

Accumulation of ^{99m}Tc -sestamibi in tissue is analogous to that of thallium and uptake is proportional to blood flow. In addition, tissues that are mitochondria-rich show a longer retention of ^{99m}Tc -sestamibi (18). Sandrock et al. (11) showed that parathyroid adenomas are mitochondria-rich and that ^{99m}Tc -sestamibi is taken up more avidly and released more slowly by these adenomas than by the surrounding thyroid (11). Early and delayed images with ^{99m}Tc -sestamibi take advantage of its differential kinetics: ^{99m}Tc -sestamibi, like ^{201}Tl , washes out of the thyroid gland quickly; unlike ^{201}Tl , however, it is retained in hyperfunctioning parathyroid tissue thereby allowing better visualization (19). This differential in washout times results in a 90% sensitivity for detecting parathyroid adenomas when ^{99m}Tc -sestamibi is used as a single agent (double-phase study) (20).

Initial studies have suggested improved localization with the addition of SPECT (21–26). SPECT offers the advantages of greater tissue contrast, reasonable resolution at depth, and three-dimensional localization. Neumann et al. (27) recently reported demonstration of a mediastinal parathyroid adenoma with SPECT. The report did not indicate whether planar imaging was attempted. In comparison to ^{201}Tl , ^{99m}Tc has higher energy that allows better penetration of the thorax. In addition, the larger administered dose of ^{99m}Tc -sestamibi permits shorter imaging times and facilitates the use of SPECT (28,29).

CONCLUSION

In our patient, ^{99m}Tc -sestamibi SPECT demonstrated an abnormal focus of activity in the middle mediastinum, which correlated with a pathologically proven parathyroid adenoma that was not detected with planar imaging or prior undirected mediastinal exploration. We suggest routine use of ^{99m}Tc -sestamibi SPECT of the mediastinum when standard planar images are negative. This case illustrates the usefulness of ^{99m}Tc -sestamibi SPECT in localizing mediastinal parathyroid adenomas preoperatively.

REFERENCES

- Levin KE, Gooding GAW, Okerlund M, et al. Localizing studies in patients with persistent or recurrent hyperparathyroidism. *Surgery* 1987;102:917–925.
- Edis AJ, Beahrs OH, Sheedy PF II. Reoperation for hyperparathyroidism. *World J Surg* 1977;1:731–738.
- Satava RM Jr, Beahrs OH, Scholz DA. Success rate of cervical exploration for hyperparathyroidism. *Arch Surg* 1975;110:625–627.
- Shaha AR, Jaffe BM. Cervical exploration for primary hyperparathyroidism. *J Surg Oncol* 1993;52:14–17.
- Roe SM, Burns RP, Graham LD, Brock WB, Russell WL. Cost-effectiveness of preoperative localization studies in primary hyperparathyroid disease. *Ann Surg* 1994;219:582–586.

- Wang CA. Parathyroid re-exploration: a clinical and pathological study of 112 cases. *Ann Surg* 1977;186:140–145.
- Akerstrom G, Malmaeus J, Bergstrom R. Surgical anatomy of human parathyroid glands. *Surgery* 1984;95:14–21.
- Ferlin G, Borsato N, Camerani M, Conte N, Zotti D. New perspectives in localizing enlarged parathyroids by technetium-thallium subtraction scan. *J Nucl Med* 1983;24:438–441.
- Winzelberg GG, Hydovitz JD. Radionuclide imaging of parathyroid tumors: historical perspectives and newer techniques. *Semin Nucl Med* 1985;15:161–170.
- Winzelberg GG. Parathyroid imaging. *Ann Intern Med* 1987;107:64–70.
- Sandrock D, Merino MJ, Norton JA, Neumann RD. Parathyroid imaging by Tc/Tl scintigraphy. *Eur J Nucl Med* 1990;16:607–613.
- Rantis PC Jr, Prinz RA, Wagner RH. Neck radionuclide scanning: a pitfall in parathyroid localization. *Am Surg* 1995;61:641–645.
- Coakley AJ, Kettle AG, Wells CP, O'Doherty MJ, Collins REC. Technetium-99m-sestamibi—a new agent for parathyroid imaging. *Nucl Med Commun* 1989;10:791–794.
- Hindie E, Melliere D, Simon D, Perlemuter L, Galle P. Primary hyperparathyroidism: is technetium-99m-sestamibi/iodine-123 subtraction scanning the best procedure to locate enlarged glands before surgery? *J Clin Endocrinol Metab* 1995;80:302–307.
- Thule P, Thakore K, Vansant J, McGarity W, Weber C, Phillips LS. Preoperative localization of parathyroid tissue with technetium-99m-sestamibi/iodine-123 subtraction scanning. *J Clin Endocrinol Metab* 1994;78:77–82.
- Casas AT, Burke GJ, Mansberger AR Jr, Wei JP. Impact of technetium-99m-sestamibi localization on operative time and success of operations for primary hyperparathyroidism. *Am Surg* 1994;60:12–16.
- Wei JP, Burke GJ, Mansberger AR Jr. Prospective evaluation of the efficacy of technetium-99m-sestamibi and iodine-123 radionuclide imaging of abnormal parathyroid glands. *Surgery* 1992;112:1111–1116.
- O'Doherty MJ, Kettle AG, Wells P, Collins EC, Coakley AJ. Parathyroid imaging with technetium-99m-sestamibi: preoperative localization and tissue uptake studies. *J Nucl Med* 1992;33:313–318.
- Oates E. Improved parathyroid scintigraphy with ^{99m}Tc -MIBI, a superior radiotracer. *Applied Radiol* 1994;23:37–40.
- Taillefer R, Boucher Y, Potvin C, Lambert R. Detection and localization of parathyroid adenomas in patients with hyperparathyroidism using a single radionuclide imaging procedure with technetium-99m-sestamibi (double-phase study). *J Nucl Med* 1992;33:1801–1807.
- Sfakianakis G, Foss J, Georgiou M, Irvin G III, Levis-Dusseau S, Chandraratna SKC. The role of preoperative SPECT ^{99m}Tc -sestamibi imaging and intraoperative PTH measurement in para-thyroidectomy [Abstract]. *J Nucl Med* 1994;35(suppl):68P.
- Staudenherz A, Telfeyan D, Steiner E, et al. Comparison of 3 imaging methods for the localization of parathyroid tumors [Abstract]. *J Nucl Med* 1994;35(suppl):167P.
- Suzuki Y, Hiramatsu K. Parathyroid adenoma demonstrated with Tl-201 SPECT. *Clin Nucl Med* 1993;18:561–563.
- Neumann DR. Simultaneous dual-isotope SPECT imaging for the detection and characterization of parathyroid pathology. *J Nucl Med* 1992;33:131–134.
- Jenkins BJ, Newell MS, Goode AW, Boucher BJ, Monson JP, Brown CL. Impact of conventional and three-dimensional thallium-technetium scans on surgery for primary hyperparathyroidism. *J R Soc Med* 1990;83:427–429.
- Ziffer JA, Fajman WA. Ectopic parathyroid gland localization with thallium-201 SPECT. *Clin Nucl Med* 1987;12:617–619.
- Neumann DR, Esselstyn CB, Eastwood J, Rice TW. Localization of mediastinal parathyroid adenoma in recurrent postoperative hyperparathyroidism with ^{99m}Tc -sestamibi SPECT. *Clin Nucl Med* 1995;20:175.
- Morita ET, Kwan WP, Clark OH. Technetium-99m-sestamibi for parathyroid imaging. *West J Med* 1994;161:413.
- Kwan WP, Morita E, Clark O. Technetium-99m-sestamibi is a superior agent to thallium-201 pertechnetate subtraction in evaluating patients for repeat parathyroidectomy for either adenoma or hyperplasia [Abstract]. *Clin Nucl Med* 1993;18:927.

Somatostatin-Receptor Scintigraphy of Subcutaneous and Thyroid Metastases from Bronchial Carcinoid

Yodphat Krausz, M. Raphael Pfeffer, Benjamin Glaser and Joel Lafair

Departments of Nuclear Medicine, Oncology, Endocrinology and Pulmonary Unit, Hadassah University Hospital, Jerusalem, Israel

We present a case of bronchial carcinoid tumor with multiple metastases in the retina, subcutaneous tissues and thyroid gland. These metastatic lesions were detected by ^{111}In -pentetreotide scintigraphy 15 yr after removal of the primary tumor. The extensive

metastatic involvement documented on scintigraphy spared the patient unnecessary total thyroidectomy and directed the attention of the primary physician to previously unknown and potentially more important foci of metastatic disease.

Key Words: carcinoid; subcutaneous metastases; thyroid; retinal metastases; indium-111-pentetreotide

J Nucl Med 1996; 37:1537–1539

Received Dec. 27, 1995; revision accepted Feb. 15, 1996.

For correspondence or reprints contact: Yodphat Krausz, M.D., Department of Nuclear Medicine, Hadassah University Hospital, P.O. Box 12000, Jerusalem, 91120, ISRAEL, Phone: 972 2 777860, Fax: 972 2 437940.

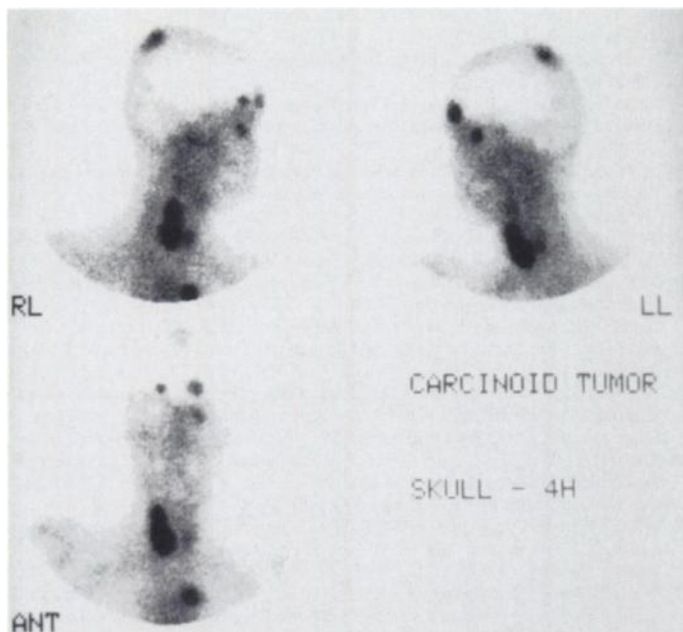


FIGURE 1. Right lateral (RL), left lateral (LL) and anterior (ANT) views of the skull demonstrating multiple foci in the parietal and frontal bones, right frontal lobe and left orbit. Additional lesions are seen in the thyroid gland and left upper mediastinum.

CASE REPORT

A 36-yr-old woman was referred to our nuclear medicine department for ^{111}In -pentetreotide scintigraphy. Fifteen years earlier, the patient underwent a left upper lobectomy for a polypoid endobronchial carcinoid tumor, following symptoms of dyspnea and hemoptysis. The patient was completely asymptomatic for 6 yr following resection of the tumor, when she developed blurred vision in the left eye. On fundoscopy, a subretinal nodule causing mild retinal detachment in the left eye and a nodule anterior to the equator in the right eye were identified. Because of the location and size of the lesions, tissue diagnosis was not feasible without endangering the eye. The patient underwent several local treatments to the eye with laser, cryotherapy, radioactive cobalt plaque and proton beam radiotherapy with limited success.

During this time, the patient was found to have enlarged nodes in the right axilla and supraclavicular area. Biopsies demonstrated metastatic carcinoid tumor.

Fifteen years after the initial surgery, an enlarged thyroid gland was detected on physical examination. Ultrasonography disclosed multiple solid nodules in both lobes of the thyroid gland ranging in size from 3 (left) to 19 mm (right), and TcO_4^- scintigraphy detected a dominant cold area in the right thyroid lobe. Fine-needle aspiration (FNA) of the palpable cold nodule disclosed multiple epithelial cells in clusters, with positive stain for chromogranin, suggestive of carcinoid tumor, and surgical removal was advised.

To determine the extent of the metastatic process prior to the suggested total thyroidectomy, ^{111}In -pentetreotide scintigraphy was performed. Static views of the skull, neck, chest, abdomen and pelvis, together with SPECT images of the chest and abdomen, were obtained at 4 and 24 hr after tracer injection, using a single-head rotating gamma camera equipped with a medium-energy collimator.

Scintigraphy revealed multiple pathological foci in the skull, right frontal lobe of the brain, left orbit (Fig. 1), thyroid gland, mediastinum, paraortic lymph nodes and pelvis (Fig. 2). In addition, multiple foci were also observed in the subcutaneous tissues of both arms and in the left humerus (Fig. 3). CT confirmed the findings in the skull, brain parenchyma, neck and mediastinum. It did not, however, identify the abdominal and ischial foci.

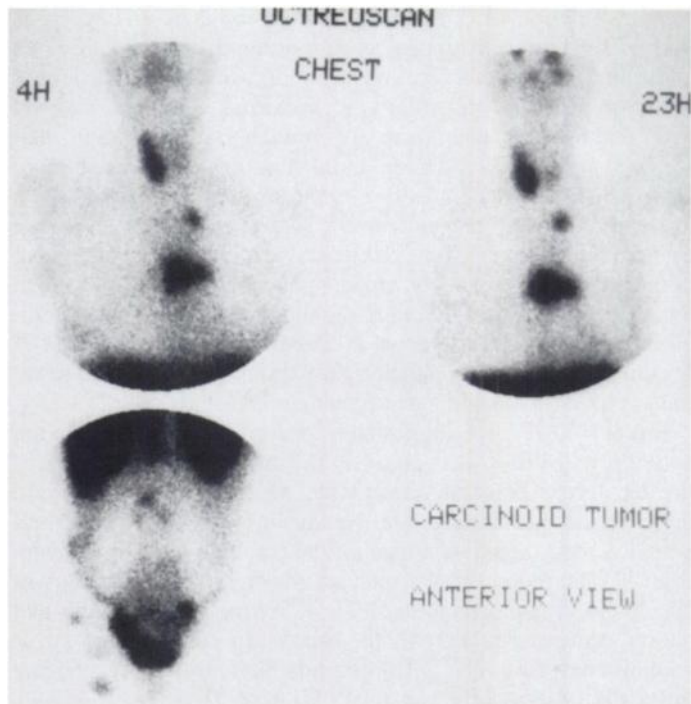


FIGURE 2. Anterior view of the chest, abdomen and pelvis demonstrating pathologic foci in the thyroid gland, upper left and middle mediastinum, para-aortic nodes and right inguinal region.

Aside from the visual defect associated with the retinal lesion, the patient has remained completely asymptomatic. Urinary 5-hydroxyindolacetic acid excretion is, however, elevated to 11.6 mg (upper limit of normal 8 mg/24 hr).

No surgical procedure was performed because of the extensive metastatic spread demonstrated scintigraphically, and the patient is now being considered for somatostatin analog therapy.

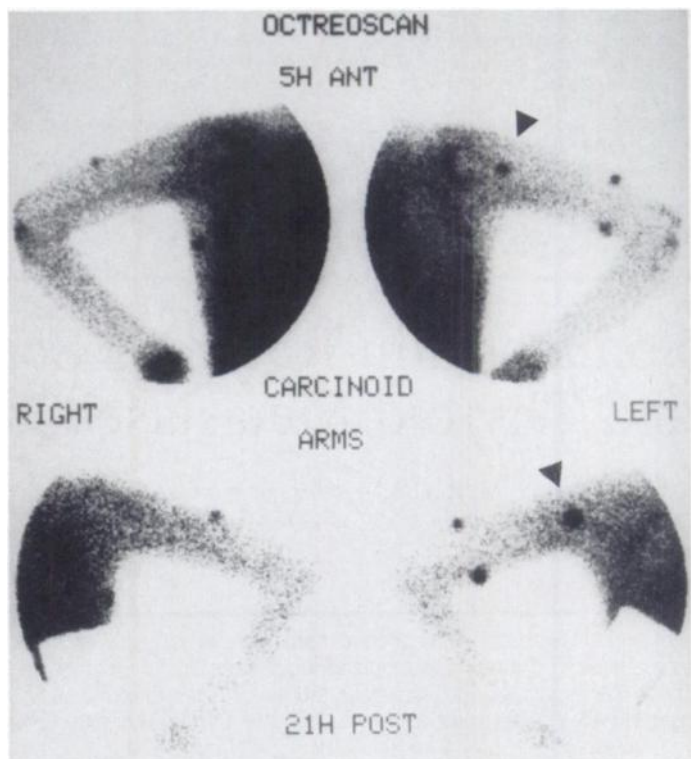


FIGURE 3. Anterior (top) and posterior views (bottom) of the arms demonstrating multiple subcutaneous lesions and pathologic uptake in the left proximal humerus (arrow).

DISCUSSION

The typical carcinoid of the bronchus has a favorable prognosis (1) with a 5-yr survival of above 90% (2,3). Our patient is alive 15 yr after initial diagnosis; retinal metastases were, however, documented 6 yr after diagnosis and surgical removal of the primary tumor. Metastases to the subcutaneous tissues, bone, paraortic nodes, thyroid gland and mediastinum were detected 9 yr later.

Subcutaneous metastases of carcinoid origin have been rarely described. These lesions may be either asymptomatic (4) or tender (5). They may be the initial manifestation of a midgut tumor (4) or of a pulmonary carcinoid (5) and may precede the carcinoid syndrome by several years (4). Our patient was found to have several asymptomatic subcutaneous nodules 6 yr after the primary tumor had been removed, at the time of visual manifestations.

Recently, metastases to the thyroid gland were also observed. Metastatic involvement of the thyroid is not commonly considered in the differential diagnosis of a patient with a thyroid mass but had been reported in 4 of 70 patients (5.7%) with thyroid nodules referred for FNA in a 12-mo period (6). In that study, one patient had carcinoid tumor metastatic to the thyroid with an unlocalized primary site. Others have reported rectal (7) or small-bowel (8) carcinoid tumors metastatic to the thyroid, although these tumors usually metastasize to the regional lymph nodes or to the liver (3). Our patient has metastatic involvement of the thyroid from a primary tumor originating in the lung.

The presence of high-density somatostatin receptors on neuroendocrine tumors may suggest responsiveness to long-term octreotide therapy, as documented by Kvols et al. (9). In carcinoid patients, somatostatin analog therapy has been associated with excellent symptomatic relief and improved survival, despite the paucity of convincing evidence for in vivo tumor

regression. Continued treatment of somatostatin-receptor positive patients with somatostatin analogs may be advantageous, even in the absence of hormone-related symptoms, as is the case for this patient.

Surgical resection of isolated metastatic foci may have been indicated in this patient, given the poor response of carcinoid tumors to chemotherapy. In fact, thyroidectomy was recommended despite the presence of metastases in the eye, since these were partially controlled by local treatment. However, the extensive metastatic disease documented on ¹¹¹In-pentetreotide scintigraphy spared the patient unnecessary thyroid surgery. Furthermore, it directed the primary physician to a previously unsuspected lesion in the brain parenchyma.

REFERENCES

1. Bonato M, Cerati M, Pagani A, et al. Differential diagnostic patterns of lung neuroendocrine tumours. A clinicopathological and immunohistochemical study of 122 cases. *Virchows Arch Pathol Anat Histopathol* 1992;420:201-211.
2. Martini N, Zaman MB, Bains MS, et al. Treatment and prognosis in bronchial carcinoids involving regional lymph nodes. *J Thorac Cardiovasc Surg* 1994;107:1-6.
3. Vadasz P, Palfy G, Egervary M, Schaff Z. Diagnosis and treatment of bronchial carcinoid tumors: clinical and pathological review of 120 operated patients. *Eur J Cardiothorac Surg* 1993;7:8-11.
4. Naschitz JE, Yeshurun D, Nash E, Lev L, Shajrawi, Boss JH. Cervical soft-tissue metastasis of typical carcinoid tumor preceding diagnosis of ileal primary by 4 years. *Am J Gastroenterol* 1992;87:1665-1668.
5. Oleksowicz L, Morris JC, Phelps RG, Bruckner HW. Pulmonary carcinoid presenting as multiple subcutaneous nodules. *Tumori* 1990;76:44-47.
6. Watts NB. Carcinoma metastatic to the thyroid: prevalence and diagnosis by fine-needle aspiration cytology. *Am J Med Sci* 1987;293:13-17.
7. Lertprasertsuke N, Kakudo K, Satoh S, Tada N, Osamura Y. Rectal carcinoid tumor metastasizing to the thyroid and pancreas: an autopsy case exploiting immunohistochemistry for differentiation from tumors involving multiple endocrine organs. *Acta Pathol Jpn* 1990;40:352-360.
8. Marks WH, Strodel WE, Lloyd RV, Eckhauser FE, Thompson NW, Vinik AL. Cervical metastases from small-bowel carcinoid tumors. *J Surg Oncol* 1983;24:135-141.
9. Kvols LK, Reubi JC, Horisberger U, Moertel CG, Rubin J, Charboneau JW. The presence of somatostatin receptors in malignant neuroendocrine tumor tissue predicts responsiveness to octreotide. *Yale J Biol Med* 1992;65:505-518.