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PRIMARY TUMOURS OF BONE – A MORPHOLOGICAL STUDY

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ABSTRACT

INTRODUCTION: Bone tumours are rare, amounting to only 0.2% of the overall human tumour burden. A systemic approach to clinical history, radiological evaluation and histopathology data is necessary for an accurate diagnosis. In this study, the clinicopathological features of primary bone tumours were analysed. METHOD: The cases were retrieved from the archives of the Department of Pathology from January 2016 to December 2018. RESULT: A total of 50 cases were found. The patients were aged 6 to 70 years. Out of these 36 (72%) patients were males and 14 (28%) were females. Most of the bone tumours observed in our study were benign 39/50 (78%). Giant cell tumour was the most common with 25/50 cases (50%), followed by osteochondroma 8/50 (16%), chondroblastoma 3/50 (6%), ossifying fibroma 2/50 (4%), and aneurysmal bone cyst 1/50 (2%). Primary malignant bone tumours in our study were 11/50 (22%), including osteosarcoma 5/50 (10%) and chondrosarcoma 5/50 (10%) were the most common followed by Ewing's sarcoma 1/50 (2%).
CONCLUSION: Benign bone tumours were found to be more common than malignant tumours. Histopathological diagnosis of bone tumours should always be made in conjunction with clinical and radiological findings.

INTRODUCTION:

Primary neoplasms of the skeleton are rare, amounting to only 0.2% of the overall human tumour burden.[1] These present with nonspecific sign and symptoms.[2] Bone tumours are extremely heterogeneous groups of neoplasm consisting of varieties of benign and malignant conditions which develop from embryonic mesoderm and are categorized according to their differentiated histology.[3] Therefore, an integrated approach involving clinical, radiographic and histologic data are necessary to form an accurate diagnosis so as determine the degree of activity and malignancy of each lesion. A proper histopathological diagnosis is useful in confirming the diagnosis. Bone tumours commonly present with progressive pain, swelling, tenderness and in some cases as an acute pathological fracture.[4] Early diagnosis and treatment are important for improving the quality of life and survival rate in patients with malignant bone tumors.[5] In this study the histopathological features of primary bone tumours were studied along with the clinico-radiological findings.

METHOD:

A combined retrospective and prospective study was conducted from January 2016 to December 2018, in the Department of Pathology. The relevant clinical and radiological information (X-ray, CT scan, and MRI) of these patients was obtained by reviewing records maintained by the institution.

RESULTS:

This study of clinical presentation, radiological examination corroborated with histological appearances yielded 50 cases of primary bone tumours between the ages 6 to 70 years. Among the 50 cases, 36(72%) cases were males and 14 (28%) were females. Commonest bone tumours observed in our study were benign 39(78%), and 11 (22%) were malignant. Details of the primary bone tumours in our study are given in Table 1. The radiological and microscopic findings of the tumours encountered in our study are shown in figures 1 to 7.

Table 1: Distribution of frequency, age and sex of primary malignant bone tumours

Serial No	HPE diagnosis	No. of cases (percentage)	Age range in years	Male	Female	Site
	BENIGN					
1.	Giant cell tumour	25(50%)	13-57	17	8	Femur(18) Tibia(7)
2.	Osteochondroma	8(16%)	6-25	6	2	Femur (5), Tibia (3)
3.	Chondroblastoma	3 (6%)	18	3	-	Femur (3)
4.	Ossifying fibroma	2 (4%)	11-45	2	-	Mandible(2)
5.	Aneurysmal Bone cyst	1 (2%)	18	-	1	Femur
MALIGNANT						
6.	Chondrosarcoma	5(10%)	17-70	4	1	Ilium (3), vertebra (1), ribs(1)
7.	Osteosarcoma	5 (10%)	10-19	3	2	Femur (2), Ilium (2), Tibia (1)
8.	Ewing's sarcoma	1 (2%)	18	1	-	Pelvic tubercle
	TOTAL	50		36(72%)	14 (28%)	

Figure 1: Giant cell tumour: A: X-ray showed lobulated lytic lesion in the epiphysis of the left upper tibia.B: MRI showed a heterogenously enhancing lobulated lytic lesion in the epiphysis of the left upper tibia. C: Microscopy showed multinucleated giant cells and neoplastic stromal cells (H&E, x40).

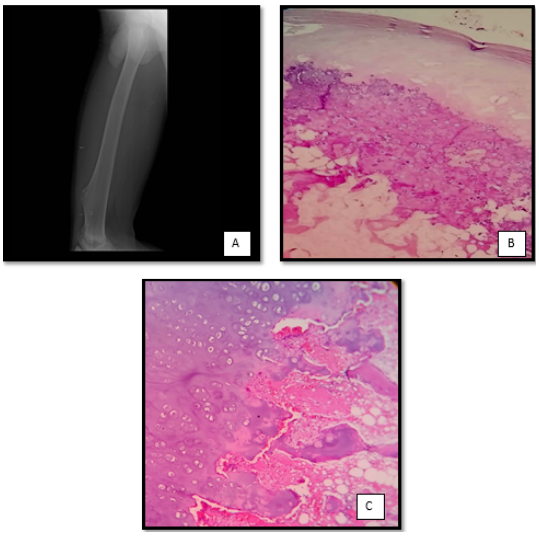


Figure 2: Osteochondroma;
A. X-ray showed a focal growth in the distal humerus.
B. The lesion is composed of benign cartilaginous cap covered by perichondrium and with underlying bone (H& E, x10)
C. The cartilaginous cap composed of lobules of cartilage with benign chondrocytes within the lacunae. (H& E, x40)

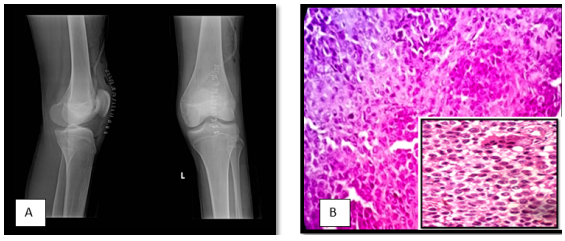


Figure 3: Chondroblastoma:
A. X-ray showed a radiolucent expansile lytic lesion in the distal epiphysis of femur with marginal sclerosis. B. Neoplasm composed of sheets of round to oval cells with cells having bland nuclear chromatin, some showing small nucleoli. Occasional nuclei show grooves (H&E, x10). Inset; Showing nuclear grooves (H&E, x40).

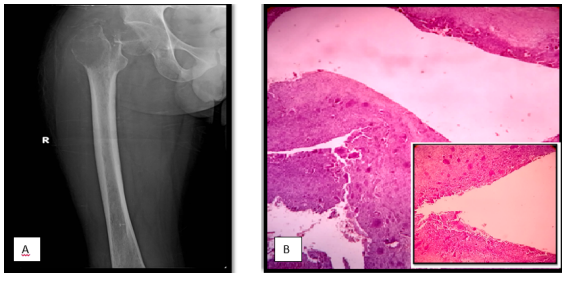
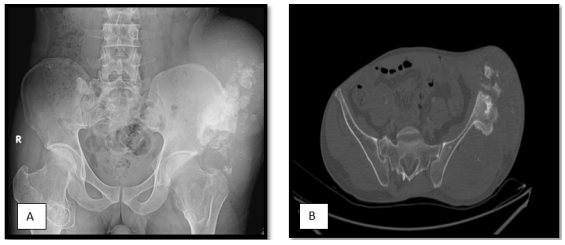


Figure 4: Aneurysmal bone cyst:
A. X-ray showed an eccentric cystic lesion of the right proximal femur.
B. Large luminal spaces lined by fibrous tissue along with giant cell tumor like areas (H&E, x10). Inset; Showing multinucleated small-sized osteoclast like giant cells (H&E, x40).



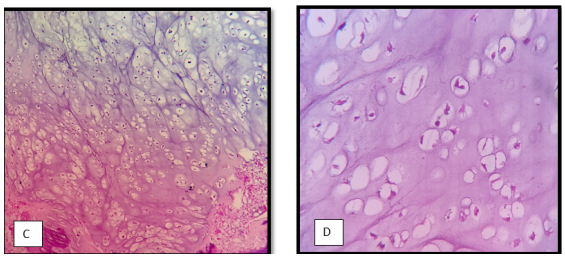


Figure 5: Chondrosarcoma:
A: X-ray showed hetrogenous lesion with intra lesional calcification of the left iliac bone.

B: CT scan showed heterogenously enhancing large well-defined lobulated lesion of the left iliac bone with "cloud-like calcification."

C. Neoplasm composed of irregular lobules of cartilage separated by fibrous septae (H&E, x10).

D. Neoplasm showing chondrocytes which are atypical, varying in size and exhibiting moderate atypia in a background of abundant blue grey cartilage matrix (H&E, x40).

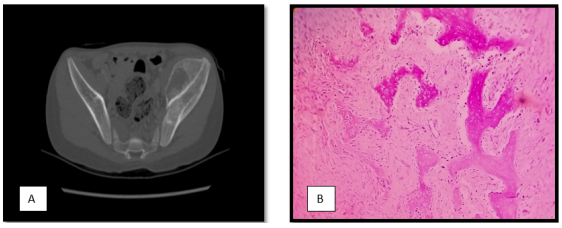


Figure 6: Osteosarcoma

A. CT scan showed an expansile eccentric osteolytic lesion with osteoid matrix involving left iliac bone.

B. Neoplasm composed of pleomorphic cells. The intervening areas between the cells show pink osteoid rimmed by tumour cells(H&E, x10).

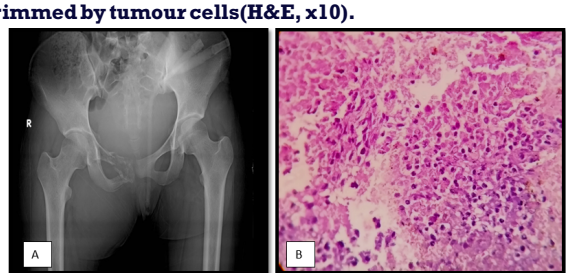


Figure 7: Ewings sarcoma

A. Ewing's sarcoma involving right pelvic tubercle.

B. The tumour has small round blue cell morphology, with tumour cells having round nuclei, scant cytoplasm, coarse chromatin and inconspicuous nucleoli (H&E, x40).

DISCUSSION

According to the WHO classification, 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 characterstics.[6] Primary lesions of the bone are rare and account for < 0.5% of all world cancers.[7] Complete clinical details including age, gender, site and radiological findings are prerequisites before making the histopathological diagnosis of any bone tumour. Certain entities can be confused clinically with acute osteomyelitis or tuberculosis.[4]

In the present study and in other studies benign lesions were more common with male predominance as shown in Table 2.

Table 2: Comparison of our study with other similar studies.

Serial No	Present study (2018)	Kumavat PV et al (2017)[10]	Modi D et al (2016)[9]	Kethireddy S et al (2016)[4]	Sharma S et al (2015)[8]
Total cases	50	70	26	28	110
M:F Ratio	2:1	0.9:1	2:1	1.2:1	1:1
Benign	39	43	18	25	79
Malignant	11	27	8	3	31
Osteochondroma	8	30	4	6	15
Giant cell tumor	25	27	4	12	17
Osteosarcoma	5	0	3	2	12
Chondrosarcoma	5	5	1	0	6

Giant cell tumors (50%) followed by osteochondroma were the most common benign tumours in the present study and similar to studies by Kethireddy S et al.[4] and Shrama S et al.[8] Giant cell tumours are classified as benign, intermediate locally aggressive (rarely metastasizing) and malignant. Histology shows a moderately vascularised stroma with oval, spindle-shaped mononuclear cells, uniformly interspersed with multinucleated giant cells.[10] Radiography shows a purely lytic destructive lesion at the end of the bone. The macroscopic appearance of a giant cell tumour can be quite distinctive. The lesion is soft and typically has dark brown color.[11] We had twenty five cases of giant cell tumour mostly seen in the femur followed by tibia between the ages 13 to 57 years. X-ray showed lobulated lytic lesion in the epiphysis of the bone. Histopathology showed numerous multinucleated osteoclast-type giant cells and neoplastic stromal cells similar to other studies.[4,8]

Osteochondroma was the second most common benign tumour most of which were seen in the femur and showed a male predominance with the patients between the ages 6 to 17 years. These tumours radiologically show a pedunculated growth arising from the metaphyses of long bones. External surface shows a lobulated cartilage cap covered by a fibrous membrane that is continuous with periostium covering the stalk. Histology reveals that the cartilage cap is composed of moderately cellular hyaline cartilage. At the junction with underlying cancellous bone, cartilage shows enchondral ossification. In one study Osteochondroma was the most common benign lesion followed bt giant cell tumour, and was commonly seen in 2nd decade with male predominance, femur being the commonest site involved.[10]

Chondroblastoma is classified according to latest WHO classification as intermediate grade (rarely metastasizing) tumour.[1] It is an aggressive tumour which destroys the cortex and grows into the soft tissues. Recurrences may occur in the bone or adjacent soft tissue. Rare cases of chondroblastoma metastasizing to the lungs after 34 years have been reported.[10] We had three cases of chondroblastoma. Tumour were located in the distal epiphysis of the femur with male predominance and mean age of 18 years, finding similar to Kumavat et al where one case of chondroblastoma located in distal end of femur in a 17 year old male was reported.[10] Histology shows a neoplasm composed of sheets of round to oval cells with cells having bland nuclear chromatin, some showing small nucleoli and nuclear grooves.

Ossiying fibroma is a benign fibro-osseous lesion of the bone, frequently seen in the third and fourth decades of life. Radiologic features include the presence of a sharply demarcated lesion with smooth contours. Histologically, ossifying fibromas are composed of randomly distributed mature (lamellar) bone spicules rimmed by osteoblasts admixed with fibrous stroma.[11]In the present study two cases of ossifying fibroma were reported one in a 11 years old male and other in a 45 years old male both arsing from the mandible. Microscopy showed stromal cells having hyperchromatic nuclei, moderate amount of cytoplasm with no marked atypia.

Aneurysmal bone cyst (ABC) is a benign but locally aggressive bone lesion, considered as a reactive lesion mostly involving bone although soft tissue variants have also been described. Patients are usually in the first two decades of life with a slight female predominance. The majority of lesions occur in the metaphysis of long bones. Radiography reveals a purely lytic lesion, involving the metaphysis of a long bone, is eccentric and shows a blowout appearance with extension into soft tissues. Microscopicaly ABC shows cysts of varying sizes separated by septa. Septa are composed of loosely arranged spindle cells with osteoclast-like giant cells and capillary proliferation.[11] We had one case of aneurysmal bone cyst in our study. Radiographic imaging showed eccentric cystic lesion of the right proximal femur in an 18 years old male. Histology showed large luminal spaces lined by fibrous tissue along with giant cell tumour-like areas.

Osteosarcoma was the most common malignant bone tumours in various studies.[4, 8, 9, 10.] In present study osteosarcoma and chondrosarcoma were the most common malignant bone tumours. Chondrosarcoma is the most common primary malignant bone tumour in the age group of 40-60 years. It commonly involves pelvis, femur, ribs, shoulder girdle, and vertebra with male predilection similar to another study.[10] Radiographically, chondrosarcomas appears more aggressive and destructive lesion, typically demonstrate significant endosteal scalloping, cortical thickening, cortical destruction and periosteal reaction.[11] Histologically chondrosarcomas show abundant blue-grey cartilage matrix production. Irregular shaped lobules of cartilage of variable sizes separated by fibrous bands.[1] We had five cases of chondrosarcoma. Pelvis was the commonest site with three cases in our study. CT scan taken of the pelvis revealed speckled calcification which is hallmark of these tumours. The neoplasm was composed of irregular lobules of cartilage separated by fibrous septae showing chondrocytes varying in size and exhibiting moderate atypia in a background of abundant blue grey cartilage matrix.

Osteosarcoma is a malignant tumour composed of osteoblastic cells that produce bone matrix, accounting for approximately 20% of primary malignant bone tumours. It may present at any age but the most common at the second decade and late adulthood with a male preponderance. Fifty percent of all osteosarcomas occur in the knee joint area; the proximal humerus is the next common site.[1,3,11] In various studies osteosarcoma was the most common primary malignant bone tumour between age 4-20 years with male predominance mostly located in femur, tibia and humerus. MRI manifestations of osteosarcoma often consisted of low mixed signals on T1WI and high mixed signals on T2WI. Histopathological section of the tumor shows pink osteoid and malignant osteoblast. [3,4,5] Osteosarcomas accounted for 10% of primary malignant bone tumours in our study. It was found that it was more common in 10 – 19 year old age group with male predominance. All osteosarcomas were histologically of conventional (classical) variety,

microscopically identified by the presence of eosinophilic glassy osteoid material arranged in a lace-like pattern surrounded by malignant osteoblasts.

Ewing's sarcoma is relatively uncommon, accounting for 6-8% of primary malignant bone tumours. Nearly 80% of patients are younger than 20 years.[1] Commonest site for the involvement of Ewing's tumour is tibia and femur. Radiologically, femur showed a moth-eaten, permeative, destructive tumour at the diaphysis with lamellar or onion skin periosteal bone reaction. Histology shows solid areas of uniform undifferentiated cells, with minimal amount of cytoplasm.[2,10] One case of Ewings sarcoma in a 18 year old male involving right pelvic tubercle was seen in our study. Histology showed cells having small round blue cell morphology with round nuclei, scant cytoplasm, coarse chromatin and inconspicuous nucleoli similar to other studies.[2,9,10]

Both our study and other studies showed male predominance in bone tumors. Also benign tumours were more than malignant tumors.[4.8.9.10]

CONCLUSION:

It has become quite a challenging task for pathologist, radiologist and surgeon to reach to a correct diagnosis of bone lesion. Histopathological diagnosis is still the crucial and gold standard for precise diagnosis of bone tumours and should always be made in conjunction with clinical and radiological findings.

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