Technetium-99m-MIBI Versus Fluorine-18-FDG in Diffuse Multiple Myeloma

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Experience of scintigraphic detection of bone lesion and active bone marrow involvement of multiple myeloma, especially with sestamibi and FDG-PET scans is in evolution. We report a case of intense sestamibi uptake in bone marrow correlating with the extent of the disease, while FDG-PET scans showed activity only in areas of active disease progression associated with pain. Technetium-99m-sestamibi appears to indicate the extent of the disease, while [^{18}F]FDG-PET scans show sites of active tumor proliferation and may be useful in directing local therapy such as radiation.

Key Words: multiple myeloma; sestamibi; fluorine-18-FDG; PET
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Several radiopharmaceuticals have been used for detection of bone involvement in patients with multiple myeloma (*1,2*). Bone scintigraphy with ^{99m}Tc-MDP is relatively insensitive when compared with conventional radiographs (*3,4*). Experience with ^{99m}Tc-sestamibi and [^{18}F]FDG, both well-known tumor imaging agents, is scarce. A review of the literature shows only one series comparing ^{99m}Tc-sestamibi with MDP bone scans, with the former showing higher sensitivity for myeloma detction (*5*) and one case of [^{18}F]FDG uptake in multiple myeloma (*6*).

We report a case of multiple myeloma with extensive bone marrow involvement detected by ^{99m}Tc-sestamibi while performing a stress myocardial perfusion scan. We also correlate the findings of ^{99m}Tc-sestamibi and [^{18}F]FDG PET scans with the patient's known bone involvement and suggest that the latter technique is important in multiple myeloma, particularly in distinguishing active bone involvement from inactive lesions.

CASE REPORT

A 67-yr-old man with past medical history of anemia presented with chronic leg pain in 1991 when his hemoglobin was 10.3, with normal white blood cell count and platelets. He had an elevated IgA with relatively normal IgM and IgG levels. Serum protein electrophoresis was normal. The diagnosis was monoclonal gammopathy of unknown significance. He remained well until May 1995 when he sustained a left elbow fracture. A radiograph showed a lytic lesion in the olecranon process of the ulna. The elbow was surgically repaired and biopsy of the lesion was consistent with multiple myeloma. Bone marrow aspiration showed 52% plasma cells and kappa clonal excess. Skeletal survey showed diffuse osteopenia of the spine and diffuse permeative pattern involving both femora extending from the diaphysis to the distal metaphysis, a lytic lesion in the distal left radius and mottling of the distal right radius and ulna, consistent with myelomatous involvement. An MRI of the spine showed diffusely abnormal signal in the bone marrow, consistent with infiltration by multiple myeloma (Fig. 1). Hematological workup showed hemoglobin of 9.3, IgA kappa of 5700 mg/dl (normal = 68–423), B2 microglobulin of 6 mg/liter (normal = 1.1–2.4) and depressed IgG. The patient was diagnosed as Stage III IgA multiple myeloma and was treated with alpha-interferon and decadron from May to October 1995. In January 1996, after a brief remission, laboratory workup revealed monoclonal IgA of 4505 mg/dl. At this time, the patient complained of new bone pain in the knees and left elbow.

The patient was referred to the nuclear medicine department for evaluation of myocardial perfusion in preparation for bone marrow transplant. Myocardial scintigraphy was performed with 10 and 30 mCi ^{99m}Tc-sestamibi for the rest and stress images, respectively. A large fixed defect in the inferior wall consistent with an old infarct was seen. Intense radiotracer uptake was observed in the rib cage and thoracic spine. A whole-body image was obtained approximately 4 hr following the injection of 30 mCi ^{99m}Tc-sestamibi. The image confirmed the presence of diffuse radiotracer uptake in the spine, ribs, pelvis, both knees and the left elbow (Fig. 2).

A whole-body [^{18}F]FDG PET scan was obtained 10 days later. After a 6-hr fast, 10 mCi [^{18}F]FDG were given intravenously. Emission images of the whole body were obtained about 1 hr later followed by a transmission scan. Increased [^{18}F]FDG uptake was observed in the left elbow as well as in the condylar regions of both femora (Fig. 3). Mildly increased [^{18}F]FDG uptake was also noted in the right proximal tibia and in the right elbow. The rest of the skeletal system showed normal [^{18}F]FDG activity.

Bone scanning performed 1 wk later with 25 mCi ^{99m}Tc-MDP showed increased radiotracer uptake in the condylar regions of both femora, both elbows and the mid sternum (Fig. 4). The latter lesion was traumatic in origin due to a previous car accident and most likely represents a healing fracture. It was not detected on the sestamibi or [^{18}F]FDG PET scans.

DISCUSSION

Multiple myeloma is characterized by malignant proliferation of clonal plasma cells and excessive formation of nonoclonal immunoglobulin. Detection of bone lesions in the early phase of the disease and evaluation of changes during treatment are often difficult. Radiographic changes are not reliable indicators of prognosis (*1*), often showing only occasional punched out lesions or diffuse osteopenia which is difficult to quantitate. Quantitative analysis of serum and urine M-protein is useful after the general progression of the disease, but does not reflect the status of developing or existing bone lesions (*1*). Radionuclide imaging offers a potential alternative or supplement to radiographic detection and assessment of bone lesions. Recently, there has been a growing interest and recognition of the important role of ^{99m}Tc-sestamibi in imaging malignant tumors (*5,7–9*). Abnormal bone marrow uptake of ^{99m}Tc-sestamibi has also been reported in patients with multiple myelomas (*5*).

Fluorine-18-FDG is a glucose analog currently used to evaluate glucose metabolism in a variety of cancers, including bone lesions (*10–12*). However, the biodistribution and mech-

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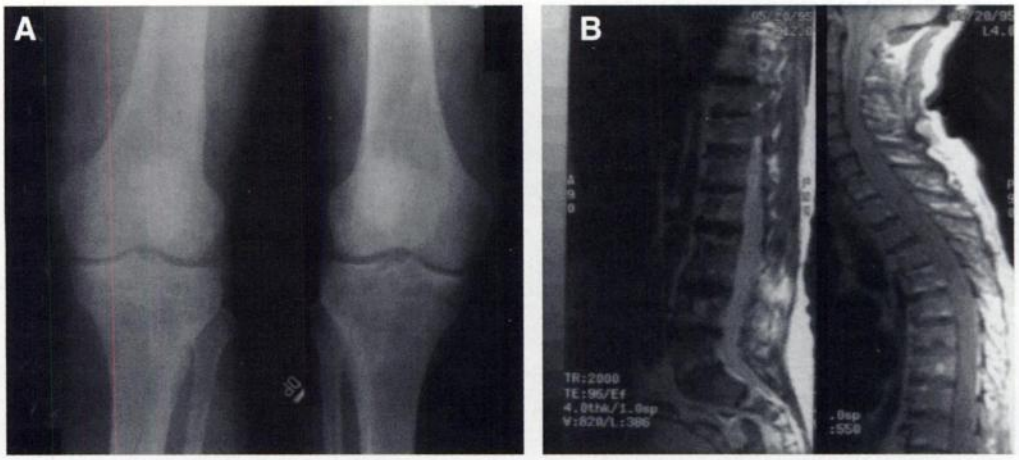

FIGURE 1. (A) Radiograph of the knee joint showing diffuse permeative pattern. (B) T2-weighted pulse sequence MR of the spine showing diffuse abnormal signal in the bone marrow.

anism of uptake of sestamibi and [^{18}F]FDG are different, reflecting two separate biological phenomena. Chiu et al. (*13*) have demonstrated that sestamibi is sequestered within the cytoplasm and mitochondria of cultured mouse fibroblast and the net cellular uptake and retention occur in response to the electrical potential generated across the membrane bilayers. Therefore, tissues with larger numbers of mitochondria will show avid sestamibi uptake. Other factors such as the lipophilicity of sestamibi, local blood flow and transcapillary exchange are also involved.

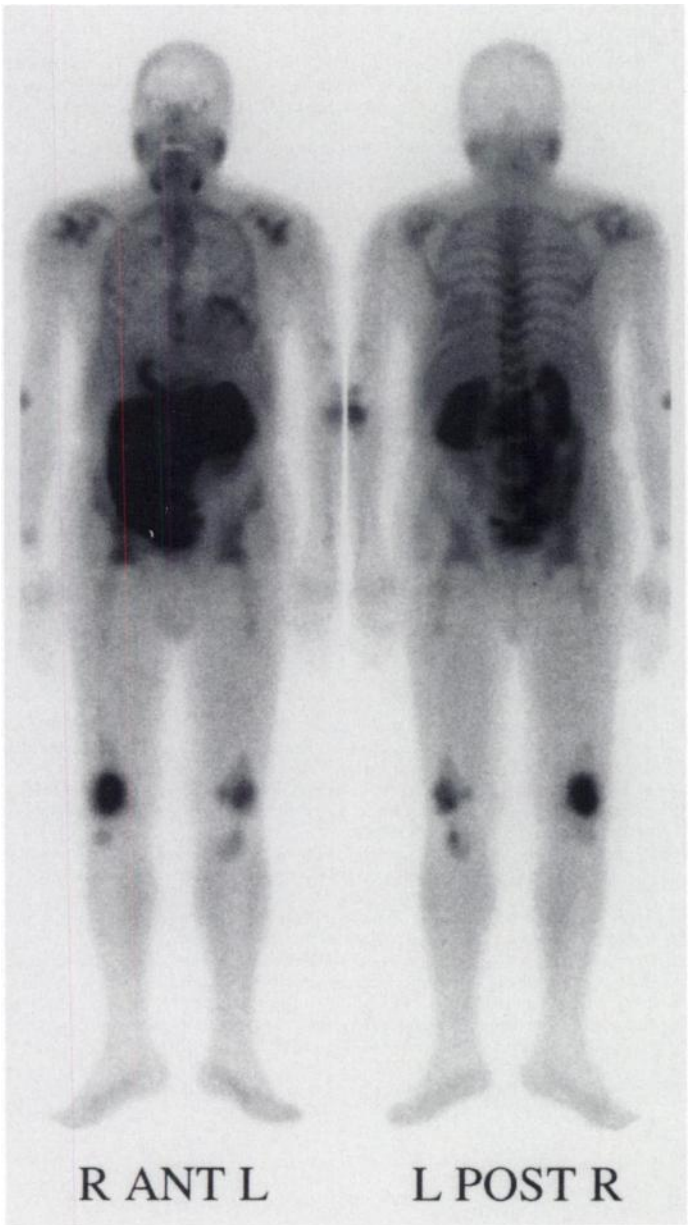

FIGURE 2. Whole-body sestamibi scan showing diffuse uptake in the ribs, thoracic and lumbar vertebrae, distal ends of both femora, proximal left tibia and both elbows.

On the other hand, [^{18}F]FDG uptake by tumor reflects the accelerated glycolysis usually occurring in malignant cells. The enhanced glycolytic rate of malignant cells, which is associated with increased activities of rate-controlling enzymes for glycolysis, facilitates tumor detection with [^{18}F]FDG-PET (*14*). Recently, several functional facilitative glucose transporters (GTs) were identified and cloned (*15–17*), and some of these have been recognized to be overexpressed in patients with anaplastic glioma (*18*). In particular, Fulham et al. (*19*) suggested that GTs may play a role in explaining the paradoxical findings of increased [^{18}F]FDG uptake as compared to the relatively benign clinical course in patients with juvenile pilocytic astrocytoma.

In this case, the sestamibi images showed abnormal uptake throughout the axial skeleton as well as the ribs, proximal femora, shoulders, elbows and knees. These most likely represented sites of viable tumors. Diffuse marrow abnormality was also noted in the MRI of the spine, corresponding to the sestamibi findings.

The PET scan showed abnormally increased [^{18}F]FDG uptake only in the regions of the knees and the left elbow, sites of intense pain. This may reflect the rapid growth and highly invasive features of the tumor in these regions as compared to others where the [^{18}F]FDG uptake was the same as normal bone marrow. Changes in the biologic nature of the tumor in certain locations may be associated with up-regulation of the GTs gene, thus leading to increased [^{18}F]FDG uptake. This may explain the pattern of uptake and the discrepancy between the ^{99m}Tc-sestamibi and [^{18}F]FDG PET scan findings. Associated inflammatory activity with tumor proliferation may also be a factor leading to increased [^{18}F]FDG uptake.

Bone scans are notoriously insensitive in detecting bone marrow disease and is positive only at sites of extensive bone involvement (i.e., the knees and elbows). Bone scans are also nonspecific, as exemplified in this case report by the traumatic lesion of the sternum which was very hot on the bone scan but not seen on the sestamibi and PET scans.

CONCLUSION

Technetium-99m-sestamibi scans appear to indicate the extent of multiple meloma while [^{18}F]FDG PET scans may show

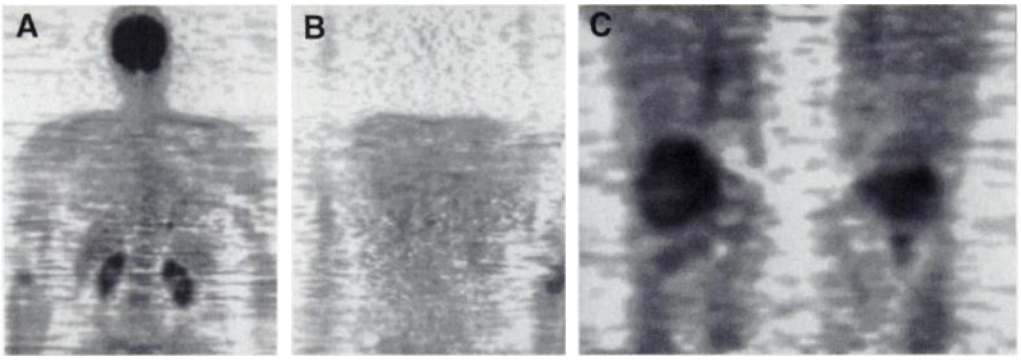

FIGURE 3. (A) Fluorine-18-FDG PET scan showing increased uptake in the left elbow. (B) Normal spine uptake. (C) Increased uptake in condylar regions of both femurs.

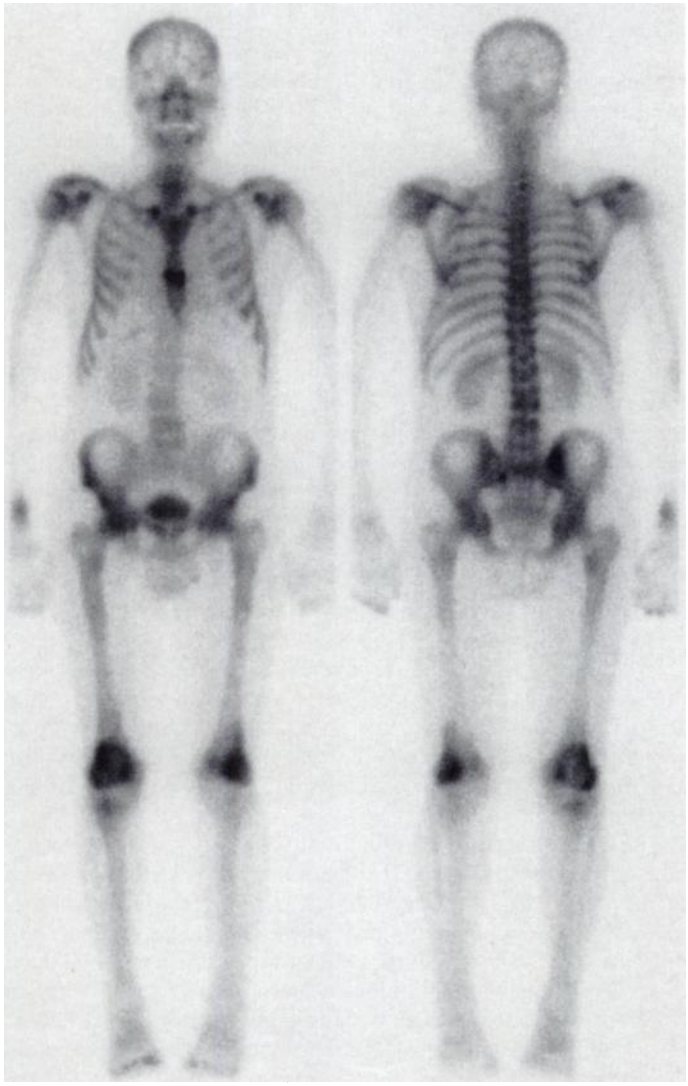

FIGURE 4. Whole-body bone scan shows increased uptake in distal ends of both femora, midsternum, both elbows and irregular activity in the SI joint.

sites of active tumor proliferation and may be useful in directing local therapies such as radiation. Further studies with larger series of patients are needed to better characterize the role of ^{99m}Tc-sestamibi scans versus [^{18}F]FDG PET scans in diffuse multiple myeloma.

REFERENCES

1. Hubner KF, Andrews GA, Hayes RL, Poggenburg JK, Solomon A. The use of rare earth radionuclides and other bone seekers in the evaluation of bone lesions in patients with multiple myeloma or solitary plasmacytoma. *Radiology* 1977;125:171–176.
2. Kanoh T, Ohno T, Uchino H, Yamamoto I, Torizuka K. Avid uptake of ^{67}Ga in multiple myeloma. An additional indicator of the aggressive phase. *Clin Nucl Med* 1987;12:482–484.
3. Ludwig H, Kumpan W, Sinzinger H. Radiography and bone scintigraphy in multiple myeloma: a comparative analysis. *Br J Radiol* 1982;55:173–181.
4. Scutellari PN, Spanedda R, Feggi LM, Cervi PM. The value and limitations of total body scan in the diagnosis of multiple myeloma: a comparison with conventional skeletal radiography. *Hematologica* 1985;70:136–142.
5. Unlu M, Haznedar R, Atavci S, Inanir S, Turgut B. Detection of bone lesions in multiple myeloma using ^{99m}Tc-MIBI scintigraphy [Abstract]. *J Nucl Med* 1995; 36(suppl):190P.
6. Sasaki M, Ichiya Y, Kuwabara Y, et al. FDG-PET in ^{99m}Tc-MDP negative bone tumors. *J Nucl Med* 1993;34:288–290.
7. Hassan IM, Sahweil A, Constantinides C, et al. Uptake and kinetics of ^{99m}Tc-hexakis-2-methoxyisobutyl isonitrile in benign and malignant lesions in the lungs. *Clin Nucl Med* 1989;14:333–340.
8. Caner B, Kitapci M, Aras T, Erbengi G, Ugur O, Bekdik C. Increased accumulation of 2-methoxyisobutyl-isonitrile technetium in osteosarcoma and its metastatic lymph nodes. *J Nucl Med* 1991;32:1977–1978.
9. Abdel-Dayem HM, Scott AM, Macapinlac HA, Larson SM. Role of ^{201}Tl-chloride and ^{99m}Tc-sestamibi in tumor imaging. In: *Nuclear medicine annual*. New York: Raven Press; 1994:181–234.
10. Paul R, Ahonen A, Roeda D, Nordman E. Imaging of hepatoma with FDG. *Lancet* 1985;1:50–51.
11. Di Chiro G, DeLaPaz RL, Brooks RA, et al. Glucose utilization of cerebral gliomas measured by FDG and PET. *Neurology* 1982;32:1323–1329.
12. Nolop KB, Rhodes CG, Brudin LH, et al. Glucose utilization in vivo by human pulmonary neoplasms. *Cancer* 1987;60:2682–2689.
13. Chiu ML, Kronauge JF, Piwnica Worms D. Effect of mitochondrial and plasma membrane potentials on accumulation of hexakis (2 methoxyisobutyl isonitrile) technetium in cultured mouse fibroblasts. *J Nucl Med* 1990;31:1646–1653.
14. Weber G. Enzymology of cancer cells. *N Engl J Med* 1977;296:486–493, 541–551.
15. Mueckler M, Caruso C, Baldwin SA, et al. Sequence and structure of human glucose transporter. *Science* 1985;229:941–945.
16. Birnbaum MJ, Haspel HC, Rosen OM. Cloning and characterization of a cDNA encoding the rat brain glucose-transporter protein. *Proc Natl Acad Sci* 1986;83:5784–5788.
17. Pessin JE, Bell GI. Mammalian facilitative glucose transporter family: structure and molecular regulation. *Ann Rev Physiol* 1992;54:911–930.
18. Guerin C, Laterra J, Hruban RH, Brem H, Drewes LR, Goldstein GW. The glucose transporter and blood brain barrier of human brain tumors. *Ann Neurol* 1990;28:758–765.
19. Fulham MJ, Melisi JW, Nishimiya J, Dwyer AJ, Di Chiro G. Neuroimaging of juvenile pilocytic astrocytoma: an enigma. *Radiology* 1993;189:221–225.