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Hepatic and splenic uptake of Tc-99m HDP in multiple myeloma: Additional findings on Tc-99m MIBI and Tc-99m sulfur colloid images

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The authors present a case of multiple myeloma with intense hepatic and splenic uptake on Tc-99m HDP bone scan and discuss its clinical implications and possible uptake mechanisms. Tc-99m MIBI and Tc-99m sulfur colloid were used to demonstrate bone marrow involvement and focal lesions of multiple myeloma.

Key words: multiple myeloma, spleen, liver, bone scan, Tc-99m MIBI

INTRODUCTION

SEVERAL RADIONUCLIDE IMAGING PROCEDURES have been used in patients with multiple myeloma.[1–3] Radionuclide bone scan is of limited value in uncomplicated multiple myeloma and thus not frequently performed because of its low sensitivity compared with conventional radiography[4–7] but metastatic bone disease may sometimes mimic multiple myeloma both clinically and biochemically, resulting in a substantial number of multiple myeloma patients undergoing bone scan. Various scintigraphic features are described. It may be completely normal in some cases but massive skeletal uptake (a superscan) may sometimes dominate the scintigraphic appearance on bone scan.[4,8,9] Soft tissue uptake of a bone-seeking agent was previously reported, particularly in the presence of secondary amyloidosis with organ involvement.[10,11] We report a patient with multiple myeloma with marked accumulation of a bone-seeking agent in the liver and spleen and poor skeletal uptake on bone scan and additional findings on technetium-99m methoxy isobutyl isonitrile (Tc-99m MIBI) and technetium-99m sulfur colloid scans.

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CASE REPORT

A 52-year-old man presented with a 4-month history of back and chest pain and fatigue. He had lost 10 kg in weight in 2 months. He was admitted to the Neurosurgery Department because of suspected discal hernia. Physical examination revealed sensorial deficit below the Th-4 level.

Hemoglobin was 8.89 g/*l* with a normal mean cell volume and mean cell hemoglobin. Erythrocyte sedimentation rate was up to 115 mm/h. Blood calcium and alkaline phosphatase levels were high (12.9 mg/d*l* and 125 U/*l*, respectively). Renal function was poor; serum urea and creatinine were high (99 mg/d*l* and 3.5 mg/d*l*, respectively).

The patient underwent detailed diagnostic imaging procedures including computerized tomography (CT), magnetic resonance imaging (MRI) and bone scintigraphy. A hypodense soft tissue mass was detected anterior to thoracic 3rd and 4th vertebrae on a CT scan (not included). Also lytic lesions were detected in thoracic vertebrae and ribs. MR imaging of the thorax revealed compression in the 4th thoracic vertebra with an accompanying anterior mass of 2×3 cm in size suggesting metastatic bone disease or plasmacytoma (Fig. 1). Then a radionuclide bone scan was performed to assess the whole skeleton. Tc-99m HDP (740 MBq) was administered intravenously, and whole body imaging was performed after an interval of 4 hours. Images showed poor visualization of the skeleton with relatively increased soft tissue

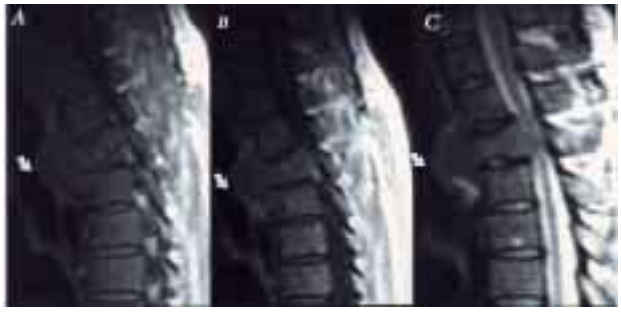

Fig. 1 Magnetic resonance image. Sagittal pre-contrast (a) and post-contrast (b) T1-weighted and T2-weighted (c) images. There is marked compression in the fourth thoracic vertebra with an accompanying anterior soft tumoral tissue component of about 2 × 3 cm (*white arrow*).

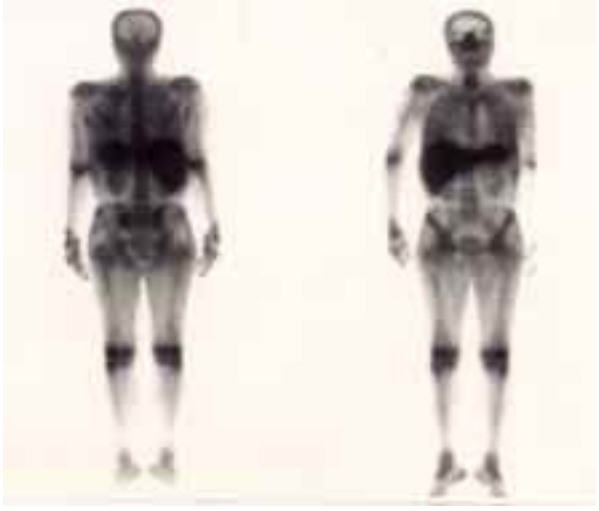

Fig. 2 Tc-99m HDP whole-body images in anterior and posterior projections. Bone scan images showed poor visualization of skeleton with relatively increased soft tissue uptake and markedly increased uptake in the liver and spleen. Multiple focally increased uptake in the ribs, and generalized diffusely increased uptake in the joints of both arms, hands and legs, and a photopenic defect in left sacro-iliac joint were also noted.

uptake and noticeably increased uptake in the liver and spleen. Multiple focally increased uptake with in the ribs, and generalized diffusely increased uptake in the joints of both arms, hands and legs, and a photopenic defect in the left sacro-iliac joint were also noted (Fig. 2). Differential diagnosis included malignancy of hematologic origin with possible bone marrow involvement.

Our radiopharmaceutical quality control records showed that the aluminum concentration was well below 10 ppm and no radiocolloid formation was noted. Labeling efficiency was 99%. The other four bone scan patients who underwent bone scanning on the same day had normal *in vivo* distribution of the agent. These findings therefore exclude the possibility of artifactual uptake of bone-seeking agent in the liver and spleen.

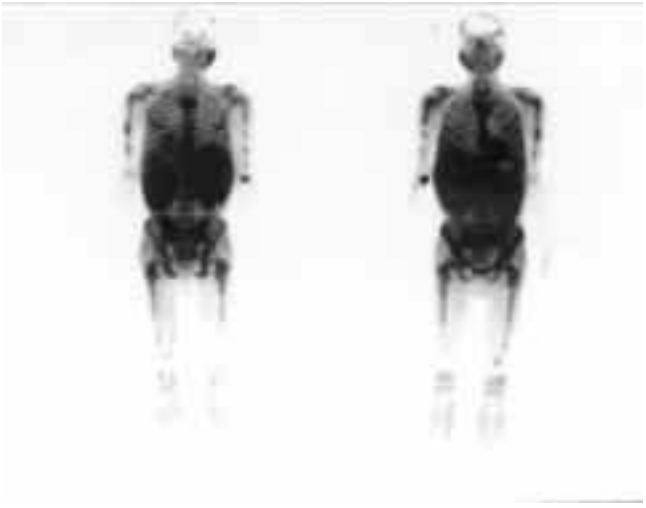

Fig. 3 Tc-99m MIBI whole body images. Markedly increased irregular uptake in the bone marrow was detected in the cranium, arms and legs in addition to diffusely increased uptake in the all other parts of skeleton with possible bone marrow expansion.

Considering previously published reports emphasizing the use of Tc-99m MIBI in the diagnostic work-up of bone marrow involvement of hematological malignancies,[12,13] we performed tumor imaging 10 minutes after the intravenous injection of 740 MBq Tc-99m MIBI. Noticeably increased irregular uptake in the bone marrow was detected in the cranium, arms and legs in addition to diffusely increased uptake in the all other parts of the skeleton with possible bone marrow expansion (Fig. 3). Focal uptake was also observed in the left iliac wing just above to the sacro-iliac joint. A focally increased uptake was detected in the Th-4 vertebra in the posterior image and SPECT slices (Fig. 4).

A bone marrow scan was carried out 60 minutes after the intravenous injection of 740 MBq sulfur colloid (Fig. 5). This showed extensive uptake in the liver and spleen. Irregular uptake with hot and cold spots in the extremities suggesting the expansion of bone marrow was detected.

Further biochemical analysis showed positivity for Bence Jones' protein in urine, and serum IgA was noticeably increased to 44.9 g/*l* (normal range 0.7–3.75 g/*l*). Bone marrow aspiration biopsy led to a final diagnosis of multiple myeloma (Fig. 6).

DISCUSSION

The sensitivity of bone scan is poor in establishing the skeletal involvement of multiple myeloma.[4–7] Various bone-scanning agents have been used for the detection of multiple myeloma, including strontium-85, strontium-87 and the Tc-99m phosphate compounds,[15–17,4–7] which accumulate in the skeleton by chemical adsorption onto hydroxyapatite crystals of bone formation. Bone involve-

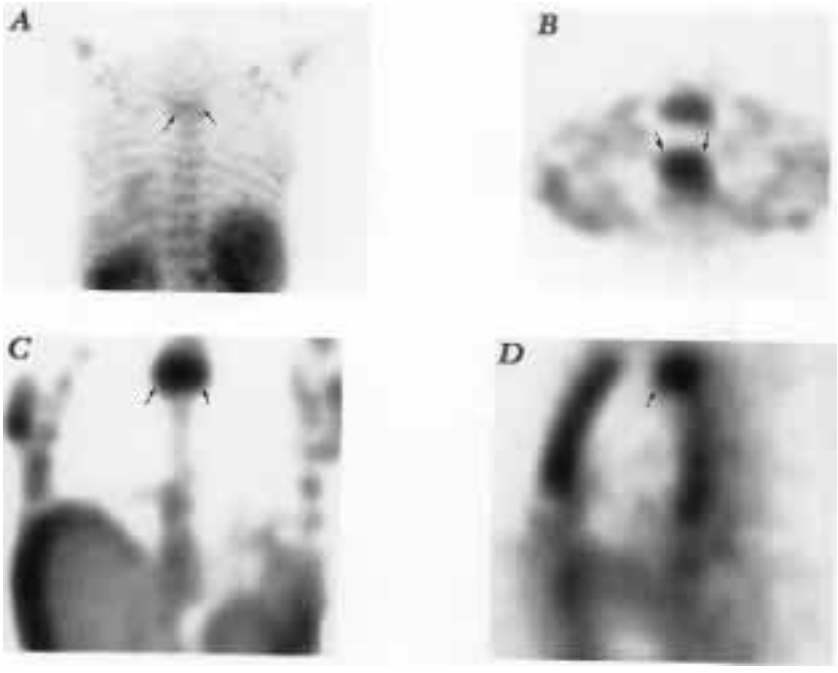

Fig. 4 Tc-99m MIBI SPECT and spot images of thorax. A focally increased uptake was detected in the Th-4 vertebra in posterior spot image (A), transverse (B), coronal (C) and sagittal (D) SPECT slices.

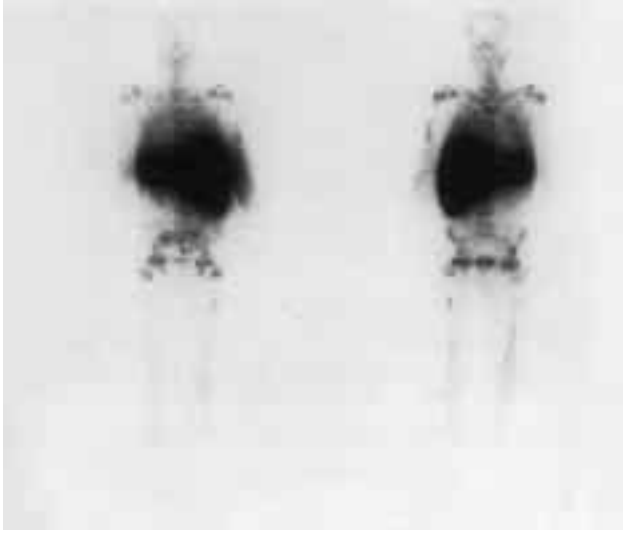

Fig. 5 Bone marrow scan showed extensive uptake in the liver and spleen. Irregular uptake with hot and cold spots in the extremities suggesting the expansion of bone was detected.

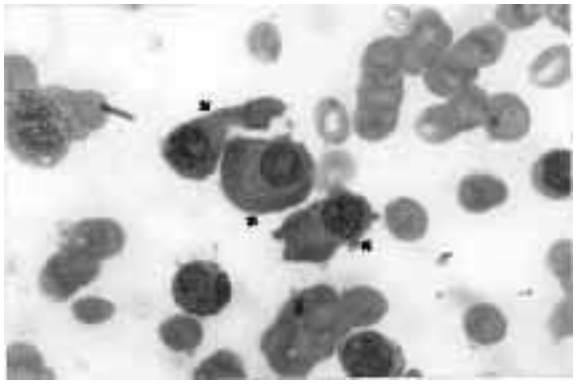

Fig. 6 Bone marrow aspiration biopsy. Photomicrograph showing 3 atypical plasmocytes with bigger-than-normal size (×1000 Giemsa-May Gruenwald) (*arrows*).

ment is likely to be underestimated and the bone scan may be completely normal.[4–6] Radiographic skeletal survey is therefore the investigation of choice, usually combined with biochemical investigations and bone marrow biopsy to confirm the final diagnosis and extent of the disease. Nevertheless, bone scan is often performed because clinical, biochemical and plain X-ray appearances can mimic widespread metastatic bone disease.

Radionuclide bone scan can provide additional diagnostic information in multiple myeloma, and in some cases it could identify a biopsy-proven myeloma deposit invisible on X-rays.[8] Another scintigraphic pattern is the "superscan," commonly associated with extensive metastatic or metabolic bone disease. The superscan shows prominent skeletal uptake of radionuclide with little or no tracer reaching the renal tract, leading to absent renal and delayed bladder visualization.[9]

Amyloidosis is clinically evident in less than 5% of multiple myeloma patients, but, in post-mortem studies, it

is found in over 10% of cases as a result of light chain deposition within solid organs, blood vessels and connective tissues.[18] The liver, spleen, heart, gastrointestinal tract, tongue and peripheral nerves are commonly involved in amyloidosis. Tc-99m labeled diphosphonate has been used to demonstrate solid organ and soft-tissue involvement of amyloid protein in multiple myeloma patients.[10,11]

In one case with associated refractory hypercalcemia reported in the literature,[11] there was abnormal accumulation of Tc-99m MDP in the lungs and stomach; at postmortem examination, micro-calcification was found only in the stomach; whereas amyloid was present in both organs. It was therefore concluded that the radionuclide uptake was due to the presence of amyloid protein rather than microcalcification.[11]

In another case, the bone scan showed extensive uptake of isotope in muscles with virtually no uptake in bone.[14] The authors concluded that extensive marrow deposition of myeloma cells could prevent any significant skeletal uptake of Tc-99m MDP and led to the preferential accumulation in soft tissue.

Uremic myopathy and hypercalcemia are known to cause soft tissue uptake on bone scan,[19,20,7] Renal function was poor in our patient, but the serum calcium level was only slightly above normal limits (result 12.9 mg/d*l*; normal range 8.4 to 10.2 mg/d*l*). In the cases reported so far, soft tissue calcification occurred when the calcium phosphate ion product exceeded 70 mg/d*l*.[19]

In our case, the patient had advanced disease and died in a short time after diagnosis so that more detailed and definitive tissue tests for a more clear-cut histochemical diagnosis were not performed due to ethical concerns. But we observed that the bone marrow and the rest of the reticuloendothelial system (RES) including the liver and spleen were notably visualized on Tc-99m MIBI images, possibly suggesting malignant involvement of these tissues[14] considering the affinity between Tc-99m MIBI and malignant cells.

Tc-99m MIBI imaging clearly depicted the bone marrow distribution throughout the whole skeleton of the patient reported here. The bone marrow uptake patterns were similar on Tc-99m MIBI and Tc-99m sulfur colloid images. The hypoactive defect originally seen on bone scan in the left iliac wing also accumulated Tc-99m MIBI ("filled in"), suggesting its possible use as a complementary tool when further evaluation is clinically indicated for any bones showing hypoactive or photopenic appearances in suspicious cases, including multiple myeloma which has a strong possibility of photopenic lesions on bone scan.

We suggest that bone marrow involvement of multiple myeloma could be studied by Tc-99m MIBI or Tc-99m sulfur colloid imaging, and solid organ uptake of bone seeking agents can be observed even in the absence of a significantly increased level of serum calcium. Tc-99m MIBI may demonstrate focal areas of multiple myeloma.

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