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Uptake of In-111 Pentetreotide by Normally Functioning Nodular Goiters

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After the intravenous administration of a radiolabeled somatostatin analogue (octreotide), normal thyroid and neoplastic and nonneoplastic thyroid lesions can be visualized. The authors present the cases of two patients who underwent somatostatin receptor scintigraphy (SSRS) using In-111 pentetreotide: one for the study of suspected paraneoplastic ACTH hypersecretion, and the other for a restaging of breast carcinoma with neuroendocrine features. In both patients, SSRS revealed increased uptake in the thyroid, corresponding to "cold" nodules on Tc-99m pertechnetate imaging. Cytologic and histologic examinations showed the typical features of thyroid goiters without lymphocytic infiltration.

Key Words: Somatostatin Receptor Scintigraphy, Octreotide, Thyroid Diseases.

IT IS KNOWN that the uptake of radiolabeled octreotide by normal thyroid is a possible physiologic finding during somatostatin (SS) receptor scintigraphy (SSRS). It has been reported that the gland can be clearly seen on delayed images in approximately 70% of patients (1), with a maximum uptake at 5 hours (2) and strong variations between individual subjects (3).

On the other hand, increased uptake of In-111 pentetreotide has been described in several pathologic conditions of the thyroid (4,5). In fact, SSRS has been used in the study of either neuroendocrine (NE) tumors, such as medullary carcinoma (6–9) or non-NE neoplasms, such as papillary, follicular, insular, and anaplastic cancers (10–12), which show increased accumulation of the radionuclide in a large number of cases.

Some nonmalignant diseases, such as Graves' hyperthyroidism (13–15), Hashimoto's disease, De Quervain's thyroiditis (4,5), and follicular adenomas (5) can show abnormal uptake on SS imaging.

Increased radiolabeled octreotide uptake in thyroid nodular goiters has been described in only one article (16). In this study, we report two cases with marked In-111 pentetreotide accumulation in normally functioning nodular goiters.

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Case Reports

Case 1

SSRS was performed in a 56-year-old woman with Cushing's syndrome who had a poor ACTH response to suppressive dynamic tests.

Imaging revealed increased uptake in the right lobe of the thyroid (Fig. 1), corresponding to a neck swelling. This nodule was a "cold" lesion on Tc-99m pertechnetate imaging and hypoechogenic on US. Fine-needle aspiration was suggestive of nodular colloid goiter and c-cells were not found (17).

Selective venous sampling of the inferior petrosal sinus was performed, and a left pituitary ACTH microadenoma was found. The lesion was confirmed by a second MRI and the patient underwent stereotaxic radiosurgery with excellent results.

Case 2

A 52-year-old woman underwent SSRS during a follow-up restaging after a left radical mastectomy for breast carcinoma with neuroendocrine features performed 1.5 years earlier.

SSRS revealed only increased uptake of In-111 pentetreotide in the left lobe of the thyroid (Fig. 2) corresponding to a "cold" area on Tc-99m pertechnetate imaging and to a hypoechogenic nodule on US.

Fine-needle aspiration was suggestive of a thyroid colloid goiter. This patient did not undergo surgical treatment.

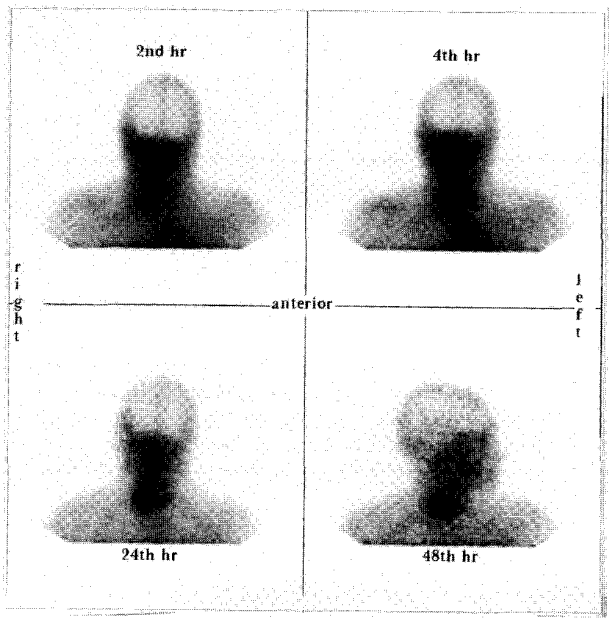

Fig. 1. Anterior planar scans at 2, 4, 24, and 48 hours showing an abnormal increased uptake of In-111 pentetreotide in the right lobe of the thyroid.

Discussion

Peptide hormone activity is mediated by binding to specific high-affinity receptors, generally located at the cellular membrane level. Using radiolabeled hormones or analogues, it is possible to visualize cells or tissues bearing receptors for these peptides. Diseases in which pathologic tissues express SS-receptors can be studied using radiolabeled octreotide, an analogue peptide of SS. SSRS can be employed in the study of some thyroid diseases, such as medullary thyroid carcinomas (MTC) (6–9). These neoplasms, which belong to the family of NE tumors, are composed of neoplastic C-cells, which express SS-receptors, such as in other types of NE cells. Using SSRS, tumor localization was seen in approximately 65% of patients with MTC in one series (7). In this study, the authors demonstrated SS-receptors in vitro in all neoplasms that were visualized in vivo. The demonstration of SS-receptors in this and other types of tumors has important implications both in the diagnostic approach and in treatment (18,19).

Accumulation of radiolabeled octreotide has been reported in normal thyroid glands (1–3) and in some thyroid lesions not related to C-cell proliferation (4,5,13–16). Adrian et al (1) described octreotide uptake in normal thyroid in approximately 70% of patients who underwent SSRS. The gland became clearly delineated on delayed images, at least 4 hours after injection, but generally at 24 hours. The mechanism responsible for this imaging is unclear because SS-receptors have not yet been found in normal thyroid tissue (6,20). It has been hypothesized that the visualization of the gland is related to octreotide binding to SS-receptors of the C-cells (5). In our series, the thyroid gland was visualized in approximately 70% of 20 patients who underwent SSRS for evaluation and staging of SS receptors expressing NE tumors.

Increased thyroid octreotide uptake has been reported in Graves' hyperthyroidism (13–15), Hashimoto's disease, De Quervain's thyroiditis (4,5), endemic goiters (16), follicular adenomas and carcinomas, and papillary, insular, and anaplastic cancers (5,10–12). It has been speculated that in Graves' and Hashimoto's disease, the presence within the thyroid of activated lymphocytes, which possess SS-receptors, might explain the accumulation of the radiolabeled SS analogue (4,5). Interestingly, the other diseases mentioned previously (papillary, insular, anaplastic, and follicular carcinoma, follicular adenomas, endemic goiters) are not related to C-cell proliferation and are not associated with significant lymphocytic infiltration. All of them have been visualized during SSRS (10–12,16).

These findings may suggest the possible presence of SS-receptors in follicular cells. Some authors have demonstrated a direct action of SS on follicular thyroid cells. Degli Uberti et al (21) showed that SS inhibited both the basal and TSH-induced tritiated thymidine incorporation of human normal and goitrous thyroid follicles in

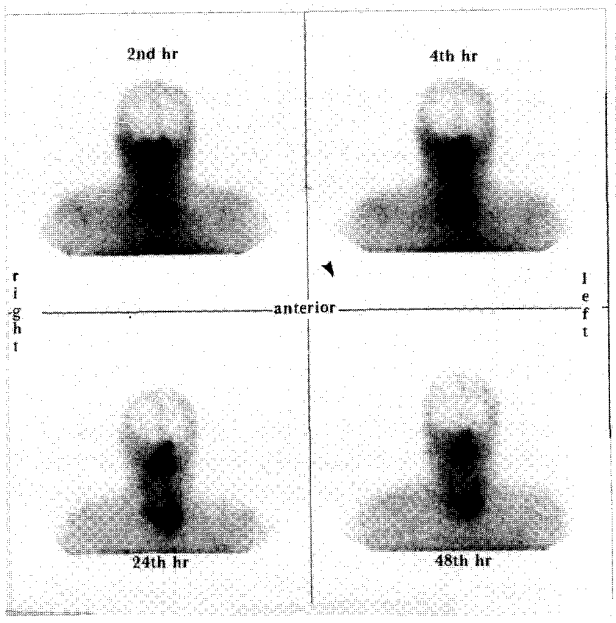

Fig. 2. Anterior planar scans at 2, 4, 24, and 48 hours showing abnormal increased uptake of In-111 pentetreotide in the left lobe of the thyroid.

suspensions. Systemic administration of SS was found to be able to block thyroid hormone secretion induced by injection of TSH in humans (22). More recent studies have shown that SS inhibits basal and TSH-stimulated adenilate cyclase activity in normal and neoplastic human thyroids (23), and that octreotide is able to inhibit cell growth and protease activity in papillary and follicular thyroid cancers (24).

In both cases cytologic smears were obtained by fine-needle aspiration and we did not find a significant lymphocyte component that might suggest a possible thyroiditis associated with the goiters. In the case studied histologically, it was possible to verify that there was not a lymphocytic infiltration in the lesion and, using immunohistochemical technique, it was also possible to demonstrate the absence of C-cells. These results, together with those reported by other authors, suggest that follicular thyroid cells may really express SS-receptors on their cellular membrane. This hypothesis is in agreement with the results obtained in a recent study (25), in which the authors demonstrated ligand binding to SS-receptors in membranes and cell lines of human thyroid carcinoma, but they did not identify the receptor subtypes which were expressed. Because the radiolabeled octreotide uptake seems to be greatly increased in thyroid diseases related to follicular cell proliferation, such as nodular goiter, follicular adenoma, follicular, papillary, and anaplastic cancers, compared to normal thyroid, it may be speculated that in these lesions the amount of SS-receptors might be increased.

Our findings show that abnormal thyroid In-111 pentetreotide uptake may be simply due to a nodular goiter that should be considered in the differential diagnosis of "cold" nodules of the thyroid, among the possible lesions characterized by positive SSRS.

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