Technetium-99m-Methoxyisobutylisonitrile in Localization of Ectopic Parathyroid Adenoma

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Preoperative localization of ectopic parathyroid lesions is crucial for the correct treatment of patients with primary hyperparathyroidism. Invasive and noninvasive procedures, including selective venography, ultrasound, CT and MRI provide limited sensitivity in the detection of ectopic lesions. We report three patients in whom ^{99m}Tc-MIBI scintigraphy accurately detected ectopic parathyroid adenomas and was instrumental in the cure for these patients. Technetium-99m-MIBI scintigraphy provides a simple and accurate noninvasive test for the detection of ectopic parathyroid adenomas.

Key Words: primary hyperparathyroidism; ectopic parathyroid adenomas; technetium-99m-MIBI

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Single adenoma is the most frequent etiology of primary hyperparathyroidism. Surgical treatment of hyperparathyroidism is successful in 95% of patients undergoing initial neck exploration (*1*). Failure to find the parathyroidal lesion may be related to ectopia and anatomic variations in the location of the tumor. Preoperative lesion localization, with a sensitive and specific imaging technique, can help in achieving better surgical results in those cases of ectopia or anatomic variation. Several noninvasive procedures, such as ultrasonography, CT, MRI and ^{201}Tl/^{99m}Tc scanning, have been tried for this purpose. In addition, invasive procedures such as selective venography, intra-arterial digital angiography and needle aspiration combined with high-resolution ultrasonography have been tested. None of these procedures provided enough diagnostic reliability to be considered the first elective procedure in the preoperative evaluation of these patients.

A few years ago, Coakley et al. (*2*) introduced the use of ^{99m}Tc-MIBI as a new agent for parathyroid imaging, and other groups have subsequently confirmed its usefulness (*3,4*). This technique may be helpful in the preoperative management of ectopic adenomas. We present three patients in whom ^{99m}Tc-MIBI scintigraphy accurately detected ectopic parathyroid adenomas and significantly contributed to their cure.

CASE REPORTS

Patient 1

A 42-yr-old woman was diagnosed with primary hyperparathyroidism after 15 yr of recurrent nephrolithiasis. Neck exploration was performed on the patient and three apparently normal parathyroid glands were partially removed. The left inferior parathyroid gland was not found and the left hemithyroid and upper thymus were removed. Histologic studies of all samples did not disclose abnormal parathyroid tissue. Due to persistent hypercalcemia, cervicothoracic MRI and CT, and selective venography were performed, failing to localize the ectopic parathyroid tissue. Finally, a planar ^{99m}Tc-MIBI scintigraphy was performed, showing a well-delineated mediastinal hot-spot (Fig. 1). During surgery, a 660-mg parathyroid adenoma (Fig. 2) within the residual thymus was found. After surgery, the patient's blood calcium levels have been within the normal range for 2 yr of follow-up.

Patient 2

A 59-yr-old woman was admitted to the hospital because of a 6-yr history of repeated episodes of nephrolithiasis. During the last 3 yr, she also reported bone pain and weight lost of 20 kg. Laboratory tests showed hypercalcemia, hypophosphatemia, PTH 2214 pg/ml (n = 10–65) and alkaline phosphatase 2149 U/liter (n = 81–263). Radiographs showed subperiosteal bone resorption and sclerosis of the vertebral bodies. Abdominal echography showed bilateral nephrolitiasis while neck ultrasonography demonstrated the presence of multinodular goiter without parathyroid abnormalities. A cervico-thoracic CT showed the multinodular goiter and a hypodense image in the inferior portion of the left thyroid lobule that could correspond to a parathyroidal lesion. A planar ^{99m}Tc-MIBI scintigraphy of the neck and thorax showed a mediastinal lesion (Fig. 3). A subtotal thyroidectomy was then performed and three apparently normal parathyroid glands were identified, while the inferior left gland was not found. Surgery revealed that the hypodense lesion seen on CT was due to multinodular goiter and did not correspond to a parathyroid adenoma. At the same time, sternotomy was performed and a mediastinal adenomatous lesion was removed. Pathology revealed a parathyroid adenoma of 2470 mg (Fig. 4). Laboratory tests normalized after surgery.

Patient 3

A 48-yr-old woman was considered to have primary hyperparathyroidism after a history of recurrent nephrolithiasis, hypercalcemia and increased PTH levels. During surgical exploration of the neck, four apparently normal parathyroidal glands were identified and confirmed after pathological examination of small biopsy specimens. In addition, most of the thymic remnant was removed

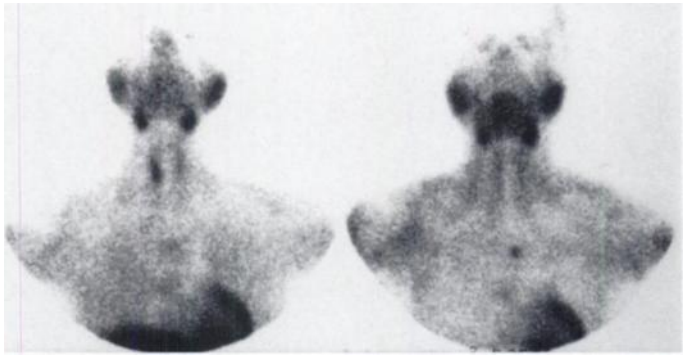

FIGURE 1. Technetium-99m-MIBI scintigraphy of Patient 1. On the delayed image (right) there is increased focal uptake in the mediastinum corresponding to a parathyroid adenoma of 660 mg.

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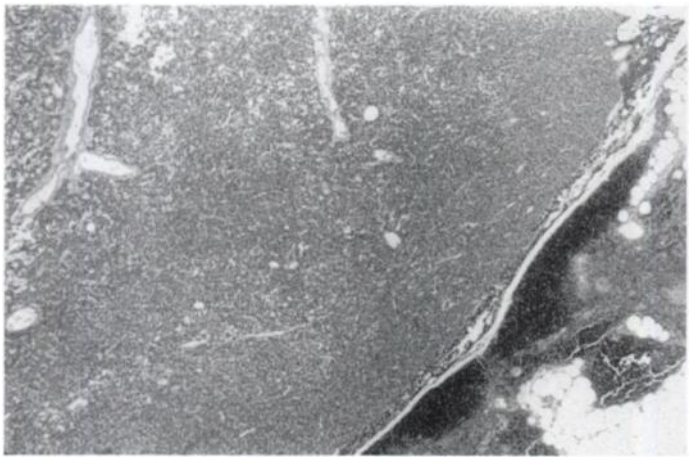

FIGURE 2. Microscopic appearance of the parathyroid adenoma of Patient 1. There is a predominant population of chief cells, intermingled with variable amounts of oxyphil and transitional oxyphil cells.

and analysis of the specimen did not reveal histologic abnormalities. Due to persistence of hyperparathyroidism, an MRI study and a ^{99m}Tc-MIBI scintigraphy (Fig. 5) were performed. Both studies showed a mediastinal lesion located next to left pulmonary hilum. With findings of MIBI as the guide, thoracotomy was performed and a parathyroid adenoma of 950 mg was removed (Fig. 6). Calcium levels decreased to normal values after surgery.

DISCUSSION

For years, a classical consensus among surgeons has been that localization techniques in patients with primary hyperparathyroidism should not be performed unless the initial surgery proved unsuccessful. Localization and removal of a single abnormal parathyroid gland is usually possible without any particular preoperative imaging technique, as demonstrated by cure rates up to 95% in the hands of experimented surgeons (*1*). In addition, a consensus also seems to exist for patients with postoperative recurrent or persistent hyperparathyroidism that imaging studies are required before additional surgery is performed (*5*). Ultrasonography is at its best in detecting adenomas around the lower pole of the thyroid, but it is not efficient for visualizing ectopic adenomatous glands in either the posterior or superior mediastinum. Computed tomography has a sensitivity around 65% in detecting parathyroid lesions in patients who have already undergone surgery; MRI has a sensitivity of 75%, and reported sensitivities for ^{201}Tl/^{99m}Tc scintigraphy for this group of patients range from 26% to 80% (*6,7*).

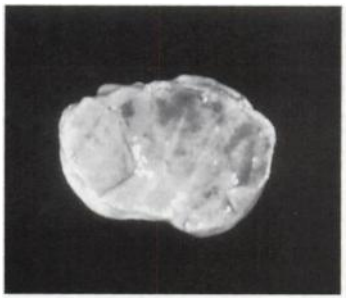

FIGURE 4. Gross appearance of the parathyroid adenoma of Patient 2.

Since Coakley et al. (*2*) introduced the use of ^{99m}Tc-MIBI as a new agent for parathyroid imaging, several groups have shown its utility (*3,4*). We present three patients in whom ^{99m}Tc-MIBI scintigraphy was accurate in depicting ectopic parathyroid adenomas. Patients 1 and 3 had unsuccessful initial surgeries; CT failed to diagnose the parathyroid lesion in Patients 1 and 2. In Patient 1, MRI and selective venography failed to identify the parathyroid adenoma, and only in Patient 3 did MRI depict the ectopic parathyroid lesion. In Patients 1 and 2, ^{99m}Tc-MIBI scintigraphy was the only method that correctly identified the lesion responsible for primary hyperparathyroidism; in Patient 3, MRI findings were concordant with the scintigraphic image.

MIBI uptake has been reported in different types of thyroid carcinoma, osteosarcoma, breast cancer, lymphoma, bronchogenic carcinoma, parathyroid carcinoma, undifferentiated mesenchymal tumors, carcinoid tumor and in ACTH-producing tumors (*8,9*). In these different types of tumors, the biological uptake mechanism of ^{99m}Tc-MIBI is not well known (*8,9*). Some studies suggest that ^{99m}Tc-MIBI uptake may be related to the mitochondrial content of a particular tissue, with higher avidity in those having larger numbers of them (*10*). This would be the case for parathyroid adenomas, since these lesions usually show a large number of this organelle (*11*). Furthermore, it has been reported that ^{99m}Tc-MIBI is selectively and more avidly taken up by parathyroid adenomas than by the thyroid tissue (*3,4*). Interestingly, the washout from parathyroid adenoma is slower than that from surrounding tissues, resulting in a higher target-to-background ratio (*3,4*). Taillefer et al. (*4*) described these double-phase kinetics of ^{99m}Tc-MIBI for parathyroid adenomas and showed that late image fairly detects abnormal parathyroid tissue. In our studies, images obtained 2–3 hr after injection of 20 mCi ^{99m}Tc-MIBI showed marked accumulation in Patients 1 and 2 but only faint uptake in Patient 3 in the mediastinum that corresponded to parathyroid adenomas. The scintigram was extremely useful in the management and treatment decision of these patients.

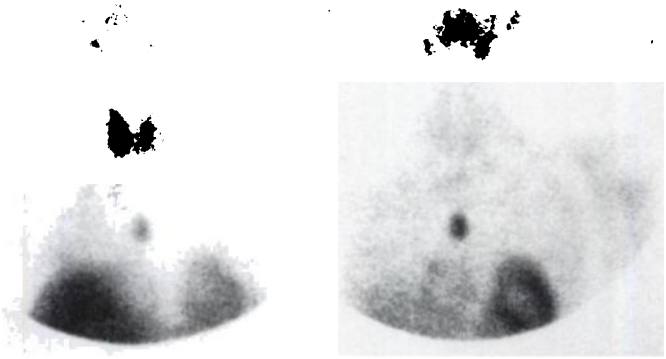

FIGURE 3. Early and delayed ^{99m}Tc-MIBI scintigraphy of Patient 2. Increased focal uptake in the mediastinum corresponding to a parathyroid adenoma of 2470 mg.

FIGURE 5. Left lateral planar view of Patient 3. There is a faint focal uptake above the heart corresponding to a parathyroid adenoma of 950 mg.

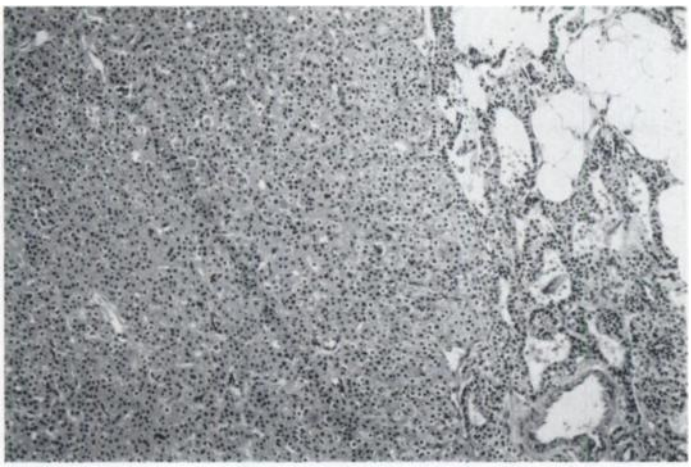

FIGURE 6. Microscopic appearance of the parathyroid adenoma of Patient 3.

CONCLUSION

Technetium-99m-MIBI scintigraphy provides a simple, reliable, accurate and noninvasive method for the detection of ectopic parathyroid adenomas. Our results suggest that ^{99m}Tc-MIBI scintigraphy could be considered as the first elective imaging technique and part of the routine in the management and localization of parathyroid adenomas.

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Disseminated Bone Marrow Metastases of Insular Thyroid Carcinoma Detected by Radioiodine Whole-Body Scintigraphy

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We present ^{131}I scintigraphic findings in a patient with insular carcinoma of the thyroid showing diffuse abnormal uptake throughout the skeleton. The scintigraph closely resembled the pattern of [^{131}I]MIBG distribution in children with bone marrow metastases of neuroblastoma. The extent of involvement was underestimated by bone scintigraphy and radiography. Insular carcinoma of the thyroid in the bone marrow was subsequently demonstrated by biopsy. The patient was treated with 242 mCi ^{131}I given in two courses, which led to severe myelosuppression and died as a result of progressive disease and severe pancytopenia 10 mo after initial therapy.

Key Words: insular thyroid carcinoma; bone marrow metastases; iodine-131

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Whole-body ^{131}I scintigraphy is the method of choice for postoperative evaluation of differentiated thyroid carcinoma for the detection of metastatic lesions, the positive rate of ^{131}I whole-body scan for metastases in differentiated thyroid carcinoma being approximately 75% (*1–6*).

Uptake of ^{131}I has also been demonstrated in recurrent and metastatic insular carcinoma of the thyroid, a recently recognized histologic entity believed to be of follicular cell origin and having a characteristic histopathologic appearance, consisting of nests or "insulae" of medium sized tumor cells (*7,8*). This tumor demonstrates an aggressive clinical course with distant metastases developing in many cases (*9*).

We present a case with unusual scintigraphic finding of intense, diffuse ^{131}I accumulation throughout the skeleton in a patient with insular carcinoma of the thyroid. The images resembled the scintigraphic pattern of MIBG distribution in patients with diffuse bone marrow infiltration by neuroblastoma (*10*). Bone marrow involvement by insular carcinoma of the thyroid was subsequently confirmed by iliac crest biopsy.

CASE REPORT

A 61-yr-old woman presented in April 1993 with a fixed nodule in the right thyroid lobe. For several years she suffered from diffuse bone pain, which had been interpreted as being due to osteoporosis and which had been treated with calcium and calcitonin. A ^{131}I

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