Pattern of Skeletal Metastasis in Breast Cancer Patients Attending INMAS, Rajshahi

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ABSTRACT

Breast cancer is the most common malignant tumor of females, the incidence increases with age. Bone is the most common site to which breast cancer metastasizes. Between 30% to 85% of patients with metastatic breast cancer develop bone metastases during the course of the disease. Bone scan is the most commonly used means of detecting bone metastasis; it visualizes increases in osteoblastic activity and skeletal vascularity. Many radio-pharmaceuticals (radionuclides) have been used in bone scan including technetium-99m bound to methylene diphosphonate (MDP). Published sensitivity and specificity rates of bone scan for diagnosis varies, with sensitivity ranging from 62% to 100% and specificity from 78% to 100%. However, bone scan is generally considered sensitive for detecting bone metastases on whole-body images.The aim of this study was to evaluate the pattern of distribution of skeletal metastases in patients with breast carcinoma by using Tc-99m MDP bone scan. A retrospective study was conducted on 245 consecutive female breast carcinoma patients irrespective of clinical staging, menopausal status and pre-operative / post- mastectomy status, referred for bone scan to Institute of Nuclear Medicine and Allied Sciences, Rajshahi from July 2015 to June 2017. The mean age of the patients was 43.4 ± 13.8 years (mean ± SD) with range from 29 to 66 years. Bone scan was performed by an intravenous bolus injection of 20 mCi Tc99m-MDP. Bone phase images were taken at three hours after injection of the radiotracer. Out of 245 studied patients, 163 patients (66.53%) were negative for skeletal metastasis and 82 patients (33.47%) were positive for skeletal metastasis. Out of 82 patients with positive skeletal metastasis, 68 (82.93%) patients had multiple sites (two or more) and 14 (17.07%) patients had solitary site of bony involvement. Out of 68 patients with multiple sites of skeletal metastasis, highest number was noted in thoraco-lumbar spine (80.89%), followed by ribs including sternum and clavicle (57.35%), pelvic bones (47.06%), upper extremities including scapula (41.18%), lower extremities (33.82%), cervical spine (23.53%) and skull bone (8.82%). Among 14 patients with solitary skeletal metastasis, maximum number was noted in thoraco-lumbar spine (64.29%), followed by cervical spine (14.29%), pelvic bone (07.14%), ribs (07.14%) and sternum (07.14%). Skeletal metastases were much more common in multiple sites than solitary lesion in breast cancer patients. Thoraco-lumbar spine was the most common site of involvement in both solitary and multiple lesions in our study. Axial skeleton was more commonly involved than the appendicular skeleton. Bone scan may pick up bone metastases up to 18 months earlier than conventional radiology, with an average lead of four months. 99m Tc-MDP bone scan is very cost effective in comparison to other imaging modalities (CT, MRI, and PET) and play a major role in early detection of skeletal metastasis in breast cancer patients.

Key words: Breast cancer, 99m Tc-MDP bone scan, skeletal metastasis.

INTRODUCTION

Breast cancer is the most common malignant tumor of females, the incidence increases with age (1-3). Bone is the most common site to which breast cancer metastasizes. About 30% to 85% of patients with metastatic breast cancer develop bone metastases during the course of the disease. Bone also represents the first site of metastasis for 26% to 50% of patients with metastatic breast cancer. Complications of bone metastasis include bone pain, pathologic fractures (the incidence of which ranges from 16% to 60%), hypercalcemia, and spinal cord compression, any of which can profoundly impair quality of life (4-10).

Approximately 70% of patients with breast cancer treated with placebo experienced at least one skeletal complication during a two-year follow-up period. Although literature shows that most of the skeletal metastases from breast carcinoma are osteolytic, more sclerotic lesions are observed now a days probably due to increasing use of zoledronic acid and bisphosphonates. Skeletal metastases also herald a poor prognosis with a median survival being 2-3 years (11-14).

Bone scan is the most commonly used means of detecting bone metastasis; it visualizes increased

osteoblastic activity and skeletal vascularity. Many radiopharmaceuticals (radionuclides) have been used in bone scan including technetium-99m bound to MDP. Published sensitivity and specificity rates of bone scan for diagnosis have varied, with sensitivity ranging from 62% to 100% and specificity from 78% to 100%. However, bone scan is generally considered sensitive for detecting bone metastases on whole-body images (15-17).

The aim of this retrospective study was to evaluate the pattern of distribution of skeletal metastases in patients with breast carcinoma by using Tc-99m MDP bone scan.

PATIENTS AND METHODS

A retrospective study was conducted on 245 consecutive female breast carcinoma patients irrespective of clinical staging, menopausal status and pre-operative / post- mastectomy status, referred for bone scan to Institute of Nuclear Medicine and Allied Sciences, Rajshahi from July 2015 to June 2017. The mean age of the patients was 43.4 ± 13.8 years (mean ± SD) with range from 29 to 66 years. Patient's clinical records and bone scan reports were reviewed retrospectively. In our institute we used SPECT digital dual head gamma camera (e-cam series, Siemens from Germany) with a low-energy high resolution parallel hole collimator. Bone scan was performed by an intravenous bolus injection of 20 mCi Tc99m-MDP. Bone phase images were taken at three hours after injection of the radiotracer and the scan time was about 15 minutes for a whole body scan. Whole body scan in anterior and posterior projections were obtained. All scans were interpreted for metastatic deposits by two independent nuclear medicine physicians.

RESULTS

Out of 245 studied patients, 163 patients (66.53%) were having either normal bone scan or some other benign pathology like history of trauma or rheumatoid arthritis as documented with the assistance of clinical history, physical examination and other radiological imaging. Rest 82 patients (33.47%) were positive for skeletal metastasis (Figure 1).

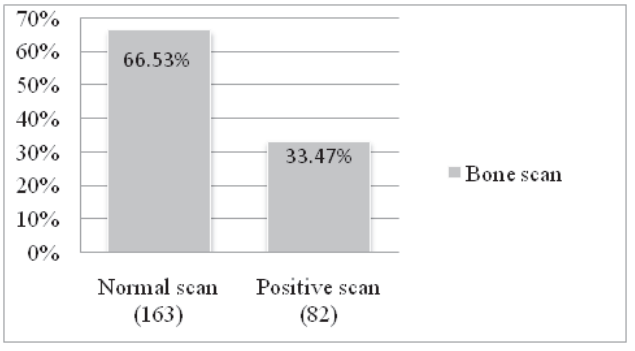

Figure 1: Distribution of bone scan findings in frequency and percentage in study group (n= 245)

Out of 82 patients with positive skeletal metastasis 68 (82.93%) patients had multiple sites (two or more) and 14 (17.07%) patients had solitary site of bony involvement (Figure 2).

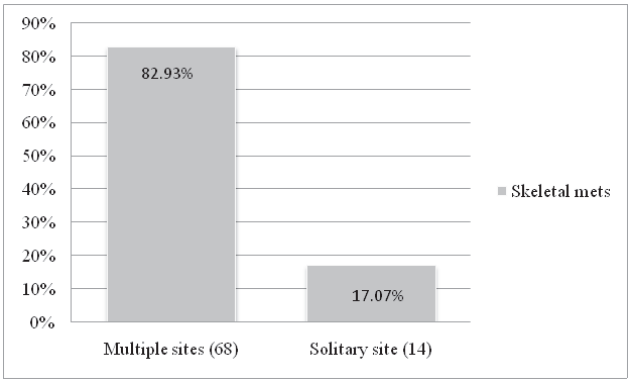

Figure 2: Distribution of skeletal metastases in frequency and percentage by number of sites in study group (n= 82)

Out of 68 patients with multiple sites of skeletal metastasis, highest number was noted in thoraco-lumbar spine (80.89%). Other sites of metastases were in ribs including sternum and clavicle (57.35%), pelvic bones (47.06%), upper extremities including scapula (41.18%), lower extremities (33.82%), cervical spine (23.53%) and skull bone (8.82%) (Figure 3).

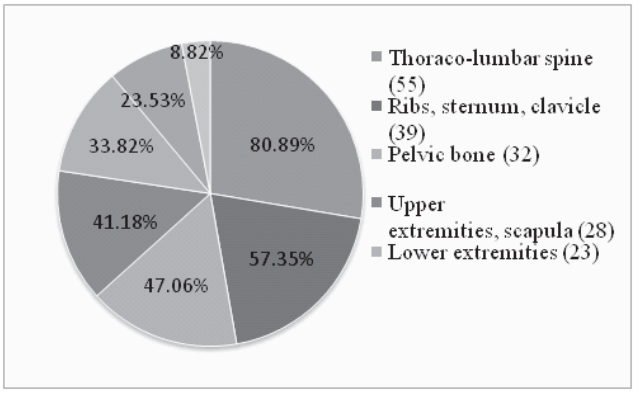

Figure 3: Distribution of multiple skeletal metastases in frequency and percentage by anatomical sites (n= 68)

Among 14 patients with solitary skeletal metastasis, maximum number was noted in thoraco-lumbar spine (64.29%). Other sites of metastases were in cervical spine (14.29%), pelvic bone (07.14%), ribs (07.14%) and sternum (07.14%) (Figure 4).

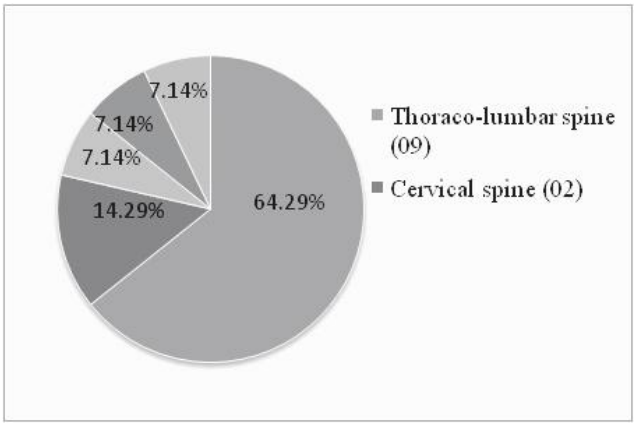

Figure 4: Distribution of solitary skeletal metastasis in frequency and percentage by anatomical sites (n= 14)

DISCUSSION

Bone scan is a highly sensitive technique in detecting metastatic deposits within skeleton, 50% to 80% more sensitive than radiographs. The high sensitivity of this technique is based on physiological basis for preferential uptake of methyl diphosphonate, which identifies as little as 5-15% alteration in local bone turnover. Delineation of a lytic lesion by conventional radiology requires a minimum size of one cm and a focal loss of at least 50% of bone mineral, while at least 30% increase in bone mineral content is essential to appreciate sclerotic lesion. That's why bone scan may pick up bone metastases up to 18 months earlier than conventional radiology, with an average lead of four months. The usual appearance of skeletal metastases on bone scan is focal hot spot; however, rarely focal cold defects are also noted (18-21).

The routes of skeletal metastasis are direct extension or invasion, lymphatic spread, hematogenous dissemination and intraspinal spread. Skeletal metastases of breast cancer will mainly occur from hematogenous dissemination. Two potential vascular routes are possible for hematogenous dissemination. One is the arterial system and the other is venous system. The mechanism or a route of venous system dissemination to develop skeletal metastasis was proposed by Batson. He insisted that owing to the extensive communications of this venous system and to the variability of the direction of this blood flow, tumors arising in many sites release cells that could be deposited anywhere along the course of vessels, including the skeleton, even in the absence of pulmonary and hepatic metastasis. A part of the sternal metastasis could occur via lymphatic vessels to parasternal lymph node (22, 23).

In our study, out of 245 patients, 82 patients (33.47%) were positive for skeletal metastasis, either solitary or multiple sites. Afzal M S et al. found positive bone scan in 38% patients out of 465 breast cancer patients (18). The present study showed, in positive bone scan patients 82.93% had multiple sites (two or more) of skeletal metastases. Common sites of involvement were in thoraco- lumbar spine (80.89%), followed by ribs including sternum and clavicle (57.35%), pelvic bones (47.06%), upper extremities including scapula (41.18%), lower extremities (33.82%), cervical spine (23.53%) and skull bone (8.82%). The findings were almost similar with other studies. Afzal M S et al.

found in patients having multiple skeletal lesions, highest number in spine (84.5%- most common in thoracolumbar), followed by ribs (55.5%), pelvis (37.3% - most frequent in iliac bone), skull (32%), scapula (27.3%), sternum (26.4%), femur (19.1%), humerus (14.5%), clavicle (3.6%) and tibia (0.9%). In another study of patients with breast cancer (24), out of 23 subjects with skeletal metastases, 16 cases were having multiple secondaries; the most involved site was the ribs (18 cases), followed by the spine (in 17 cases), iliac bone (9 cases), the femur (7 cases), the skull (3 cases). In spine, the more frequently involved vertebrae were dorsal (49.23%), followed by lumbosacral (26.13%) and lastly cervical vertebrae (12.3%). On the dorsal vertebrae, in 91% the metastases were localized between D8 and D12. Other studies (25) also showed that vertebral column is the most common site of skeletal metastases. Spinal metastases are a very frequent manifestation of systemic neoplasia, with up to 70% of cancer patients harboring secondary spinal disease. Our study showed more frequent involvement of thoracolumbar spine than cervical vertebrae. Classic autopsy investigations have demonstrated that the distribution of extradural spinal metastases is related to the size of the vertebrae. Thus, metastatic lesions are most commonly located in the thoracolumbar region, less so in the cervical spine (18, 24-26).

In the present study, among 14 (17.07%) patients with solitary skeletal metastasis, maximum number was noted in thoraco-lumbar spine (64.29%), followed by cervical spine (14.29%), pelvic bone (07.14%), ribs (07.14%) and sternum (07.14%). The findings were quite similar with other studies. Afzal M S et al. found in patients having solitary focal lesion, highest number was noted in spine (45.5%- most common in thoracolumbar spine), followed by ribs (22.7%), sternum & pelvis (13.6% each), and skull (6.8%) (18).

In a study of comparison between solitary and multiple skeletal metastatic lesions of breast cancer patients by Koizumi M et al. found that out of 703 patients with metastatic bone lesions, 289 (41%) had solitary bone lesions and 414 (59%) had multiple bone lesions at the time of diagnosis. For 206 patients with a solitary bone lesion, skeletal metastasis was the first evidence of recurrence (206 of 289; 71%), and for 291 patients with multiple bone lesions, bone metastasis was the first evidence of recurrence (291 of 414; 70%). For patients whose bone metastasis was the first recurrence, patients whose metastasis was restricted only to bone at initial diagnosis of osseous metastasis were 169 for the solitary metastatic bone lesion group (169 of 206; 82%) and 230 for the multiple metastatic bone lesion group (230 of 291; 79%) (27).

Boxer et al. found that out of 160 consecutive studied breast cancer patients, 79% were having multiple metastatic lesions. Similar to our results, he observed that spine was the most frequent site for both solitary (52%) and multiple (87%) metastases. He stated that solitary metastases are much more common in cases of breast cancer, than they are thought to be. Reported incidence of solitary skeletal metastases in breast cancer patients having skeletal metastases ranges from 11% to 21% (28).

CONCLUSION

Skeletal metastases are much more common in multiple sites than solitary lesion in breast cancer patients. Thoraco-lumbar spine was the most common site of involvement in both solitary and multiple lesions in our study. Axial skeleton was more commonly involved than the appendicular skeleton. Tc-99m MDP bone scan is very cost effective in comparison to other imaging modalities (CT, MRI, and PET) and play a major role in early detection of skeletal metastasis in breast cancer patients; and thus helping oncologist for proper treatment strategies.

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