

Hepatic metastasis arising from diverse primary pathologies diagnosed on ^{99m}Tc-Methylene diphosphonate bone scan

M. L. Narayan, N. Ravishwar, A. Y. Lakshmi¹, N. Rukmangadha², T. C. Kalawat, R. G. Manthri

Departments of Nuclear Medicine, ¹Radiology and ²Pathology, Sri Venkateswara Institute of Medical Sciences, Tirupati, Andhra Pradesh, India

ABSTRACT

We are presenting two cases that illustrate nonosseous localization of ^{99m}Tc-Methylene diphosphonate (MDP) in hepatic metastases arising from varied primary pathology and review of the literature. This series emphasizes the evidence of MDP localization in hepatic metastases arising from adenocarcinoma of rectum and infiltrating duct cell carcinoma of the breast.

Keywords: ^{99m}Tc-Methylene diphosphonate extra osseous uptake, adenocarcinoma rectum, hepatic metastasis, infiltrating duct cell carcinoma breast

INTRODUCTION

^{99m}Tc-Methylene diphosphonate (MDP) bone scintigraphy is one of the most common investigations routinely performed for screening of suspected bone metastases. Increased MDP uptake in the extraosseous tissues has been reported in various benign and neoplastic diseases.^[1-4] Precise localization of anatomical site with single photon emission computed tomography/computed tomography (SPECT/CT) and identification of disease pathology enhances the diagnostic utility of MDP bone scan.^[2,4]

Incidental detection of hepatic metastases from adenocarcinoma of rectum and infiltrating duct cell carcinoma breast on MDP bone scan is described in present cases.

CASE REPORTS

Case 1

A 57-year-old male who presented with a history of locally advanced, well-differentiated adenocarcinoma of the rectum,

post 4 cycles of chemotherapy (CT) and external beam radiotherapy for pelvis. He was referred for bone scan for metastatic work up. ^{99m}Tc-MDP whole body imaging was performed 3 Hrs postinjection. Planar whole body images showed evidence of multiple osteoblastic skeletal metastases involving L-4 lumbar vertebra, bilateral pelvic bones and right proximal femur. In addition to skeletal metastasis, MDP avid multiple rounded, extraosseous lesions of varying size were seen in right upper quadrant of the abdomen, suggestive of intrahepatic pathology [Figure 1a and b]. On correlative SPECT/CT images these MDP avid foci were corresponding to sites of multiple heterogeneous density lesions seen extensively involving bilateral hepatic lobes, suggestive of metastases. The largest lesion measured 2.5 × 2.5 cms in size. MDP uptake seen in these intrahepatic lesions was congruent with sites of coarse calcification seen at periphery of these metastatic lesions, on CT [Figure 1c].

Case 2

The 41-year-old lady who was diagnosed as the case of infiltrating duct cell carcinoma of right breast and subsequently underwent modified radical mastectomy, CT and local radiotherapy in 2005. She presented with recurrence in the right axilla after 7 years and referred to Nuclear Medicine Department for a bone scan to evaluate skeletal metastases. Planar whole body and SPECT images showed evidence of mild reactive changes involving right lateral border of the sternum. In addition to this, a small rounded focus of MDP uptake was noted in right upper quadrant of the abdomen, suggestive of extraosseous soft tissue uptake. Ultrasound (USG) evaluation revealed a congruent

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DOI:
10.4103/0972-3919.152981

Address for correspondence:

Dr. Manishi L. Narayan, Department of Nuclear Medicine, Sri Venkateswara Institute of Medical Sciences, Tirupati - 517 507, Andhra Pradesh, India. E-mail: manishi.Ln@gmail.com

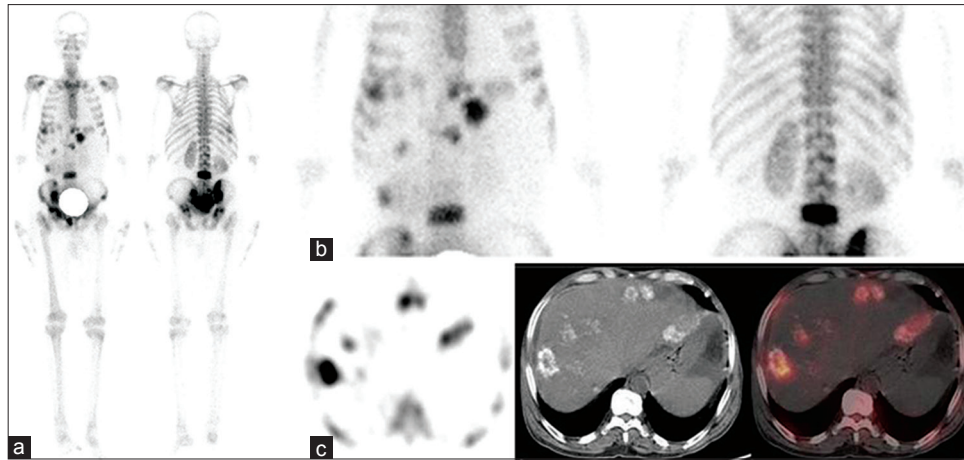


Figure 1: (a) Anterior and posterior whole body views of the ^{99m}Tc -Methylene diphosphonate (MDP) whole body planar images, showing multiple rounded foci of extraosseous uptake in right upper quadrant of abdomen, in addition to multiple osteoblastic skeletal metastases, involving L-4 lumbar vertebra, bilateral pelvic bones and right proximal femur (b) Planar and (c) single photon emission computed tomography/computed tomography (CT) images, showing multiple rounded foci of MDP uptake corresponding to sites of multiple heterogeneous density, metastatic lesions seen extensively involving bilateral hepatic lobes. MDP uptake seen in these intrahepatic metastases is congruent with sites of coarse calcification seen at the periphery of these lesions on CT images

focal lesion with heterogeneous echotexture and calcification involving segment IV of liver, suggestive of metastases. Patient underwent USG guided hepatic biopsy, and histopathological evaluation [Figure 2d] confirmed the carcinomatous deposits. Immunohistochemistry showed estrogen-receptor and progesterone-receptor positivity, but it was negative for Her-2/neu expression.

Subsequently patient received 6 cycles of palliative CT. Follow-up bone scan done after 1-year show mild MDP uptake in hepatic metastases [Figure 2a]. Correlative CT images revealed an irregular heterogeneous density mass lesion with coarse calcifications, measuring 2.5×2.0 cm in size involving segment IV of the liver [Figure 2c].

DISCUSSION

^{99m}Tc -MDP and its analogs bind to bone, by adsorption to the surface of hydroxyapatite crystal. Areas of new bone formation exhibit elevated uptake because of increased flow with expanded surface.^[4,5]

The proposed mechanism of soft tissue uptake of MDP include (a) local tissue necrosis or damage leading to increased calcium deposition in the tissue, (b) hyperemia, (c) altered capillary permeability, (d) adsorption onto tissue calcium, (e) presence of iron deposits, and (f) binding to enzyme receptors or denatured proteins.^[6-9]

Calcium localizes to variety of soft tissue through a number of common pathways.^[5] These pathways also result in uptake of ^{99m}Tc -MDP, through chemisorptions of radiopharmaceutical onto surface of calcium salts. The causes of soft tissue uptake of bone seeking radiopharmaceuticals have been divided into five broad categories (1) metastatic calcification of hypercalcemia, (2) dystrophic calcification, caused by

trauma, ischemia or cellular necrosis, (3) metabolic uptake, related to affinity of pharmaceutical to certain metabolites produced by tumors and calcification in some of the benign conditions, (4) compartmental sequestration or (5) artefactual, that is related to faulty preparation, misadministration and altered tissue handling of radiopharmaceutical.^[3,10]

Methylene diphosphonate uptake in hepatic metastases has been described in the past.^[2,3,7,11] Liver is the most frequent site of metastasis as it is highly vascular organ, has dual blood supply and high blood flow.^[9] MDP concentration in metastatic lesions is favored by variation in blood flow, necrosis and dystrophic calcification.^[1,7]

The degree and pattern of hepatic uptake may differentiate between likely etiologies. Mild hepatic and splenic uptake is usually seen with radiopharmaceutical faults, whereas, in hepatic necrosis, the uptake is usually intense and diffuse. Diffuse and intense hepatic uptake of bone imaging agent can also be due to a variety of causes including, diffuse hepatic necrosis, repeated iron injections, administration of contrast media after bone scan agent injection, idiopathic hepatic uptake, acute hypoxic hepatitis or hypoxia secondary to respiratory failure, amyloidosis associated with plasma cell dyscrasia and also in late stage of multiple myeloma.^[10,12]

In hepatic metastases, pattern of MDP uptake is usually focal and scattered than diffuse.

Distinct pathological characteristics of certain tumours also contribute to MDP uptake e.g., Osteogenic sarcoma producing osteoid matrix that binds to ^{99m}Tc -MDP, mucin producing tumors possess a glycoprotein that is biochemically similar to ossifying cartilage and binds calcium (Ca^{2+}) salts.^[3] Classically mucinous adenocarcinoma tumors of lung, breast and gastrointestinal tract are associated with elevated ^{99m}Tc -MDP uptake.

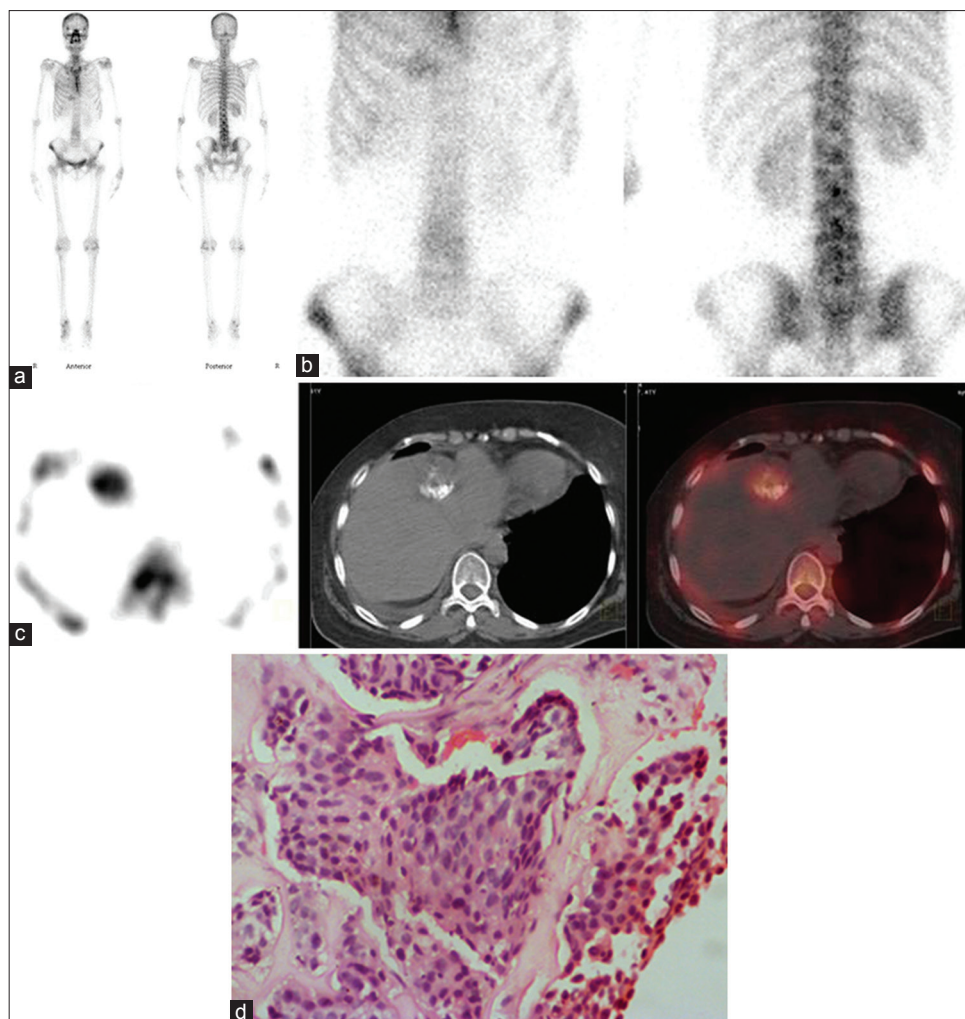


Figure 2: (a) ^{99m}Tc - Methylene diphosphonate (MDP) whole body scan images after palliative chemotherapy, showing mild reactive changes involving sternum and an extra osseous small rounded focus of MDP uptake in right upper quadrant of abdomen (b) ^{99m}Tc - MDP Bone scan Planar and (c) single photon emission computerized tomography/computed tomography (SPECT/CT) images showing extra osseous focus of MDP uptake localizing to site of an ill-defined (2.5×2.0 cm) size, heterogeneous density lesion involving segment IV of liver with evidence of coarse calcifications seen within this lesion, suggestive of metastases. (d) Histopathologic image of liver biopsy (H and E $\times 20$): Showing tumour deposits in background of fibrous stroma. Cells arranged in the form of solid nests with intervening stroma showing congested blood vessels. Tumor cells are round to oval with pleomorphic vesicular nuclei and moderate amount of eosinophilic cytoplasm arranged in solid nests

SUMMARY

These cases show evidence of MDP uptake in hepatic metastases arising from adenocarcinoma of the colon in the first case and infiltrating duct cell carcinoma of the breast in the second case. Although the main purpose of bone scan is to detect the skeletal abnormalities. When extraosseous abnormalities are noted on bone scan, precise identification of extraosseous site, pattern, degree of tracer uptake as well as likely pathology, not only increases the specificity of Bone scintigraphy but also adds to its diagnostic value.

ACKNOWLEDGMENTS

The authors would like to express their appreciation to Mr. P. Ravi and Mr. B. Chandrashekhar of Department of Nuclear Medicine, SVIMS, Tirupati, for their technical support.

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How to cite this article: Narayan ML, Ravishwar N, Lakshmi AY, Rukmangadha N, Kalawat TC, Manthri RG. Hepatic metastasis arising from diverse primary pathologies diagnosed on ^{99m}Tc-Methylene diphosphonate bone scan. *Indian J Nucl Med* 2015;30:154-7.

Source of Support: Nil. **Conflict of Interest:** None declared.