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## PATTERN OF BONY METASTASIS IN DIFFERENT TYPES OF MALIGNANCY

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#### ABSTRACT

Bone pain is very common in different types of malignancy and is present in one third of patients suffering from carcinoma. After liver and lung bone is the third most common site of metastatic disease. Prostate, breast, lung, kidney and thyroid cancers accounts for 80% of skeletal metastasis. The most common site of bony metastasis are spine, pelvis, ribs, skull, and proximal femur. Aim of the present study is to evaluate pattern of bony metastasis, its side, laterality in different types of carcinoma. This is a retrospective nonrandomized study of 35 patients of differents type of malignancy with bone metastasis. Age ranges from 16 years to 90 years. Majority of patients 19(54.2%) belongs to 5<sup>th</sup> and 6<sup>th</sup> decade. 11(31.4%) were male and 24 (68.5%) were female. Out of 35 patients - 14(40%) were of breast cancer, 7(20%) cervical cancer patients, 4(11.4%) multiple myeloma, 4(11.4%) prostate, 4 (11.4%) head and neck cancer and 1 (2.8%) patient belongs to each group of ovary and renal cell carcinoma. Among all, spine was the most common site of metastasis. The domon site of femure. Ribs were most common site for breast cancer. Other sites were skull, sternum and scapula.

**KEYWORDS:** Bone scan, Bony metastasis, Pattern, Side, Laterality.

### INTRODUCTION

In the United State approximately 1. 2 million patients present with cancer each year. Of these, approximately 600,000 persons have metastases to bone. In contrast, 2,700 patients per year develop primary bone sarcoma. Metastases distal to the knee and elbow are extremely rare, 50% of these acral metastases are secondary to primary lung tumors (Healey et al 1986, Libson E et al 1987).

Bony pain is most common type of pain in cancer and is present in one third patients of carcinoma. After liver and lung bone is the third most common site of metastatic disease (Buckalter et al 1997,Jaffe et al 1958).Prostate, breast,lung, kidney and thyroid cancers account for 80% of skeletal metastasis(Buckalter et al 1997).The most common site of bony metastasis isspine, pelvis, ribs, skull, and proximal femur. Due to venous blood flow in Batsonsplexus predilection towards axial skeleton were seen.

The age range of patients with sarcoma is different from that of individuals with carcinoma of bone; most metastatic bone lesions occur in adults older than 50 years, while most sarcomas occur in adolescents or young adults below 30years of age. In females, the breastand lungs are the most common primary cancer sites; approximately 80% of cancers that spread to bone arise in these locations (Keens et al, 1986). In males, cancers of the prostate and lungs make up 80% of the carcinomas that metastasize to bone. <sup>[Edwards J et al 2010]</sup> The remaining 20% of primary disease sites in patients of both sexes are the kidney, gut, and thyroid as well as sites of unknown origin.

Most common complaint is pain is usually insidious in onset and is present in 70% of patients at presentation(Tillman et al 1999).Night pain and pain incompletely relieved by rest are not specific for metastasis, but they are typical symptoms. MBD damages and weakens bone and increase risk of fracture. This type of fracture is called pathological fracture. It detoriates the quality of life. Anaemia is the common blood abnormality in patients with metastatic breast disease.

For final diagnosis beside proper medical history, physical examination, different imagingare required. Xray of affected parts, CT scan and /or magnetic resonance imaging in cases where spine, or pelvis may be involved. Technetium Bone scan is not specific for metastatic bone disease. Positron Emission Tomography have both high sensitivity, and high specificity.

Biopsy should be confirmed the final diagnosis and various tumour marker like prostatic serum antigen, aiphafeto protein.

According to Fidler fractures are highly unlikely (2.3%) when less than 50% of cortical bone is involved. Risk increases to 80% if cortical bone involved 75% (Fidler Metal 1981). Pure lytic lesion are more likely to cause bone failure and least likely to heal. Blasticlesion are least likely to fracture. Mixed lesion are of intermediate risk (Harrington KD 1995,1986). Present study aims to understand pattern of bone metastasis in different types of malignancy.

### MATERIAL AND METHODS

This is a non-randomized, retrospective study conducted at department of Radiation Oncology, Mahavir Cancer Sansthan, Patna. Total number of 35 patients of metastatic bone disease wasevaluated during a period from March 2015 to March 2016which was approved by their ethical committee.

This study included patients of different types of malignancy who was treated for primary and developed bony metastasis on follow up or newly diagnosed cases for bony metastasis.All patients were examined to see primary disease status, or searched for primary in case of unknown primary. History regarding symptom, risk factor like addiction, chronic infection, exposure of prior ionizing radiation, family history were asked.Examination of thyroid, breast prostate, lung, skin is examined.Lab investigation include complete blood count, erythrocyte sedimentation rate, bloodchemistries, liver function tests, kidney function test, tumour marker. Painful site was examined by X ray, CTscan, Bonescan. MRI done in case of spine, pelvis. Once patients were diagnosed as metastatic bone disease and not relieved by narcotic then assessed for palliative radiotherapy to most painful site. In case of pathological fracture internal fixation done prior to radiotherapy. Majority of patients were treated with palliative radiotherapy dose depends on performance status of patients. In case of pathological fracture internal fixation done prior to radiotherapy.

### RESULTS

In this retrospective nonrandomized study out of 35 patients age ranges from 16 years to 90 years. Majority of patients 54.2% belongs to 5<sup>th</sup> and 6<sup>th</sup> decade (Table-1, Graph-1).Out of total patients 31.4% were male and 68.5% were female (Table-2, Graph-2). Out of totalpatients 71.4% patients had no addiction,11.4% patients were addicted to tobacco chewing, and 11.4% patients were addicted to smoking, none of the patients addicted to alcohol alone. In combination group tobacco and smoking 2.8% patient, tobacco and alcohol 2.8% patient (Table-3, Graph-3).In our study different types of

malignancyinclude40% were of breast cancer, cervical cancer 20% patients, multiplemyeloma 11.4%, and prostate11.4%. Head and neck cancer11.4%. 2.8% patient belongs to each group of ovary, renal cell carcinoma (Table-4, Graph-4).

Histologically37.1% were of invasive duct carcinoma, 25.7% patients belongs to squamous cell carcinoma, 14.2% patients were adenocarcinoma,11.4% patients of plasma cellmyeloma, 2.8% patient in each group of lobularcarcinoma, adenosqamous, clear cell carcinoma and sarcoma. For the laterality of bony metastasis in patients, unilateral site were seen in 25.7%, bilateral site in 14.2%, vertebrae alone 11.4% patients. Unilateral and vertebrae in 17.1%, bilateral and vertebrae in 31.4% patients (Table-5).

Among all site spine were the most common site of metastasis in 60% patients. Out of which 22.8% patients were of breast, 14.2% were of cervix, 8.5% patients belongs toprostate and multiple myeloma each 2.8% patient belongs to renal cell carcinoma and head and neck carcinoma each.In51.4% patient pelvis were second common site for metastasis. Breast cancer 20%, prostate cancer 11.4%, cervical cancer and multiple myeloma 5.7% patient in each group. Third most common site were proximal end of femur. Total 25.7% patients metastasizes to above site. Breast cancer 11.4% patients, head and neck cancer 8.5% patients, 2.8% patient of each group of multiple myeloma and cervical cancer. Ribs were most common site for breast cancer 14.2% patients. Skull were most common site for multiple myeloma 5.7% and breast cancer 5.7% patients. Sternum and scapula were observed in11.4% patients of breast cancer. Less common site were humerus 8.5% and clavicle 5.7%. No metastasis seen in tibia, fibula (Table-6).Out of total patients 8.5% had a pathological fracture so they underwent internal fixation prior to radiotherapy (Table-7, Graph-5).

#### Table 1: Age.

Age range(years)	Number	%
10-29	2	5.7
30-49	10	28.5
50-69	19	54.2
70-89	3	8.5
90-109	1	2.8

Table 2: Sex.

Sex	number	%
Male	11	31.4
Female	24	68.5

## Table 3: Addiction.

Addiction	number	%
Tobacco chewing	4	11.4
Smoking	4	11.4
Alcohol	0	0
Tobacco+Smoking	1	2.8
Tobacco+Alcohol	1	2.8
Smoking+Alcohol	0	0
None	25	71.4

## Table 4: Site.

Site	number	%
Breast	14	40
Cervix	7	20
Ovary	1	2.8
Multiple myeloma	4	11.4
Prostate	4	11.4
Renal cell carcinoma	1	2.8
Head and neck	4	11.4

## Table 7: frequency of anatomical distribution.

## Table 5: Histopathology.

	number	%
Invasive duct ca	13	37.1
Lobular ca	1	2.8
Squamous cell ca	9	25.7
Adenoca	5	14.2
Adenosquamous	1	2.8
Clear cell ca	1	2.8
Sarcoma	1	2.8
Plasma cell myeloma	4	11.4

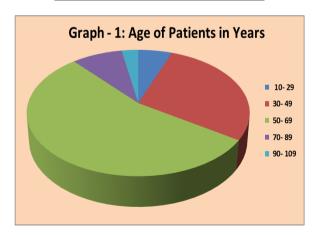
## Table 6: Laterality of bony metastasis.

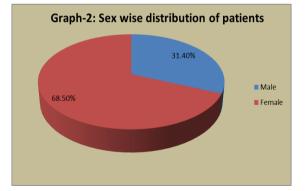
Side of mets	number	%
Unilateral	9	25.7
Bilateral	5	14.2
Unilateral+vertebra	6	17.1
Bilateral+vertebra	11	31.4
Vertebra alone	4	11.4

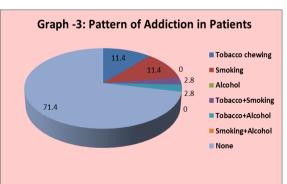
Site	Totaln=35	Breast	Prostate	Cervix	<b>Ovary</b>	M.myeloma	RCC	Head &neck
Spine	21(60%)	8(22.8%)	3(8.5%)	5(14.2%)	0	3(8.5%)	1(2.5%)	1(2.5%)
Pelvis	18(51.4%)	7(20%)	4(11.4%)	2(5.7%)	1(2.5%)	2(5.7%)	1(2.5%)	1(2.5%)
Ribs	7(20%)	5(14.2%)	0	1(2.5%)	0	0	1(2.5%)	0
Sternum	4(11.4%)	2(5.7%)	0	0	0	0	1(2.5%)	1(2.5%)
Femur	9(25.7%)	4(11.4%)	0	1(2.5%)	0	1(2.5%)	0	3(8.5%)
Scapula	4(11.4%)	3(8.5%)	0	1(2.5%)	0	0	0	0
Skull	5(14.2%)	2(5.7%)	0	1(2.5%)	0	2(5.7%)	0	0
Humerus	3(8.5%)	1(2.5%)	1(2.5%)	0	0	0	0	1(2.5%)
Clavicle	2(5.7%)	1(2.5%)	0	1(2.5%)	0	0	0	0
Tibia,fibula	0	0	0	0	0	0	0	0

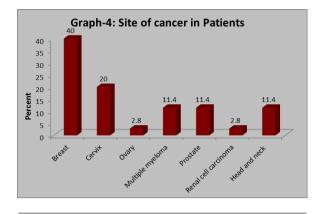
## Table 7: Pathological fracture.

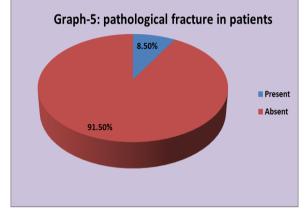
Status	Number	%
Present	3	8.5
Absent	32	91.4











### DISCUSSION

However, there have been only limited guidelines published on early detection and management of metastasis. Screening for bone metastasis is not currently recommended for all types of primary cancer. Some bone metastases, e.g., rapidly progressive cancers including lung cancer, can be concomitantly found before the primary site diagnosis has been accomplished (Nguyen et al., 2009). Breast cancer with bone metastasis presents a better prognosis compared with other sites of distant metastasis. The long survival period might be expected to found the second and third skeletal related events (McDougall et al., 2016; Tanaka et al., 2016).

Identification of primary cancer in patients suspected bone metastasis in adults and elderly patients is a critical step. Decision-making regarding metastasis is even more difficult in urgent situations including spinal cord compression and pathological fracture. At the same time, primary tumor identification is time-consuming and involves multiple investigative steps (Takagi et al., 2015).

A study of 2,641 bone metastases in Japan found the origins of the three most common carcinoma metastases were from lung, prostate and liver cancer (Takagi et al., 2015). The three leading bone metastases in the US originated from breast, prostate and lung cancer (Li et al., 2012; Oster et al., 2013). In Germany, the top three originated from breast, lung and prostate cancer (Tarnoki et al., 2016), in the UK the top three bone metastases originated from breast, prostate and thyroid cancer

(Coleman, 2001), and in Malaysia the top three originated from breast, lung and prostate cancer (Singh et al., 2014). In our study, the primary cancers with the lowest incidence of metastatic bone disease were seen in carcinoma of the ovary and Renal cell carcinoma.

Lung cancer is known to have a fast progression and short latency time, which was relating to skeletal-related events presentation before or concurrent primary tumor was diagnosed. Bone metastasis concurrent with lung cancer diagnosis has been reported in between 38.4% and 41.0% of cases (Tsuya et al., 2007).

Bone metastasis in hepatocellular carcinoma presents in 16 to 25.4% of cases (Uchino et al., 2011; Abbas et al., 2014). Coleman showed that close to 80% of advanced breast and prostate cancer patients would eventually develop skeletal metastases.( Coleman RE 2006). A postmortem study by Harrington reported high incidences of bone metastasis in breast and prostate cancers (84%). Breast, lung and prostate cancers commonly metastasize to the spine, as they have a higher prevalence and predilection toward bone metastasis (Quattrocchi et al, 2007). In our study, there was a lower percentage of bone metastasis for prostate cancer compared to breast cancers. This could be due to the low number of patients of prostate cancer and higher number of breast cancer in our hospital.

## CONCLUSION

Spine was the most common site of metastasis, pelvis were second common site for metastasis Third most common site was proximal end of femur. Ribs were most common site for breast cancer. Other sites were skull, sternum and scapula.

### REFERENCES

- 1. Abbas A, Medvedev S, Shores N, et al Epidemiology of metastatic hepatocellular carcinoma, a nationwide perspective. Dig Dis Sci, 2014; 59: 2813-20.
- 2. Alarmo EL, Kallioniemi A. Bone morphogenetic proteins in breast cancer dual role in tumourigenesis?. EndocrRelat Cancer, 24 Mar 2010.
- Buckwalter J. A, Brandser E A. Metastatic disease of the skeleton. Am Fam Physician, 1997; 55: 1761-8.
- 4. Chow E, Hoskin P, Vander Linden Y, Bottomley A, Velikova G. Quality of life and symptom end points in palliative bone metastasis trials. Clin Oncol (R CollRadiol), 2006; 18: 67-9.
- 5. Coleman RE Metastatic bone disease: clinical features, pathophysiology and treatment strategies. Cancer Treat Rev, 2001; 27: 165-76.
- 6. Coleman RE Clinical features of metastatic bone disease and risk of skeletal morbidity. Clin Cancer Res, 2006; 12: 6243s-9s.

- Coleman RE. Clinical features of metastatic bone disease and risk of skeletal morbidity. Clin Cancer Res, 2006; 12: 6243s-9s.
- Coleman RE. Metastatic bone disease: clinical features, pathophysiology and treatment strategies. Cancer Treat Rev, 2001; 27: 165-76.
- 9. Coleman RE. Metastatic bone disease: clinical features, pathophysiology and treatment stategies. Cancer Treat Rev, 2001; 27: 165-76.
- Doot RK, Muzi M, Peterson LM, Schubert EK, Gralow JR, Specht JM, et al. Kinetic analysis of 18F-fluoride PET images of breast cancer bone metastases. J Nucl Med, 2010; 51(4): 521-7.
- 11. Edwards J. Src kinase inhibitors: an emerging therapeutic treatment option for prostate cancer. Expert OpinInvestig Drugs, 5 Apr 2010,
- 12. Fidler M. Incidence of fracture of metastasis in long bones. Acta Orthop Scand, 1981; (249): 256-64.
- 13. Harrington KD. Impending pathologic fractures from metastatic malignancy: evaluation and management. Instr Course Lect, 1986; 35: 357-81.
- Harrington KD. Orthopaedic management of extremity and pelvic lesions. ClinOrthopRelat Res, 1995; (312): 136-47.
- 15. Healey JH, TurnbullAD, MiedemaB, LaneJM. Acrometastasis. A study of twenty nine patients with osseous involvement of hand and feet. J Bone Joint Surg Am, 1986; 68: 743-6.
- Hung JJ, Jeng WJ, Hsu WH, Wu KJ, Chou TY, Hsieh CC, et al. Prognostic factors of postrecurrence survival in completely resected stage I non-small cell lung cancer with distant metastasis. Thorax, 2010; 65(3): 241-5.
- 17. Jaffe HL.Tumors metastatic to the skeleton .In:Jaffe HL editor.Tumors and tumorous condition of bones and joints. Philadelphia: Lea and Febiger, 1958.
- Keene JS, Sellinger DS, McBeath AA, et al. Metastatic breast cancer in the femur. A search for the lesion at risk of fracture. ClinOrthopRelat Res., 1986; (203): 282-8.
- 19. Li S, Peng Y, Weinhandl ED, et al Estimated number of prevalent cases of metastatic bone disease in the US adult population. ClinEpidemiol, 2012; 4: 87-93.
- LibsonE, BloomRA, HusbandJE, StokerDJ, Metastatictumours of bones of hand and foot. A comparative review and report of 43 additional cases. Skeletal Radiol, 1987; 16: 387-92.
- 21. McDougall JA, Bansal A, Goulart BH, et al The clinical and economic impacts of skeletal-related events among medicare enrollees with prostate cancer metastatic to bone. Oncologist, 2016; 21: 320-6.
- 22. Mirels H. Metastatic disease in long bones. A proposed scoring system for diagnosingimpending pathologic fractures. ClinOrthopRelat Res, 1989; 256-64.
- Nguyen DX, Bos PD, Massagué J Metastasis: from dissemination to organ-specific colonization. Nat Rev Cancer, 2009; 9: 274-84.

- 24. Oster G, Lamerato L, Glass AG, et al Natural history of skeletal-related events in patients with breast, lung, or prostate cancer and metastases to bone: a 15-year study in two large US health systems. Support Care Cancer, 2013; 21: 3279-86.
- 25. Quattrocchi CC, Piciucchi S, Sammarra M, et al. Bone metastases in breast cancer: higher prevalence of osteosclerotic lesions. Radiol Med (Torino), 2007; 112(7): 1049-59.
- SundaresanN, Digiacinto G V,KrolG,Hughes J E.Spondylectomy for malignant tumour of the spine. JClinOncol, 1989; 7: 1485-91
- 27. Takagi T, Katagiri H, Kim Y, et al Skeletal Metastasis of Unknown Primary Origin at the Initial Visit: A Retrospective Analysis of 286 Cases. PLoS One, 2015; 10: 129428.
- 28. Tanaka R, Yonemori K, Hirakawa A, et al Risk factors for developing skeletal-related events in breast cancer patients with bone metastases undergoing treatment with bone-modifying agents. Oncologist, 2016; 21: 508-13.
- 29. Tarnoki DL, Tarnoki AD, Ohlmann-Knafo S, et al Pattern of Tumour Spread of Common Primary Tumours as Seen on Magnetic Resonance Imaging. PatholOncol Res, 2016; 22: 79-85.
- 30. Tillman RM. The role of the orthopaedic surgeon in metastatic disease of the appendicular skeleton. Working Party on Metastatic Bone Disease in Breast Cancer in the UK. J Bone Joint Surg Br, 1999; 81: 1-2.
- 31. Townsend PW,RosenthalHG,Smalley SR et al.Impact of postoperative radiation therapy and other perioperative factors on outcome after orthopaedic stabilization of impending or pathological fracture due to metastasicdisease.JClinOncol, 1994; 12: 2345-50.
- 32. Tsuya A, Kurata T, Tamura K, et al Skeletal metastases in non-small cell lung cancer: a retrospective study. Lung Cancer, 2007; 57: 229-32.
- Uchino K, Tateishi R, Shiina S, et al Hepatocellular carcinoma with extrahepatic metastasis: clinical features and prognostic factors. Cancer, 2011; 117: 4475-83.