Pattern of Bone Tumours Seen at Addis Ababa University, Ethiopia.

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Background: Primary bone tumors are uncommon malignancy, but they are important causes of cancer morbidity and mortality, especially among young people. To measure the strength of agreement in Clinical, Radiological and Histopathological diagnosis of all Bone Tumors in a -5-year study period from December, 2003 – March, 2008. Faculty of Medicine, Black-Lion Teaching Hospital, Addis Ababa University, Ethiopia. The study was also aimed at looking into the spectrum of bone tumors referred to BLH.

Methods: All bone tumor patients, who presented to all the three departments at BLH between the study periods of December, 2003 – March, 2008 were recruited. All files related to these patients were reviewed. All patients had a clinical examination, plain radiographs and biopsies of the affected part of the extremity. Radiographs of few selected difficult cases were usually discussed at the weekly joint Orthopedic & Radiologic sessions. The Radiological and Histopathological diagnoses made were categorized separately using WHO classification of bone tumors. Strength of agreement between Radiological and Histopathological diagnoses was measured using Cohen's Kappa test.

Results: From the total of 216 bone tumor patients presented and biopsied in the five year period, complete information could not be gathered only for 11 (5%) of the patients and these are excluded. Hence there were 111(51.3%) males and 94(48.7%) females with Histopathological tissue diagnosis of the bone tumor. Male to female ratio was nearly 1. The ages ranged from 7 to 55 years with a peak in the 15-29 years age group. There were 32 different types of tumors histopathologically diagnosed. In 74 (36 %), the tumors were malignant. The commonest primary malignant tumour was Osteosarcoma (28.5%). It was also the single most common Clinical, Radiological and Histological diagnosis made. Exostosis was second. Considering all bone tumors together, the study indicated that radiological diagnosis was confirmed by similar histological diagnosis in 172 out 205 cases (84 %) and the corresponding Cohen's kappa value (0.82) showed excellent agreement between radiological and histological diagnoses of all bone tumors. The agreement between radiological and Histopathological diagnoses of Osteosarcoma of the limbs was 84.5%.

Conclusion: There is an excellent agreement between Clinical, Radiological and Histopathological diagnoses of bone tumors in general and Osteosarcoma in particular. All mixed density lesions located in the metaphysis of long bones around the knee joint in young adults with sharp pain should be investigated as Osteosarcoma until proven otherwise. In set-ups where there is limited or no Histopathological service, joint Clinical and Radiological decision could lead to a higher degree of accuracy in diagnosis of bone tumors, especially Osteosarcoma. Radiological diagnosis of bone tumors at Black Lion Hospital, Addis Ababa is excellent.

Introduction

Bone tumor is an abnormal growth arising from bone. It could be benign or malignant but most commonly the term is used for primary tumors; it is less exactly applied to secondary or metastatic tumors found in bone. Bone tumors may be classified as "primary tumors" which originate in the bone, and "secondary tumors" which originate elsewhere and involving the bone secondarily. Primary tumors of bone can be divided into benign tumors and malignant tumors. Common benign bone tumors may be neoplastic, developmental, traumatic, infectious, or inflammatory in etiology. Primary bone tumor accounts for 0.2% of all tumors in humans, whereas involvement of skeletal tissue by metastatic disease

is much more common[1]. Bone tumors are mostly mesenchymal in origin, though, for example Ewing's sarcoma is thought to have neuroectodermal precursor cells. Primary bone tumors are uncommon malignancy, but they are important causes of cancer morbidity and mortality, especially among young people. Although relatively rare in childhood, primary bone tumor represents the sixth most common neoplasm in children, while in adolescents and young adults; they are the third most frequent, exceeded only by leukemia and lymphoma. Examples of benign bone tumors include osteoma, osteochondroma, aneurysmal bone cyst, and fibrous dysplasia. Malignant primary bone tumors include osteosarcoma, chondrosarcoma, Ewing's sarcoma, and other sarcoma types. Multiple myeloma is a Hematologic malignant tumor which also frequently presents as one or more bone tumors.

Secondary bone tumors include metastatic tumors which have spread from other organs, such as the breast, lung, and prostate. Metastatic tumors more frequently involve the axial skeleton than the appendicular skeleton. Tumors which originate in the soft tissues may secondarily involve bones through direct invasion. A review of literature reveals that malignant bone lesions were demonstrated in bones of ancient Egyptian mummies[2]. For a long time, osteosarcoma has been associated with a low social-economic stratum[3]. This is a major problem in the developing countries where limb-sparing surgery is not yet possible. Amputation is therefore often the mode of treatment making the patient disabled, non productive and a burden to the family[4,5,6].

Literature on bone tumors in Africa is scarce. In a study carried out in Uganda between 1964 and 1968, osteosarcoma was found to be the commonest primary malignant bone tumour with a peak age of 10 - 19 years. The commonest site was the lower femur[3]. This is similar to what has been reported elsewhere[7]. It has been suggested that major histocompatibility complex linked genes may determine susceptibility to some types of tumors[8]. Other epidemiological factors mentioned to be linked are mechanical trauma, ionizing radiation and chronic osteomyelitis[9,10,11,12,13]. Radiological diagnosis of any bone tumor takes into account the clinical history, site of lesion, borders of the lesion, type of matrix, type of bone destruction, type of periosteal reaction, nature and extent of soft tissue involvement and number of lesions. A systematic approach to clinical history, radiographic evaluation and histopathology is necessary for accurate diagnosis -all three are important. As many bone lesions overlap, an experienced clinician systematically integrates the radiological and histopathological results to plan and offer the best possible management to the patient. This study is the first of its kind in the East African region to address 32 types of bone tumors and aims at assessing the level of agreement between Histopathological radiological diagnoses of bone tumors at AAU-MF and profiling the spectrum of bone tumors presenting to BLH.

Patients and Methods

All bone tumor patients, who presented to all the three departments at BLH between the study periods of December, 2003 – March, 2008 were recruited for the study. Histopathological and Radiological diagnoses of the tumors were identified and their clinical profile looked in detail. All files related to the patients were reviewed. There was no complete information only for 11 patients and were not considered in this study. Hematologic tumors including malignant myeloma were also excluded from the study, as they are mainly diagnosed by bone marrow cytology and not bone tissue biopsy. All patients had a clinical examination, plain radiographs and biopsies of the affected part of the extremity. Radiographs of few selected difficult cases were usually discussed at the weekly joint Orthopedic & Radiologic sessions.

The Radiological and Histopathological diagnoses made were categorized separately using WHO classification of bone tumors. The tumors were then classified according to the recent WHO classification of bone tumors[14,15]. Locations were divided into nine groups namely: Bones of the limbs, bones of the limbs and spine, clavicle, cranio-facial bones, pelvic bones, ribs, scapula, spine, and sternum. The collected information was then analyzed using SPSS and Microsoft Excel. Cohen's Kappa test to determine the level of Radiological and Histopathological diagnostic agreement was calculated online[16].

Results

After exclusions by criteria, a total of 205 bone tumor patients were enrolled. By far the majority, 182 (182/205, 89%) of the biopsied bone lesions were neoplastic whereas 23 (23/205, 11%) of the lesions were non-neoplastic conditions. Primary tumors accounted for 94.5% (172/182) of the neoplastic lesions. Metastasis was diagnosed in 10 (10/182, 5.5%) of the neoplasms. Benign lesions accounted for 57% (74/172) and malignant lesions for 43% (74/172) of the primary neoplasms. The histological diagnosis shows over one third (74/205, 36.1%) of the tumors are malignant: 22% (45/205) Osteosarcoma, 5.36% (11/205) Ewing's Sarcoma, 0.5% Leiomyosarcoma, 2.0% Lymphoma, 1% Malignant Fibrous Histiocytoma and 0.5 % Spindle Cell Neoplasm. The age ranged from 4 months to 65 years with median age 19 years.

Table 1. Distribution of Radiological and Histopathological Diagnoses of All Bone Tumors in Each Sex.

Diagnoses	Males		Females		Total Number		Percent	
	(Rad.)	(Histopath.)	(Rad.)	(Histopath.)	(Rad.)	(Histopath.)	(Rad.)	(Histopath)
ABC	1	1	3	3	4	4	1.95	1.95
Ameloblastoma	14	12	7	5	21	17	10.22	8.27
Bone Islands	0	0	1	0	1	0	0.49	0
Bony Dysplasia	0	0	1	0	1	0	0.49	0
Brodie Abscess	0	0	1	0	1	0	0.49	0
Cementifying Fibroma	0	0	0	2	0	2	0	0.98
Chondromyxoid Fibroma	1	2	1	1	2	3	0.98	1.46
Dentigerous Cyst	1	1	0	0	1	1	0.49	0.49
Enchondroma	2	2	2	3	4	5	1.95	2.44
Eosinophilic Granuloma	0	0	2	0	2	0	0.98	0
Ewing's Sarcoma	10	8	2	3	12	11	5.85	5.37
Exostosis	26	27	17	18	43	45	20.98	21.95
Fibrous Dysplasia	3	8	5	6	8	14	3.9	6.83
GCT	13	14	8	8	21	22	10.24	10.73
Haemangioma	1	1	3	4	4	5	1.95	2.44
Leiomyosarcoma	0	1	0	0	0	1	0	0.49
Lymphoma	1	1	5	3	6	4	2.93	1.95
Malig Fibrous Histocyt.	0	1	0	1	0	2	0	0.98
Maxillary Sarcoma	1	0	0	0	1	0	0.49	0
Metastasis	3	3	8	7	11	10	5.37	4.88
Myositis Ossificans	1	0	0	0	1	0	0.49	0
Non-Ossifying Fibroma	1	1	0	0	1	1	0.49	0.49
Normal report	1	0	0	0	1	0	0.49	0
Ossifying Fibroma	0	0	1	2	1	2	0.49	0.98
Osteoblastoma	0	1	0	1	0	2	0	0.98
Osteoid Osteoma	1	1	0	0	1	1	0.49	0.49
Osteoma	1	1	2	2	3	3	1.46	1.46
Osteosarcoma	27	23	23	22	50	45	24.39	21.95
Pathological Fracture	1	0	0	0	1	0	0-49	0
Pleomorphic Adenoma	0	1	0	0	0	1	0	0.49
Simple Bone Cyst	1	1	2	2	3	3	1.46	1.46
Spindle Cell Neoplasm	0	0	0	1	0	1	0	0.49
TOTAL	**111**	**111**	**94**	**94**	**205**	**205**	**100**	**100**

The majority of bone lesion occurred below 30 years of age (n=158, 77.1 %) among these 55.1% (42.4 % of the total) were in the age range of 10 to 19 years. 111 patients were male making male to female ratio 1.08:1 Bone tumor in children below the age of 15 occurred in 52 cases out of which the highest is osteosarcoma (n=18, 34.6%), followed by Exostosis (n=10, 19.2%), Ewing's Sarcoma (n=7, 13.5%)

Table 1 shows the categorical distribution of Radiological & Histopathological diagnoses of all bone tumors in each sex. The table clearly shows that the distribution of bone lesion in each sex is varying from one type to other, for example; the male to female ratio is 1:1 in the case of Osteosarcoma, 3:2 in Exostosis, 2:1 in Ameloblastoma, 2:1 in GCT, and 8:3 in Ewing's Sarcoma. The three most common bone lesions histopathologically proven were: osteosarcoma and Exostosis equally first (n=45, 21.95 % each), GCT (n=22, 10.73%) and Ameloblastoma (17, 8.29%) respectively. Radiologically, the

commonest tumor singled out was osteosarcoma, (24.5%, 50/205). The distribution of bone tumor groups is indicated in table 2.5. Table 2 shows the distribution of Bone tumor Groups based on Histopathological Matrix. As clearly seen, the most common group of tumors were cartilaginous in origin (n=53, 25.9%) followed by osteogenic tumors (n=51, 24.9%).Table 3 shows the site/location of the tumor based on WHO classification[14,15]. The majority of specimen were from bones of the limbs (n=135, 65.8 %), followed by Craniofacial bones (n=41, 20.0 %), pelvic bones (n=10, 4.9 %), Ribs (n=6, 2.9 %), and Scapulae (n=5, 2.4%). Considering all bone tumors together, the study indicated that radiological diagnosis was confirmed by histological diagnosis in 172 out 205 cases (84 %) and the corresponding Cohen's kappa value (0.82) calculated online, showed excellent agreement between radiological and histological diagnoses of all bone tumors[16,17].

Only one patient was reported radiologically normal and histopathologically diagnosed to have Osteoblastoma. There was no patient reported normal after biopsy. The main diagnostic disagreement was noticed in diagnosing osteosarcoma. Radiological and Histopathological diagnoses were not in agreement in eight (15.7%, 8/51) of the Osteosarcoma patients. While the lesion was finally histopathologically proven to be benign, radiological diagnosis of malignant bone tumor was made only in six ((6/51, 11.8%) of the cases. These are shown on Table 4.

Table 2. Distribution of Bone Tumor Groups Based on Histopathological Matrix.

Tumor Group	**Histological Diagnosis**	**tumor (% in group)**	**Total**	
			n	%
Cartilaginous Tumors			**53**	25.85
	Exostosis Enchondroma Chondromyxoid Fibroma	84.9 1 9.43 5.66	45 5 3	21.95 2.44 1.46
Osteogenic Tumors			**51**	24.88
	Osteoma Osteoid Osteoma Osteoblastoma Osteosarcoma	5.88 1.96 3.92 88.24	3 1 2 45	1.46 0.49 0.98 21.95
Fibrogenic Tumors			**4**	1.95
	Cementifying Fibroma Malig Fibrous Histocyt.	50.00 50.00	2 2	0.98 0.98
Ewing's Sarcoma	Ewing's Sarcoma		**11**	5.37
Hematologic neoplasm	Lymphoma		4	1.95
GCT	Gct		**22**	10.73
Vascular Tumor	Haemangioma		5	2.44
Miscellaneous Tumors			**32**	15.61
	Ameloblastoma Metastasis Leiomyosarcoma Spindle Cell Neoplasm Non-Ossifying Fibroma Ossifying Fibroma	53.13 31.25 3.13 3.13 3.13 6.25	17 10 1 1 1 2	8.29 4.88 0.49 0.49 0.49 0.98
Miscellneous Lesions			**23**	11.22
	ABC Dentigerous Cyst Simple Bone Cyst Pleomorphic Adenoma Fibrous Dysplasia	17.39 4.35 13.04 4.35 60.87	4 1 3 1 14	1.95 0.49 1.46 0.49 6.83
	Total		**205**	

Discussion:

This comparative study of bone tumors as a spectrum of lesions is the first of its kind from Ethiopia, if not from Africa. We have noted that the documentation of bone tumor patients at Black-Lion Hospital is excellent, only 5% (11/216) files were lost. This could be due to the fact that the analysis focused only on the last five years, which are very recent. We also noted that, the Pathology Department has made spectrum of 32 different types of Histopathological bone lesions. This shows the Department's long years of experience in detecting different bone lesions and it also indicates the presence of many types of bone tumors in a referral Hospital.

Table 3. WHO Distribution of Site of Bone Tumor.

Histopathological Diagnosis	WHO Site of bone tumor									
	BL	BL +S	C	CFB	PB	Rib	Scapula	Spine	Sternum	No
ABC	2	-	-	-	2	-	-	-	-	4
Ameloblastoma	-	-	-	17	-	-	-	-	-	17
Cementifying Fibroma	-	-	-	2	-	-	-	-	-	2
Chondromyxoid Fibroma	2	-	-	-	1	-	-	-	-	3
Dentigerous Cyst	-	-	-	1	-	-	-	-	-	1
Enchondroma	2	-	1	-	-	2	-	-	-	5
Ewing's Sarcoma	9	-	1	-	-	-	1	-	-	11
Exostosis	35	-	-	1	2	3	4	-	-	45
Fibrous Dysplasia	4	-	-	9	-	1	-	-	-	14
Gct	21	-	-	-	1	-	-	-	-	22
Haemangioma	3	-	1	1	-	-	-	-	-	5
Leiomyosarcoma	1	-	-	-	-	-	-	-	-	1
Malig Fibrous Histo	2	-	-	-	-	-	-	-	-	2
Metastasis	5	1	-	-	1	-	-	2	1	10
Lymphoma	-	-	-	3	-	-	-	-	1	4
Non-Ossifying Fibrous	1	-	-	-	-	-	-	-	-	1
Ossifying Fibroma	-	-	-	2	-	-	-	-	-	2
Osteoblastoma	2	-	-	-	-	-	-	-	-	2
Osteoid Osteoma	1	-	-	-	-	-	-	-	-	1
Osteoma	-	-	-	3	-	-	-	-	-	3
Osteosarcoma	42	-	-	-	3	-	-	-	-	45
Pleomorphic Adenoma	-	-	-	1	-	-	-	-	-	1
Simple Bone Cyst	2	-	-	1	-	-	-	-	-	3
Spindle Cell Neoplasm	1	-	-	-	-	-	-	-	-	1
Total	**135**	**1**	**3**	**41**	**10**	**6**	**5**	**2**	**2**	**205**

Key: BL= Bone of the Limb, S=Spine, C= Clavicle, CFB= Craniofacial bone, PB= Pelvic bone.

Table 4. Disagreements between Radiological and Histopathological Diagnosis of Osteosarcoma of the Limbs at BLH.

Radiological diagnosis	Pathological Diagnosis	Frequency
Osteosarcoma	*MFH	2
Osteosarcoma	#GCT	2
Lymphoma	Osteosarcoma	1
Osteosarcoma	Lieomyosarcoma	1
Osteosarcoma	Ossifying fibroma	1
Osteosarcoma	Fibrous dysplasia	1

* MFH=Malignant Fibrous Histiocytoma, #GCT= Giant Cell Tumor.

In general terms, the age, sex, site and distribution of the tumors is comparable to most reports from elsewhere[18]; we found the same groups of common tumors like Osteosarcoma, osteochondroma, chondrosarcoma and giant cell tumors. Hematologic malignancies, like multiple myeloma, seem to be lower in our study. This is due to the fact that these tumors are diagnosed based on bone=marrow smear and not bone by biopsy.

Excluding Ameloblastoma of the jaw, 39.7% (n=60) of the primary non-Hematologic bone tumor were malignant. Lower when compared to 63% in other series[19]. As the most common primary non-Hematologic malignant tumors of the bone, the frequency of osteosarcoma in the present study is relatively higher (n=45, 75%) compared to those studies conducted in Chiang Mai University (67.4%) [18]; this could be explained by the fact that most patients with malignancy are referred to this Hospital as it is the country's highest referral institution. The most common primary malignant bone tumor is osteosarcoma and its frequency is similar to the frequency in other study[14]. The second most common malignant tumor of the bone seen in children and adolescent was Ewing's sarcoma [20]. Osteosarcoma typically is a long bone tumor and rarely affects flat bones of the axial or appendicular skeleton. The cases examined in this study show 42 out of 45 incidences of osteosarcoma are in long bone and 3 out of 45 in the pelvic bones. This observation agrees very well with the study conducted at La Timone adults University Hospital for a 16 years period[21]. The present study showed that Exostosis is the most common benign bone tumor accounted for 49.5% of all benign bone tumors. This is higher when compared with the study done in Chiang Mai University (23.58%) and we noticed low incidence of GCT (24.2 %) compared to Chiang Mai University (34.9% .This may reflect the fact that most of these tumors are handled at lower level institutions as they are clinically benign; hence not referred to our Hospital.

Specific types of tumors targeted certain age groups and anatomic sites[22]. As a group, bone neoplasms affect all ages and arise in virtually every bone but most bone tumors presenting during the first decades of life have a propensity to originate in the long bones of the extremities[23]. In our study, approximately 77.1% bone tumors were younger than 30 years and bone of the limb were the major site affected 65.8%. The predilection bone in specific tumor types correlates well with most of the results of previous reports[14, 20].

Cohen's (1960) kappa statistic (*K*) has long been used to quantify the level of agreement between two raters in placing persons, items, or other elements into two or more categories[22]. Hence this test –statistic can be used to measure the level/strength of agreement between different raters (Orthopedists, radiologists and pathologists) in placing/diagnosing bone tumors into the different WHO categories. Kappa values are easily calculated online. Our corrected Cohen's kappa value of 82% (0.82) is an excellent level of agreement ($k > 0.75$) between radiological and histological diagnoses of all bone tumors. But as still some histologically benign bone tumors which are easily treated by simple surgery were diagnosed as radiologically malignant lesions which usually demands radical surgery, radiotherapy and chemotherapy; Histopathological confirmation must always accompany bone tumor diagnosis whenever possible. Therefore bone tumor diagnosis should be made by joint consideration of clinical presentation, radiological appearance and Histopathological results whenever possible.

Conclusion and Recommendations

Spectrum of bone tumors presented to Black Lion Hospital. There is an excellent/high level of agreement between Radiological and Histopathological diagnoses of bone tumors at Black Lion Hospital. In set-ups where there is limited or no Histopathological service, joint Clinical and Radiological decisions could lead to a higher degree of accuracy in diagnosis of bone tumors. Based on the findings of this study, we recommend the following:

1. As exact diagnosis of bone tumors is at times difficult, joint approach integrating Clinical, Radiological and Histopathological findings is recommended to increase accuracy. This is an excellent learning point to be adopted from BLH, AAU-MF.
2. Where there is no or limited Histopathological service, the surgeon could decide on patient's management based on radiologist's report and his clinical findings.
3. Where ever available, Histopathological diagnosis helps the Surgeon in planning limb-salvaging surgery for early malignant and all benign bone lesions.

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