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Pattern and distribution of bone metastases in common malignant tumors

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Abstract

BACKGROUND: Bone scan is a sensitive but not specific method for evaluation of bone metastases. However, the clinical data and the pattern of bone scan findings help the physician to narrow the diagnostic differentials. We tried to investigate the distribution of bone metastases in common cancers using bone scintigraphy.
MATERIAL AND METHODS: 160 consecutive patients with malignancy (prostate cancer: 32, breast cancer: 107, lung cancer: 8, and gastrointestinal cancers: 13) underwent bone scan.
RESULTS: From the 160 patients, 58 patients (36.3%) had abnormal bone scans attributable to metastatic tumor. Bone metastases were found in 32.7%, 40.6%, 38.5% and 62.5% of patients with breast, prostate, GI and lung cancers, respectively (P = 0.35). The most frequently involved area was the spine, followed by ribs and pelvic bones. Spine was the most frequent site of bone metastases in breast and GI cancers. Except for the spine, common locations of bone metastases from breast cancer were ribs and sternum. In prostate cancer, the most frequent site were spine and pelvis, with similar incidences. In lung cancer, ribs followed by spine were most frequent sites of bone metastases. 97 (60.6%) of the cancer patients studied had symptoms of bone pain. The highest incidence was associated with metastatic lesions in bone scan (P = 0.004). Significant correlation between location of bone pain and evidence of bone metastasis in the same region was noticed in the pelvis (P = 0.001), skull (P = 0.04), sternum (P = 0.01), spine (P = 0.003) and femur (P < 0.001).
CONCLUSIONS: Our results indicate that the spine and pelvis in prostate carcinoma and the spine, ribs and sternum in breast carcinoma as well as ribs and spine in lung cancer are most frequently invaded. Bone pain in the skull, sternum, lumbar vertebrae, pelvis and proximal portion of femurs are more important to keep in mind for metastatic bone involvement.
KEY words: bone scan, bone metastases, metastatic pattern, cancer
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Background

Common malignant tumors, such as breast, prostate and lung cancers, frequently have bone metastasis at presentation or during follow-up. Bone metastases are responsible for significant morbidity and usually have prognostic impact [1, 2]. The bone scan has high sensitivity and the ability to examine the whole skeleton, so it is of utmost prognostic significance and still remains the most important investigation in the evaluation of bone metastases [1]. Bone scan is a sensitive but not specific method. However, the clinical data and the pattern of bone scan findings help the physician to narrow the diagnostic differentials. In the present study, we tried to investigate the distribution of bone metastases in breast, prostate, gastrointestinal (GI) and lung cancers using bone scintigraphy and determine the relationships of bone scan findings and bone pain symptoms.

Material and methods

160 consecutive patients (44 males and 116 females; average age 55.67 ± 14.08 years; age range 29 to 83 years) with histologically proved malignant disease (32 prostate, 107 breast, 8 lung and 13 gastrointestinal cancers) referred to the Nuclear Medicine Department underwent bone scan. Each patient received 20 mCi of the Tc99m-MDP intravenously. After an approximately 3 hours, scintigraphy was performed using a dual head gamma camera (E.cam

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Table 1. Frequency of anatomical distribution of bone metastases in prostate, breast, gastrointestinal (GI) and lung cancers

Anatomical site	Total	Breast cancer	Prostate cancer	GI cancer	Lung cancer
Spine	30 (18.8%)	18/103 (16.8%)	5/27 (15.6%)	5/13 (38.5%)	2/7 (25%)
Ribs	23 (14.4%)	16/103 (15.0%)	2/27 (6.3%)	2/13 (15.4%)	3/7 (37.5%)
Pelvis	15 (9.4%)	9/103 (8.4%)	5/27 (15.6%)	1/13(7.7%)	0/7
Sternum	12 (7.5%)	12/103 (11.2%)	0/27 (0%)	0/13	0/7
Femur	8 (5.0%)	6/103 (5.6%)	2/27 (6.3%)	0/13	0/7
Scapula	6 (3.8%)	4/103 (3.7%)	2/27 (6.3%)	0/13	0/7
Skull	6 (3.8%)	5/103 (4.7%)	1/27 (3.1%)	0/13	0/7
Humerus	3 (1.9%)	3/103 (2.8%)	0/27 (0%)	0/13	0/7
Clavicle	2 (1.3%)	1/103 (0.9%)	1/27 (3.1%)	0/13	0/7
Tibia and fibula	1 (0.6%)	0/103 (0%)	1/27 (3.1%)	0/13	0/7

Simens). Whole body scan in anterior and posterior projections and in individuals spot views were obtained. All bone scans were reviewed by two well-trained nuclear medicine physicians. Bone scan results were compared with available radiographs and assessed taking into account all available clinical information; any positive findings were considered as metastatic bone disease, when they could not be attributed to any other known disorder in the patient (such as degenerative changes). In patients for whom previous conventional bone scans were available, we compared the scan findings with previous bone scan results.

The involved area was divided into ten portions: 1. skull, 2. sternum; 3. vertebrae; 4. ribs; 5. pelvic bones, including sacroiliac joints and sacrum; 6. humeri; 7. scapulae; 8. femora; 9. tibiae and fibulae; and 10. clavicles.

Statistical analysis. Initially, frequency of the involvement of particular anatomical regions were ranked. Student's t-test, Chi-squared test, Fisher's exact test and one way ANOVA in post-hoc analysis were used for statistical analysis. $P < 0.05$ was considered as statistically significant difference.

Results

Of the 160 patients, 107 patients (66.9%) had breast cancer, 32 patients (20.0%) had prostate carcinoma, 13 patients (8.1%) had gastrointestinal carcinoma and 8 patients (5.0%) had lung cancer.

Of the 160 patients, 58 patients (36.3%) had abnormal bone scans attributable to metastatic tumor. 12 patients (7.5%) had single bone metastasis while 10 patients (6.2%) had widespread bone metastases throughout the axial skeleton. Mean age of patients with and without bone metastasis was 57.21 ± 15.55 and 54.79 ± 13.18, respectively ($P = 0.32$). Bone metastases were found in 32.7%, 40.6%, 38.5% and 62.5% of patients with breast, prostate, GI and lung cancers, respectively ($P = 0.35$). Table 1 shows the frequency of specific anatomical regions of bone involvement. Of the 30 patients with metastases to the spine, 3 had lesions in cervical, 20 in thoracic and 23 in lumbar vertebrae, respectively.

Table 2. Frequency of bone pain and metastatic bone involvement

	No pain	Symptom of bone pain	Total
No bone metastasis	49 (77.8%)	53 (54.6%)	102 (63.8%)
Evidence of bone metastasis	14 (22.2%)	44 (45.4%)	58 (36.2%)
Total	63 (100%)	97 (100%)	160 (100%)

97 patients (60.6%) of the cancer studied had symptoms of bone pain. The highest incidence was associated with metastatic lesions in bone scan (Table 2) ($P = 0.004$). We analyzed the correlation between the location of bone pain and evidence of bone metastatic lesion in the same area. Significant correlation was found for following locations: pelvis ($P = 0.001$), skull ($P = 0.04$), sternum ($P = 0.01$), spine ($p = 0.003$), and femur ($P < 0.001$). We performed more detailed analysis of the recorded data and found that there was a correlation between the presence of lumbar pain and lumbar vertebral metastatic lesions ($P = 0.005$), while there was no correlation for the cervical and thoracic vertebrae. There was also a correlation between presence of pain and metastatic lesion in the proximal half of the femur ($P < 0.001$) while there was no correlation for the distal portion of the femur.

Discussion

Bone is one of the most common locations of distant metastases in malignancy.

Bone scintigraphy has been a perfect method for evaluation of bone metastasis and cancer staging for several decades and it is still a procedure of choice in many of these clinical settings [1–14]. In the present study, the incidence of bone metastasis from prostate carcinoma (40.6%%) did not differ significantly from that of breast carcinoma bone metastasis (32.7%). In agreement to our results, Wilson et al. [3] as well as Tofe et al. [4] reported that the difference in bone metastasis incidence between breast and prostate carcinomas was not significant. Although Tofe et al. reported the higher incidences of bone metastasis of breast and prostate cancers (67 vs. 62%, P = 0.25), Wilson reported similar frequency to our study (28% vs. 35%, P = 0.52). Some differences are likely due to the different study populations.

Our study focused on the area most commonly involved in the bone metastases. According to our data, the most frequently involved area was the spine, followed by ribs and pelvic bones. Spine was most frequent site of bony metastases in breast and GI cancers. Except for the spine, common locations of bone metastases from breast cancer were the ribs and sternum. In prostate cancer, the most frequent sites were spine and pelvis, with similar incidences. However, as compared to the breast cancer, the lower incidence of involving the ribs and, particularly, the sternum was noticed in the prostate cancer. On the other hand, in the lung cancer, ribs followed by spine were most frequent sites of bone metastases.

It has been observed that malignant tumors metastasize according to predictable patterns. Several theories were proposed to explain this tumor behavior [5]. The ''seed and soil'' theory proposed by Paget was an explanation for the non-random patterns of cancer metastases. This theory is still relevant today, although different factors involved in the attraction and subsequent growth of prostate cancer cells to the bone have been discovered. These factors include: accumulation of genetic changes within cancer cells, the preferential binding of cancer cells to bone marrow endothelial cells, and the release of cancer cell chemo-attractants from bone elements [6].

Other theory proposed by Ewing indicates that metastatic deposits were primarily a mechanical phenomenon [5]. Cancer cells were directed to a specific site based on the anatomy of the blood flow and lymphatics. It is likely that both of these theories are correct, at least in part [6]. Indeed, both anatomical components (i.e., Batson venous plexus) and site-specific molecular interactions were responsible for prostate cancer spread to the bone [7].

In agreement to the seed and soil theory, bone metastases occur almost exclusively in areas containing active red marrow. Active red bone marrow represents an attractive site for metastatic involvement because of sinusoidal vascular spaces and relatively easy barrier for penetration of tumor cells [5].

We showed that the pelvis and spine are the main predilection sites of prostate cancer, rather than the ribs and sternum. Spreading through the Batson venous plexus explained the following hypothesis that prostatic cancer cells are directed into the pelvis and spine early in the disease and later metastasize to other parts of the skeleton, such as ribs [3].

However, in breast cancer rib metastases were more frequent than in prostate cancer. It's may be due to different spreading pathways. At early stage, breast cancer may directly invade the nearby ribs or may also spread to the ribs via the aorta following metastasis to lung [8]. It is suggested that breast cancer spread to the sternum via the parasternal lymph nodes [9]. So breast cancer involves the spine, ribs and sternum with a high frequency.

Although, in our study the number of lung cancer patients was low, ribs followed by spine are most frequent sites of bone involvement. In other studies, it has been suggested that lung cancers via the pulmonary veins and then arterial system involve appendicular skeleton more frequently than other cancers, which is in accordance with Ewing's hypothesis [5].

Our results show that the spine, pelvis and ribs are the main sites of bone metastases and the extremities, especially the distal portions, are non-predilection sites. Of the extremities, proximal portions of femurs are most frequent involvement site.

Of 58 patients with bone metastases, 75.9% had symptoms of bone pain. Of all patients with bone pain, 45.4% had bone metastasis. Concordance between the bone pain area and metastatic involvement in the same region was noticed in the skull, sternum, pelvis, lumbar vertebrae, and proximal portion of the femurs. So, we have to pay more attention to the symptoms in this area which is more likely suggestive of bone metastasis.

Study limitations: The sample of our data for GI and lung cancer was not large. Therefore it is recommended to investigate more patients with these cancers.

Conclusions

The distributions of metastatic bone lesions in the prostate cancer involved mainly the pelvis and spine, while breast cancer showed high frequency of involvement of the spine, ribs and sternum. Most frequent involvement sites in lung cancer were spine and ribs. Our results indicate that the spine and pelvis in prostate carcinoma and the spine, ribs and sternum in breast carcinoma are frequently invaded, which in agreement with Ewing theory. On the other hand, distribution of bone metastases in the regions of the red bone marrow supports Paget's theory. Bone pain in the skull, sternum, lumbar vertebrae, pelvis and proximal portion are more important to keep in mind for metastatic bone involvement.

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