Comparison Between Whole body Bone Scintigraphy and Regional CT Scan in the Diagnosis to Bone Metastasis of Cancer Patients

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Abstract

The detection of skeletal metastases is an essential step in the staging and treatment planning of the primary tumor. Tc-99m MDP bone scan is widely available and an important imaging technique for detection of bone metastases. For most types of cancer, CT scan is the modality of choice for cancer staging & serial follow up. The aim of this study was to investigate the diagnostic potential of CT scan in bone metastases detection by comparing with bone scan in a variety of cancer patients. Twenty eight patients with multiple bone metastases detected on Tc-99m MDP bone scan were enrolled for current study. Images were interpreted by two experienced nuclear medicine physicians having sound knowledge of CT diagnosis. In 10 of 28 patients (35.7%), multiple metastases were detected by both bone scan and CT scan. Eight of 28 patients (28.6%), fewer metastases could be detected on CT scan compared to bone scan. Six cases (21.4%) showed false negative in CT possibly due to earlier stage. To evaluate post chemotherapy patients, in 4 of 28 cases (14.3%) bone scan shows better results in two cases because of rapid metabolic response than anatomical change. In conclusion, however the delectability of metastases is less in CT than bone scintigraphy but due to its collaborative imaging as well as additional information about soft tissue structures CT is useful in this situation.

Keywords: Bone metastases, bone scan, CT detection ability, bony window

1. Introduction

The skeleton is one of the most common sites of distant metastases in many cancers. Bone scan or scintigraphy (BS) using Tc-99m methylenediphosphonate (MDP) or hydroxymethylene diphosphonate (HMDP) is considered the most sensitive method of detecting skeletal metastases. It has been used routinely in higher-risk cancer patients, especially in breast, prostate and lung cancers, which are known for their high incidence rate of bone metastases [1-2].

Skeletal metastases are associated with a high morbidity which may be reduced by early detection and treatment. The detection of skeletal metastases is also an essential step in the staging and treatment planning of the primary tumor.

For most types of cancer, Computed Tomography (CT) is the modality of choice for staging in the chest and abdomen and for serial follow up imaging. CT scan for these purposes encompasses a large part of the axial skeleton and can thus detect not just soft-tissue lesions, but osteoplastic or osteolytic bone metastases as well. The study was designed to evaluate the diagnostic ability of CT scan (in usual clinical conditions) in the detection of bone metastases in a variety of cancer patients compared to bone scan.

2. Materials and Methods

The study population comprised of 28 patients (Age: 25-85 years, Mean: 52.2 years, Male: 18, Female: 10) of different cancers with multiple bone metastases. We enrolled these 28 patients in our study from 225 consecutive patients with various cancers who underwent whole body bone scan in our institution during a period of Jan 2014 through April 2015. A standard whole body BS (from toes to top of the head) was performed using Dual-head gamma-camera (Siemens E-cam signature series) 3-4 hours after IV injection of 15 mCi of Tc-99m MDP.

CT scan was performed in our institution within 02 months of BS using Siemens Somatom Emotion before and after using IV contrast material.

Regional contrast enhanced CT (CECT) scan of chest/abdomen or both were done according to clinicians referral. We extended the field of view (FOV) in all patients for only plain CT from lower neck to mid thigh to detailed study of bone in bony window. Ten of them underwent CT guided-FNAC for further confirmation. Written consent was taken for each patient.

3. Image Analysis

For all patients, Tc-99m MDP BS images only were independently reviewed by two experienced NM physicians who had no knowledge of any clinical information, including the primary cancer. BS images were assessed for the presence of bone metastases by using a five point grading as follows; 0: definitely negative, 1: probably negative, 2: equivocal, 3: probably positive, and 4: definitely positive for bone metastases.

CT scan images were reviewed by two NM physicians having experience with diagnostic CT scan who had the clinical information including the primary cancer. The physicians knew that the lesions had been given grades of 4 at BS. They used a workstation to display CT scans with bone and soft tissue windows. For diagnostic certainty at CT the same five-point grading system (0-4) was used as BS. CT images were evaluated by using CT planes that corresponded to the planes in which the lesion appeared at BS. In true positive lesions that were clearly localized to the bone, CT findings were recorded (location, morphologic changes).

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Table 1. Distribution of location of metastasis at BS (n=28) and number of metastasis interpreted as true-positive at CT (n=22)

Location	No. of Lesions in BS	No. of Lesions in CT	χ^2 test Significance
Vertebrae	40	27	P = 0.290 ^{NS}
Pelvic Bones	28	16	P = 0.885 ^{NS}
Ribs	23	09	P = 0.336 ^{NS}
Sternum	10	05	P = 0.857 ^{NS}
Proximal Upper Limbs	04	01	P = 0.463 ^{NS}
Proximal Lower Limbs	06	03	P = 0.891 ^{NS}
Total Lesions	111	61	

** NS = Not Significant (P > 0.05)*

Table 2. Distribution of primary cancers of metastasis (BS, n=28) and number of metastasis interpreted as true- positive at CT (n=22)

Primary Cancers	No. of Lesions in BS	No. of Lesions in CT	χ^2 test Significance
Ca Prostate	25	15	P = 0.759 ^{NS}
Ca Lung	22	13	P = 0.816 ^{NS}
Ca Breast	21	14	P = 0.530 ^{NS}
Ca Rectum	12	06	P = 0.842 ^{NS}
Ca Esophagus	10	05	P = 0.857 ^{NS}
RCC	09	06	P = 0.701 ^{NS}
Cholangio-carcinoma	06	00	P = 0.065 ^{NS}
Ca Scalp	03	02	P = 0.830 ^{NS}
Ca Glans Penis	03	00	P = 0.195 ^{NS}
Total Lesions	111	61	

** NS = Not Significant (P > 0.05)*

4. Results

Ten of 28 patients (35.7%), multiple metastases were detected by both bone scan and CT scan. Eight of 28 patients (28.6%), fewer metastases could be detected on CT scan compared to bone scan. Six cases (21.4%) showed false negative in CT. To see the treatment effect evaluation in post chemotherapy patients, 4 of 28 cases (14.3%), bone scan showed better results.

Twenty eight adults were found to have 111 lesions that were classified with consensus of the two readers as being definite bone metastases at whole body bone scan (grade 4). Among the 111 lesions, corresponding morphologic findings of metastases were identified at CT for 61 lesions (54.95%) in 22 patients; considered true-positive lesions for bone metastases (were given a CT visual grade of 4). Fifty of 111 lesions (45.05%) that did not show definite morphological changes at CT were considered false-negative for bone metastases.

Ten lesions in 10 patients had histological confirmation of bone metastases. Ten more patients showed progressive disease at follow up bone scan. Four out of 28 patients reviewed after chemotherapy. Liver metastases were also detected in 4 patients of breast (2) and lung (2) cancers.

Table 1 depicts metastatic lesions according to location with true-positive CT lesions; there were no significant difference of CT detection among the locations (p>0.05).

In addition, according to the classification of primary cancers, there were no significant difference of CT detection of bone lesions on cancer type (p>0.05)-shown in table 2.

There were 4 cases, either solitary or a few lesions located outside the FOV of CT scan in upper cervical vertebrae, skull and knee and were not included in current study.

4.1 False Negative Lesions

Thirty one of 50 lesions (62%) did not show any morphological change in CT scan. Rest 19 lesions (38%) showed non-specific findings on CT scan (degenerative, neoplastic, density change, others). Six patients with false negative CT scan included, Ca prostate (3), Ca breast (1), Ca glans penis (1) & cholangiocarcinoma (1).

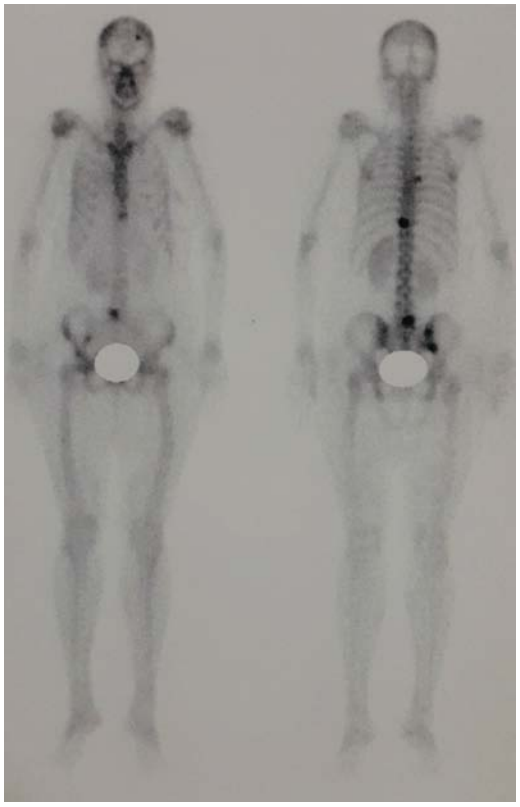

Fig. 1 Tc-99m MDP BS showing multiple metastases in breast cancer patient at transverse process (TP) of T6 on right side, T10 body on left, L5 body on right, right iliac bone near SI joint

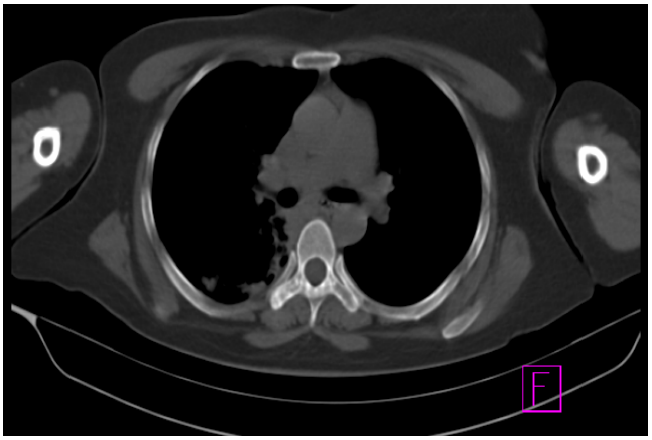

Fig. 2 CT bone window shows mild sclerotic change in corresponding TP (NS)

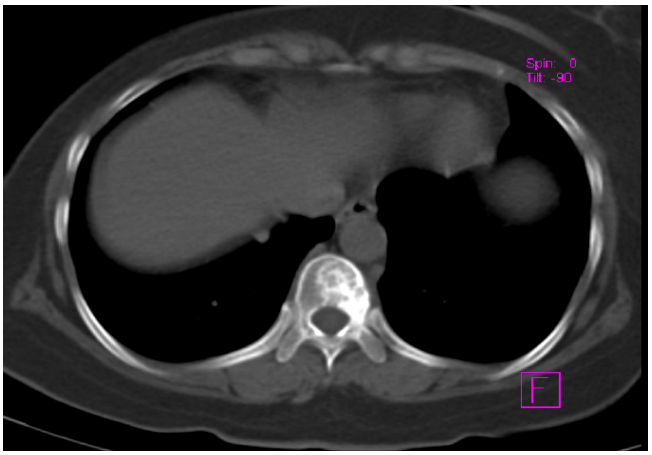

Fig. 3 CT scan bone window shows predominantly sclerotic lesion in T10 on left side

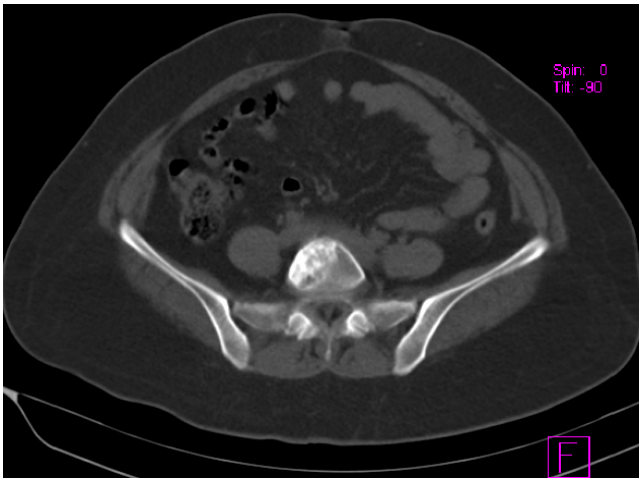

Fig. 4 CT scan bone window shows predominantly sclerotic lesion in L5 on right side

5. Discussion

Bone involvement in metastases occurs by means of 3 main mechanisms: (1) direct extension, (2) retrograde venous flow, and (3) seedling with tumor emboli via the blood circulation. Seedling occurs initially in the red marrow; this process accounts for the predominant distribution of metastatic lesions in the red marrow-containing areas in adults. As a metastatic lesion grows in the medullary cavity, the surrounding bone is remodeled by means of either osteolclastic or osteoblastic processes. The relative degree of resultant bone resorption or deposition is highly variable and depends on the type and location of the tumor. The relationship between the osteoclastic and osteoblastic remodeling processes determines whether a predominant

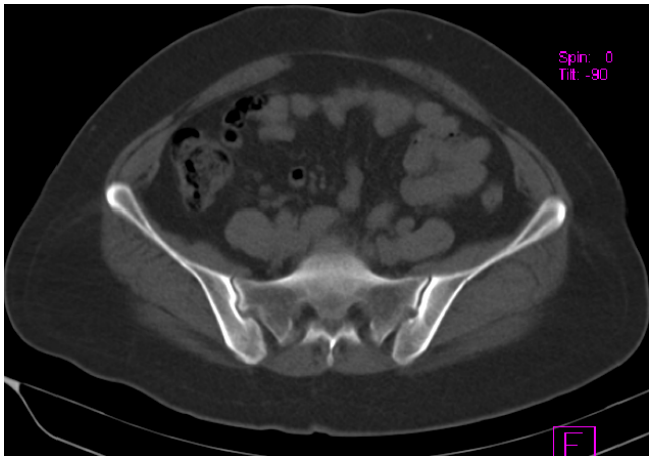

Fig. 5 No change/minor non-specific change in right iliac bone (↑ CT density)

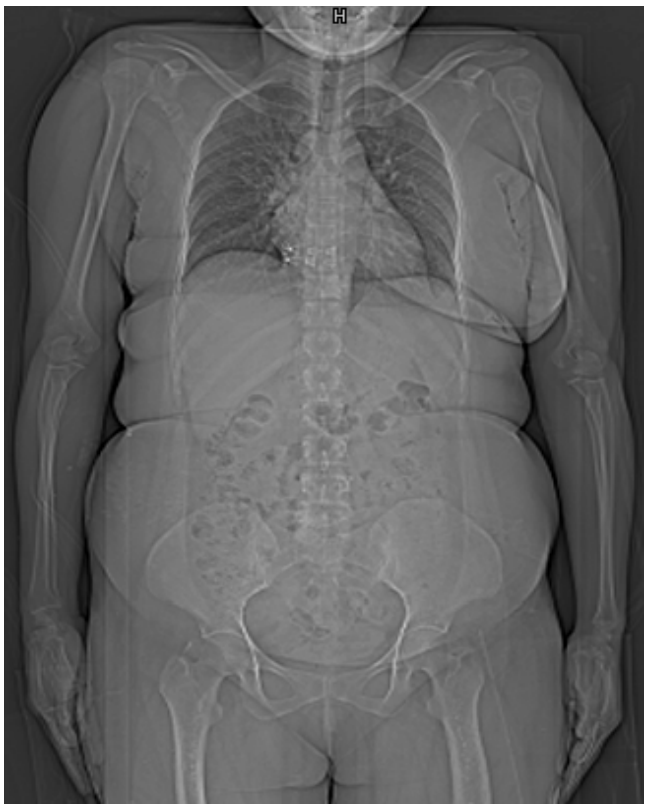

Fig. 6 Topogram of CT scan (FOV) for bony window

lytic, sclerotic, or mixed pattern is seen on radiographs [3-4].

In our study, among the lesions that were graded as definite metastases at Tc-99m MDP bone scan (grade 4) and that were finally diagnosed as metastases with all available data, 54.95% were characterized as definite metastases at CT (lytic, sclerotic and mixed pattern).

We did not get any definite morphological changes to suspect metastases at CT in remaining 45.05% (50) lesions. Though, we have experienced some non-specific changes (increased density, degenerative change etc) in 19 lesions (17.1%) are not necessarily related to the diagnosis of suspected bone metastases with confidence.

CT is highly sensitive for osteolytic and osteoplastic bone lesions involving cortical bone, but less so for tumors restricted to the marrow space. However, tumor within the marrow causes an increase in attenuation due to fat replacement. An attenuation difference of more than 20 HU compared to corresponding area on other side is abnormal [5] as in our case (Fig. 5, 145 HU compared to 120 HU). Such findings are subtle and easily overlooked by the radiologist.

In the comparative study Yang et al.[6] found that CT has a sensitivity of 73% and specificity (per patient) of 95% for the detection of bone metastases. In our current study, lesion based sensitivity & patient based sensitivity were 54.95% & 78.57% respectively with a specificity of 100%.

Yuji Nakamoto et al. [7] showed no statistical significant difference of CT detection among the locations of bone metastases ($p= .665$), as in our study ($p>0.05$). We did not find any significant difference of CT detection of bone metastases according to the classification of primary cancers type ($p>0.05$). However, Yuji Nakamoto et al. in their study found that metastatic lesions from lymphoma and digestive cancers (pancreatic and rectal cancer) were consistently diagnosed as negative for metastases at CT more often than were metastases from other tumor types ($p<0.01$).

Technetium-99m (Tc-99m) scintigraphy is an established imaging modality as a first choice for detecting bone metastases, but also known for its drawback in detecting pure osteolytic bone metastases [1, 8-9]. The diagnostic ability of plain films of skull, spine and pelvis is limited by superposition effect with the sensitivity of only in the range of 44-50% [10-12]. Computed tomography (CT) is routinely and widely used for cancer detection & staging and also to evaluate the treatment response in post therapy patient. In addition to see the organ lesions including primary cancer and metastases, detail bony anatomy can be well studied in bony window. CT is also useful in guiding needle biopsy, particularly in vertebral lesions. False negative lesions in CT scan may be due to earlier stage disease/ disease confined to marrow space. However many of these lesions show minute non-specific changes at CT scan.

Four patient received chemotherapy on the basis of bone scintigram & CT findings and for these patients a further bone scan & CT examination were carried out three months later. Post chemotherapy cases showed improvement of image findings at BS in two patients after successful treatment, however CT showed sclerosis. This is possibly due to earlier recovery of metabolic status rather than anatomical/ morphological changes. Two of the four remaining patient showed progressive disease in both scintigraphy and CT.

6. Conclusion

The delectability of metastases is less in CT than bone scintigraphy but due to its collaborative imaging as well as additional information about soft tissue structures CT is useful in this situation.

References

1. W. B. Eubank and D. A. Mankoff, Evolving Role of Positron Emission Tomography in Breast Cancer Imaging, Semin Nucl Med, **35**, 84-99 (2005).
2. S. D. Yeh, M. Imbriaco, S. M. Larson, D. Garza, J. J. Zhang and H. Kalaigian, et al., Detection of Bony Metastases of Androgen Independent Prostate Cancer by PET-FDG. Nucl Med. Biol., **23,** 693-697 (1996).
3. J. M. Salmon and S. E. Kilpatrick, Pathology of Skeletal Metastases, Orthop Clin. North Am., **31(4),** 37-44 (2005).
4. G. A. Clines and T. A. Guise TA, Molecular Mechanisms and Treatment of Bone Metastasis, Expert Rev Mol Med., **10,** e7 (2008).
5. C. A. Helms, C. E. Cann, F. O. Brunelle, L. A. Gilula, N. Chafetz and H. K. Genant, Detection of Bone-Marrow Metastases Using Quantitative Computed Tomography, Radiology, **40,** 745-750 (1981).
6. H. L. Yang, T. Liu, X. M. Wang and et al., Diagnosis of Bone Metastases: A Meta-Analysis Comparing FDG-PET, CT, MRI and Bone Scintigraphy, EUR Radiol., **21**, 2604-2617 (2011).
7. Yuji Nakamoto, Christian Cohade, Mitsuaki Tatsumi, Dima Hammound and L. Richard Wahi, CT Appearance of Bone Metastases Detecyted with FDG PET as Part of The Same PET/CT Examination, Radiology, **237,** 627-634 (2005). .
8. L. Maffioli, L. Florimonte, L. Pagani, I. Buti and I. Roca, Current Role of Bone Scan With Phosphonates In The Follow-Up of Breast Cancer, Eur J Nucl Med Mol Imaging, **31 (supl 1),** S143-148 (2004).
9. M. Abe K. Sasaki, Y. Kuwabara, H. Koga, S. Baba, K. Hayashi and et al., Comparison of 18FDG-PET with 99mTc-HMDP Scintigraphy for The Detection of Bone Metastases in Patients With Breast Cancer, Ann Nucl Med., **19,** 573-579 (2005).

10. E. A. Bellamy, D. Nichilas, M. Ward and et al., Comparison of Computed Tomography and Conventional Radiology in The Assessment of Treatment Response of Lytic Bone Metastases in Patients With Carcinoma of The Breast, Clin Radiol., **38(4),**. 351-355 (1987).
11. H. I. Libshitz and G. N. Hortobagyl, Radiographic Evaluation of Theraputic Response in Bony Metastases of Breast Cancer, Skeletal Radiol., **7(3),** 159-165 (1981).
12. M. V. Merrick, J. S. Beales, N. Garve and R. C. Leonard, Evaluation and skeletal Metastases. Br J Radiol., **65(7),** 803-806 (1992).