

cemia and hyperphosphatemia. Technetium-99m-MDP binds avidly to the tissue crystals that are present.

Extracellular fluid expansion and enhanced regional vascularity and permeability due to granulomatous inflammation may also cause this high extraosseous ^{99m}Tc-MDP uptake (16).

The findings in our patient are unique because his hypercalcemia is not caused by malignant disease, hyperparathyroidism or drug-induced vitamin D intoxication. Elevated soft-tissue uptake of ^{99m}Tc-MDP caused by drug-induced vitamin D intoxication has been reported (10,13). The patients in these reports had elevated uptake in the lungs and/or in the stomach. One patient (13) took roughly 2000 U of vitamin D and 3 g of calcium a day. Massive gastric uptake ^{99m}Tc-MDP without elevated lung uptake has been reported only once in a patient who had a milk-alkali syndrome (13). In our patient, drug-induced hypervitaminosis D could be ruled out.

Rapidly calcifying sites are frequently pure amorphous calcium phosphate accumulations with a large surface area. The reason why only the stomach and the lungs were visualized could be explained by the fact that calcification can occur in normal tissue when the acid-base balance allows precipitation of calcium and phosphate (1). Intracellular pH is high in the lungs because of low pCO₂ and because of acid secretion in the kidneys and stomach (17). These are the predominant places where calcium salt precipitates (13). In our patient, the fundus of the stomach showed higher activity than in the antrum, which we believe confirms the pH dependency of the calcium deposition. Gastric fixation in bone scintigraphy due to preparation failure (18) can occur but was ruled out in our patient.

Interestingly, during the first bone scan, the calcium-phosphorus ionization product in the blood was already normal. Probably the injected ^{99m}Tc-MDP bound avidly to the tissue crystals that were still present. After 6 wk, the gastric and lung uptake had disappeared, apparently because the tissue crystals were dissolved because of the relatively long period of a normal calcium/phosphorus ionization product. There is one other published report on this reversible phenomenon (17).

CONCLUSION

We expect, because organ involvement and hypercalcemia in sarcoidosis are often asymptomatic, that calcinosis occurs more often in patients than previously described. Usually bone scans are not obtained in patients with sarcoidosis, despite the fact that bone scintigraphy has been described as a sensitive modality for recognition of bony involvement by sarcoidosis (19).

REFERENCES

1. Heck LL. Extraosseous localization of phosphate bone agents. *Semin Nucl Med* 1980;10:311-313.
2. Padhy AK, Gopinath PG, Amini AC. Myocardial, pulmonary, diaphragmatic, gastric, splenic and renal uptake of ^{99m}Tc-MDP in a patient with severe hypercalcemia. *Clin Nucl Med* 1990;15:648-649.
3. Wynchank S, Brendel AJ, Leccia F, Lacoste D, Maire JP, Ducassou D. Transient intense gastric fixation of ^{99m}Tc-MDP. *Eur J Nucl Med* 1983;8:458-460.
4. Reitz MD, Vasinrapee P, Mishkin FS. Myocardial, pulmonary and gastric uptake of ^{99m}Tc-MDP in a patient with multiple myeloma and hypercalcemia. *Clin Nucl Med* 1986;11:730.
5. Valdez VA, Jacobstein JG, Perlmutter S, Brusman H. Metastatic calcification in the lungs and stomach demonstrated on bone scan in multiple myeloma. *Clin Nucl Med* 1979;4:120-121.
6. Rosenthal DI, Chandler HL, Azizi F, Schneider PB. Uptake of bone imaging agents by diffuse pulmonary metastatic calcification. *AJR* 1977;129:871-874.
7. Richards AG. Metastatic calcification detected through scanning with ^{99m}Tc-polyphosphate. *J Nucl Med* 1974;15:1057-1060.
8. Grames GM, Sausser DD, Jansen C, Soderblom RE, Hodgkin JE, Stilson MS. Radionuclide detection of diffuse interstitial pulmonary calcification. *JAMA* 1974;230:992-995.
9. McDevitt GR, Heironimus JD, Toney MO, Bilingsley JL. Diffuse abdominal uptake of technetium-99m-methylene diphosphonate in a patient on continuous ambulatory dialysis during bone scintigraphy. *J Nucl Med* 1992;33:2052-2054.
10. Jayabalan V, De Witt B. Gastric calcification detected in vivo by ^{99m}Tc-pyrophosphate imaging. *Clin Nucl Med* 1978;3:27-29.
11. Schlangen JT, Pauwels EKJ. Die diagnostik der calcinosis pulmonis durch szintigraphische untersuchungen. *Fortschr Geb Roentgenstr Nuclearmed* 1976;124:119-123.
12. Van Leendert FJ, Flendrig JA. A patient with primary hyperparathyroidism and an abnormal bone scan. *Clin Nucl Med* 1986;11:701-703.
13. Corstens F, Kerremans A, Claessens R. Resolution of massive technetium-99m-methylene diphosphonate uptake in the stomach in vitamin D intoxication. *J Nucl Med* 1986;27:219-222.
14. Akmal M, Sharma OP. Renal sarcoidosis: a reminder. *Chest* 1990;97:1284-1285.
15. Marinides GN, Hadju I, Gans RO. A unique association of renal carcinoma with sarcoid reaction in the kidney. *Nephron* 1994;67:477-480.
16. Peller PJ, Ho VB, Kransdorf MJ. Extraosseous ^{99m}Tc-MDP uptake: a pathophysiologic approach. *Radiographics* 1993;13:715-734.
17. Delcourt E, Baudoux M, Neve P. Technetium-99m-MDP bone scanning detection of gastric calcification. *Clin Nucl Med* 1980;5:546-547.
18. Dhawan V, Yeh DJ. Labeling efficiency and stomach concentration in methylene diphosphonate bone imaging. *J Nucl Med* 1979;20:791-793.
19. Yaghma I. Radiographic, angiographic and radionuclide manifestations of osseous sarcoidosis. *Radiographics* 1983;3:374-376.

Accelerated Thyrotoxicosis Induced by Iodinated Contrast Media in Metastatic Differentiated Thyroid Carcinoma

Mordechai Lorberboym and Jeffrey I. Mechanick

Division of Nuclear Medicine, Department of Radiology, and Division of Endocrinology, Department of Medicine, Mount Sinai School of Medicine, New York, New York

A 67-yr-old woman who underwent total thyroidectomy 32 yr ago developed accelerated hyperthyroidism after injection of iodinated contrast media to evaluate a left hemipelvis mass. The patient was managed with propylthiouracil, beta-blockers and digoxin. Whole-body ²⁰¹Tl and ¹³¹I scans demonstrated a functioning metastasis in the left hemipelvis where biopsy revealed a well differentiated follicular thyroid carcinoma. Palliative external beam radiotherapy was

administered. The patient then received radioiodine treatment with granulocyte colony-stimulating factor to minimize bone marrow toxicity. Clinically significant thyrotoxicosis occurring in metastatic thyroid carcinoma is rare and results from abnormal ectopic thyroid tissue iodine metabolism. Iodide-containing medications and contrast media should be avoided in patients with functioning thyroid metastases to prevent abrupt increases in circulating thyroid hormone levels.

Key Words: thyroid carcinoma; thyrotoxicosis; granulocyte colony-stimulating factor

J Nucl Med 1996; 37:1532-1535

Received Dec. 5, 1995; revision accepted Mar. 6, 1996.

For correspondence or reprints contact: Mordechai Lorberboym, MD, Department of Nuclear Medicine, Mount Sinai Medical Center, One Gustave L. Levy Pl., New York, NY 10029.

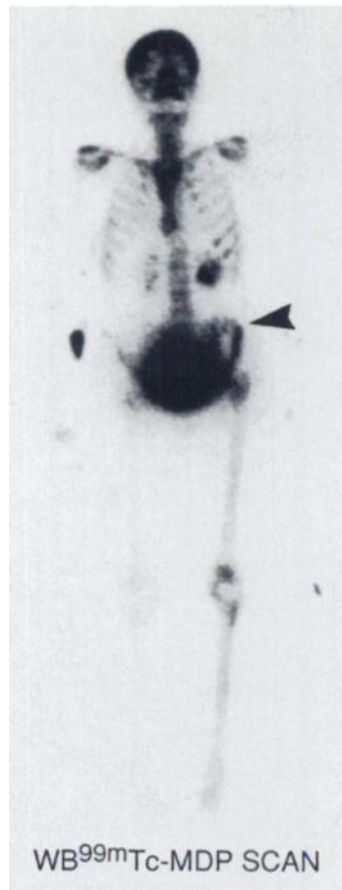


FIGURE 1. Whole-body bone scan shows a photopenic defect in the left iliac bone with intense peripheral uptake (arrow).

Exposure to increased quantities of iodine may induce thyrotoxicosis in a previously euthyroid patient (the Jod-Basedow phenomenon), presumably by production and secretion of excessive hormone in functionally autonomous thyroid tissue (1). It usually occurs in areas of endemic iodine deficiency (2), primarily in patients with nontoxic multinodular goiter. In normal animals and humans, the administration of large doses of iodide leads to transient inhibition of organic iodination and of thyroid hormone synthesis (the Wolff-Chaikoff effect) (3–5). Iodides have also been utilized to treat patients with Grave's disease as preoperative preparation.

However, after the initial exposure to iodide, more efficient

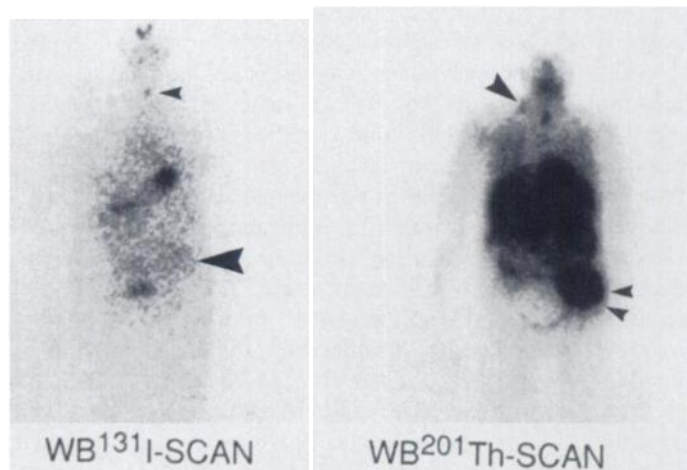


FIGURE 2. Whole-body iodine scan (left) shows increased activity in the left hemipelvis (large arrowhead) and a faint focus in the neck (small arrowhead). Whole-body thallium scan (right) shows intense uptake in the left iliac fossa (double arrowheads), a focus of activity in the right neck (single arrowhead) and in the thyroid fossa (additional focus in the right scapula is not shown).

organic iodination resumes by an autoregulatory mechanism of adaptation, resulting in diminished iodide trapping (6–8). We report on a patient with a functioning metastatic follicular thyroid carcinoma who produced sufficient thyroid hormone to induce accelerated hyperthyroidism and required complex medical management. Iodide-associated thyrotoxicosis is a potentially fatal complication in patients with thyroid carcinoma due to abnormal ectopic thyroidal tissue iodine autoregulation (9).

CASE REPORT

A 67-yr-old woman was admitted for evaluation of a pelvic mass. She had a history of hypertension and arthritis. At age 35, she underwent total thyroidectomy for a substernal goiter but did not receive L-thyroxine therapy or have subsequent clinical follow-up. On admission, a noncontrast CT scan of the pelvis demonstrated a destructive mass lesion invading the entire left iliac crest. Pelvic angiography performed with iodide-containing dye disclosed a large vascular neoplasm and tumor biopsy using local anesthesia revealed a well differentiated metastatic follicular thyroid carcinoma. A bone scan was obtained 3 hr after intravenous injection of 20 mCi ^{99m}Tc-methylene diphosphonate (MDP) and showed a photopenic area in the left iliac fossa surrounded by a rim of increased activity in the left hemipelvis (Fig. 1).

Four days after angiography, the patient developed severe agitation, high fever (103°F) and atrial fibrillation with a rapid ventricular response. Thyroid function tests showed an elevated T4 to 15.7 (normal 4.5–12.5 μg/dl), T3 273 (normal 100–200 ng/dl), TSH 0.1 (normal 0.2–5.0 μIU/ml), TBG 20.3 (normal 14.5–32.0 μg/ml) T4/TBG 7.7 (normal 2.5–6.5) and urinary iodide 190 mcg/dl (normal 2–48 mcg/dl). A whole-body thallium scan (Fig. 2) was performed 10 min after intravenous injection of 3 mCi ²⁰¹Tl-chloride and showed increased uptake in the left iliac fossa, right lower neck and right scapula. A focus of activity was also noted in the thyroid bed. A whole-body iodine scan was performed 48 hr after oral administration of 1.25 mCi ¹³¹I and showed increased activity in the left hemipelvis despite the increased body pool of stable iodide and faint uptake in the thyroid bed (Fig. 2). However, the other two foci noted on the thallium scan were not observed on the iodine scan. The patient was treated with propranolol (20 mg) every 6 hr, dexamethasone (0.5 mg) every 6 hr, propylthiouracil (200 mg) every 8 hr and digoxin (0.25 mg) daily followed by conversion to a normal sinus rhythm and normalization of body temperature and thyroid hormone levels. Three days later, the patient received radiation therapy to the pelvis for symptomatic relief of her leg pain. The therapeutic course was complicated by neutropenia 2 wk later (WBC 2300/mm³) and she was treated with human granulocyte colony-stimulating factor (G-CSF) 300 mcg/day subcutaneously for 5 days followed by a dramatic increase in WBC to 12,500/mm³. Following the radiation therapy course, the patient eventually became hypothyroid (T4 1.3 μg/dl, TSH 26 μIU/ml). Four weeks later, after normalization of total iodine in urine (19 mcg/dl), the patient received 75 mCi ¹³¹I for therapy and was eventually placed on thyroid hormone suppression therapy. Figure 3 illustrates the dynamic change in thyroid function tests, WBC count and the appropriate medical management.

DISCUSSION

The classic studies of Wolff and Chaikoff in 1948 (10–11) showed that large doses of iodide inhibited organification in the rat, and this finding was soon confirmed by Stanley in humans (12). The Wolff-Chaikoff effect is thought to depend on high intrathyroidal free iodide concentrations which create a thyroperoxydase-iodide complex incapable of organification and coupling. The rate of hormone secretion is also diminished

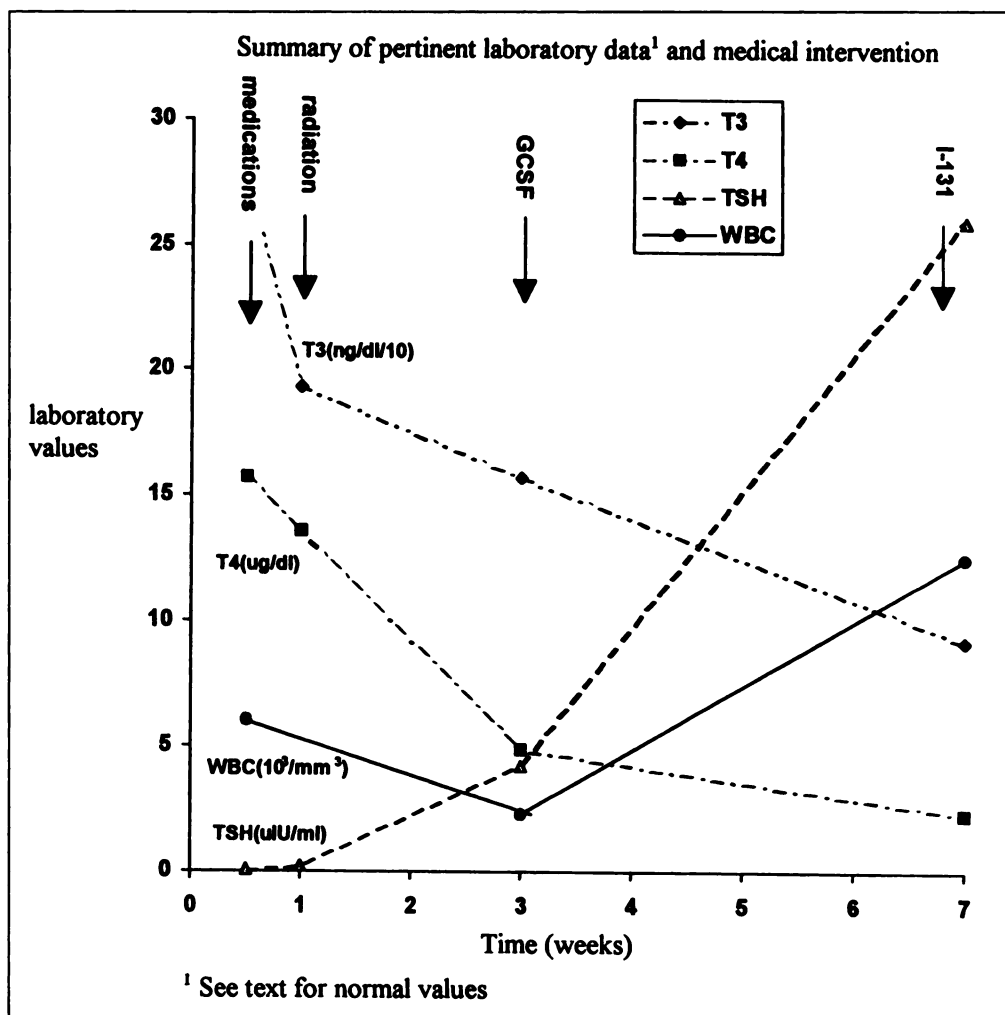


FIGURE 3. Summary of pertinent laboratory data and medical intervention.

through an inhibition of the proteolytic release of iodothyronines from thyroglobulin. The Wolff-Chaikoff effect has been reported after oral and vaginal administration of iodide and may even result from external iodine application to the skin (13). Wolff et al. (4) found that hormonogenesis resumes despite the high serum iodide levels when iodides are given at inhibitory concentrations for a prolonged period of time. This "escape" from the Wolff-Chaikoff effect is presumably related to a qualitative change in thyroidal function resulting in diminished iodide trapping and may be mediated by an iodinated organic inhibitor of iodine transport (6-8). Decreased trapping would theoretically decrease intrathyroidal free iodide concentrations and disinhibit organification.

Iodine-induced hyperthyroidism in patients with pre-existent endemic goiter with autonomous nodular elements was first termed "Jod-Basedow" by Kocher in 1910 (5,14). In 1925, Kimball (15) studied 2659 patients with hyperthyroidism and found that prescribed iodine was the precipitating factor in 12%. This phenomenon is thought to result from an underlying defect in intrathyroidal iodine regulation. Specifically, iodine-induced hyperthyroidism occurs in many thyroid follicular adenomas which appear less functional than the thyroid tissue on imaging (9,16) despite a defective trapping mechanism. Administration of excess iodide can also induce hypersecretion of thyroid hormones from autonomously functioning and nonfunctioning thyroid nodules (16-17). This same metabolic defect may apply in thyroid carcinomas (18-19). Well-differentiated papillary and follicular thyroid carcinomas arise from thyroid follicular cells and retain their ability to concentrate radioio-

dine. Even papillary carcinomas without detectable colloid usually concentrate radioiodine (20). Thyrotoxicosis in patients with predominantly well-differentiated follicular thyroid carcinoma was reported previously (21). The clinical presentation was similar to that of Graves' patients. Asymptomatic thyrotoxicosis induced by iodide in a patient with metastatic thyroid carcinoma was also reported (22).

Our patient developed severe, life-threatening hyperthyroidism. The most significant contributing factor to the severity of hyperthyroidism was the large volume of tumor which occupied the entire left hemipelvis and was likely autonomous prior to the administration of the contrast material. Initial medical management consisted of glucocorticoids, beta-blockers and antithyroid drugs aimed to decrease, in concert, thyroid hormone production and peripheral conversion of T4 to T3 as well as target organ (e.g., cardiac) hypermetabolism.

Radiation therapy was then necessary for palliation, but our patient developed significant neutropenia. The recently purified recombinant glycoprotein-granulocyte colony-stimulating factor (GCSF) promotes the proliferation and differentiation of granulocytes both in vitro and in vivo (23). Therapy with GCSF has been shown to increase neutrophil counts in patients with congenital, idiopathic, or cyclic neutropenia (24-25). Our patient showed a remarkable increase in white cell count in response to GCSF therapy without notable side effects. The beneficial effect of this therapy in our patient suggests that this potent hormone may complement radiation therapy and reduce the morbidity associated with neutropenia. GCSF was ulti-

mately necessary to allow prompt, definitive therapy of metastatic thyroid cancer with radioiodine.

Both ^{131}I and ^{201}Tl scintigraphy are the most useful diagnostic modalities for the diagnosis of residual, recurrent or metastatic thyroid cancer, in conjunction with serum thyroglobulin measurements (22,26). The higher sensitivity of the thallium scan in identifying additional foci not seen on the ^{131}I scan may stem from the lower avidity of these lesions to iodine, particularly in view of the increased stable iodide pool.

CONCLUSION

We presented a complex case of thyroid carcinoma illustrating a tailored medical management: acute medical treatment of accelerated hyperthyroidism, palliative radiation therapy and definitive therapy with radioiodine. The beneficial effect of GCSF in stimulating bone marrow activity should be considered when neutropenia complicates the course of combined modality therapies for thyroid cancer.

REFERENCES

1. Woebber KA. Iodine and thyroid disease. *Med Clin North Am* 1991;75:169-178.
2. Martins MC, Lima N, Knobel M, Medeiros-Neto G. Natural course of iodine-induced thyrotoxicosis (Jod Basedow) in endemic goiter area: a 5-year follow-up. *J Endocrinol Invest* 1989;12:239-244.
3. Galton VA, Pitt-Rivers R. The effect of excessive iodine on the thyroid of the rat. *Endocrinology* 1959;64:835-839.
4. Wolff J, Chaikoff IL, Goldberg RC, Meier JR. The temporary nature of the inhibitory action of excess iodide on organic iodine synthesis in the normal thyroid. *Endocrinology* 1949;45:504-513.
5. Mechanick JI, Davies TF. Medical management of hyperthyroidism: Theoretical and practical aspects. In: Falk SA. *Thyroid disease: endocrinology, surgery, nuclear medicine and radiotherapy*. New York: Raven Press; 1990:197-232.
6. Braverman LE, Ingbar SH. Changes in thyroidal function during adaptation to large doses of iodide. *J Clin Invest* 1963;42:1216-1231.
7. Childs DS, Keating FR, Rall JE, Williams MMD, Power MH. The effect of varying quantities of inorganic iodide (carrier) on the urinary excretion and thyroidal accumulation of radioiodine in exophthalmic goiter. *J Clin Invest* 1950;29:726-738.
8. Halmi NS. Thyroidal iodine transport. *Vitam Horm* 1961;19:133-163.
9. Shiroozu A, Inoue K, Nakashima T, et al. Defective iodide transport and normal organification of iodide in cold nodules of the thyroid. *Clin Endocrinol* 1981;15:411-416.
10. Wolff J, Chaikoff IL. Plasma inorganic iodide as a homeostatic regulator of thyroid function. *J Biol Chem* 1948;174:555-564.
11. Wolff J, Chaikoff IL. The inhibitory action of excessive iodide upon the synthesis of diiodotyrosine and of thyroxine in the normal rat. *Endocrinology* 1948;43:174-179.
12. Stanley MM. The direct estimation of the rate of thyroid hormone formation in man. The effect of the iodide ion on thyroid iodine utilization. *J Clin Endocrinol Metab* 1949;9:941-954.
13. Clemens PC, Neumann RS. The Wolff-Chaikoff effect: hypothyroidism due to iodine application [Letter]. *Arch Dermatol* 1989;125:705.
14. Kocher T. Uber Jodbasedow. *Archiv für Klinische Chirurgie* 1910;92:1166-1193. As cited in: Lividas DP, Koutras DA, Souvatzoglou A, Beckers C. The toxic effects of small iodine supplements in patients with autonomous thyroid nodules. *Clin Endocrinol* 1977;7:121-127.
15. Kimball OP. Induced hyperthyroidism. *JAMA* 1925;85:1709-1710.
16. Vagenakis AG, Wang C, Burger A, Maloof F, Braverman L, Ingbar SH. Iodide-induced thyrotoxicosis in Boston. *N Engl J Med* 1971;287:523-527.
17. Ermans AM, Camus M. Modifications of thyroid function induced by chronic administration of iodide in the presence of autonomous thyroid tissue. *Acta Endocrinol* 1976;70:463-475.
18. Field JB, Larsen PR, Yamashita K, Mashiter K, Dekker A. Demonstration of iodide transport defect but normal iodide organification in nonfunctioning nodules of human thyroid glands. *J Clin Invest* 1973;52:2404-2410.
19. Thomas-Morvan C, Nataf BM, Tubiana M. In vivo and organ culture studies of thyroid proteins and hormone synthesis in human thyroid cancer tissues. *Ann Radiol (Paris)* 1977;20:739-742.
20. Hurlley JR, Becker DV. The use of radioiodine in the management of thyroid cancer. In: Freeman LM, Weissman HS, editors. *Nuclear medicine annual 1983*. New York: Raven Press; 1983:329-384.
21. Paul SJ, Sisson JC. Thyrotoxicosis caused by thyroid cancer. *Endocrinol Metab Clin North Am* 1990;19:593-612.
22. Yoshinari M, Tokuyama T, Okamura K, Sato K, Kusuda K, Fujishima M. Iodide-induced thyrotoxicosis in a thyroidectomized patient with metastatic thyroid carcinoma. *Cancer* 1988;61:1674-1678.
23. Morstyn G, Campbell L, Lieschke G, et al. Treatment of chemotherapy induced neutropenia by subcutaneously administered granulocyte colony-stimulating factor with optimization of dose and duration of therapy. *J Clin Oncol* 1989;7:1554-1562.
24. Hammond WP, IV, Price TH, Souza LM, Dale DC. Treatment of cyclic neutropenia with granulocyte colony-stimulating factor. *N Engl J Med* 1989;320:1306-1311.
25. Bonilla MA, Gillio AP, Ruggiero M, et al. Effects of recombinant human granulocyte colony-stimulating factor on neutropenia in patients with congenital agranulocytosis. *N Engl J Med* 1989;320:1574-1580.
26. Murthy S, Webner P, Mechanick JI, Morris JC. Clinical utility of thallium-201 scintigraphy in the follow-up of differentiated thyroid cancer [Abstract]. *J Nucl Med* 1994;35(suppl):167P.

Technetium-99m-Sestamibi SPECT Localization of Mediastinal Parathyroid Adenoma

Elizabeth L. Teigen, Erik J. Kilgore, Robert J. Cowan and David A. Albertson

Departments of Radiology and Surgery, Bowman Gray School of Medicine, Winston-Salem, North Carolina

We report a case in which $^{99\text{m}}\text{Tc}$ -sestamibi SPECT was used to localize a middle mediastinum parathyroid adenoma that was not detected with planar sestamibi imaging on two previous occasions. Despite prior surgical exploration of the neck and mediastinum, the patient had a 20-yr history of hyperparathyroidism.

Key Words: hyperparathyroidism; technetium-99m-sestamibi; SPECT; parathyroid adenoma

J Nucl Med 1996; 37:1535-1537

The usefulness of preoperative localization of hyperfunctioning parathyroid tissue in patients with recurrent or persistent hyperparathyroidism after previous neck surgery is well estab-

lished (1). When preoperative imaging is performed, the success rate for reoperation in patients with persistent or recurrent hyperparathyroidism increases from approximately 60% to 90% (1-3). We report a case of $^{99\text{m}}\text{Tc}$ -sestamibi SPECT localization of a middle mediastinum parathyroid adenoma which was not detected either with planar sestamibi imaging on two occasions or with prior mediastinal exploration.

CASE REPORT

A 48-yr-old man had a history of hyperparathyroidism and hypercalcemia since 1975. A 3 1/2-gland parathyroidectomy and neck exploration were performed in 1975, but the patient had persistent hyperparathyroidism thereafter. Exploration of the neck was repeated in June 1976 but did not reveal any hyperfunctioning parathyroid tissue. In April 1977, the patient underwent cervical exploration with thymectomy, pericardial exploration and bilateral subtotal thyroid lobectomies. Again, he had no relief of his hyperparathyroidism, and he subsequently experienced pathologic

Received Dec. 14, 1995; revision accepted Mar. 6, 1996.

For correspondence contact: Elizabeth L. Teigen, MD, Department of Radiology, Bowman Gray School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157-1088.

Reprints are not available from the author.