

## RESEARCH ARTICLE

# Metastatic Bone Disease as Seen in Our Clinical Practice - Experience at a Tertiary Care Cancer Center in Pakistan

Asim Qureshi<sup>1\*</sup>, Usman Shams<sup>2</sup>, Azra Akhter<sup>2</sup>, Sabiha Riaz<sup>2</sup>

### Abstract

**Aim:** Metastatic tumor of bone is the most common malignancy involving bone and is an important predictor of prognosis in advanced cancers. The prognosis depends upon the primary site of origin and the extent of disease. In current study, we present the pattern and distribution of metastatic bone disease seen in the leading cancer care center of Pakistan, Shaukat Khanum Cancer Hospital & Research Center (SKMCH & RC), Lahore. **Materials & Methods:** All cases of bony metastatic disease were included that presented in the Pathology Department, from Jan 2005 to July 2011. Patients of all ages and both sexes were included. Primary bone tumors, lymphomas, sarcomas and other malignancies were excluded. The data were recorded and analyzed with SPSS 16.0. **Results:** A total of 146 cases of metastatic bone disease were included in the study. Out of the total cases, 79 were male and 67 were female. Age range 25-82 years (median 52). Hip bone was the most frequent bone involved, with femur and vertebrae as second and third in the list. The commonest bone involved in males was vertebrae with 23 cases and in females was hip bone with 22 cases. Regarding primary site, cancers of breast, prostate and gastrointestinal tract were at the top of the list with prostate and breast being the most frequent primary sites of metastasis in males and females respectively. **Conclusion:** Bone metastasis is an important entity to consider in the differential diagnosis whenever a bony tumor especially carcinoma present in older age. Our data are comparable with international findings and the literature available regarding the site and distribution of skeletal metastatic lesions. A slight deviation noted was more common bony metastatic lesions with ovarian primaries in females and gastrointestinal tract cancers in males in our study.

**Keywords:** Bone - metastatic tumor - cancer - Pakistan

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### Introduction

Metastatic bone disease is the most common malignancy involving bone. The skeleton is the third most frequent organ involved by metastatic tumors and comes after lungs and liver in the list (Coleman, 2006). Most of the metastatic tumors are carcinomas and rarely sarcomas. Different studies have shown that 30-90% patients of common carcinomas have skeletal metastasis in their course of disease. The disease often affects older patients. In children, osseous metastasis is rare and occurs in cases of clear cell sarcoma of kidney, neuroblastoma, Ewing's sarcoma/PNET and rhabdomyosarcoma.

The common routes of involvement of bone include direct extension and/or lymphovascular spread. In this regard, location of the primary tumor and the local pattern of blood flow determine involvement of skeletal sites. At molecular level, it has been found that genetic evolution of metastatic cells confers tropism of metastatic deposits for specific bones. The growth of metastatic implant is regulated by its interaction with an array of

chemokines, cytokines and growth factors present in the bone microenvironment.

The metastatic bony lesions can be osteolytic, osteoblastic or mixed. Lung and breast cancerous bone implants show osteolytic lesions mostly. Thyroid and kidney deposits are purely lytic, while prostatic deposits are osteoblastic. Local symptoms produced by these lesions include pain, with or without swelling, pathological fractures and neurological symptoms. Systemic manifestations are frequent too and include hypercalcemia secondary to osteolysis.

Radiologically most metastases are located in the marrow cavity. Conventional plain radiograph is very helpful in initial assessment in most cases of bone metastases, except in case of vertebral lesion where X-rays can detect only one quarter of cases. Computed tomography (CT) scan and magnetic resonance imaging (MRI) are useful in determining extent of disease and guiding needle biopsies. Radioisotope scintigram bone scan is handy in detecting multiple skeletal metastases.

Regarding morphology of the metastatic bone disease,

<sup>1</sup>Department of Pathology Sultan Qaboos University Hospital, Muscat, Oman, <sup>2</sup>Department of Pathology Shaukat Khanum cancer Hospital, Lahore Pakistan \*For correspondence: [asimqureshi32@hotmail.com](mailto:asimqureshi32@hotmail.com)

gross appearance is non-specific. These may be grayish white and firm as in case of breast primary or soft or hemorrhagic as in case of renal cell carcinoma. Osteoblastic metastatic lesions simulate osteosarcoma macroscopically as well as microscopically. Microscopically osseous metastatic carcinomas tend to resemble the primary tumour. Metastatic adenocarcinomas and squamous cell carcinomas pose little diagnostic problem. In case of poorly differentiated or undifferentiated carcinomas, it may be difficult to determine the primary site. Sarcomatoid carcinomas can masquerade primary spindle cell sarcomas of bone. An accompanying fibroblastic, vascular, osteoblastic and/or osteoclastic response is a frequent finding. Immunomarkers are helpful in detecting the primary site and histologic type. IHC stains for EMA and keratins are frequently positive in epithelial tumors and negative in mesenchymal lesions.

Metastatic tumors of bone represent advanced disease and associated with a poor outcome. It usually heralds incurability and palliative options only that commonly include relief of pain and prevention of fracture. The prognosis depends on primary site of the tumour, histologic type of neoplasm and extent of disease.

The rationale of this study is to assess the distribution and pattern of skeletal metastasis in the local population as presented in our clinical practice at the leading cancer center of Pakistan.

**Materials and Methods**

The objective of this study was to assess the frequency and distribution of metastatic bone disease in our local population. This was a descriptive study carried out on 146 cases who presented with bone metastases. Both genders and all ages were included. Study was carried out at Department of Pathology, Shaukat Khanum Memorial Cancer Hospital and Research Centre (SKMCH and RC) from July 2005 to July 2011. The biopsies came to our department because of some bone morbidity and histopathological diagnosis was made on routine hematoxylin and eosin (H&E) staining and immunohistochemistry. The data was recorded and analyzed. Mean, median and mode were calculated for quantitative variables like patients age. Frequencies and percentages were calculated for qualitative variables like gender, age group and results of histopathological diagnosis.

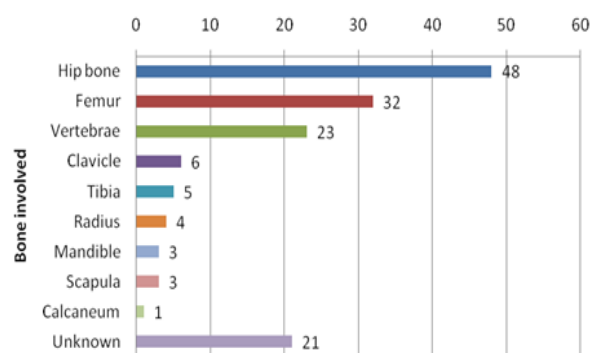
**Results**

A total of 146 cases of metastatic bone disease were included in the study. There were 79 (54.1%) males and 67 (45.9%) females. This graph shows that hip bone, femur and vertebrae are the most favored sites of bone metastases constituting 32.1%, 21.9% and 15.8% cases respectively. Other significant entity is ‘unknown’ that includes cases for site of bone metastases was not mentioned in the history forms attached with the biopsy. In females, the most frequent bones involved are hip bone, femur and clavicle, while in males, vertebrae, femur and scapula were the most common bones involved. The data regarding

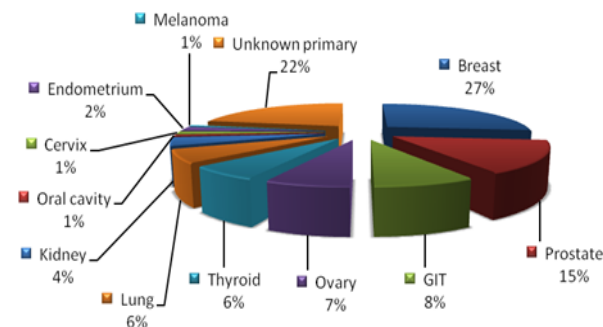
most frequent involved bones according to gender is summarized in Table 1.

Regarding the primary site of origin, breast, prostate and gastrointestinal tract are at the top with 39, 22 and 12 cases respectively. Ovary and thyroid primaries proceed with 9 cases each. For 32 cases, the primary lesion could not be found. The individual percentage for each site is given in pie chart 2.

Here again the commonest sites for origin of skeletal metastases vary between two genders. In females, breast, ovary and thyroid were the commonest primary sites, whereas prostate, gastrointestinal tract and lung are the three top most culprits in males. The data is summarized in the Table 2.



**Figure 1. Bone Involved by Skeletal Metastatic Disease.**



**Figure 2. Percentage of Primary Site of Bone Metastases.**

**Table 1. Commonest Bone Involved**

Bone Involved	No. Of Cases	%
Female:		
Hip bone	32	47
Femur	18	26.9
Clavicle	5	7.5
Tibia	3	4.5
Male:		
Vertebrae	23	29.1
Hip bone	18	20
Femur	5	17.7
Scapula	3	3.8

**Table 2. Commonest Primary Site**

Bone Involved	No. Of Cases	%
Female:		
Breast	39	58.2
Ovary	10	14.9
Thyroid	8	11.9
Male:		
Prostate	22	27.8
GIT	10	12.7
Lung	9	11.4

## Discussion

Metastatic bone disease causes significant morbidity and constitutes most of the cases of malignancies seen in skeleton. The bone involved depends upon the location and blood supply of the primary site.

Age and gender comparison revealed that More than 60% of the patients are in sixth to seventh decade of life. Over two thirds of patients with bone metastases are between 40-60 years of age (Chirgwin et al., 2000; Feller et al., 2011).

Regarding the involvement of skeleton by the metastatic deposits, our data is comparable with the literature. In our study, out of 125 cases for which skeletal site of metastasis was known, 71 (56.8%) cases involved axial skeleton and 54 (43.2%) cases involved appendicular skeleton. In literature, axial skeleton is involved in nearly 70% cases of bone metastases by one textbook and 44.3% cases by the other (excluding cases with multiple sites) (Reddi et al., 2003; D'Silva et al., 2006). Conversely 30% of bone metastasis is reported to be involved appendicular skeleton by the former textbook and 28.8% by the later. Metastatic tumour involving the small bones of hands and feet is rare (Chen et al., 2010) and our data supports this fact. Not a single case in our study involved these rare sites. The lumbar spine and proximal femur are favored sites by various studies (Coleman, 2006; Virk, 2007). Here also our data matches with the literature as femur and spine or vertebrae are second and third most frequent sites of involvement. However, in our study hip bone is the most frequent bone involved which has been reported in literature as favored site but not the commonest. According to gender, bone involvement comparison (Coleman, 1997)

Regarding the nature of primary lesion, sarcomas metastasize to bone rarely. Our data shows the same as all the cases with known primary were having different carcinomas, no sarcomas. Lung, breast, prostate, kidney and thyroid gland account for more than 80% and more than 93% of all skeletal metastases according to different textbooks (Tsuya et al., 2008). According to our data, these primary sites constitute 74.6% cases out of a total of 114 cases with known primary. A slight difference in the pattern of metastatic bone disease which we found was that lung, thyroid and kidney cancer implants in bone are less common and secondary bone involvement by ovarian and gastrointestinal cancers is more common as compared to international data available (Berruti et al., 2000; Yavas et al., 2007).

In pathology, IHC has a key role in detection of unknown primary. Specific immunostains for detecting primary sites are in frequent use. Some examples include thyroid transcription factor-1 (TTF-1) for lung cancer, prostatic specific antigen (PSA) for carcinoma of prostate, GCDFP-15 and hormone receptors for breast cancer, S-100, Melan-A for malignant melanoma and chromogranin for neuroendocrine tumors. These stains were used in our study with reasonable success.

In literature, clinical, laboratory and radiological search identifies the primary site in up to 80% cases by some authors and 85% cases by others. According to our data, histopathological and clinical data alone remained

successful in detecting primary site in 78.1% cases. This percentage is quite reasonable in context of unavailability of molecular and genetic typing for cancers.

In conclusion, our data is comparable to international data most common bone involved in females is hip bone whereas most common bones in males is vertebral column. Primary site in females is breast while that in males is prostate, these are comparable to international data.

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