

Recurrent Medullary Carcinoma of the Thyroid Demonstrated by Thallium-201 Scintigraphy

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Thallium-201 scintigraphy has been used in the evaluation of thyroid neoplasms, but uptake in recurrent or persistent medullary thyroid cancer has not been reported. We present two cases where focal ^{201}Tl activity localized superior mediastinal recurrences which were subsequently resected. Postoperative ^{201}Tl scans in both cases showed elimination of the focal uptake seen before surgery, as well as return of previously elevated serum calcitonin levels to normal. Scanning with ^{201}Tl may be useful in the preoperative localization of recurrent medullary thyroid cancer.

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Medullary carcinoma of the thyroid (MCT) is an uncommon malignancy with a 10-yr survival rate of 46% if lymph node metastases are present (1). Recurrent or persistent disease may be detectable by measurement of serum calcitonin levels, either alone or with pentagastrin or calcium provocation (2), but is often difficult to localize using computed tomography (CT) or ultrasound. Accurate localization of recurrent disease is a prerequisite for successful surgical excision. We present two cases where regional recurrence of medullary thyroid cancer was accurately localized by thallium-201 (^{201}Tl) scintigraphy, leading to successful surgical removal and return of elevated serum calcitonin levels to normal.

CASE REPORTS

Case 1

A 40-yr-old man with no family history of thyroid cancer or multiple endocrine neoplasia (MEN) was initially evaluated for an asymptomatic left thyroid mass which was cold on technetium-99m ($^{99\text{m}}\text{Tc}$) imaging and was ~1 cm in diameter. A total thyroidectomy was carried out after frozen section of the left lobe revealed medullary carcinoma. There was no right lobe or extra-thyroidal involvement. Aside from transient

hypocalcemia, recovery was uneventful and the patient did well on thyroid replacement until left lateral cervical lymph node recurrences were found and resected 8 and 13 yr later. Three months after removal of the second neck node recurrence, serum calcitonin levels were elevated (16.34 ng/ml, normal = <0.32 ng/ml), despite the absence of lymphadenopathy. Plain films and CT of the chest and neck were normal, as well as serum calcium and parathyroid hormone (PTH).

Scintigraphy of the neck and upper thorax was performed with a large field-of-view gamma camera and a low-energy, all-purpose collimator, using both [$^{99\text{m}}\text{Tc}$]pertechnetate and thallium-201 (^{201}Tl) chloride. The $^{99\text{m}}\text{Tc}$ image was obtained first, using 2 mCi, to rule out the presence of functioning residual thyroid tissue. A 10-min acquisition was started at 20 min postinjection. Two millicuries of ^{201}Tl were then administered, and the same region was imaged for 10 min, starting 5 min after ^{201}Tl injection. A 20% window centered about 140 keV was used for $^{99\text{m}}\text{Tc}$ and a 20% window about 80 keV for ^{201}Tl imaging. The resulting images demonstrated minimal $^{99\text{m}}\text{Tc}$ activity but a clear focus of ^{201}Tl uptake in the left superior mediastinal region (Fig. 1). A recurrence of medullary carcinoma was subsequently resected from this location through the patient's previous collar thyroidectomy incision. Three contiguous lymph nodes were found; these were grossly and microscopically involved with tumor (Fig. 2). One node was dissected from the left recurrent laryngeal nerve. Eight days following surgery, a repeat ^{201}Tl scan of the neck and upper chest showed absence of the superior mediastinal uptake seen preoperatively (Fig. 3). The serum calcitonin level obtained 2 days after surgery had fallen to 0.53 ng/ml, and 2 wk later to 0.10 ng/ml (normal = <0.32 ng/ml).

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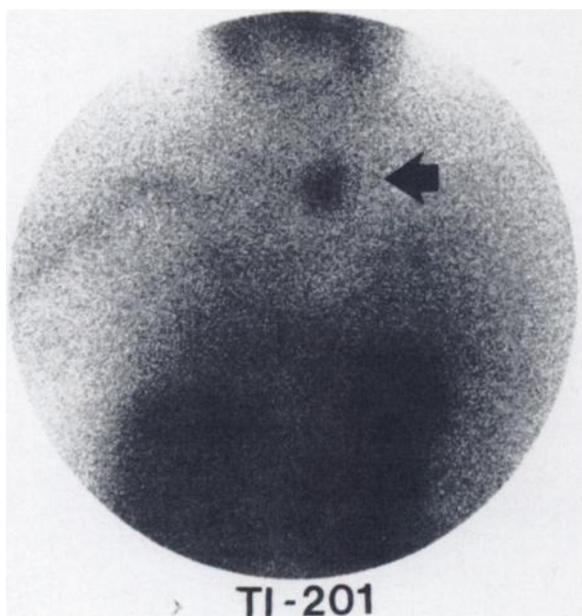
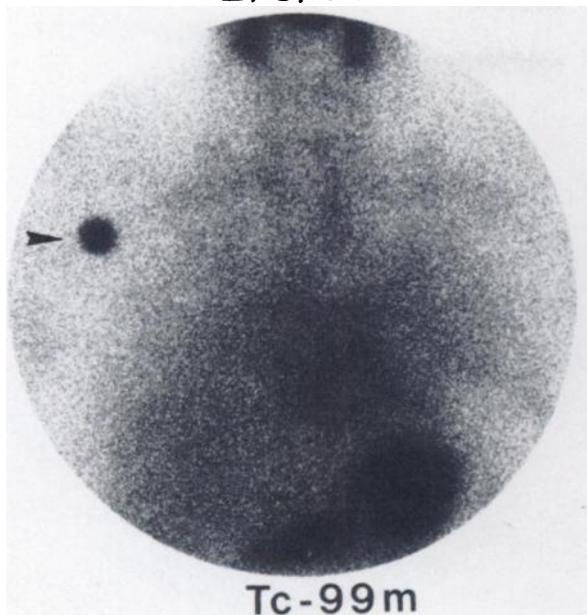


FIGURE 1
Preoperative thallium and ^{99m}Tc images for Case 1. Discrete focus of thallium uptake in mediastinum (arrow) is not seen on ^{99m}Tc image. Right-sided focus on ^{99m}Tc image is axillary marker (arrowhead)

Case 2

A 57-yr-old woman with a 6-yr history of chronic lymphocytic thyroiditis and no family history of MEN presented with a firm nodule in the right thyroid lobe, approximately 2½ cm in diameter. Total thyroidectomy was carried out after fine needle aspiration of the nodule was suspicious for carcinoma. The right lobe was enlarged by a 3.5 × 3.0 × 2.5 cm primary

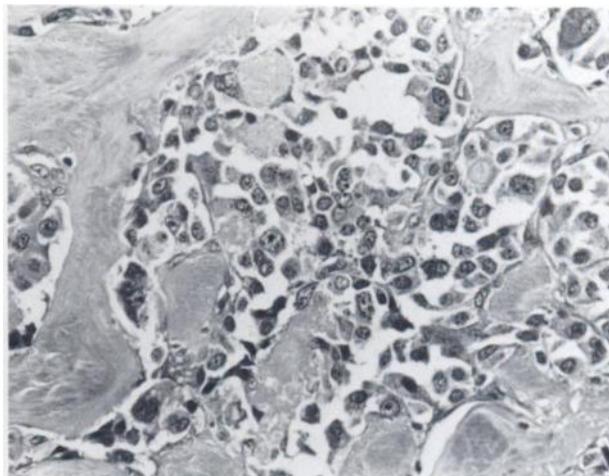


FIGURE 2
Microscopic section of lymph node resected from Case 1, showing infiltrating medullary thyroid carcinoma with amyloid stroma surrounding nests of tumor cells. Hematoxylin and eosin, 330X

medullary cancer; multiple right cervical lymph nodes were also involved. The diagnosis of MCT was confirmed by electron microscopy and immunohistochemical staining for calcitonin. Following surgery, the patient received 6,000 rad of external beam irradiation to the neck, which she tolerated well.

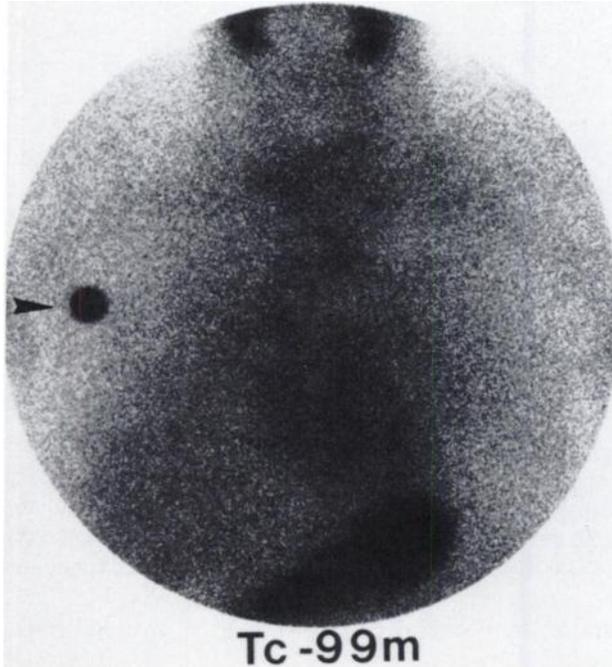
After completion of radiotherapy, the serum calcitonin was found to be elevated at 1.70 ng/ml (normal = <0.32 ng/ml), and a CT of the chest (Fig. 6) showed a nonspecific right paratracheal asymmetry. Six months later, serum calcitonin had fallen to 0.8 ng/ml. Calcium and PTH levels were normal.

Scintigraphy of the upper chest and neck was performed using ^{201}Tl and ^{99m}Tc pertechnetate as previously described. A small focus of thallium uptake not apparent on the technetium image was noted (Fig. 4). During a subsequent surgical exploration, two involved nodes were found in the lateral compartment of the neck at the junction of the right common carotid and subclavian arteries. These were ½ and 1½ cm in diameter and were contiguous. These were grossly and microscopically involved with tumor. Eight days postoperatively, a follow-up ^{201}Tl scan (Fig. 5) no longer demonstrated the previous focus of uptake. The serum calcitonin level fell to 0.10 ng/ml one week after operation and remained at that level even after pentagastrin provocation (0.5 µg/kg i.v.).

DISCUSSION

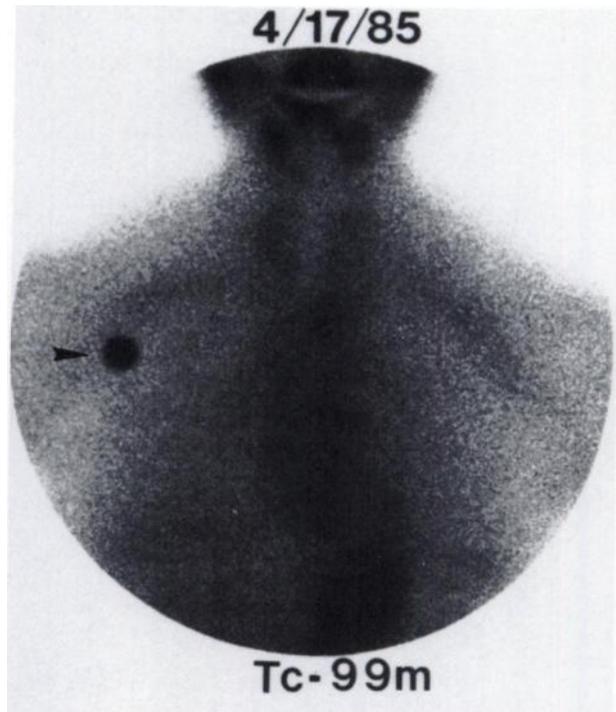
Thallium-201 scintigraphy has been used in the evaluation of thyroid neoplasms (3,4), but uptake in recurrent medullary carcinoma after thyroidectomy has not been reported. Ochi et al. (3) reported in his discussion of ^{201}Tl uptake in thyroid malignancy, absence of such uptake in the one case with primary medullary cancer. Senga et al. (4) described slight accumulation of ^{201}Tl in a primary medullary carcinoma, while 10 of 11

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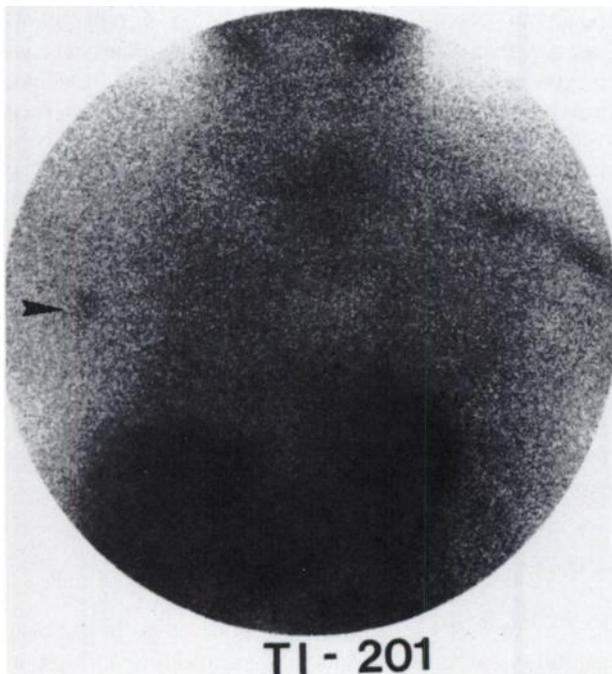


Tc-99m

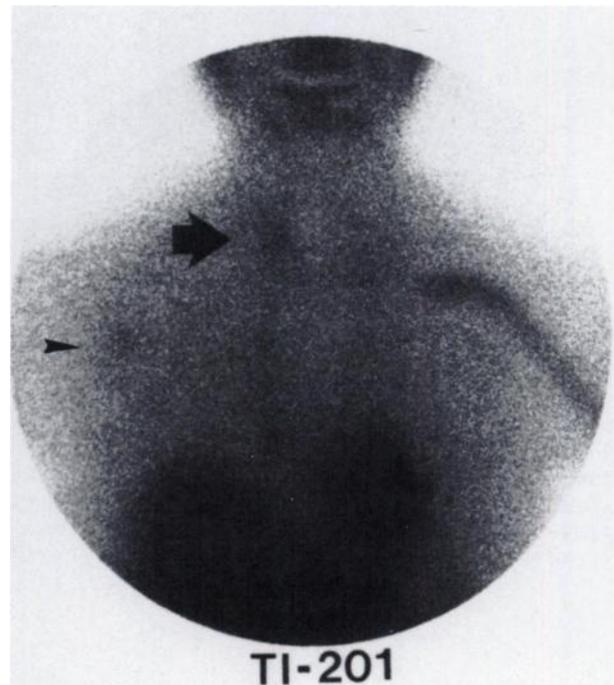
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Tc-99m



TI - 201



TI-201

FIGURE 3

Postoperative thallium and ^{99m}Tc images for Case 1. Mediastinal focus is no longer present. Axillary marker on ^{99m}Tc image, as well as its downscatter on thallium image, is indicated by arrowhead

FIGURE 4

Preoperative thallium and ^{99m}Tc images of neck and chest for Case 2. Focus of thallium activity is present in upper mediastinum (arrow). Arrowheads indicate axillary marker on ^{99m}Tc image and its downscatter on thallium image

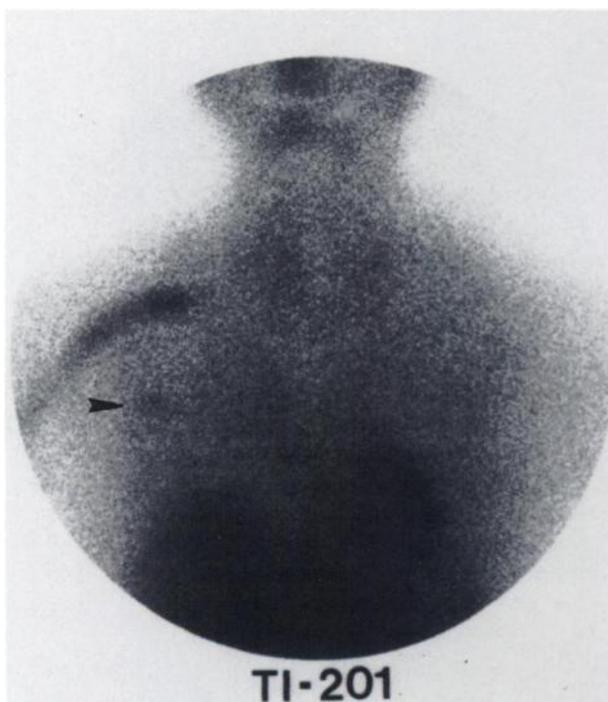
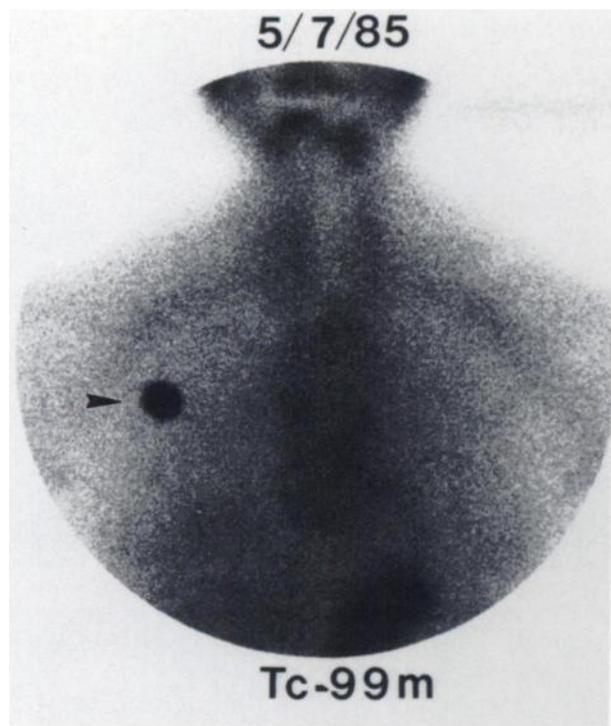


FIGURE 5
Postoperative thallium and ^{99m}Tc images for Case 2. Mediastinal thallium activity is no longer present. Axillary marker and its downscatter are marked by arrowheads

patients with papillary or follicular cancer took up the radiotracer.

Uptake of other radiotracers by medullary thyroid cancer has been described by several authors. These include phosphate bone agents (5), radioiodine (6), and a new agent, [^{99m}Tc (V)]dimercaptosuccinic acid (7), which was demonstrated in primary, metastatic, and residual tumors. Iodine-131 metaiodobenzylguanidine (^{131}I]MIBG), an agent known to accumulate in pheochromocytoma (8) and some neuroblastomas (9), has been demonstrated in an occasional primary medullary thyroid carcinoma. Sone et al. (10) recently reported [^{131}I]MIBG uptake in distant metastases of medullary thyroid cancer. Endo et al. (11) described [^{131}I]MIBG uptake in both medullary thyroid cancer and pheochromocytoma in a patient with Sipple's syndrome (MEN-2a). Our first patient demonstrated faint uptake of [^{131}I]MIBG in the same location as the ^{201}Tl uptake previously described (Fig. 7). The second patient showed no [^{131}I]MIBG uptake at the site of tumor. Our experience in a number of other patients with proven MCT has shown that [^{131}I]MIBG is unlikely to give consistent results.

The present cases are of interest for several reasons. In each, ^{201}Tl scintigraphy provided a means of localizing recurrent tumor, indicated by elevated serum calcitonin levels but not detected by conventional studies. Furthermore, in both cases, resection of the tumor resulted in normalization of the serum calcitonin and disappearance of the focal ^{201}Tl uptake. Finally, ^{201}Tl has not been reported to localize in a recurrence of sporadic medullary cancer after thyroidectomy. We conclude that these scintigraphic procedures may be useful in the preoperative localization of recurrent or persistent medullary carcinoma of the thyroid after total thyroidectomy when calcitonin levels are elevated and conventional localizing studies are negative.

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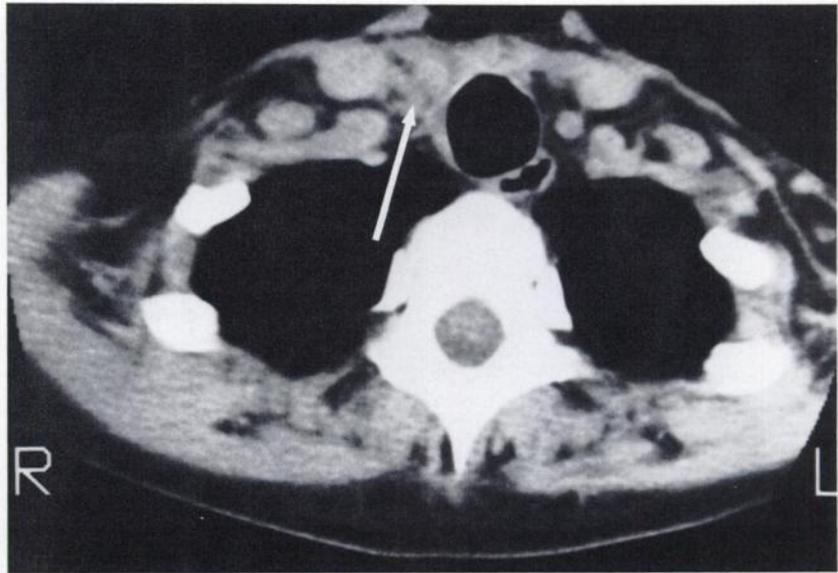


FIGURE 6
Preoperative chest CT for Case 2. White arrow indicates paratracheal asymmetry which in retrospect is suggestive of recurrent tumor but was interpreted as nonspecific

chloride thyroid scintigraphy to evaluate benign and/or malignant nodules. *Cancer* 50:236-240, 1982

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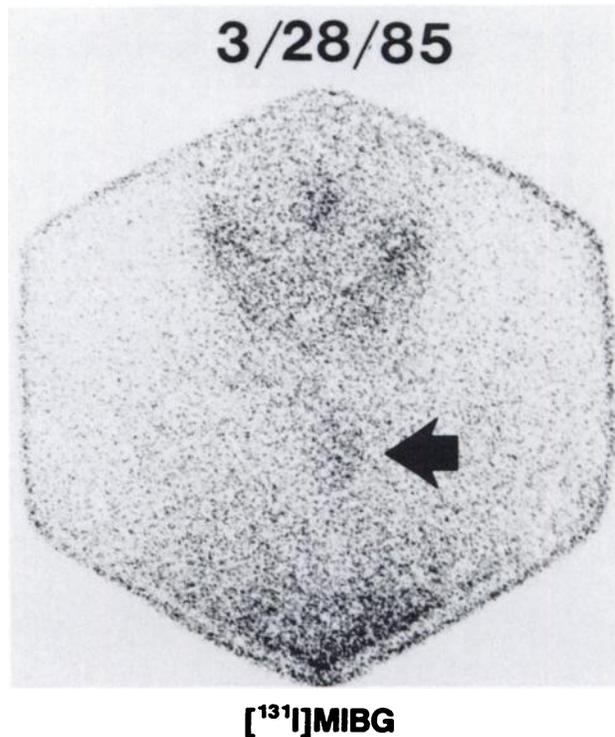


FIGURE 7
Preoperative [¹³¹I]MIBG image for Case 1. Area of increased activity is noted in upper mediastinum (arrow)