Technetium-99m MIBI Uptake in Recurrent Parathyroid Carcinoma and Brown Tumors

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Demonstrable parathyroid adenoma in delayed (3-hr) ^{99m}Tc-MIBI neck imaging and localization of ^{201}Tl-chloride in brown tumors mimicking skeletal metastases have been reported. Technetium-99m-MIBI scintigraphy is currently the imaging modality of choice for localizing parathyroid tumors in patients with recurrent hyperparathyroidism. This report is a good example of the use of ^{99m}Tc-MIBI in the diagnostic work-up of a patient with recurrent hyperparathyroidism, which turned out to be due to parathyroid carcinoma rather than the initial histopathologic diagnosis of parathyroid adenoma. Additionally, the patient's total body ^{99m}Tc-MIBI and ^{99m}Tc-MDP bone images showed multiple focal lesions in the bone-mimicking metastases.

Key Words: parathyroid carcinoma; brown tumors; technetium-99m-MIBI; double-phase imaging; hyperparathyroidism; technetium-99m-MDP; bone imaging

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Parathyroid carcinoma is rare, showing itself in approximately 0.047%–4% (*1–4*) of all cancer cases. Parathyroid adenoma (*1–4*) patients develop the classic bone disease, osteitis fibrosa cystica, 25%–60% of the time. We report a patient with recurrent hyperparathyroidism associated with bone pain and fractures as a result of parathyroid carcinoma. This patient had multiple neck surgeries with recurrent symptoms of hyperparathyroidism. Technetium-99m-MIBI double-phase (early and 2–4 hr delayed) imaging demonstrated recurrent parathyroid carcinoma. Technetium-99m-MDP and ^{99m}Tc-MIBI total-body images showed multiple hot spots in the bones.

CASE REPORT

A 44-yr-old woman complained of bone pain in her right leg, which became worse after walking. Three months later, rib fractures occurred. Laboratory data revealed serum calcium 14.1 mg/dl (n = 9–11), phosphorus 2.6 mg/dl (n = 2.4–4.4) and elevated parathyroid hormone, all of which indicate hyperparathyroidism. The patient underwent neck exploration and a 2.8 × 1.7 × 1.1-cm brownish mass was excised at another hospital. Histological study of the mass was reported as parathyroid adenoma. After the surgery, her bone pain disappeared and she was able to ride a bicycle to work. Four years later, however, she underwent reexploration of the neck because of recurrent bone pain. Despite the second neck surgery, the patient's condition worsened. She was bedridden most of the time and fractured her left humerus while picking up a bowl of rice. In addition, she fractured her right femoral neck while turning over in bed. The patient was transferred to the PUMC Hospital. Laboratory data analysis revealed: calcium 12 mg/dl (n = 9–11), phosphorus 3.2 mg/dl and (n = 2.4–4.4), alkaline phosphatase 253 IU/liter (n = 38–126) and parathyroid hormone 7.24 ng/ml (normal <0.27 ng/ml). Her hemoglobin was 6.8 g/dl, and red blood cells were 2.1 × 10^{12}/liter. Twenty-four hour urinalysis (total 2000 ml) revealed: calcium 4.4 mg/dl phosphorus 25 mg/dl. Double-phase ^{99m}Tc-MIBI imaging over the neck 15 min and 3 hr after intravenous injection of 10 mCi of the radiopharmaceutical showed abnormal radiotracer localization in the left thyroid bed in the delayed phase (Fig. 1). The total-body planar ^{99m}Tc-MIBI image showed remarkable multiple hot spots in the bone (Fig. 2, right). The ^{99m}Tc-MDP total-body bone scan was obtained 2 days after MIBI imaging revealed multiple large and small areas of increased uptake in the skull, spine, ribs and long bones. These lesions were more prominent than those shown by ^{99m}Tc-MIBI imaging (Fig. 2, right). Chest CT demonstrated normal lungs, mediastinum and multiple cystic lesions in ribs, scapula and vertebrae compatible with osteitis fibrosa cystic (brown tumor) (Fig. 3). Neck surgery was performed for a third time. A mass resected from the left thyroidal bed, 3 × 2.5 × 1.4 cm in size, was confirmed to be parathyroid carcinoma with invasion of the adjacent thyroid. There was no evidence of lymph node metastasis. Postoperatively, the patient's bone pain was alleviated after calcitonin therapy. The patient's serum calcium was 10.8 mg/dl, phosphorus 4.2 mg/dl, alkaline phosphatase 38 IU/liter, parathyroid hormone 1.52 ng/ml, hemoglobin 8.0 g/dl and red blood cells 2.68 × 10^{12}/liter.

DISCUSSION

This patient's parathyroid malignancy had histological evidence of carcinoma with invasion of adjacent thyroid tissue as well as recurrent clinical manifestations of hyperparathyroidism. From the initial surgery, the pathological diagnosis was parathyroid adenoma, but the tumor from the last surgery turned out to be parathyroid carcinoma. These conflicting diagnoses suggest that distinguishing adenoma and carcinoma can be difficult (*4,5*). Fraker et al. reported on four patients with parathyroid carcinoma: one patient was initially diagnosed as such, two patients were

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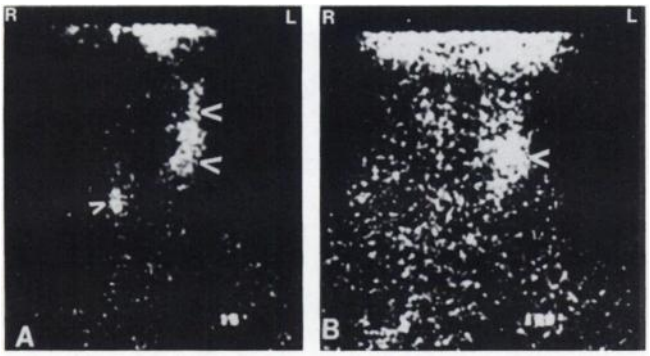

FIGURE 1. (A) Technetium-99m-MIBI anterior neck images obtained 15 min after injection show radiotracer localization in the left thyroidal bed (double arrowheads) and a small area of uptake in the region inferior to the right thyroidal bed (single arrowhead) indicate residual thyroid tissue. (B) Technetium-99m-MIBI anterior neck image obtained 3 hr after injection shows a focal area of increased uptake in the left thyroidal bed (single arrowhead), which is consistent with recurrent tumor (carcinoma).

initially diagnosed as parathyroid adenoma and one as hyperplasia (*3*). Another explanation of our patient's pathological status is that adenoma and carcinoma often co-exit in the same patient (*5*). Our patient fits the common clinical characteristics of parathyroid carcinoma: age range 44–48 yr, hypercalcemia, recurrent bony symptoms and repeat neck exploration (*1,4,5*).

Thallium-201-chloride has been reported to localize in parathyroid glands (*6*). Increased cellular density and vascularity of parathyroid adenoma has been postulated as an increase in ^{201}Tl uptake in these lesions. Technetium-99m-MIBI is an alternative to ^{201}Tl as a myocardial perfusion imaging agent and has been used successfully in parathyroid imaging (*7,8*). Tumor uptake of ^{99m}Tc-MIBI is probably related to increased perfusion, cell metabolism, AT-Pase pump activity and mitochondrial activity (*9,11,12*). Taillefer et al. (*13*) reported a sensitivity of 90% for double-phase ^{99m}Tc-MIBI imaging in parathyroid adenoma patients with hyperparathyroidism; cervico-thoracic planar imaging was performed 15 min and 2–3 hr after intravenous injection of 20–25 mCi of tracer (*13*). In another study, Cesani et al. (*9*) reported good visualization of a parathyroid adenoma on delayed 4-hr ^{99m}Tc-MIBI images of the neck.

Primary hyperparathyroidism due to parathyroid carcinoma is rare (*4*). Parathyroid adenoma contributed about 80%–95% of patients with primary hyperparathyroidism. Osteitis fibrosa cystica is a generalized bone disease caused by hyperparathyroidism. It may be manifested by fractures with little or no trauma, bony pain, bone tenderness and deformity. Localized destructive lesions are known as brown tumors of the bone. Thallium-201 uptake in brown tumors (*14–17*) and bone fracture mimicking metastases (*17*) has been reported. Localized bone remodeling induces increased blood flow and local metabolic activity that results in ^{201}Tl accumulation in brown tumors of the bone (*11*).

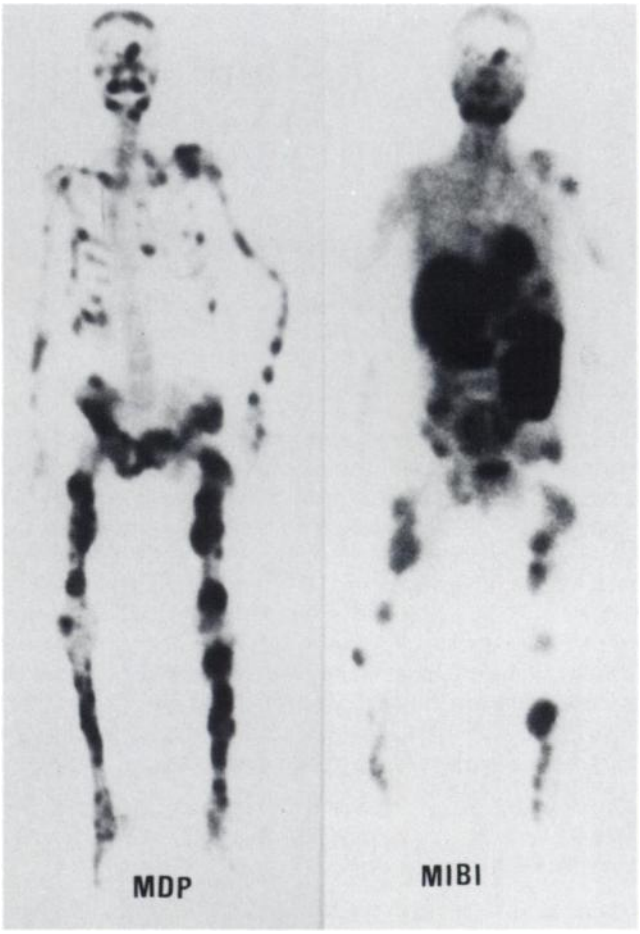

FIGURE 2. (Left) Anterior ^{99m}Tc-MDP total-body image obtained 2 days after ^{99m}Tc-MIBI imaging shows multiple areas of increased uptake in the skull, facial bones, ribs, pelvic bones and long bones. (Right) Anterior ^{99m}Tc-MIBI total-body image shows mild increased uptake in the right neck, areas of increased uptake in the skull and multiple small and large areas of increased uptake in the facial bones, long bones, pelvis and rib.

In a comparison of ^{99m}Tc-MDP and ^{201}Tl scans of brown tumors, ^{99m}Tc-MDP detection of lesions was superior to ^{201}Tl-chloride (*15*). In previous studies by Durak (*15*) and Joyce (*16*), ^{99m}Tc-MDP bone studies revealed more lesions than ^{201}Tl, and the MDP lesion-to-background-ratio was higher. This finding may be explained by the lack of ^{201}Tl accumulation in all lesions or insignificant ^{201}Tl accumulation (*15*). Although ^{201}Tl localizes in brown tumors, our patient's MIBI accumulation in these tumors was less apparent than that on ^{99m}Tc-MDP images (Fig. 2). Therefore, increased accumulation of ^{99m}Tc-MIBI may indicate parathyroid carcinoma, not only parathyroid adenoma or thyroid pathology (*18*). Total-body ^{99m}Tc-MIBI imaging can be used to detect metastatic disease of parathyroid cancer. Aggressive surgical management of parathyroid carcinoma and resection of its metastases can prolong a patient's life. Thus, ^{99m}Tc-MIBI imaging may give prognostic information.

In summary, double-phase ^{99m}Tc-MIBI neck and chest imaging may be used in parathyroid carcinoma patients to

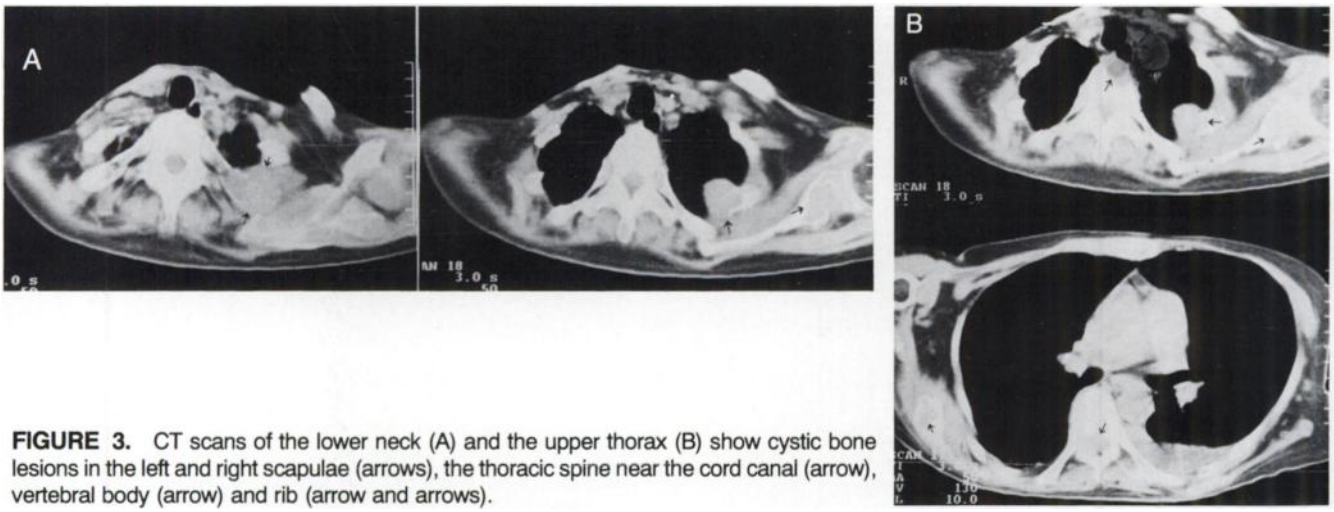

FIGURE 3. CT scans of the lower neck (A) and the upper thorax (B) show cystic bone lesions in the left and right scapulae (arrows), the thoracic spine near the cord canal (arrow), vertebral body (arrow) and rib (arrow and arrows).

detect recurrences. Technetium-99m-MIBI may also be used to detect parathyroid carcinomas in patients with recurrent hyperparathyroidism.

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REFERENCES

1. Hakaim AG, Esselstyr CB. Parathyroid carcinoma: 50 yr experience at the Cleveland Clinic Foundation. *Cleve Clin J Med* 1993;60:331–335.
2. Shane E, Bilezikian JP. Parathyroid carcinoma: a review of 62 patients. *Endocrinol Rev* 1982;3:218–226.
3. Franker DL, Travis WD, Merendino JJ, et al. Locally recurrent parathyroid neoplasms as a cause for recurrent and persistent primary hyperthyroidism. *Am J Surg* 1991;213:58–65.
4. Wang CA, Gar RD. Natural history of parathyroid carcinoma. Diagnosis treatment and results. *Am J Surg* 1984;149:522–527.
5. Vetto JJ, Brennan MF, Woodruf J, et al. Parathyroid carcinoma: diagnosis and clinical history. *Surgery* 1993;114:882–892.
6. Fukunaga M, Morita R, Yonekura Y, et al. Accumulation of ^{201}Tl chloride in a parathyroid adenoma. *Clin Nucl Med* 1979;4:229–230.
7. Coakley AJ, Kettle AG, Well C, et al. Technetium-99m-sestamibi—a new agent for parathyroid imaging. *Nucl Med Commun* 1989;10:791–794.
8. O'Doherty MJ, Kettle AG, Wells P, et al. Parathyroid imaging with technetium-99m-sestamibi: preoperative localization and tissue uptake studies. *J Nucl Med* 1992;33:313–318.
9. Cesani F, Ernst R, Walser E, Villaneva-Meyer J. Technetium-99m MIBI imaging of a pancreatic VI POMA and parathyroid adenoma in a patient with multiple Type I endocrine neoplasia. *Clin Nucl Med* 1994;19:532–534.
10. Delmar-Moningeon LI, Piwnica-Worms D, Van den Abbeele AD, et al. Uptake of the cation hexakis (2-methoxyizobutz lisonitrile) technetium-99m by human carcinoma cell lines in vitro. *Cancer Res* 1990;50:2198–2201.
11. Chiu ML, Kronauge JF, Piwnica-Worms D. Effect of mito chondrial and plasma membrane potentials on a accumulation of hexakis (2-methoxy-isobutylisonitrile) technetium (I) in cultured mouse fibroblast [Abstract]. *J Nucl Med* 1990;31:1646.
12. Aktotum C, Bayham H, Kir M. Clinical experience with Tc-99m MIBI imaging in patient with malignant tumors preliminary results and comparison with Tl-201. *Clin Nucl Med* 1992;17:171–175.
13. Taillefer R, Bouchor Y, Potvin C, Raymond L. Detection and localization of parathyroid adenomas in patients with hyperparathyroidism using a single radionuclide imaging procedure with Tc-99m MIBI (double-phase study). *J Nucl Med* 1992;33:1801–1807.
14. Yang CJ, Seabold JE, Gurll NJ. Brown tumor of bone: a potential source of false-positive thallium-201 localization. *J Nucl Med* 1989;30:1264–1267.
15. Durak H, Aras T, Sungur C, et al. Thallium-201 uptake in brown tumors of hyperparathyroidism. *Clin Nucl Med* 1991;16:931–935.
16. Joyce JM, Idea RJ, Grossman SJ, et al. Multiple brown tumors in unsuspected primary hyperparathyroidism mimicking metastatic disease on radiograph and bone scan. *Clin Nucl Med* 1994;19:630–635.
17. Adalet I, Aktay R, Sirali M, Cantez S, Terzioglu T, Alagel F. Uptake of Tl-201 in Brown tumor and bone fracture. *Clin Nucl Med* 1994;19:542–543.
18. Kitapsi MT, Tastekim G, Turgut M, et al. Preoperative localization of parathyroid carcinoma using Tc-99m MIBI. *Clin Nucl Med* 1993;18:217–219.
19. Shortell CK, Andus CH, Phillips CE, et al. Carcinoma of the parathyroid gland: a 30-yr experience. *Surgery* 1991;110:704–708.
20. Ohara T, Okamoto T, Ito Y, et al. Surgical and medical management of patients with pulmonary metastasis from parathyroid carcinoma. *Surgery* 1993;114:1040–1048.