ing Ca × PO_4 products by manipulating Ca and PO_4 levels can lead to drastic resolution of these calcifications (*11*). Alfrey et al. (*12*) have already demonstrated radiologically the disappearance of gross tumoral calcifications of chronic uremia after transplantation, either by phosphate supplementation or parathyroidectomy.

We could not correlate the metastatic calcium deposits by bone scan with the anatomic presence of calcification. Radiological diagnosis of diffuse metastatic calcification has proven to be difficult, as the particles are extremely small (microscopic in most cases) (*13*). Lack of MDP uptake by metastatic calcium deposits does not mean the disappearance of the anatomic presence of calcification but represents the metastatic activity of the pathologic calcification.

Among the important bone scintigraphic findings in hyperparathyroidism, uniformly increased bone-to-soft tissue ratios generally associated with faint or absent renal visualization (*14–16*) are a well known classical findings. The mechanism for the super scan is due to low excretion of injected ^{99m}Tc-MDP (10% in 4 hr versus 60% in normal subjects) and a fivefold increase in the total bone-to-soft tissue uptake ratio (*17*). Faint or absent kidney images are due to low soft-tissue activity common to any metabolic bone disease with high bone uptake of ^{99m}Tc-diphosphonate (*11*).

In our patient, the skeletal and renal uptake appeared normal in the first bone scan, whereas the second one, obtained 1 wk after surgery, showed generalized increased activity symmetrically, particularly in the calvarium, the mandible and the diaphysis of long bone (*18*). Relatively higher ^{99m}Tc-MDP uptake in extraskeletal sites may have prevented the appearance of this characteristic feature of hyperparathyroidism in the first bone scan. After surgery, extraskeletal uptake of the radiopharmaceutical decreased, thus allowing the appearance of hyperparathyroidism features on the bone scan.

CONCLUSION

Hepatic, pulmonary and gastric uptake of ^{99m}Tc-MDP could be reversed in primary hyperparathyroidism as the cause of hypercalcemia is resolved. Therefore, the resolution of the extraskeletal metastatic calcification can be correctly assessed with repeat follow-up bone scintigraphy.

REFERENCES

1. Janowitz WR, Serafani AN. Intense myocardial uptake of ^{99m}Tc-diphosphonate in a uremic patient with secondary hyperparathyroidism and pericarditis: case report. *J Nucl Med* 1976;17:896–898.
2. Francis MD. The inhibition of calcium hydroxyapatite crystal growth by polyphosphonates and polyphosphates. *Calcif Tiss Res* 1969;3:151–162.
3. Krane SM, Glindher MJ. Transphosphorylation from nucleoside di- and triphosphates by apatite crystals. *J Biol Chem* 1962;237:2991–2998.
4. Watson NW, Cowan RJ, Maynard D, Richards F. Resolution of metastatic calcification revealed by bone scanning: case report. *J Nucl Med* 1977;18:890–892.
5. Scarpelli DG, Iannaccone PM. Cell injury and errors of metabolism. Kissane JM, ed. In: *Anderson's pathology*. St Louis: Mosby; 1990:1–65.
6. Velentzas C, Meindok H, Oreopoulos DG, et al. Detection and pathogenesis of visceral calcification in dialysis patients and patients with malignant disease. *Can Med Assoc J* 1978;118:45–50.
7. Cohen AM, Maxon HR, Goldsmith RE, et al. Metastatic pulmonary calcification in primary hyperparathyroidism. *Arch Intern Med* 1977;137:520–522.
8. Herry JY, Chevet D, Moison A, et al. Pulmonary uptake of ^{99m}Tc-labeled methylene diphosphonate in a patient with a parathyroid adenoma. *J Nucl Med* 1981;22:888–890.
9. Amico S, Lucas P, Diebold MD, et al. Metastatic calcification in the thyroid gland demonstrated on bone scan in a patient with primary hyperparathyroidism. *J Nucl Med* 1986;27:373–376.
10. Rosenthal DI, Chandler HL, Azizi F, et al. Uptake of bone imaging agents by diffuse pulmonary metastatic calcification. *Am J Roentgenol* 1977;129:871–874.
11. de Jonge FAA, Pauwels EKJ, Hamdy NAT. Scintigraphy in the clinical evaluation of disorders of mineral and skeletal metabolism in renal failure. *Eur J Nucl Med* 1991;18:839–855.
12. Alfrey AC, Jenkins D, Croth CG, et al. Resolution of hyperparathyroidism renal osteodystrophy and metastatic calcification after renal homotransplantation. *N Engl J Med* 1968;279:1349–1356.
13. Mootz JR, Sagel SS, Roberts TH. Roentgenographic manifestations of pulmonary calcifications. A rare cause of respiratory failure in chronic renal disease. *Radiology* 1973;107:55–60.
14. Sy WM, Patel D, Faunce H. Significance of absent or faint kidney sign on bone scan. *J Nucl Med* 1975;16:454–456.
15. Thrupkaew AK, Henkin R, Quinn J. False-negative bone scans in disseminated metastatic disease. *Radiology* 1974;113:383–386.
16. Osmond JD, Pendergrass HP, Potsaxid MS. Accuracy of ^{99m}Tc-diphosphonate bone scans and roentgenograms in the detection of prostate, breast and lung carcinoma metastases. *Am J Roentgenol* 1975;125:972–977.
17. Constable AR, Cranage RW. Recognition of the super scan in prostatic bone scintigraphy. *Br J Radiol* 1981;54:122–125.
18. Sy WM. Bone scan in primary hyperparathyroidism. *J Nucl Med* 1974;15:1089–1091.

Localization of Technetium-99m-Sestamibi in Diffuse Myelodysplastic Processes

Robert E. Reiman and Julie K. Fetters

Departments of Radiology and Medicine, Duke University Medical Center, Durham, North Carolina

We present two patients with skeletal localization of ^{99m}Tc-sestamibi in patients with ringed sideroblastic anemia and polycythemia vera who were undergoing routine myocardial perfusion studies.

Key Words: myelodysplastic disorders; technetium-99m-sestamibi

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Technetium-99m-sestamibi (hexakis-2-methoxyisobutylisonitrile ^{99m}Tc(I)) was originally developed as a myocardial perfusion imaging agent and has been widely used in the diagnosis of coronary artery disease since its introduction. It has, however, been shown to preferentially concentrate in a variety of solid tumors. We report the incidental finding of skeletal localization of ^{99m}Tc-sestamibi in two patients with diffuse myelodysplastic processes.

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For correspondence or reprints contact: Robert Reiman, MD, Department of Radiology, Box 3808, Duke University Medical Center, Durham, NC 27710.

CASE REPORT

Patient One

A 73-yr-old man was referred for evaluation of a 3-wk history of dyspnea on exertion and palpitations in view of a family history of coronary artery disease. He underwent a myocardial perfusion study utilizing a one-day imaging protocol and received 296 MBq (8.0 mCi) ^{99m}Tc-sestamibi at rest, followed 60 min later by planar imaging in the anterior, 45° LAO and left lateral projections. Imaging was repeated following treadmill exercise using 888 MBq

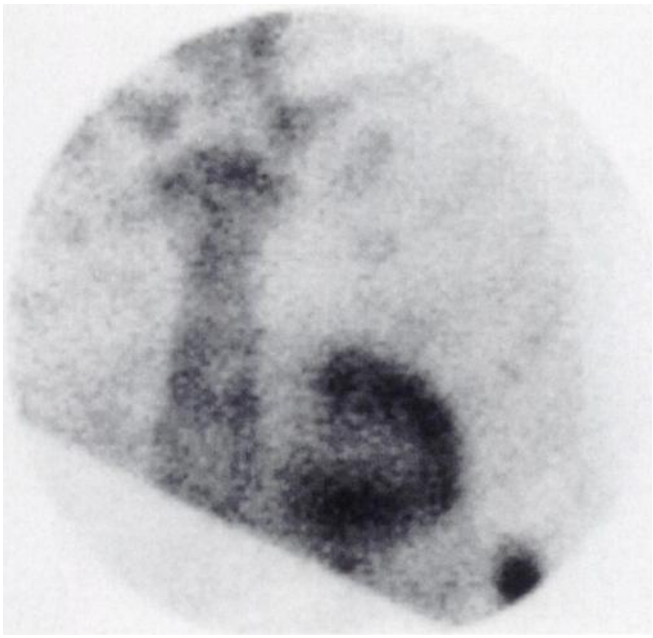

FIGURE 1. Image of the thorax (45° LAO planar projection) of Patient 1 who had a 2-yr history of stable, ringed sideroblastic anemia. Image was acquired 60 min after administration of 296 MBq (8 mCi) ^{99m}Tc-sestamibi at rest. There is prominent, homogeneous tracer uptake in the sternum, clavicle and ribs, which is not typical in routine myocardial studies.

(24 mCi) ^{99m}Tc-sestamibi. Review of the rest images demonstrated a normal left ventricle with the exception of a mild inferior wall defect. Abnormal, prominent radiotracer accumulation, however, was noted in the sternum, clavicle and ribs in a homogeneous pattern (Fig. 1). The patient denied having undergone a prior radionuclide imaging procedure.

Chromatographic analysis of the residual material in the preparation vial demonstrated a radiochemical purity greater than 97.0% at 24 hr. Further investigation into the patient's medical history revealed that he had a 2-yr history of chronic, stable macrocytic anemia with high ferritin and normal vitamin B12 levels. A bone marrow biopsy obtained at the time of the initial evaluation demonstrated a myelodysplastic syndrome characterized by ringed sideroblastic anemia. At the time of his sestamibi study, the patient had no evidence of leukemic transformation or myelofibrosis.

Patient Two

A 67-yr-old man with a history of chronic abdominal pain, narcotic dependence, polycythemia vera and coronary artery disease was hospitalized for major depression, cellulitis and pain control. During his hospital course, he had intermittent episodes of atrial fibrillation and chest pain. He was referred for myocardial perfusion imaging and underwent a sestamibi study using the imaging protocol described above. Abnormally prominent skeletal uptake was noted on the resting sestamibi images in a pattern similar to that seen in Patient 1.

DISCUSSION

The localization of ^{99m}Tc-sestamibi has been described in benign and malignant solid tumors such as parathyroid adenoma (*1*), giant lymph node hyperplasia (*2*), lung cancer (*3*), astrocytoma (*4*), undifferentiated mesenchymal tumor (*5*), osteogenic sarcoma (*6*), thyroid carcinoma (*7,8*) and primary cardiac lymphoma (*9*). The patients reported here demonstrate its homogeneous localization in diffuse bone marrow disease.

Ringed sideroblastic anemia and polycythemia vera are included in the broad category of hematological diseases referred to as myelodysplastic disorders. Ringed sideroblastic anemia is manifested in the peripheral blood by megaloblastic anemia, the appearance of red cell precursors with ring-shaped deposits of ferruginous granules and abnormalities in serum levels of iron transport proteins. In a variable number of patients, ringed sideroblastic anemia will eventually transform into more malignant processes, including acute or chronic leukemia and myelofibrosis (*10–12*). Polycythemia is characterized by increased erythropoiesis and variable degrees of leukocytosis and thrombocytosis; myeloid metaplasia and myelofibrosis may also be manifested (*13*).

The localization of ^{99m}Tc-sestamibi in cardiac myocytes, which is the basis for its utility in cardiac perfusion imaging, is believed to be related to its high lipophilicity and subsequent intracellular binding in metabollically active tissues. Metabolic inhibition studies in cultured myocardial cells and the correlation of sestamibi binding with mitochondrial membrane potential (*14,15*) suggest that its localization is within mitochondria. Nonspecific uptake of sestamibi in ringed, sideroblastic anemia and polycythemia may therefore be related to marrow expansion and the accompanying increase in oxidative metabolism. Increased marrow perfusion also likely plays a role; morphometric studies have demonstrated marrow hypervascularity in the form of dilated venous sinusoids and increased blood flow in polycythemia (*16,17*). Finally, marrow abnormalities such as anemia are known to alter blood flow in adjacent bone and this may also contribute to the increased skeletal uptake seen in our patients.

CONCLUSION

We described the localization of ^{99m}Tc-sestamibi in two diffuse myelodysplastic processes which have the potential for malignant transformation. Further studies will be needed to assess the clinical utility of this incidental finding in the evaluation of bone marrow disorders.

REFERENCES

1. 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.
2. Oktolun C, Bayhan H, Celasun B, et al. Unexpected uptake of technetium-99m hexakis-2-methoxy-isobutylisonitrile in giant lymph node hyperplasia of the mediastinum (Castleman's disease). *Eur J Nucl Med* 1991;18:856–859.
3. Hassan IM, Sahweil A, Constantinides C, et al. Uptake and kinetics of ^{99m}Tc hexakis 2-methoxyisobutylisonitrile in benign and malignant lesions in the lungs. *Clin Nucl Med* 1989;14:333–340.
4. O'Tuama LA, Packard AB, Treves ST. SPECT imaging of pediatric brain tumor with hexakis (methoxybutylisonitrile) technetium(I). *J Nucl Med* 1990;31:2040–2041.
5. Caner B, Kitapci M, Erbengi G, et al. Increased accumulation of ^{99m}Tc MIBI in undifferentiated mesencymal tumor and its metastatic lung lesions. *Clin Nucl Med* 1992;17:144–145.
6. Caner B, Kitapci M, Aras T, et al. Increased accumulation of hexakis (2-methoxybutylisonitrile) technetium(I) in osteosarcoma and its metastatic lymph nodes. *J Nucl Med* 1991;1977–1978.
7. Briele B, Hotze A, Kropp J, et al. Vergleich von ^{201}Tl und ^{99m}Tc MIBI in der nachsorge des differentzierten schilddrusenkarzinoms. *Nuklearmedizin* 1991;30:115–124.
8. O'Driscoll CM, Baker F, Casey MJ, et al. Localization of recurrent medullary thyroid carcinoma with technetium-99m-methoxybutylisonitrile scintigraphy: a case report. *J Nucl Med* 1991;32:2281–2283.
9. Medolago G, Virotta G, Piti A, et al. Abnormal uptake of technetium-99m hexakis-2-methoxyisobutyl isonitrile in a primary cardiac lymphoma. *Eur J Nucl Med* 1992;199:222–225.
10. Valentine W. Sideroblastic anemias. In: Williams WJ, Beutler E, Erslev AJ, Rundles RW, eds. *Hematology*, 2nd ed. New York: McGraw-Hill; 1977.
11. Meckenstock G, Fonatsch C, Heyll A, et al. T-cell receptor gamma/delta expressing acute leukemia emerging from sideroblastic anemia: morphological, immunological and cytogenetic features. *Leukemia Res* 1992;16:379–384.
12. Gatterman N, Aul C, Schneider W. Risk of leukemic transformation in two types of acquired idiopathic sideroblastic anemia. *Hematologie und Bluttransfusion* 1990;33:374–381.
13. Glass JL, Wasserman LR. Primary polycythemia. In: Williams WJ, Beutler E, Erslev AJ, Rundles RW, eds. *Hematology*, 2nd ed. New York: McGraw-Hill; 1977.

14. Piwnica-Worms D, Kronauge JF, Delmon L, et al. Effect of metabolic inhibition on technetium-99m-MIBI kinetics in cultured chick myocardial cells. *J Nucl Med* 1990;31:464–472.
15. Chiu ML, Kronauge JF, Piwnica-Worms D. Monitoring mitochondrial plasma membrane potentials with a new ^{99m}Tc-based lipophilic cation [Abstract]. *J Gen Physiol* 1989;94:41A.
16. Vykoupil KF, Thiel J, Stangel W, et al. Polycythemia vera. I. Histopathology, ultrastructure and cytogenetics of the bone marrow in comparison with secondary polycythemia. *Virchows Archiv A Path Anat Histol* 1980;389:307–324.
17. Van Dyke D, Anger HO, Parker H, et al. Markedly increased blood flow in myelofibrosis. *J Nucl Med* 1971;12:506–512.

Scintigraphic Diagnosis of Intrathoracic Extramedullary Hematopoiesis in Alcohol-Related Macrocytosis

Frank De Geeter and Dirk Van Renterghem
Departments of Nuclear Medicine and Pneumology, Saint John's General Hospital, Brugge, Belgium

We report the scintigraphic diagnosis of thoracic extramedullary hematopoiesis in a case of alcohol-related macrocytosis. A patient with liver cirrhosis and alcohol-related macrocytosis showed multiple rounded masses in the low thoracic paraspinal region on chest radiography and CT. Whole-body scintigraphy and SPECT imaging of the thorax, after nanocolloid administration, demonstrated expansion of the bone marrow in the humeri and femora and uptake of the tracer in the mediastinal masses, establishing the diagnosis of mediastinal extramedullary hematopoiesis. Thoracic extramedullary hematopoiesis may occur in conjunction with alcohol-related macrocytosis. Scintigraphy with ^{99m}Tc-nanocolloids is a suitable noninvasive method to establish the presence of extramedullary marrow.

Key Words: technetium-99m-colloid; bone marrow scintigraphy; extramedullary hematopoiesis; posterior mediastinal tumor; macrocytosis

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Extramedullary hematopoiesis is defined as the recurrence after birth of normal marrow outside the skeleton. It occurs in chronic hemolytic states, ineffective erythropoiesis, myelophtisic conditions and in myeloproliferative disorders as an attempt to compensate for the anemia (*1–3*). Most frequently, the extraskeletal marrow is present in liver and spleen. We report on a case of intrathoracic extramedullary hematopoiesis in conjunction with alcohol-related macrocytosis. Scintigraphy with nanocolloids was instrumental in the differential diagnosis of the intrathoracic masses.

CASE REPORT

A 73-yr-old man with known alcoholic liver cirrhosis presented with dyspnea and asthenia. Fifteen months earlier, he had been examined because of macrocytic anemia. At that time, bone marrow biopsy had revealed a megaloblastic appearance of the red and myeloid precursors and a bone marrow aspirate had shown dyserythropoietic characteristics such as megaloblastic elements, deshemoglobinisation, anisocytosis and anisokaryosis. Serum levels of vitamin B12 and folic acid as well as erythrocytic levels of folic acid were normal. Bone marrow findings were attributed to substantial alcohol abuse.

The patient, now admitted, continued consumption of 4-to-5 alcoholic beverages a day. At physical examination, an anemic facies, spider naevi, a slightly enlarged liver and ascites were found. Chest radiography showed small bilateral pleural effusion and suggested a space-occupying lesion projected upon the right hilum. Computed tomography of the thorax (Fig. 1) revealed the presence of a paraspinal polynodular mass at the mid and low dorsal levels. A diagnosis of neurinoma was suggested by the radiologist. The erythrocyte sedimentation rate was 36 mm/hr; the hematocrit was 29% and the hemoglobin level 9.7 mg/dl. The mean corpuscular volume was 117.8 fl. White blood cell counts as well as platelet counts were normal. Gamma-glutamyl transferase was 100 m*U*/ml (normal values up to 65 m*U*/ml).

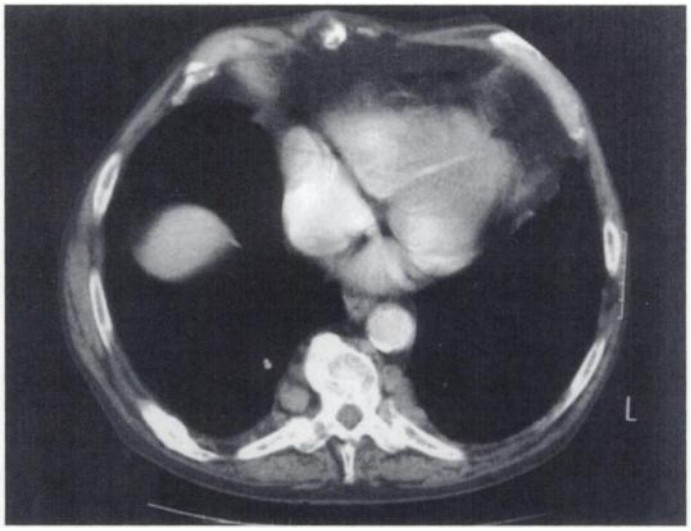

FIGURE 1. CT shows multiple rounded masses in the paraspinal region at the low thoracic level.

Since thoracic extramedullary hematopoiesis was considered as a differential diagnosis, bone marrow scintigraphy was performed 1 hr after intravenous injection of 20 mCi ^{99m}Tc-nanocolloid. Whole-body images (Fig. 2) revealed marked activity in the femora and humeri, extending to their most distal parts, and thus were indicative of marrow expansion (*4*). Moreover, paraspinal activity was present at the low thoracic level. SPECT (Fig. 3) enabled us to locate the activity in the paraspinal region corresponding to the masses seen on CT.

We therefore concluded that these represented foci of extramedullary hematopoiesis secondary to alcoholic macrocytosis. The patient refused further examination and treatment. No histologic confirmation could be obtained.

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For correspondence or reprints contact: Frank De Geeter, MD, Department of Nuclear Medicine, Algemeen Ziekenhuis Sint-Jan, Ruddershove 10, 8000 Brugge, Belgium.