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A Study on Histological Classification of Bone Lesions and Features of Malignant Lesions: Descriptive Study

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Abstract

Introduction: Osteosarcoma is by far the greatest histological imitator of bone tumours. Both radiologically and histologically, osteosarcoma mimics many other benign and malignant bone lesions.Accurate diagnosis of bone-forming tumors, including correct subclassification of osteogenic sarcoma is critical for determination of appropriate clinical management and prediction of patient outcome. *Methodology:* All patients with clinical and radiological suspicion of primary and secondary tumours and tumour like lesions of the bone which require biopsy or surgical excision. Biopsy specimens were fixed in 10% formalin for 24 hrs after recording the gross morphological features. Specimen was sampled carefully and bone tissue was cut with hand and electrical saw in to thin slices. Samples containing bone tissue were decalcified before routine processing and paraffin embedding. *Results:* Among the bone forming tumours, benign tumours were four which constituted one osteoma and two osteoid osteoma and one osteoblastoma.. Malignant bone forming tumours were 3 which constituted conventional osteosarcoma. Among the cartilage forming tumours benign tumours were 11 amongst which osteochondromas were 8, chondromas were 2 and 1 chondroblastomas. The malignant cartilage tumour. was conventionally chondrosarcoma. Marrow origin tumours constituted 2 cases of Ewing's sarcoma *Conclusion:* Knowledge of radiological appearances of various bone tumours and tumour like lesions is essential for the pathologist in evaluating the bone tumours.

Keywords: Bone Tumours; Radiology; Osteosarcoma.

Introduction

Bone is a connective tissue (1/3), impregnated with calcium salts (2/3). The inorganic calcium salts (mainly calcium phosphate, partly calcium carbonate, and traces of other salts) make it hard and rigid. The organic connective tissue (collagen fibres) makes it tough and resilient (flexible) [1].

The term osteosarcoma is now increasingly used , replacing the older term osteogenic sarcoma and also a number of distinct entities have been recognized [2]. Several parameters have been found to be of prognostic significance, including patient age, sex, site of the tumour, and tumour classification [3]. In 1977 Krishnan, Unni K et al [4] and more recently, Kurt, Anne Marie et al described a group of low grade intraosseous osteosarcomas. The histological appearance often resembled the bland features of paraosteal osteosarcoma, with few mitoses and minimal atypia. Other cases resembled fibrous dysplasia and curlicue trabeculae of woven bone. This group of tumours, however, showed permeation of pre existing bone. As with paraosteal osteosarcoma, late differentiation to high grade osteosarcoma may occur [5]. Bertoni F et al,(1993) reported a desmoplastic fibroma like resemblance also [6].

No other benign or malignant primary tumour of bone has greater range of radiologic, pathologic presentations and sites of origin within the bone than osteosarcoma. Osteosarcoma is by far the greatest histological imitator of bone tumours. Both radiologically and histologically, osteosarcoma mimics many other benign and malignant bone

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lesions.Accurate diagnosis of bone-forming tumors, including correct subclassification of osteogenic sarcoma is critical for determination of appropriate clinical management and prediction of patient outcome [7].

Modified classification scheme of osteosarcomas have appeared in recent years. Available systems employ such features as the precise location of the tumour within the bone (intramedullary or central, intracortical, surface, periosteal or paraosteal); the degree of cellular differentiation (high grade or low grade); the histologic composition (osteoblastic, chondroblastic, fibroblastic, fibrohistiocytic, telangiectatic, small cell, clear cell); the number of foci (single or multicentric); and the status of the underlying bone (normal or the site of the disease such as Paget's disease, of injury as occurs with a vascular insult or following irradiation, or of another neoplasm, such as an osteochondroma, chondroma, or osteoblastoma). The term dedifferentiated chondrosarcoma was introduced by Dahlin and Beabout in 1971 to describe a primary bone tumour composed of low grade cartilaginous areas associated with, but sharply delineated from, high grade sarcomatous areas.

Chondrosarcoma is a malignant cartilaginous tumour arising denovo in a bone when it is called primary or superimposed on a pre existing benign cartilaginous neoplasm when it is called secondary Secondary chondrosarcomas arise from solitary or multiple enchondromas or osteochondromas [8].

A primary chondrosarcoma is rare in patients younger than 20 years in which case a likely diagnosis is cartilage rich or chondroblastic osteosarcoma. In more than 70% of cases this malignancy occurs in elderly age group of 50 to 75 years. Most important sites for primary chondrosarcomas are pelvis, femur, ribs, humerus, skull and scapula in decreasing order. Among the long bones chondrosarcomas are common at the proximal ends of femur, tibia and humerus in the meta diaphyseal locations. The size of chondrosarcomatous lesions range between 2 and 40 cms. The importance of the size has to be considered based on the site of the tumour. A 4 to 5 cms solitary cartilaginous lesion of small tubular bones or ribs is probably chondrosarcoma but not if it is in long bone or pelvis [8].

Ewing's sarcoma was first described by James Ewing in 1920 Bator, Susan M.(1986) described a periosteal origin of Ewing's sarcoma. Atypical or large cell ewing's sarcoma may lack glycogen and has increased number of mitoses. Ewing's sarcoma and malignant peripheral neuroectodermal tumor share a common chromosome translocation 11; 22. Downing, James R et al (1993) [9] demonstrated detection of (11:22) (q24:q12) translocation in ewing's sarcoma/PNET. The HBA/71 antigen is expressed in Ewing's sarcoma but not in other small cell neoplasms and can be detected through an immunohistochemical reaction [10].

Methodology

The study was conducted for 24 months subject to inclusion and exclusion criteria.

Inclusion Criteria

All patients with clinical and radiological suspicion of primary and secondary tumours and tumour like lesions of the bone which require biopsy or surgical excision.

Exclusion Criteria

1. Patients with haematopoietic tumours
2. Patients with tumours of the joints.

Informed Consent

The patients were briefed about the nature of the study and a written informed consent was obtained from the selected patients.

Method of Collection of Data

Biopsy specimens were fixed in 10% formalin for 24 hrs after recording the gross morphological features. Specimen was sampled carefully and bone tissue was cut with hand and electrical saw in to thin slices. Samples containing bone tissue were decalcified before routine processing and paraffin embedding. Sections were cut at 4-5µ thicknesses with microtome and stained routinely with Haematoxylin and Eosin. Special stains were done when necessary and these included Priodic Acid Schiff, Von Kossa and Reticulin stains.

Results

All the bone tumours and tumour like lesions from the present study are categorized according to the WHO histological classification of tumours.

Out of 50 lesions there were 7 bone forming tumours, 12 cartilage forming tumours,17 giant cell tumours, 2 marrow tumours, 4 metastatic deposits, 1

Table 1: Table showing histological classification of all bone lesions in the present study

Histological lesion	N= 50	Benign tumors		Malignant tumors	
Bone forming tumors	7(14%)	Osteoid osteoma	2	Osteosarcoma	3
		Osteoma	1		
		Osteoblastoma	1		
Cartilage forming tumors	12(24%)	Osteochondroma	8	Chondrosarcoma	1
		Chondroma	2		
		Chondroblastoma	1		
Giant cell tumors	17(34%)	-			17
Marrow tumors	2(4%)			Ewing's sarcoma	2
Others	1(2%)	Desmoplastic fibroma	1		
Metastatic deposits	4(8%)			Deposits	4
Total tumours	43(86%)	BENIGN	16	MALIGNANT	27
Tumour like lesions	7(14%)	Aneurysmal bone cyst	3		
		Fibrous dysplasia	2		
		Simple bone cyst	1		
		Non ossifying fibroma	1		

other and 7 tumour like lesions.

Among the bone forming tumours, benign tumours were four which constituted one osteoma and two osteoid osteoma and one osteoblastoma.. Malignant bone forming tumours were 3 which constituted conventional osteosarcoma. Among the cartilage forming tumours benign tumours were 11 amongst which osteochondromas were 8, chondromas were 2 and 1 chondroblastomas. The malignant cartilage tumour was conventionally chondrosarcoma. Marrow origin tumours constituted 2 cases of Ewing's sarcoma. Tumour like lesions of bone were 7 which included 3 aneurysmal bone cysts and 2 fibrous dysplasias, 1 ossifying fibroma and 1 simple bone cyst.

Malignant Bone Forming Tumours

In the present study the malignant bone forming tumours constituted 3 cases forming 6.5% of primary bone tumours. There were 3 conventional osteosarcomas. The mean age at presentation for all osteosarcomas in the present study was 18 years, youngest patient was 16 year old male child while oldest was 20 year old man. Males were affected in 2 cases while females in 1. Male to female ratio was 2:1.

Conventional Osteosarcoma

Clinical features: Clinical details were available in 3 cases. On examination tenderness over the lesion was present in all 3, one showed ulceration of the overlying skin and one case had a fungating growth.

Radiology

Data on radiologic appearance of conventional osteosarcomas were available in 3 cases. These showed the metaphyseal location of the lesion within the long bones in 2 and meta-diaphyseal in 1. Typical radiologic appearance of osteosarcomas like increased medullary density, permeative destruction with poor margins, cortical destruction, periosteal elevation and soft tissue extension with ossification were seen in two cases while atypical appearance with absence of any one of these features were present in other. Two cases showed

Table 2: Table showing localization data and site on osteosarcomas from present study

Localisation of osteosarcoma (n=3)	Site of osteosarcoma within the bone		Total
	Metaphysis	Meta-Diaphysis	
Lower end of femur	2		
Upper end femur		1	
Total	2	1	3

metastatic deposits in lung seen on chest X-ray. One case showed evidence of secondary pathological fracture.

Histopathology

The histology of conventional osteosarcomas from the present study were characterised by plump oval to spindle osteoblasts with pleomorphic and hyperchromatic nucleus showing variable mitosis in all the cases. These cells were seen producing thin lacy tumour osteoid or woven bone in various amounts. Two cases showed focal areas of malignant cartilage while giant osteoclast type giant cells were seen in one case. Also noted was areas of low grade

osteosarcoma mimicking fibrous dysplasia. Bone marrow permeation with malignant tumour was evident in one case while soft tissue infiltration of osteosarcoma into surrounding fibrous tissue and muscle plane were seen in another. There were areas of hemorrhage and necrosis in 2 cases.

Chondrosarcoma

In the present study there was one case of chondrosarcoma constituting 2 % of primary bone tumours and 3.7 % of malignant bone tumours. Age at presentation was 26 years.

Patients came with complaints of swelling with pain and restricted mobility. The duration of symptoms was 6 months. Examination revealed tumour size of 14 cm. Localisation of the growth was seen in lower end of femur.

Radiology

The lesion was located in metaphysis. The lesion was large lobulated mass showing soft tissue involvement with stippled calcification and erosion of the cortex. X-ray showed destruction of bone with soft tissue mass and calcification.

Gross

Cut surface showed shiny bluish to grey white lobules with tiny cysts and mucoid material.

Microscopy

Microscopy showed lobular growth pattern with highly cellular cartilaginous tissue. The cells were vacuolated showing varying sizes and had enlarged, plump, bizarre, multiple nuclei. There were cells with mitosis. In addition there were some myxoid and calcified areas.

Ewing's Sarcoma

In the present study 2 cases of Ewing's sarcoma constituted 4.3 % of primary bone tumours and 10.7 % of malignant bone tumours. The mean age at presentation with Ewing's sarcoma was 9 ± 5.65 years, with the age range from 5 to 13 years. Both were males.

Radiology

X-rays showed diaphyseal location of both lesions.The margins of the mass were poorly defined showing vague soft tissue mass shadows. Periosteal reaction and sclerosis of the cortex were seen in one, expansion of the bone with honeycomb trabecular pattern of destruction associated with fracture and soft tissue calcification in one.

Microscopy

Microscopy showed closely packed small round cells in sheets and nests. Cytoplasm was scant and indistinct. Nuclei were of uniform size and shape with occasional hyperchromatic forms. Mitosis were present but infrequent. Stroma showed rich vascularity with cells arranged around the blood vessels. one case showed large areas of hemorrhage and necrosis. Special stain by Periodic acid Schiff with diastase digestion showed PAS positive granules within the cytoplasm. Reticulin stain on the sections showed absence of reticulin around individual cells.

Discussion

There is probably no area in medicine in which an optimal outcome for the patient is more heavily dependent upon close co-operation between the Clinician (Orthopedic surgeon), Pathologist and Radiologist than the bone tumors [11]. Although tumors of bones are infrequently encountered, nonetheless they are of great significance because some of them assume an aggressive course and prove to be most lethal with extensive metastasis. A pathologist has a demanding role to play in early and accurate histological diagnosis as this could influence the therapeutic modality from amputation to aesthetic limb saving surgeries. More over bone tumors affect the young and adolescents in their active growth phase more commonly than other neoplasms that occur at an elderly age group [12]. Bone tumors are comparatively uncommon among the wide array of human neoplasms. This has contributed to the paucity of meaningful data on incidence rates and limited information is provided by regional centres regarding

Table 3: Table showing frequency of bone tumors according to different studies

Studies by Authors	Percentage
Paymaster (1966)	1.6%
Vyaghreshwarudu C (1973)	1.35%
Jayaram R (1997)	2.8%
Present study	1.5%

relative frequency of cases on histological confirmation [13]. In the present study the total number of bone tumors and tumor like lesions encountered were 50, of all histologically evaluated neoplastic lesions at the Department f pathology.

An epidemiological study of neoplasms in western India as reported by Paymaster show that tumors of the bone constituted 1.6% of all neoplasms [14]. A larger study extending over 20 years reported by Vyaghreshwarudu C conclude that bone tumors formed 1.35% among all other neoplasms [15]. A 3 year study done at a medical college hospital as reported by Jayaram R show that bone tumor and tumor like lesions constituted 2.8% of all neoplasms [16]. The frequency of bone tumors by histopathological evaluation in the present study was similar to that of Vyaghreshwarudu C and Paymaster [14,15].

Table 4: Table showing classification of bone lesions based on behavior from different studies and present study

Studies	Total	B:M	Benign tumors		Malignant tumors		Tumor like lesions	
			No.	%	No.	%	No.	%
Chitale AR (1987)	1222	1:2.1	300	24.5%	642	52.5%	280	22.9%
Nayar M (1979)	411	1:2.9	93	22.6%	273	66.4%	45	10.9%
Jayaram R (1997)	81	1:3	16	19.7%	48	59.2%	17	21%
Present study	50	1:1.68	16	32%	27	54%	7	14%

The precise incidence of specific bone tumors is not known because many benign bone lesions are not biopsied. Benign tumors of the bone outnumber their malignant counterparts by atleast several hundred fold.

In the present study, malignant bone tumors were more commonly encountered constituting 54% and benign bone tumors were 32% among all bone lesions. The benign to malignant ratio was 1:1.68. Similar observations were made by Chitale AR (Malignant 52.5% and B: M=1:2.2), Nayar M (Malignant 66.4%, Benign 22.6% and B:M= 1:2.9) and Jayaram R (Malignant 59.2%, benign 19.7% and B: M=1:3) [16].

Table 5: Table showing comparison of distribution of malignant bone tumors from other studies and present study

	Nayar M (1979) (n=273)	Jayaram R (1997) (n=48)	Dorfman HD (1994) (n=2627)	Present study (n=27)
Potential malignant osteoclastoma	63 (23.1%)	12 (25%)	-	17 (62.96%)
Malignant tumors osteosarcoma	64 (23.4%)	11 (22.9%)	922 (35.1)	3 (11.1%)
Chondrosarcoma	18 (6.6%)	05 (10.4%)	677 (25.8)	1 (3.70%)
Ewing's sarcoma	34 (12.4%)	05 (10.4%)	420 (16%)	02 (7.40%)
Myeloma	13 (4.8%)	03 (6.2%)	-	-
Lymphoma	18 (6.6%)	01 (2.1%)	-	-
Angiosarcoma	05 (1.8%)	-	36 (1.4%)	-
MFH	-	-	149 (5.7%)	-
Fibrosarcoma	06 (2.2%)	-	-	-
Undifferentiated	10 (3.7%)	-	32 (1.2%)	-
Chordoma	01 (0.4%)	01 (2.1%)	221 (8.4%)	-
Adamantinoma	01 (0.4%)	-	06 (5.2%)	-
Metastatic deposits	40 (14.6%)	09 (18.7%)	-	4 (14.81%)
Others	-	-	170 (6.4%)	-
Total	273	48	2627	27

All the above studies show that malignant bone tumors to be the most common histologically analysed bone lesion similar to the present study. The proportion of tumor like lesions in study reported by Chitale AR (22.9%) and Jayaram R (21%) is more than the present study (14%). The proportion of tumor like lesions is similar to the observation made by nayar M (10.9%) [16].

Among the malignant bone tumors, osteoclastoma was most commonly seen in the present study with 62.96% of malignant bone tumors. This is similar to the observation by Jayaram R which observed the potentially malignant bone tumor osteoclastoma to be the most common with 25% and osteosarcoma to be the 2nd most common (22.9%) malignant bone tumor [16]. While osteosarcoma was found to be most common malignant tumour in the study by Dorfman HD (35.1%) and Nayar M (23.4%) [17,18].

Conclusion

Newer imaging modalities like CT Scan, MR imaging and angiography can help in proper visualization of early bone neoplasms and tumour like lesions. Microscopy of bone tumour biopsies shows heterogeneous morphology. Adequate sampling of histopathological specimen with analysis of radiological pictures can help in diagnosing the lesion with certainty.

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