Res. Oncol.
Vol. 12, NO. 1, Jun. 2016:20-27

Original article

Study of distribution of bone metastases in metastatic breast cancer patients compared to other major cancers

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Introduction: Metastatic bone disease is frequent in patients with advanced breast cancer. Although it is not specific for the detection of metastatic bony lesions, bone scan is a sensitive method. The pattern of distribution of bone metastases as detected by bone scan combined with clinical data may help in reaching diagnosis.
Methods: Technetium-99m-methylene diphosphonate skeletal scintigraphy was used for evaluation of distribution pattern of skeletal metastases in patients with breast carcinoma compared to other common cancers.
Results: Out of 134 patients with positive bone scan for skeletal deposits, the primary cancer was breast cancer in 81 patients, prostate in 24, lung in 12, liver in 8, urinary bladder in 6, and head and neck in 3.
Few metastases (≤ 3 deposits) were common in breast cancer, while extensive metastatic lesions (≥10 deposits) were more common in prostate cancer (50%). The most common locations of bone metastases in patients with breast cancer were the spine, pelvic bones, femora, and ribs, respectively.
In prostate cancer patients, spine was the most common site of metastases, especially the lumber region. In lung cancer patients, thoracic spine was the most common site of metastases, while pelvic bones were the most common site in liver cancer patients.
Conclusion: In breast cancer, the most frequent sites of involvement are the spine (especially lumber region), pelvis and axial skeleton, respectively. Spinal and sternal involvements are significantly more in breast cancer than in other malignancies.

Key words: Bone scan, Breast cancer, Skeletal metastases.
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Received: 12-Jul-2016, Accepted: 1-Sep-2016

Original article

INTRODUCTION

For metastatic carcinomas, skeletal metastases are the third most common following pulmonary and hepatic. In addition, bone metastases may present as the first manifestation of cancer in 25- 30% of cases[1].

The most common malignant tumors that metastasize to bone are prostate cancer in males and breast cancer in females and lung cancer in both. Also, any malignant tumor can metastasize to bone[2].

Studying the pattern of distribution of skeletal metastases can help in diagnosis and narrow the diagnostic differentials.

This study aimed to assess the pattern of bone metastases in breast cancer patients compared to other common cancers using Technetium-99m-methylene diphosphonate skeletal scintigraphy. Besides, to explore if there is a specific distribution of bony deposits in breast cancer patients compared to other major malignancies in order to reduce diagnostic differentials.

METHODS

We studied whole-body bone scans of 150 cancer patients which was done to exclude or assess metastatic bone disease. Anterior and posterior views were obtained with a dual detector gamma camera for patients who had undergone scintigraphy with Tc-99m methylene diphosphonate (600 MBq Tc- 99m MDP).

Bone scans were interpreted as positive for bone metastasis if radiotracer activity of local bone lesion was greater or less than that of adjacent or contralateral normal bone.

Bone scan results were considered negative when:

a) No abnormal increased radiotracer uptake was detected.

b) Radiotracer uptake was characterized by medical and benign disease (e.g. arthritis, fracture and trauma).

Bony metastatic lesions in bone scan films were studied regarding their number and pattern of distribution.

Based on the number of metastatic lesions patients were divided into three categories:

I) Patients with few metastatic lesions (≤ 3lesions)

b) Patients with intermediate metastatic lesions (4-≤9 lesions)

c) Patients with extensive metastatic lesions (≥10 lesions)

To describe the pattern of distribution of bone deposits the involved areas were divided into nine portions: skull, sternum, spine, ribs, pelvic bones, sacrum, humeri, scapulae, femora, tibiae and fibulae and clavicles.

Data were computed using SPSS versions 16 for Windows. Continuous data were expressed as mean ±SD while categorical data were expressed as count and percentage. Student t test was used for comparison of continuous data, while Chi-square test was used for categorical data. P value < 0.05 was considered statistically significant.

RESULTS

From January to June, 2015, a total of 597 patients were referred to the Nuclear Medicine Unit at Menoufia Oncology Department for skeletal scintigraphy. One hundred thirty four patients had histologically-proven malignancies and positive scans for bone deposits. Of these 134 patients with positive bone scan, 81 patients had breast cancer, 24 prostate cancer, 12 lung cancer, 8 liver cancer, 6 urinary bladder cancer and 3 head and neck cancer**.** Demographic characteristics of patients are shown in table 1.

Table 2 shows the distribution of patients with different primary cancer according to onset of metastases (primary or secondary) and number of metastatic lesions (few, intermediate and extensive).

Table 3 shows the distribution of bone metastases according to the primary cancer site. Table 4 compares the distribution sites of breast cancer patients to other patients. In table 5, the distribution is compared between breast cancer patients with primary skeletal metastases and those with secondary skeletal.

Figures 1 to 3 show examples of the studied bone scans.

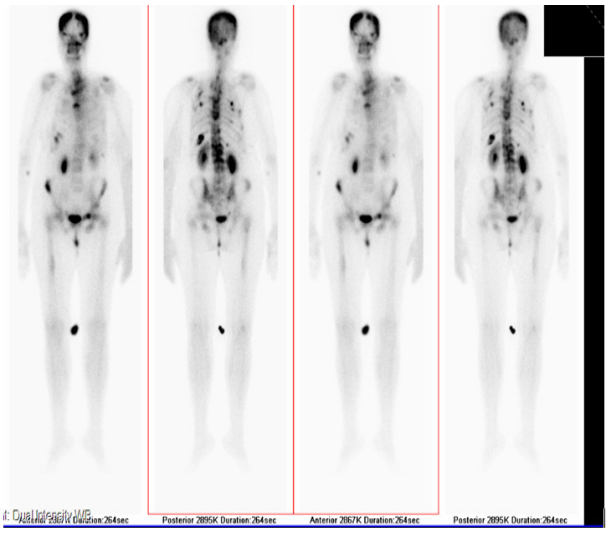

Figure 1: Metastatic breast cancer with extensive bony metastases involving most dorsal and lumber vertebrae, ribs bilaterally pelvic bones and both femora

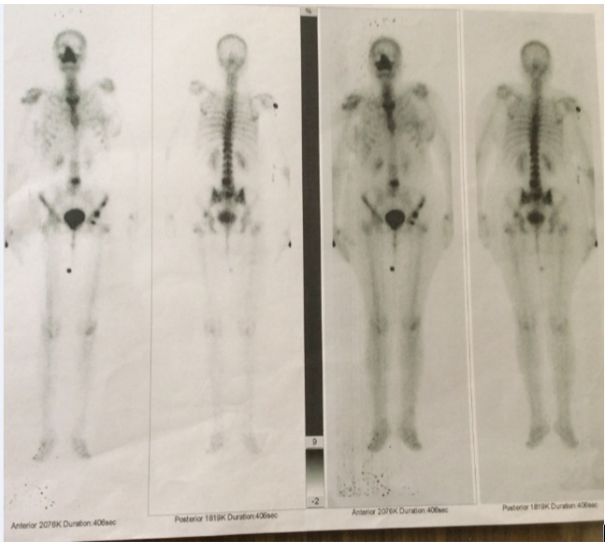

Figure 2: A case of breast cancer with limited metastases

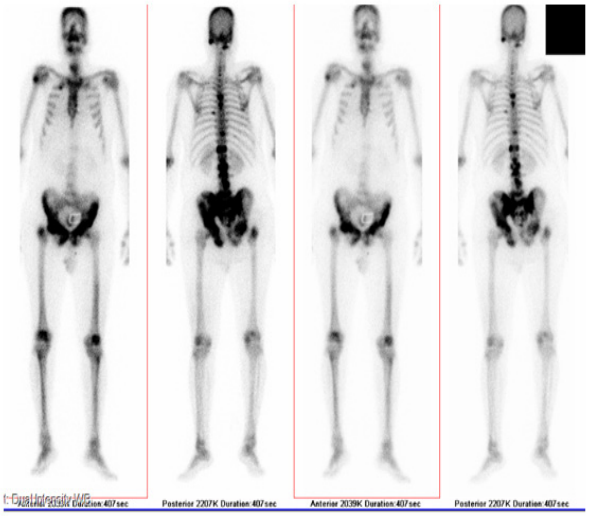

Figure 3: Prostate cancer with extensive bone metastases involving both femora, all pelvic bones, lumber and dorsal vertebrae and ribs.

Table 1: Characteristics of 134 patients.

Characteristics	*n*	%
Age		
Mean ±SD	53.88 ± 11.98	
Range	28-90	
Sex		
Female	89	66.4
Male	85	33.6
Type of cancer		
Breast	81	60.4
Prostate	24	17.9
Lung	12	9
Liver	8	6
Urinary bladder	6	4.5
Head and neck	3	2.2

Table 2: The onset and number of bone metastases in different cancer types.

	Primary cancer											
	Breast (n=81)		**Liver (n=8)**		**Prostate (n=24)**		**Lung (n=12)**		**Bladder (n=6)**		**Head & neck (n=3)**	
	no	**%**	**no**	**%**	**no**	**%**	**no**	**%**	**no**	**%**	**no**	**%**
Onset												
Primary	46	56.8	8	100	22	91.7	12	100	5	83.3	0	0
Secondary	35	43.2	0	0	2	8.3	0	0	1	16.7	3	100
Number of metastases												
Few	37	45.7	7	87.5	4	16.7	7	58.3	6	100	2	66.7
Intermediate	29	35.8	0	0	8	33.3	3	25	0	0	0	0
Extensive	15	18.5	1	12.5	12	50	2	16.7	0	0	1	33.3

Table 3: Distribution of bone metastases according to primary cancer.

	Primary cancer											
	Breast (*n*=81)		**Liver (*n*=8)**		**Prostate (*n*=24)**		**Lung (*n*=12)**		**Bladder (*n*=6)**		**Head & neck (*n*=3)**	
	no	%	no	%	no	%	no	%	No	%	no	%
Ribs	18	22.2	1	12.5	10	41.7	4	33.3	0	0	1	33.3
Scapula	3	3.8	0	0	0	0	1	8.3	0	0	0	0
Skull	7	8.6	0	0	5	20.8	0	0	0	0	0	0
Sternum	11	13.6	0	0	0	0	1	8.3	0	0	0	0
Spine	68	84	3	37.5	21	87.5	9	75	0	0	0	0
Spine site												
Cervical	1	1.5	0	0	0	0	1	11.1	0	0	0	0
Thoracic	19	27.9	0	0	1	4.8	5	55.6	0	0	0	0
Lumbar	25	36.8	0	0	6	28.6	1	11.1	0	0	0	0
Cervical + thoracic	1	1.5	0	0	1	4.8	0	0	0	0	0	0
Thoracic + lumbar	19	27.9	2	66.7	8	38.1	1	11.1	0	0	0	0
Cervical + Thoracic + Lumbar	3	4.4	1	33.3	5	23.8	1	11.1	0	0	0	0
Sacrum	14	17.3	1	12.5	8	33.3	1	8.3	0	0	0	0
Humeri	13	16	2	25	7	29.2	3	25	4	66.7	0	0
Humeri site												
Upper shaft	11	84.6	1	50	6	85.7	3	100	3	75	0	0
Lower shaft	2	15.4	1	50	0	0	0	0	1	25	0	0
Whole length	0	0	0	0	1	14.3	0	0	0	0	0	0
Femora	25	30.9	0	0	10	41.7	2	16.7	1	16.7	1	33.3
Femora site												
Upper shaft	20	80	0	0	9	90	1	50	1	100	1	100
Lower shaft	3	12	0	0	9	90	1	50	1	100	1	100
Whole length	2	8	0	0	1	10	1	50	0	0	0	0
Tibiae	2	2.5	0	0	0	0	0	0	0	0	0	0
Pelvis	30	37.0	4	50	16	66.7	3	25	2	33.3	1	33.3
Ilium	4	13.3	1	25	7	43.8	0	0	1	50	1	100
Pubis	1	3.3	0	0	0	0	0	0	1	50	0	0
Ischium	4	13.3	0	0	0	0	0	0	0	0	0	0
Hip	6	20.0	1	25	1	6.2	0	0	0	0	0	0
Ilium + pubis	1	3.3	0	0	0	0	1	33.3	0	0	0	0
Ilium + ischium	2	6.7	0	0	1	6.2	0	0	0	0	0	0
Ilium + hip	9	30.0	0	0	1	6.2	0	0	0	0	0	0
Ilium + obturator	1	3.3	0	0	0	0	0	0	0	0	0	0
Hip + ischium	0	0	0	0	2	12.5	0	0	0	0	0	0
Acetabulum	1	3.3	1	25	0	0	2	66.7	0	0	0	0
Ischium + ilium + acetabulum + hip	1	3.3	0	0	2	12.5	0	0	0	0	0	0
Ischium+ ilium+ acetabulum + pubis	0	0	0	0	2	12.5	0	0	0	0	0	0
Pubis + acetabulum	0	0	1	25	0	0	0	0	0	0	0	0

Table 4: Comparison between breast cancer patients and other patients as regard to bone metastases distribution.

	Cancer				χ^2	*p- value*
	Breast (*n*=81)		Others (*n*=53)			
	n	%	*n*	%		
Origin						
• Primary	46	56.8	46	56.8	15.34	<0.001
• Secondary	35	43.2	35	43.2		
Metastasis						
• Few	37	45.7	26	49.1	4.39	0.111
• Intermediate	29	35.8	11	20.8		
• Extensive	15	18.5	16	30.2		
Ribs	18	22.2	16	30.2	1.07	0.3
Scapula	3	3.8	1	1.9	0.35	0.55
Skull	7	8.6	5	9.4	0.02	0.875
Sternum	11	13.6	1	1.9	5.37	0.028
Spine	68	84	33	62.3	8.11	0.004
Spine site						
• Cervical	1	1.5	1	3	0.25	0.8
• Thoracic	19	27.9	6	18.2	0.81	0.415
• Lumber	25	36.8	7	21.2	1.35	0.176
• Cer+Th	1	1.5	1	3	0.25	0.8
• Th+Lum	19	27.9	11	33.3	0.33	0.745
• Cer+Th+Lumb	3	4.4	7	21.2	2.30	0.021
• Cervical	5	6.2	8	15.1	2.91	0.088
• Thoracic	41	50.6	24	45.3	0.36	0.546
• Lumber	46	56.8	24	45.3	1.70	0.192
Sacrum	14	17.3	10	18.9	0.05	0.815
Humeri	13	16.0	16	30.2	3.77	0.052
Site humeri						
• Upper shaft	11	84.6	13	81.2	0.86	0.649
• Lower shaft	2	15.4	2	12.5		
• Whole length	0	0	1	6.2		
Femora	25	30.9	14	26.4	0.30	0.579
Site Femora						
• Upper shaft	20	80	12	85.7	2.06	0.357
• Lower shaft	3	12	0	0		
• Whole length	2	8	2	14.3		
Tibii	2	2.5	0	0.0	*1.32	0.518
Pelvis	30	37.0	26	49.1	1.90	0.168
• Iliac	4	13.3	10	38.5	3.17	0.001
• Pubis	1	3.3	1	3.8	0.33	0.473
• Ischium	4	13.3	0	0	2.44	0.014
• Hip	6	20	2	7.7	1.7	0.089
• Iliac + pubis	1	3.3	1	3.8	0.33	0.743
• Iliac + ischium	2	6.7	1	3.8	0.33	0.74
• Iliac + hip	9	30	1	3.8	3.51	0.0004
• Iliac + obturator	1	3.3	0	0	0.7	0.481
• Hip + ischium	0	0	2	7.7	2.02	0.043
• Acetabulum	1	3.3	3	11.5	1.52	0.128
• Ischium + ileum + acetabulum + pubis	1	3.3	2	7.7	0.73	0.462
• Ischium + ilium + acetabulum + pubis	0	0	2	7.7	2.02	0.043
• Pubic+ acteabulum	0	0.0	1	3.8	1.04	0.297

**Fisher's exact*

Table 5: The distribution of bone metastases in breast cancer patients according to the onset of metastases (primary vs. secondary).

		Onset of metastases				X^2	P- value
		primary		secondary			
		No	%	No	%		
Ribs	Yes	10	21.7	8	22.9	0.014	NS
	No	36	78.3	27	77.1		
Scapula	Yes	2	4.4	1	2.9	0.137	NS
	No	43	95.6	34	97.1		
Skull	Yes	5	10.9	2	5.7	0.669	<0.05
	No	41	89.1	33	94.3		
Sternum	Yes	5	10.9	6	17.1	0.667	<0.05
	No	41	89.1	29	82.9		
Pelvis	Yes	18	39.1	14	40	0.006	<0.05
	No	28	60.9	21	60		
Pelvis Site	Ilium	2	11.8	2	15.4	9.299	<0.05
	Pubis	0	0	1	7.7		
	Ischium	3	17.6	1	7.7		
	Hip	4	23.5	2	15.4		
	Ilium + pubis	0	0	1	7.7		
	Ilium + ischium	2	11.8	0	0		
	Ilium + hip	3	17.6	6	46.2		
	Ilium + obturator	1	5.9	0	0		
	Acetabulum	1	5.9	0	0		
	Ischium + ilium + acetabulum + hip	1	5.9	0	0		
Spine	Yes	41	89.1	27	77.1	2.120	<0.05
	No	5	10.9	8	22.9		
Spine Site	Cervical	1	2.4	0	0	4.221	NS
	Thoracic	13	31.7	6	22.2		
	Lumber	16	39	9	33.3		
	Cervical + thoracic	0	0	1	3.7		
	Thoracic + lumbar	9	22	10	37		
	Cervical + thoracic + lumbar	2	4.9	1	3.7		
Sacrum	Yes	7	15.2	7	20	0.318	NS
	No	39	84.8	28	80		
Humeri	Yes	9	19.6	4	11.4	0.977	<0.05
	No	37	80.4	31	88.6		
Humeri site	Upper shaft	8	88.9	3	75	0.410	NS
	Lower shaft	1	11.1	1	25		
Femora	Yes	17	37	11	31.4	0.269	NS
	No	29	63	24	68.6		
Femora site	Upper shaft	13	86.7	7	70	3.264	<0.05
	Lower shaft	2	13.3	1	10		
	Whole length	0	0	2	20		
Tibiae	Yes	1	2.2	1	2.9	0.039	NS
	No	45	97.8	34	97.1		

DISCUSSION

It is important for both radiologist and nuclear medicine physician to know the pattern of distribution of metastatic skeletal deposits in breast cancer as it may help them to comment on the nature of lesions within the skeleton. Furthermore, this may aid in expecting the sites of possible skeletal related events and its early management.

Out of the studied 134 patients with positive bone scan for skeletal deposits, 81 cases had breast cancer and 53 cases had other solid malignancies. As regard number of bone metastases, few metastases (≤ 3deposits) were more common in breast cancer patients (45.7%) while extensive metastatic lesions (≥10 deposits) were more common in prostate cancer patients (50%).

As regard the site of bone metastases, the current study showed that the main sites of metastases are the ribs, pelvis and spine. Proximal femora were the most commonly involved sites in the extremities. These results are in agreement with those of *Kakhki et al*[3]. This can be explained by the fact that sinusoidal vascular spaces in the red bone marrow represent attractive sites for metastases as it is easily penetrated by cancer cells.

The most common location of bone metastases on scan images of patients with breast cancer was the spine, especially the lumber region; which is consistent with the results of *Kakhki et al*[3]. However, *Afzal et al*[4] and *Wang et al*[5] noted that the highest numbers were in the spine, mainly the thoraco-lumbar vertebrae. This is on contrary to our findings, where the lumber vertebrae were the most common metastatic site.

In our study, pelvic bones were the second most common metastatic sites in breast cancer, followed by femora (especially the proximal parts) followed by ribs. While, *Kakhki et al*[3] reported that the second most common sites in breast cancer patients were the ribs and sternum. Also, *Afzal et al*[4] and *Wang et al*[5] reported ribs as the second most common site then pelvic bones. Bieki et al[6] studied the pattern of bone metastases in breast cancer patients and found that the commonest sites were the pelvis and hip, lumbar and thoracic vertebrae and ribs. The difference in distribution between our study and that of other studies may be due to the difference in the number of patients studied.

In prostate cancer, we found the spinal vertebrae as the most common site especially the lumber region; consistent with the results of *Kakhki et al*[3]. An explanation for that is the spread of prostatic malignant cells via the Batson venous plexus to the pelvis and spine bones earlier in the course of the disease followed later by other skeletal sites. Similar results were obtained by *Wang et al*[5] and *Zytoon et al*[7] who found that metastatic bony lesions of prostate cancer are located mainly in the spine. The second most common metastatic sites in prostate cancer patients in our study were in the pelvic bones, which is in agreement with *Kakhki et al*[3] and *Wang et al*[5]. On the other hand, *Zytoon et al*[7] found the ribs and femora to be the second and third frequently involved sites. This may be due to the inclusion of relatively few prostatic cancer patients in our study (24 patients) in comparison to *Zytoon et al*[7] who included 150 patients. Other researchers reported a different pattern of bone metastases in prostate cancer patients. In 2010, *Bieki et al*[6] reported that the most common sites in prostate cancer patients were pelvis, thoracic vertebrae, proximal femur, ribs and lumbar vertebrae; respectively.

Although, in our study the number of lung cancer patients was small (12 patients), we found that the most common region was thoracic spine mostly due to direct invasion by tumor mass. While, previous researchers found that the ribs then the spinal region were the most common sites[3, 8] which can be attributed to direct tumor invasion.

Pelvic bones were the most common site in liver cancer patients; while, upper humeral metastases were the most common in urinary bladder cancer patients.

Conclusions and recommendations

In breast cancer patients, the most common involved bone metastases sites were spine (especially lumber region), pelvic bones and femora; respectively. Compared to other types of cancers, spine, sternum and iliac bone involvement were significantly more common in breast cancer.

Further research investigating the clinical application of studying the pattern of bone metastases is recommended.

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