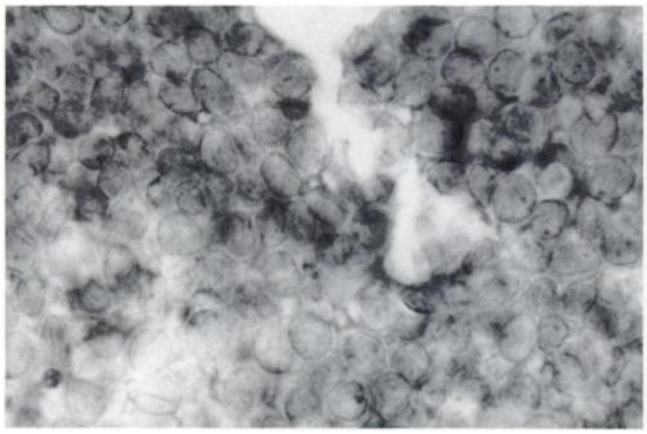

FIGURE 1. Fine-needle aspiration from a supraclavicular lymph node. Thyroglobulin staining was positive, resulting in the typical brownish color for thyroid carcinoma.

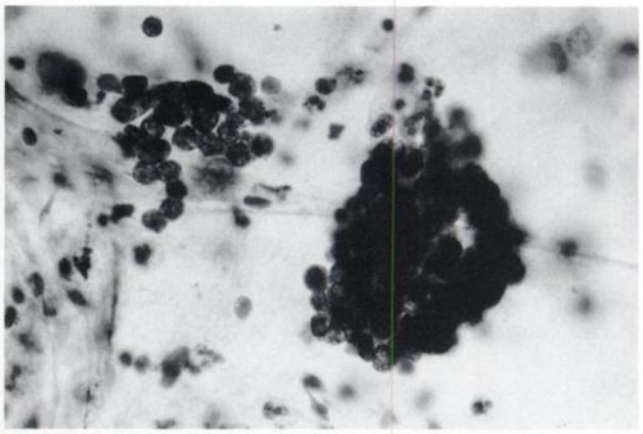

FIGURE 3. Bronchial brushing from the right bronchus intermedius. Small naked cells have slightly polymorphic nuclei and are without cytoplasm. The chromatin is coarse-grained. Synoptophysin staining was positive and proved the presence of bronchial carcinoma.

65%, however, there is a 95% specificity (*2,15,16*). False-positive ^{131}I scans, mostly of benign cases, are rare (*3–9,11,12*). There are only two descriptions of false-positive ^{131}I scans in bronchial carcinomas: one in a primary papillary adenocarcinoma of the lung (*10*) and one in a large-cell undifferentiated bronchogenic carcinoma (*13*).

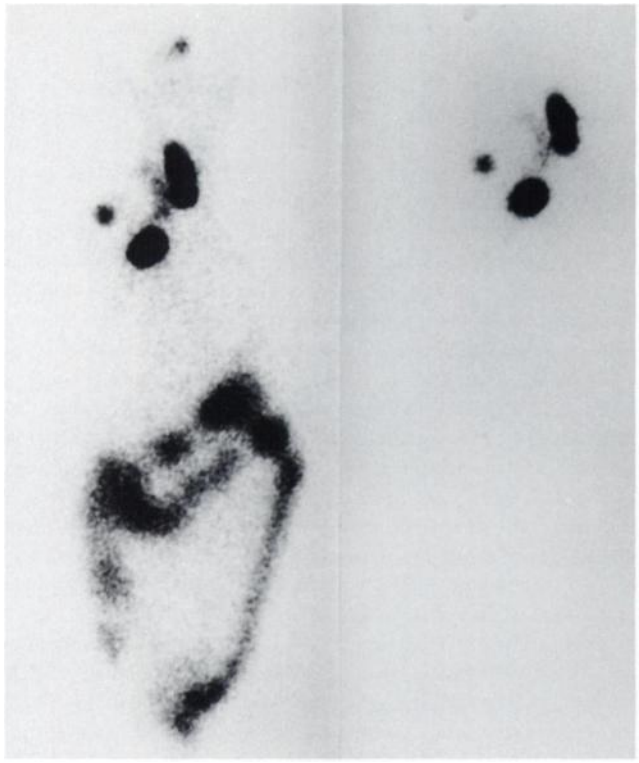

FIGURE 2. Iodine-131 scan 3 and 7 days after injection. There is prominent ^{131}I accumulation in the right hilum, upper lobe of the right lung, retrojugularly and in a small thyroid remnant. Faint accumulation in a supraclavicular lymph node is on the right. Physiological accumulation in the nasopharyngeal and the gastrointestinal mucosa occurred on the third day. After 7 days, the gastrointestinal tract is free of activity while pathological ^{131}I accumulation persists.

Our patient is exceptional in that he had a 24-yr history of suffering from three different malignancies. After recurrent Hodgkin's disease in his youth with repeated percutaneous supra- and infradiaphragmatic irradiations, he was diagnosed as having a papillary thyroid carcinoma, probably a secondary neoplasm, 24 yr later (*17*). Simultaneously, a medium-cell to small-cell undifferentiated bronchial carcinoma was diagnosed which surprisingly showed exceptional ^{131}I uptake. Positive results from staining the specimen with synoptophysin clearly proved the presence of a bronchial carcinoma, whereas negative results from thyroglobulin staining were not sufficient because false-positives can occur in differentiated metastases of thyroid carcinoma. A comparison of the two specimens, one obtained from the supraclavicular lymph node and one by bronchial brushing of the right hilum, showed totally different cell types, one typical for thyroid carcinoma (Fig. 1), the other for bronchial carcinoma (Fig. 3). Accumulation of ^{131}I is prominent, even after 7 days, where trapping in the salivary glands and the gastrointestinal tract is no longer observed and there is very little background activity. In contrast, Fernandez and Acosta reported very weak accumulation of activity (*10,13*). No explanations are available as to why a bronchial carcinoma can accumulate that much iodine (*18,19*). Acosta postulates the presence of aberrant thyroid receptors at the cell surface (*13*). It is well known that small-cell bronchial carcinomas are endocrine-active tumors that can produce ACTH and other hormones, which result in a paraneoplastic syndrome. Ratcliff et al. have shown that lung tumors, particularly anaplastic small-cell and large-cell carcinomas, influence T4/T3 metabolism (*20*). In our small-cell to medium-cell carcinoma, there was no measurable functional activity in that no thyroid

hormone could be measured in the thyroidectomized patient.

Another possible explanation is the pluripotency typically still present in tumor cells. It could be speculated that differentiated pluripotent cells, which have been proven to influence thyroid metabolism (*20*), may have developed a specific iodine uptake mechanism. The exceptional ^{131}I uptake in our patient supports this hypothesis because peritumoral edema or strong tumor vascularization do not sufficiently explain the persistent high level of ^{131}I accumulation.

In conclusion, an atypical clinical course of metastatic thyroid carcinoma should lead to a reevaluation of the diagnosis. For patients with a high risk for secondary neoplasia (preceding radiation therapy, heavy smoking), this differential diagnosis has to be considered.

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