CASE REPORTS

Hyperthyroidism with Metastatic Follicular Thyroid Carcinoma

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A 70-yr-old woman presented with hyperthyroidism and metastatic follicular carcinoma of the thyroid. The blood level of thyroid stimulating immunoglobulin (TSIg) was elevated. A total thyroidectomy was performed. One month later she remained hyperthyroid. Three weeks after therapy with 218 mCi of I-131 sodium iodide, the patient was euthyroid. Six months after the initial radioiodide therapy, she was again hyperthyroid and was given a second oral treatment dose of I-131 (220 mCi). Five months later, the patient had again become euthyroid. It is likely that initially the woman's metastases were producing sufficient hormone to render her hyperthyroid. After thyroidectomy and two large doses of radioiodide, she has remained euthyroid without having to take exogenous hormone. The blood level of TSIg had become undetectable. Based on this finding, we offer a tentative classification of the causes of hyperthyroidism in patients with thyroid carcinoma.

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It has been noted that well-differentiated thyroid cancer can produce thyroglobulin that enters the blood stream (*1*,*2*). The production of calorigenically active thyroid hormone by malignant tumors is much less common. We have followed a patient with follicular thyroid cancer and both clinical and chemical evidence of hyperthyroidism, in whom several unique mechanisms for hyperthyroidism were defined.

CASE REPORT

A 70-yr-old woman presented with fullness in her neck and 15 lb of weight loss. No lymph nodes were palpable. Radiographic studies revealed nodular infiltrates in the lungs and lytic lesions in the left humerus, right scapula, and several vertebrae. A [Tc-99m]pertechnetate image of the thyroid showed a moderate-sized gland with preservation of Tc-99m trapping. There was a photopenic nodule, 2 cm in diameter, located laterally in the midportion of the left lobe. The right thyroid lobe contained multiple areas of decreased uptake. Biopsy of a bone lesion revealed follicular carcinoma of the thyroid. She had no prior history of head or neck irradiation or antecedent medications.

Her pulse was 104/min and her skin warm and smooth. The eyes were bright but with no proptosis. Clinically she appeared hyperthyroid. Chemical findings (Table 1) were consistent with hyperthyroidism. The serum thyroid-stimulating immunoglobulin (TSIg) was greatly elevated: 32 μU TSH equivalent per ml (*3*).

A whole-body bone study revealed multiple foci of uptake. Body images were also obtained after an oral dose of 8 mCi of I-131

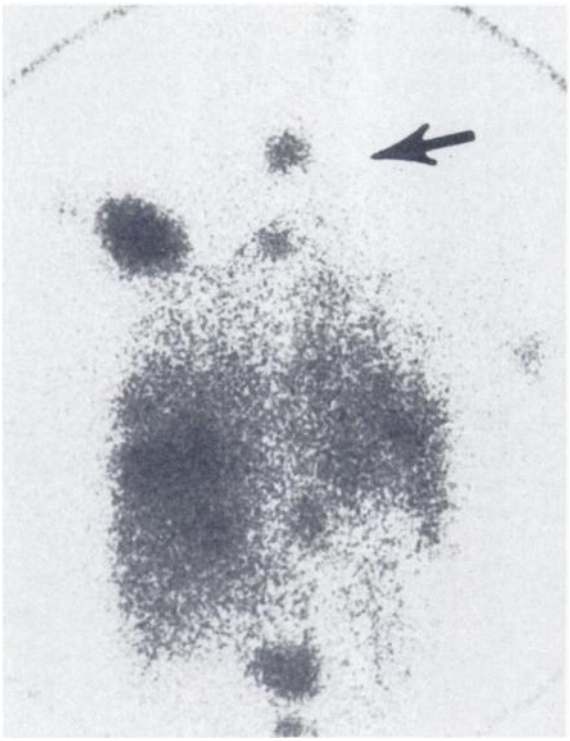

FIG. 1. Anterior scintiphoto of neck (arrow), thorax, and upper abdomen, obtained 72 hr after oral dose of 8 mCi of I-131 sodium iodide. In addition to some neck activity, there is massive uptake in right scapula, left humerus, several vertebrae, and both lungs.

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TABLE 1. SUMMARY OF SEQUENTIAL CLINICAL AND LABORATORY DATA. NORMAL VALUES ARE SHOWN IN PARENTHESES

Date	Comments	Serum thyroxine (4.5–11.5) μg/dl	Serum total T_3 (90–200) μg/dl	Serum TSH (0–6.5) μU/ml	T_3 resin (31–48)
Dec/2/81	Clinically hyperthyroid, whole-body scintigram with I-131, given propanol, PTU, KI	18.9	354	2.0	60.3%
Dec/10/81	Total thyroidectomy				
Jan/11/82	Still hyperthyroid	17.3			57.7%
Jan/12/82	Given 218 mCi $Na^{131}I$ p.o				
Feb/4/82	Euthyroid	7.4		1.1	
Mar/4/82	Euthyroid	6.3		3.8	19.6%
Jul/2/82	Clinically hyperthyroid, given 220 mCi $Na^{131}I$ p.o.	25			
Dec/2/82	Euthyroid	7.2	167	2.0	24.6%

TABLE 2. TENTATIVE CLASSIFICATION OF POSSIBLE CAUSES OF HYPERTHYROIDISM IN PATIENTS WITH THYROID CARCINOMA*

1. Exogenous
   a) Administration of exogenous thyroid hormone.
   b) Stimulation of endogenous thyroid by exogenous TSH or TSIg.
2. Endogenous
   a) Hormone produced by thyroid
      I. Hyperthyroidism from autonomous nodule
      II. Hyperthyroidism from TSIg stimulation
      III. Hyperthyroidism due to TSH-secreting tumor
   b) Extrathyroidal origin as from metastatic carcinoma (? TSH or TSIg stimulated).

* For general references, consult (*10*) on the immunology of thyroid diseases, and (*11*) for the existence of an abnormal TSH. References (*12–14*) deal with human thyroid neoplasms and their binding of TSH and activation of adenylate cyclase. TSH stimulation of lung metastases has been discussed (*15*) as well as the development of antithyrotropin antibodies (*16*).

sodium iodide (Fig. 1). The thyroid gland showed some uptake, but no massive concentration. There were multiple sites of ectopic uptake, especially in bones and in the lungs. Her hyperthyroidism was controlled with propranolol, propylthiouracil, and potassium iodide. She underwent a total thyroidectomy. The right thyroid lobe contained a well-differentiated follicular thyroid carcinoma. Both right and left lobes had follicular adenomas. Histologically the thyroid did not suggest hyperthyroidism.

One month after surgery the patient remained clinically and chemically hyperthyroid (Table 1). Hence, tissue outside of the thyroid was producing thyroid hormone. The table summarizes her I-131 treatment, relapse, second treatment, and return to euthyroidism without medication.

DISCUSSION

Hyperthyroidism and thyroid cancer can occur simultaneously (*4*). Yeo and associates reported nine cases of thyroid cancer in 720 patients with thyrotoxicosis (an incidence of 1.25%) (*5*). There are also several reports of thyroid carcinomas occurring within hyperfunctioning nodules (*6,7*).

Hyperthyroidism due to overproduction of thyroid hormone by a malignant tumor, however, is unusual. It is likely that this patient's metastatic lesions were producing quantities of metabolically active hormone, since (a) she remained hyperthyroid despite total thyroidectomy; and (b) after massive radioiodide therapy following surgical removal of the thyroid, the patient did not become hypothyroid. The initial findings of elevated TSIg and functional metastatic tissue suggested either Graves' disease coexisting with thyroid cancer, or ectopic production of TSIg by (or response to) the thyroid tumor. Nemec and co-workers have noted a case of hyperthyroidism with a functioning pelvic mass that proved to be follicular thyroid cancer (*8*). Grayzel and Bennett reported a case of follicular thyroid carcinoma in which there were functioning pulmonary metastases (*9*). In their patient, however, hyperthyroidism was relieved by removal of the main overactive tumor mass by thyroidectomy. It would be of interest (in such patients) to determine the blood levels of both thyroglobulin and calorigenically active hormones such as T_3 and T_4, and in view of the present report, thyroid-stimulating immunoglobulin (TSIg).

The I-131 scintigram, and analysis of the surgically resected thyroid, could not clearly describe the gland as being the cause of our patient's hyperthyroidism. She initially had elevated levels of TSIg. After thyroidectomy and two courses of radioiodide treatment, the TSIg level became undetectable (no interim values were available). The change, in addition to destruction of functional thyroid tumor, might be related to radiation of thyroid-associated lymphocytes, or to other reasons. This case had led us to reconsider the several possible causes of hyperthyroidism in patients with

thyroid carcinoma and to propose a tentative classification (Table 2).

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Amyloid Goiter: Preoperative Scintigraphic Diagnosis Using Tc-99m Pyrophosphate

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Amyloid goiter is a rare clinical entity. The diagnosis is rarely made preoperatively because clinical and laboratory findings are nonspecific. We report two cases of amyloid goiter in whom the diagnosis was made preoperatively using Tc-99m pyrophosphate scintigraphy.

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The incidental finding of amyloid deposits in the thyroid gland in patients with systemic amyloidosis is not unusual, occurring in 50-80% of patients. However, amyloid deposits large enough to cause thyroid enlargement are very rarely found, with only 70 such cases reported in the English literature. Although first described by Berkman in 1858, the specific term amyloid goiter was coined by von Eiselberg in 1904 (*1-3*). In view of the nonspecific clinical presentation and laboratory findings, amyloid goiter is rarely diagnosed preoperatively. We report two cases of amyloid goiter that show unique scintigraphic findings with Tc-99m-labeled pyrophosphate, a bone-seeking radiopharmaceutical. This simple scintigraphic procedure may be used to diagnose amyloid goiter in those patients clinically suspected of having this entity.

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