JK SCIENCE pISSN: 0972-1177

ORIGINAL ARTICLE

Histopathological Study of Bone Tumours- 4 Years Study in A Tertiary Care Centre

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Abstract

Background : Tumors of the bone constitute 0.5% of the total world cancer incidence. Histogenesis of these tumors is still uncertain. Relevant demographic features such as age, sex and skeletal site; detailed clinical history and radiographic findings are important for a conclusive diagnosis. **Objective:** To evaluate the histopathological features of bone tumours and to correlate these bone lesions with age, sex, clinical presentation, anatomical location and radiological findings.**Material & Method:** This retrospective study was conducted in the Postgraduate Department of Pathology, GMCH Jammu for a period of 4 years. The present study included 64 cases of bone tumours admitted to GMCH Jammu. Ethical clearance has been taken from the ethical committee of the institute GMCH Jammu. **Result:** A total of 64 cases were studied out of which 36 (56.26%) cases were benign; 17 (26.56%) cases were of primary malignant lesion and 11 (17.18%) cases were of metastasis to bone. Among benign tumours, most common tumour was Giant Cell Tumor (GCT) and among malignant tumours most common tumour was osteosarcoma. **Conclusion:** Bone tumours pose a challenge to the Pathologists, Radiologists and Orthopedic surgeon because of their varied presentation, uncertain histogenesis and their behaviour to treatment.

Key Words

Bone Tumors, Chondrosarcoma, Giant cell Tumor, Osteosarcoma

Introduction

Bone tumours are relatively rare in comparison to tumour in other parts of the body. They constitute 0.5% of the total world cancer incidence. [1] In developed countries bone tumours are quite infrequent [2], while in developing countries the prevalence of bone cancers is relatively high. In the WHO classification, most bone neoplasms are classified as either benign or malignant. Although a sharp distinction between these two categories is feasible in most of them, some neoplasms exhibit borderline and intermediate characteristics. Etiologically, most bone tumours arise de novo from somatic mutations, but other factors also contribute. The important causes include chemotherapy [3], irradiation, pre existing bone lesions and less commonly trauma, foreign body and viruses. Bone tumours occur mainly between the first and fourth decade of life and have a potential devastating effect on the most productive segment of the population. [4] Bone tumors are diverse in their clinical, radiological and morphological features and range in behaviour from non dangerous to rapidly fatal. Definitive clinical diagnosis of bone lesion is often difficult. Radiography is a first approach in a diagnosis of any bone lesion. Besides high technology techniques CT scan (Computed Tomography) MRI (Magnetic Resonance Imaging) or bones scintigraphy; histopathology provided the final and conclusive diagnosis of the bone lesions.

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Manuscript Received: 1.10. 2021; **Revision Accepted**: 21.12. 2021;

Published Online First: 10 Oct, 2022

Open Access at: https://journal.jkscience.org

Cite this article as: Rani R, Gupta I, Suri J. Histopathological Study of Bone Tumours- 4 Years Study in A Tertiary Care Centre. JK Science 2022;24(4):243-248

Benign bone tumors out-number the primary malignant tumors. The most common benign and malignant tumours were GCT and osteosarcoma respectively. Accurate diagnosis and appropriate treatment are thus necessary to ensure maximum patient survival and maintain optimal function of an affected body part. [5] An integrated approach involving clinical findings, radiologic and histologic findings are thus necessary to make an accurate diagnosis. The present study aims to evaluate the histopathological features of bone tumours and to correlate the bone lesion with age, sex, clinical presentation, anatomical location and radiological findings.

Objective

To evaluate the histopathological features of bone tumours and to correlate the bone tumours with age, sex, clinical presentation, anatomical location and radiological findings.

Material and Method

Present study was conducted retrospectively in the Postgraduate Department of Pathology, GMCH Jammu for a period of four years. The four years record from December 2020 to January 2017, of all the bone specimens and biopsies received in the Department of Pathology (histopathology section) was retrieved from archives of the histopathological section of the Department. Age, sex, clinical details, site and radiological findings were recorded from available documents. Histological slides were retrieved and reviewed. The slides which were faded or missing; the paraffin blocks were sought out and new slides were made and stained with routine Hematoxylin and Eosin stain. The histopathology diagnosis was correlated with the plain radiological features. A total of 64 cases were included in the study, which were having the complete file record, regardless of their age and sex. The relevant demographic and clinical details were recorded on a proforma designed for the study. Tumours were classified as recommended by the WHO international reference centre for histological definition and classification of bone tumours.

Patients with infective, inflammatory bone lesions and bone tumours of odontogenic origin were excluded from the study.

Result

A total of 64 cases of bone tumors were identified in the period of December 2020 to January 2017. Among neoplastic lesion incidence of benign tumors was 36 (56.26 %) and malignant tumours were 28 (43.75%). There were 52 cases of Primary Bone Tumors and 12 cases of metastatic bone tumors (*Table-1*). The long bones are frequently involved in most of the bone tumors and were around the knee joint showing a high frequency of involvement (*Table-4*).

The patients were aged between 7 to 81 years with a mean of 32 years. Among these 64 cases 27 (42.18%) were males and 37 (57.82%) were females. The peak age incidence was observed in 20 - 40 years of age (*Table- 3*). Out of 64 cases the malignant tumors were diagnosed in 28 (43.75%) cases among these 13 (46.43%) cases in male patients and 15(53.57%) cases in female (*Table-1)*. The overall benign tumors were observed in 36 (56.26%) cases, and among these 14 (38.8%) cases were male and 22 (61.2%) cases were female (*Table - 1*).

Osteosarcoma (*Fig-1*) constitutes the most common primary malignant bone tumors followed by Chondrosarcomas, and Ewing's Sarcomas (*Table-1*). Among the benign lesions Giant Cell Tumor (GCT) (*Fig-2*) was the most common followed by Osteochondroma (*Table-1*).

Osteosarcomas and Chondrosarcomas constituted the most common primary malignant bone tumors. Age range of Osteosarcoma was 9-45 years with M:F ratio of 0.3:1. 8 cases were observed at the distal end of femur and 5 cases at proximal end of tibia. Age range of Chondrosarcoma was 46-60 years and M: F approx. 1:1. One case was diagnosed in the Pelvic bone and other from the distal end of femur. 1 case of Ewing's Sarcoma was located at proximal end of humerus in present study. Giant Cell Tumor was the most common benign bone tumor. M: F ratio was 1:2. 7 cases were observed at distal end of femur, 5 cases at the proximal end of tibia and 3 at proximal end of humerus. Majority of the cases were seen between 31-45 years whereas two cases were below 15 years.

In our study metastatic bone tumors constituted 18.7% of the cases. Majority of the cases were of more than 40 years of age (90.9%). The commonest metastatic sites were vertebra (27.27%), ankle (18.18), femur (18.18%), pelvis (9.09%), scapula (9.09%), ribs (9.09%) and tibia (9.09%) (Table-4) . The sites for primary tumors were lung cancers, breast cancer, prostatic carcinoma, malignant melanoma and squamous cell cancers. Majority were metastatic adenocarcinomas (*Table-2)*.

Histopathological features were correlated with plain radiographic findings. The radiological pattern in benign osteoid tumor is a nidus with central translucent area with surrounding bone sclerosis and in benign cartilaginous lesions is an area of translucency surrounded by calcifications in some lesions. The radiological pattern in osteosarcoma show metaphyseal lesion that show cortical destruction and radiographic appearance of chondrosarcoma show lytic, metaphyseal based lesion with cortical erosion and soft tissue extension.

Table - 1 Gender and Proportion Distribution of Bone Lesion

BONE LESIONS	Male (n)	%age	Female (n)	%age	Total (n)	%age
BENIGN BONE LESIONS						
GCT	5	7.82	10	15.63	15	23.4
Osteochondroma	6	9.37	7	10.94	13	20.3
Osteoma	3	4.68	2	3.13	5	7.8
Chondroma	-	-	2	3.13	2	3.1
Chondroblastoma	-	-	1	1.56	1	1.5
MALIGNANT BONE LESIONS						
Osteosarcoma	3	4.68	10	15.63	13	20.3
Chondrosarcoma	1	1.56	1	1.56	2	3.1
Ewings Sarcoma	1	1.56	-	-	1	1.5
Metastasis to bone	8	12.5	4	6.25	12	18.7
TOTAL	27	42.17	37	57.83	64	100

Table -2 Type and Gender Distribution of Metastatic Lesions to Bone.

METASTASIS TO BONE	MALE	FEMALE
Bronchogenic adenocarcinoma	2	-
Squamous cell carcinoma	2	3
Prostatic adenocarcinoma	3	-
Breast carcinoma	-	1
Malignant Melanoma	1	-
TOTAL	8	4

Radiography of GCT shows epiphyseal based lytic lesions with well defined margins. Metastatic lesions have multiple appearance. Metastatic prostate cancer, Breast cancer and lung cancer shows sclerotic lesion; whereas malignant melanoma shows lytic lesion in plain radiograph. Of all the cases in the radiographic pattern, osteolytic types were most common followed by osteosclerotic and mixed types (*Table -5*).

Out of these 64 cases clinicoradiological diagnosis were

Table -3 Age Wise Distribution of Bone Lesions

BONE LESIONS	<15 Years	16-30 Years	31-45 Years	46-60 Years	>60 Years
Giant cell tumor (GCT)	2	3	7	3	-
Osteochondroma	6	7	-	-	-
Osteoma	2	3	-	-	-
Chondroma	-	1	1	-	-
Chondroblastoma	-	1	-	-	-
Osteosarcoma	4	5	3	-	1
Chondrosarcoma	-	-	-	2	-
Ewings Sarcoma	-	1	-	-	-
Metastatic tumors	-	1	4	4	3
TOTAL	14	22	15	9	4

Table -4 Site distribution of Bone Tumor

BONE LESIONS	SITE
Giant cell tumour (15)	Femur; lower end (LE) - 7 Humerus; upper end (UE) - 3 Tibia (UE) – 5
Osteochondroma (13)	Femur (UE) - 3 Femur (LE) - 1 Tibia (UE) – 5 Calcaneum - 1 Rib - 3
Osteoma (5)	Hard palate – 1 Left ulna (LE) – 1 Right mandible - 1 Left humerus (LE) - 1 Right hand – 1
Chondroma (2)	Right little finger- 1 Left ankle- 1
Chondroblastoma (1)	Left tibia (UE) - 1
Osteosarcoma (13)	Left Femur (LE) -6 Right Femur (LE)- 2 Left tibia (UE)- 4 Right tibia (UE) - 1
Chondrosarcoma (2)	Right iliac bone- 1 Left femur (LE) - 1
Ewings (1)	Left humerus (UE)- 1
Malignant melanoma (1)	Right ankle – 1
Bronchogenic adenocarcinoma (2)	Lumbar vertebrae - 1 Rib – 1
Squamous cell carcinoma (5)	ankle – 2 Left femur – 1 Right tibia – 1 Right scapula- 1
Breast carcinoma (1)	Right femur (UE)- 1
Prostatic adenocarcinoma (3)	Lumbar vertebrae - 2 Left iliac bone – 1

Table-5 Radiological Findings of Bone Lesions

BONE TUMORS	RADIOLOGICAL FINDINGS ON PLAIN X-RAY
Giant cell tumour	Lytic lesions with well defined non sclerotic margins at epiphysis
Osteochondroma	Projections from the bone surface
Osteoma	Round lucency at metaphysis surrounded by sclerotic bone
Chondroma	Lytic lesions with sharply defined margins at metaphysis
Chondroblastoma	Lytic lesions with lobulated margins and thin sclerotic rim at epiphysis
Osteosarcoma	Sclerotic and destructive lesions giving sunburst appearance, periosteal lifting with formation of codman's triangle with new bone formation
Chondrosarcoma	Lytic lesions with cortical thickening and endosteal scalloping at epiphysis
Ewings sarcoma	Intramedullary lytic lesion with periosteal reaction
Malignant melanoma	Lytic lesion
Metastatic tumors	70% cases presented with pathological fractures and 30% cases showed lytic lesion on plain X-ray.

Table-6 comparison of Histological Diagnosis versus Radiological Diagnosis of Bone Tumors.

RADIOLOGICAL DIAGNOSIS	HISTOLOGICAL DIAGNOSIS (gold standard)		TOTAL
	Malignant bone tumor	Benign bone tumor	
Malignant bone tumor	22	7	29
Benign bone tumor	6	29	35
TOTAL	28	36	**64**

Fig-1 H&E Stained Sections from Osteosarcoma Showing Osteoid Formed from highly Pleomorphic Tumor Cells (20X). Inset is Showing Highly Pleomorphic Tumor Cells and Multinucleated Giant Cells s (40X).

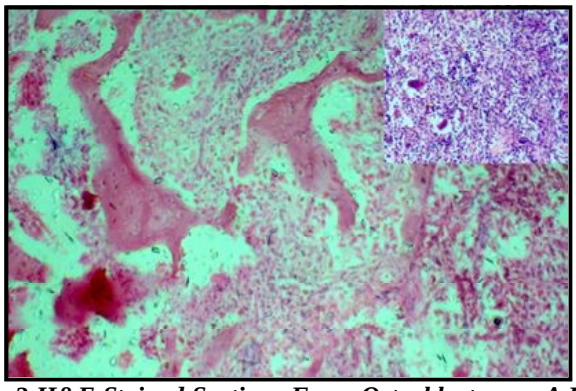


Fig.3 H&E Stained Sections From Osteoblastoma . A Foci of Cartilageneous Matrix (20X). Inset is Showing Mature Bony Trabeculae lined by Osteoblast in a Highly Vascular Stroma (40X).

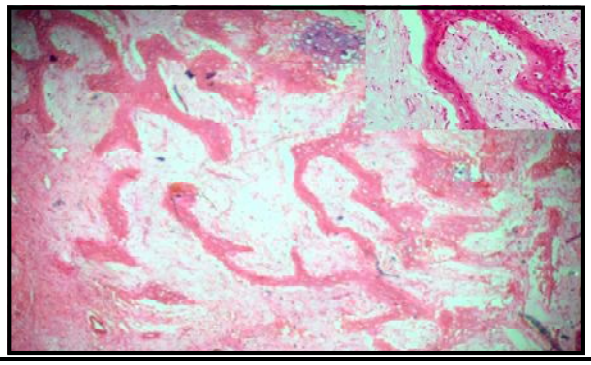
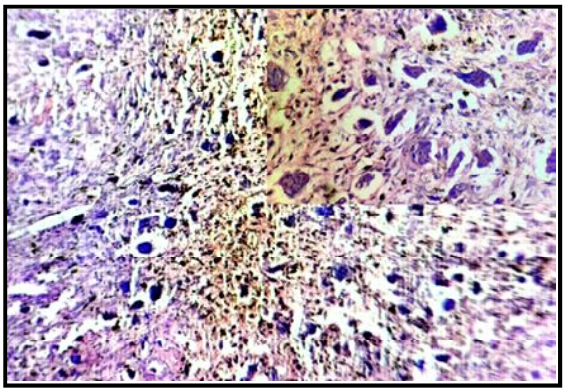


Fig-2 H&E Stained Sections from Giant Cell Tumour Showing Regular & Uniform Arrangement of Multinucleated Giant cells (20X). Inset is Showing Neoplastic Mononuclear cells and Multinucleated Giant Cells (40X).



offered in 51 cases. Radiography offered exact diagnosis in 29 cases out of total 36 benign cases and in malignant bone tumors, radiography offered diagnosis in 22 cases out of total 28 cases. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of clinicoradiological diagnosis when compared to histopathological diagnosis in case of bone tumours were found to be 78.57%, 80.56%, 75.86% and 82.86% respectively (*Table-6*).

Most of these patients presented with pain, swelling, refusal to use of the part, decrease range of motion or a hard and fixed mass that may be tender. Few patients with primary malignant bone lesions and patients with metastatic bone lesions presented with fracture after seemingly minor trauma. Pain was more common with

malignant lesions usually present at rest or at night and non responsive to non steroidal anti inflammatory drugs (NSAIDS) or weak narcotics. Few patients presented with systemic symptoms such as fever, weight loss and decrease in appetite.

Discussion

Bone tumours are rare and geographical variations in the occurrence of bone tumours have been established in many studies. [6,7] In our study, absence of major aetiological agents such as irradiation, thorotrast and alkylating agents may have had a significant role to play in the general rarity of primary bone tumors in our environment. Present study was conducted retrospectively over a period of 4 years, and during this period we have diagnosed total of 64 cases of neoplastic lesions of bones. Out of 64 cases, benign lesions were found to be more common (56.25%) than malignant lesions (43.75%) which is comparable with the studies conducted by Gururajprasad C et al and Yopovinu Rhutso *et al.* [8, 9] Age ranged from 7 years to 81 years. Most tumors showed female preponderance with male to female ratio of 0.69:1; which is in contrast to the studies conducted by Abdulkareem F B e*t al* [10] and Sharma S *et al* [11], they found male preponderance in their study which could be due to environmental and genetic factors. The peak age incidence for benign and malignant bone tumors was in the second and third decades of life. This finding is in agreement with that of Odetayo (Lagos). [12]

In our study we have found, GCT (*Fig-2*) is the most common followed by Osteochondroma among benign tumors. Study conducted by Naz *et al* [13] also shows GCT as the most common benign lesion while the study conducted by Kannan *et al* [14] shows Osteochondroma as the most common benign tumor. Radiographic findings of GCT shows epiphyseal located lesions with well defined margin. Out of total 15 GCT cases; radiography offered the diagnosis in 11 cases. GCT are locally aggressive tumor of uncertain histogenesis and it shows a range of biological behaviour from completely benign tumor to tumor producing pulmonary metastasis; even though they appear histologically benign. Radiography of Osteochondroma offered diagnosis in 8 cases out of 13 cases and 5 cases were reported as benign bone lesions. Present study shows Osteosarcoma as the most common malignant tumor of bone, particularly of long tubular bones followed by Chondrosarcoma. Study conducted by Bahebeck *et al* [15] also shows the same. Osteosasrcoma usually occurs in patients between 10 and 25 years (Primary osteosarcoms) and is exceptionally rare in preschool children. Another peak age incidence occurs after 40 years. [16] Secondary Osteosarcomas occurs following Paget's disease, chemotherapy, radiation or metallic implants. We have found that majority of the Osteosarcoma cases occurs in below thirty years of age group and pain and swelling was rhe commonest symptoms; which is comparable with the study conducted by Negash *et al* [17] Out of 13 cases of Osteosarcoma; 12 cases were reported correctely on radiography; 1 case was misdiagnosed as benign bone tumor. Radiography offered diagnosis in all 2 Chondrosarcoma cases. Chondrosarcomas arising de novo in bone and are designated as primary Chondrosarcomas. Those arising from previously benign cartilaginous lesions are referred to as secondary Chondrosarcomas. [18] Pain was the commonest symptom in most of the Chondrosarcomas. Present study shows only one case of Ewings sarcoma among all 28 malignant bone lesions. On X-ray Ewings sarcoma was classified wrongly as Osteosarcoma. It is a uncommon neoplasms with uncertain histogenesis and clubbed with PNET as both share certain molecular features and viewed as variants of each other. In our study, the most frequently involved bone in primary bone tumour is femur and this finding is consistent with that of Solomon in south Africa and Ahmed *et al* in Pakistan [19] The peak age incidence of primary bone tumors in our study was seen between 15-45 years, which is comparable with the study conducted by Settakorn *et al* . [20]

The skeletal system is the third commonest site involved by metastatic tumor after lung and liver. Vertebra was the commonest site which is also seen in the study conducted by Coleman R E *et al.* [21] Metastatic bone tumors were seen in patients with age of more than 45 years. In present study we have found 12 cases of metastatic tumors in bone, these patients were presented with pathological bone fracture and few were presented with bony pains. 8 cases were found in males whereas 4 cases were found in females. In males, primaries were identified as Bronchogenic carcinoma in 2 patients and Prostatic adenocarcinoma in 3 patients; primaries in 2 cases of SCC and 1 case of malignant melanoma remain occult. In females; 1 case was identified with carcinoma breast; whereas primaries in 3 cases of SCC remain occult. X- ray findings in cases of metastasis to bone show lytic lesions in 8 cases and in 4 cases ; sclerotic bone lesions were seen. 10 cases were presented with pathological fracture and 2 were diagnosed incidentally. Definitive diagnosis of metastasis to bone was possible only on histopathology.

The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of clinicoradiological

diagnosis when compared to histopathological diagnosis in case of bone tumours were found to be 78.57%, 80.56%, 75.86% and 82.86% respectively which is comparable with the study conducted by Salazar C *et al* [22]

Conclusion

Bone tumours pose a challenge to the Pathologists, Radiologists and Orthopedic surgeon because of their varied presentation, uncertain histogenesis and their behaviour to treatment. Histopathological diagnosis of bone tumors requires clinical & radiological correlation. A sincere effort is made to diagnose & help the patients. Histopathology is the gold standard for the precise diagnosis from a very large number of conditions leading to bone lesions. It is worth memorising that "you miss the diagnosis of a malignant bone tumour, you lose the life of the patient; you misdiagnose as a malignant lesion, you lose the limb of the patient'.

Financial Support and Sponsorship
Nil.

Conflicts of Interest
There are no conflicts of interest.

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