

Concordance between Radiological Features and Histopathological Diagnosis of Cartilaginous Lesions of Bone among Patients at a Tertiary Care Centre, Trivandrum, Kerala

JAYASREE KATTOOR¹, BALAJI RADHAKRISHNAN², SINDHU NAIR³, M VENUGOPAL⁴



ABSTRACT

Introduction: Cartilaginous tumours comprise a large, heterogeneous group of mesenchymal neoplasms. They pose a challenge in terms of accurate diagnosis and management. Histopathological findings have direct implications for treatment outcomes.

Aim: To determine the concordance between the radiological features and the histopathological diagnosis of cartilaginous lesions of bone.

Materials and Methods: This was a retrospective study conducted in the Department of Pathology, Regional Cancer Centre, Trivandrum, Kerala, India, among 109 patients with histopathologically proven benign and malignant cartilaginous tumours, received in the laboratory between January 2012 and December 2021 for a duration of 10 years, were analysed. The study was conducted between September 2019 and January 2022. The demographic data for the study, including age, tumour site, clinical findings, and radiological diagnosis, were obtained from medical records. The cases were histopathologically graded based on the World Health Organization 2020 classification of tumours of soft tissue and bone. The concordance between histopathological diagnosis and radiological features was assessed. The Chi-square test was used to find the association between two categorical variables, and the Independent sample t-test was used to find the difference between two groups with respect to mean and standard deviation.

Results: There were a total of 109 cases of cartilaginous tumours, out of which 82 cases (75.22%) were diagnosed as malignant and 27 cases (24.77%) were diagnosed as benign. Among benign neoplasms, chondroblastoma and osteochondroma were the most common, with 10 cases (37.03%) each. Among malignant chondroid tumours, 73 (89.02%) were diagnosed as conventional chondrosarcoma. There were five cases (6.09%) of secondary chondrosarcomas (malignant transformation of a benign cartilaginous lesion). Among the secondary chondrosarcomas, three cases (60%) were malignant transformation in osteochondroma, 1 (20%) in enchondroma, and 1 (20%) in synovial chondromatosis. Among the 91 cases for which radiology was available, 86 (94.50%) had a concordance between radiological and histopathological diagnosis. Five cases (5.49%) had a discordant radiological diagnosis.

Conclusion: For histologically benign tumours, the radiological findings in the study were identical and concordant. For histologically malignant tumours, there were discrepancies with radiological findings in this study when the lesion had an associated cyst, absence of cortical destruction, or absence of a clear cartilaginous component and extra cortical expansion. For histologically suspicious cases in the study, the final diagnosis was made based upon radiological findings, with a particular interest in cortical destruction.

Keywords: Benign tumours, Chondroblastoma, Cortical destruction, Imaging, Osteochondroma

INTRODUCTION

Bone tumours are uncommon, accounting for only 0.5% of total cancer incidence worldwide [1]. Cartilaginous neoplasms are defined as lesions that produce a cartilaginous matrix [2]. They are subclassified into benign and malignant lesions. Benign cartilaginous tumours behave indolently, and hence treatment is necessary only for symptomatic patients [3]. Grade I chondrosarcomas are treated with extensive intralesional excision with curettage, adjunctive burring, and bone void augmentation, whereas grade II and grade III lesions need extensive resection with reconstruction surgeries [4]. Small biopsy samples without radiological correlation can mislead in differentiating low-grade and high-grade tumours, which have entirely different management protocols.

Osteochondroma is the most common benign bone tumour, and chondrosarcoma is the third most common primary malignant bone tumour after myeloma and osteosarcoma. Chondroblastoma is the rarest, with a 1% incidence among benign bone lesions [5]. Certain benign cartilaginous neoplasms do not affect life expectancy, but certain lesions like osteochondromatosis have a higher risk of malignant transformation [6]. In the case of chondrosarcomas, a

few factors like the site and grade influence the prognosis of the patient. Particular importance must be given to identifying areas of dedifferentiation since they carry a poor prognosis compared to their well-differentiated counterparts.

The present study is limited only to cartilaginous lesions with concordant radiological assessment, similar studies are rare [7]. Hence, aim of the present study was to determine the concordance between the radiological features and the histopathological diagnosis of cartilaginous lesions of bone.

MATERIALS AND METHODS

This retrospective study was conducted in the Department of Pathology at Regional Cancer Centre, Trivandrum, Kerala, India, from September 2019 to January 2022 with data included from 1st January 2012 to 31st December 2021. The present study was conducted after obtaining ethical clearance from the Institutional Ethical Committee (IEC-IRB No.09/2019/01 dated 27.09.2019).

Sample size calculation: Sample size was calculated by applying the formula:

$$N=4 pq/e^2;$$

Where 'p' is the prevalence. The prevalence of cartilagenous tumours among bone tumours was taken as 67% [6].

So, $p=67$; $q=(1-p)$ and e =allowable error (13% in the present study). Thus, the final sample size (N) calculated was 53. A total of 109 cases of histologically diagnosed cartilagenous tumours were analysed.

Inclusion criteria: All the core needle, excision, and amputation specimens obtained from patients of all age groups, reported at the histopathology department as cartilagenous tumours, including benign, intermediate, and malignant tumours as classified under the World Health Organization (WHO) 2020 classification [8].

Exclusion criteria: Apart from cartilagenous lesions, all other tumours and inflammatory conditions of bone were excluded from the present study.

Study Procedure

The demographic data for the study, including age, tumour site, clinical findings, and radiological diagnosis, were obtained from medical records. The cases were histopathologically graded based on the WHO 2020 Classification of Tumours of Soft Tissue and Bone [8]. The concordance between histopathological diagnosis and radiological features was assessed.

STATISTICAL ANALYSIS

R-programming was used to analyse the empirical data. Categorical data was presented by frequency and percentage, whereas continuous numerical data was presented by mean and standard deviation. The Chi-square test was used to find the association between two categorical variables, and the Independent sample t-test was used to find the difference between two groups with respect to mean and standard deviation. The agreement between histopathological findings and radiological findings was assessed through sensitivity, specificity, positive predictive value, and negative predictive value. A level of significance of 5% is considered statistically significant.

RESULTS

In the present study, there were 109 cases of cartilagenous neoplasms, out of which 82 cases (75.22%) were diagnosed as malignant and 27 cases (24.77%) were diagnosed as benign. The male:female ratio was 1:1 with 54 males (49.54%) and 55 females (50.46%). The age of patients with benign cartilagenous neoplasms ranged from 7 to 65 years, and malignant cartilagenous neoplasms ranged from 8 to 76 years [Table/Fig-1].

Among the benign neoplasms, there were 10 (37.03%) cases of chondroblastoma and osteochondroma each, 3 (11.11%) enchondromas, and 2 (6.89%) cases each of chondromyxoid fibroma and synovial chondromatosis.

Among the 10 chondroblastomas, 7 (70%) were male and 3 (30%) were female, with an age range of 7 to 56 years. The most common radiological presentation was a well circumscribed lesion with preserved cortical lining [Table/Fig-2]. Microscopically, clusters of round to polyhedral chondroblasts with abundant cytoplasm and well-defined cell borders were noted [Table/Fig-3]. The most common site was the skull, with three cases (30%), followed by the humerus and tibia, with two cases (20%) each. Five cases (50%) were associated with a secondary aneurysmal bone cyst.

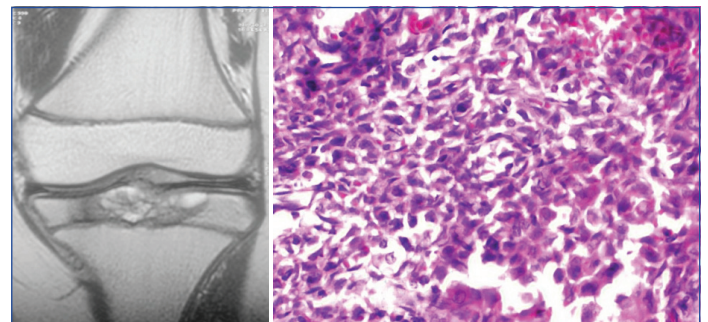
Among 10 cases of osteochondroma, 4 (40%) were males and 6 (60%) were females, with an age range of 7 to 43 years. Radiologically, only one case showed a sessile architecture with a cartilagenous cap [Table/Fig-4]. The most common site was the femur, with six cases (60%). One of the osteochondroma cases had developed multiple lesions in the femur, tibia, scapulae, right second and fifth ribs. The femoral lesion later transformed into chondrosarcoma.

Among the three cases of enchondromas, two were males and one was female, and the sites of occurrence were in the hand, foot, and humerus. Two (7.40%) of the benign cartilagenous neoplasms were chondromyxoid fibromas. One in a male and the other in a

female with lesions in the tibia and fibula respectively. Radiologically, a well-defined eccentrically located lytic lesion was found in both cases [Table/Fig-5]. Histologically, lobules of benign spindle cells in a background of chondromyxoid stroma was noted. [Table/Fig-6]. Two (7.40%) of the benign cartilagenous neoplasms were diagnosed as synovial chondromatosis [Table/Fig-7], with one case each in a male and female, both in the knee joints. Histologically, both cases had lobules of hyaline cartilage lined by benign chondrocytes with absent atypia [Table/Fig-7].

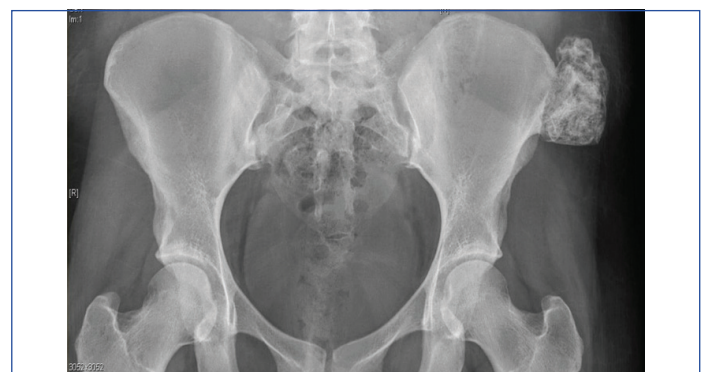
Types of tumours	Cases	Minimum age	Maximum age	Mean age	Sex		Most common site
					Male	Female	
Benign tumours (n=27)							
Chondroblastoma	10	7	56	24 years	7	3	Skull-30% (n=3)
Osteochondroma	10	7	43	23 years	4	6	Femur-60% (n=6)
Enchondroma	3	34	61	46 years	2	1	Metacarpal, Metatarsal and Humerus one (33.33%) each
Chondromyxoid fibroma	2	36	46	41 years	1	1	Tibia and Fibula one (50%) each
Synovial chondromatosis	2	46	65	56 years	1	1	Knee joint -100% (n=2)
Malignant tumours (n=82)							
Conventional chondrosarcoma	73	16	76	46 years	36	37	Humerus-17.80% (n=13)
Mesenchymal chondrosarcoma	3	8	65	27 years	1	2	Skull-66.66% (n=2)
Dedifferentiated chondrosarcoma	4	48	69	54 years	1	3	Pelvis- 75% (n=3)
Clear cell chondrosarcoma	2	32	65	49 years	1	1	Humerus and Femur- one (50%) each

[Table/Fig-1]: Demographics of patients (N=109).



[Table/Fig-2]: Magnetic Resonance Imaging (MRI) Knee of a chondroblastoma demonstrating a well circumscribed heterointense lesion in the tibial epiphysis.

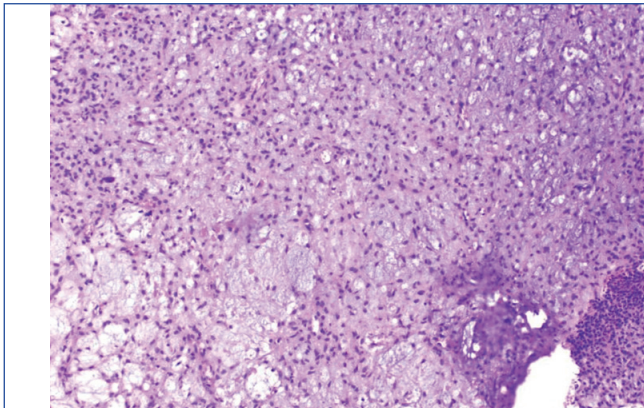
[Table/Fig-3]: Microscopic examination showing small round cells with hyperchromatic nuclei, scant cytoplasm, and surrounding chicken wire type calcification, diagnosed as chondroblastoma (H&E, 40x). (Images from left to right).



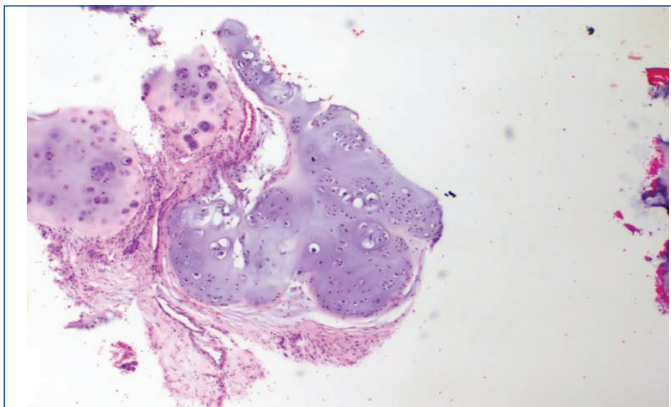
[Table/Fig-4]: X-ray pelvis of an osteochondroma showing sessile growth with a cartilagenous cap that is continuous with the underlying bone.



[Table/Fig-5]: X-ray tibia of a chondromyxoid fibroma showing a well-defined, eccentric osteolytic lesion in the proximal epiphyseal region.



[Table/Fig-6]: Microscopic examination showing lobules of spindle cells in a background of myxoid stroma, diagnosed as Chondromyxoid fibroma. (H&E, 10x).



[Table/Fig-7]: Microscopic examination showing lobules of hyaline cartilage with underlying synovium, diagnosed as synovial chondromatosis (H&E, 10x).

Out of total, 73 cases (89.02%) of malignant cartilagenous neoplasms were diagnosed as conventional chondrosarcoma and 36 (49.31%) were males and 37 (50.69%) were females, with a male-female ratio of 1:1. The most common site was the humerus, with 13 cases (17.80%), followed by the femur with 12 cases (16.43%) [Table/Fig-8].



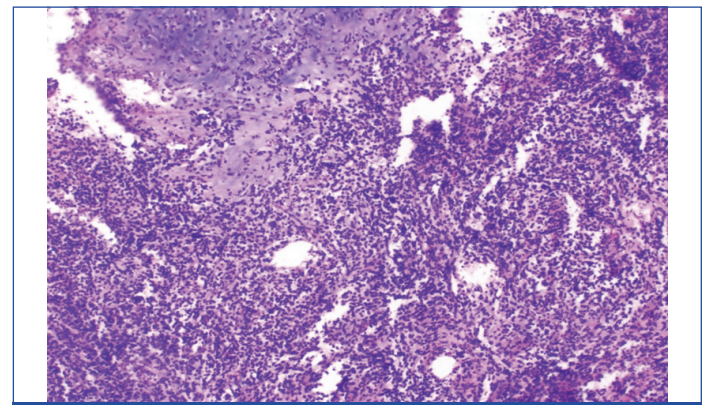
[Table/Fig-8]: Distribution of conventional chondrosarcomas by site.

One patient had a lesion both in the tibia and fibula. According to WHO, 24 cases (32.87%) were grade I, 42 cases (57.53%) were grade II, and 7 cases (9.58%) were grade III. 68 cases (93.15%) were primary chondrosarcomas. Radiologically, the most common finding was a large lytic lesion with thickened cortex, cortical erosion, and cartilagenous calcifications [Table/Fig-9]. Histologically, varying degree of cellularity, atypia, and mitotic activity was noted depending upon the chondrosarcoma grade. There were five cases (6.09%) of secondary chondrosarcomas (malignant transformation of a benign cartilagenous lesion). There were three cases (60%) of malignant transformation in osteochondroma, one case (20%) of multiple enchondromatosis, and one case (20%) of synovial chondromatosis among the secondary chondrosarcomas.



[Table/Fig-9]: X-ray pelvis of a case of conventional chondrosarcoma showing a large irregular lytic lesion in the left ilium associated with opacity and cartilagenous calcifications.

There were three cases (3.66%) of mesenchymal chondrosarcoma, two of which presented in the skull while the other was in the femur. Histologically, all cases had a small round cell component with interspersed areas of cartilage [Table/Fig-10].

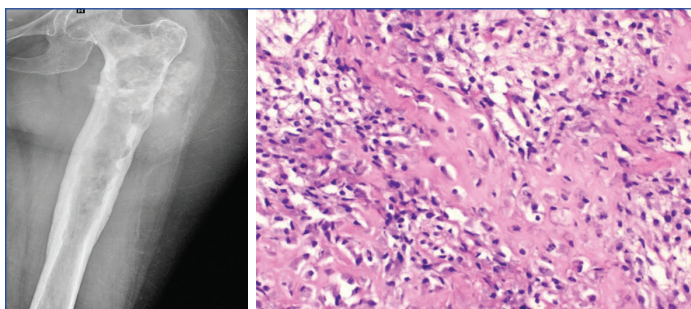


[Table/Fig-10]: Microscopic examination showing a tumour with sheets of small round cells with areas of cartilagenous tissue, diagnosed as mesenchymal chondrosarcoma. (H&E, 10x)

There were four cases (4.88%) of dedifferentiated chondrosarcoma, with three cases having an osteosarcoma component. The other case had an undifferentiated spindle cell sarcoma component. Three of the cases presented in the pelvis, with one case in the femur. Radiologically, an aggressive bone lesion with adjacent soft tissue calcification was noted. [Table/Fig-11] Histologically, interspersed islands of malignant osteoid lined by round to spindle cells with hyperchromatic nuclei and nuclear atypia were noted [Table/Fig-12]. There were two cases (2.43%) of clear cell chondrosarcoma, in the femur and humerus, respectively. Histologically, clear cell chondrosarcoma showed sheets of round to polygonal cells with clear cytoplasm, one case also showed a giant cell reaction [Table/Fig-13].

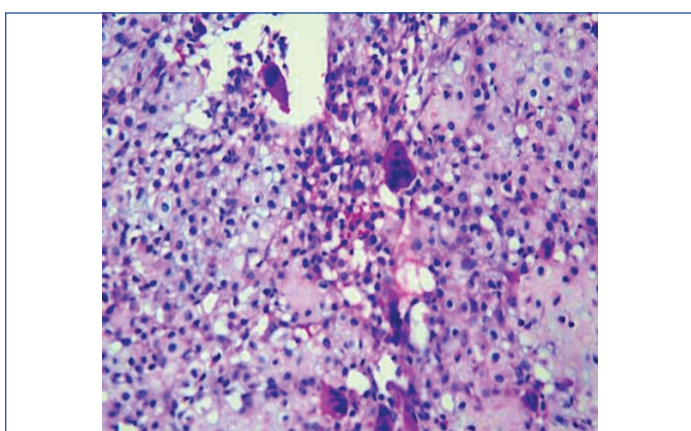
Radiological details were available for 91 cases. Eighty six (94.50%) of the 91 cases had a concordance between radiological and histopathological diagnosis. Five cases (5.49%) had histopathological and radiological discordance [Table/Fig-14]. The statistical significance value (p-value=0.406) of gender reveals that

there was no statistically significant difference in the male-female ratio among the patients with benign and malignant conditions. However, age was statistically different among the patients with benign and the patients with malignant (p-value=0.001) [Table/Fig-15]. In other words, patients with malignancy were older than patients with benign conditions.



[Table/Fig-11]: X-ray femur of dedifferentiated chondrosarcoma showing an aggressive bone lesion with cortical expansion and soft tissue ossification.

[Table/Fig-12]: Microscopic examination showing a case of dedifferentiated chondrosarcoma showing an osteosarcoma component with malignant osteoid (H&E, 10x). (Images from left to right).



[Table/Fig-13]: Microscopic examination showing a case of clear cell chondrosarcoma with adjacent giant cell reaction (H&E, 10x).

Cases	Radiological diagnosis	Site	Histopathological diagnosis
Case I	Giant cell tumour	Femur	Chondrosarcoma grade II
Case II	Primitive neuroectodermal tumour	Femur	Chondrosarcoma grade II
Case III	Tumour of neural origin	Femur	Chondrosarcoma grade II
Case IV	Chondroma	Scapula	Chondrosarcoma grade II
Case V	Benign cartilagenous lesion	Humerus	Chondrosarcoma grade I

[Table/Fig-14]: Concordance between histopathological and radiological findings. Five out of 91 cases which had discordance between histopathological and radiological findings

Variables	Histopathological findings		p-value
	Benign	Malignant	
Gender			
Male	15 (55.55%)	39 (47.56%)	0.406
Female	12 (44.44%)	43 (52.44%)	
Total	27 (100.0%)	82 (100.0%)	
Age (Mean±SD)	29.52±16.41	46.07±14.04	0.001

[Table/Fig-15]: Demographics of patients with p-value (N=109). Based on 109 patients; P-value<0.05 was considered as statistically significant

It was concluded that 93.75% of the patients with malignancy shall had positive result in radiological diagnosis (sensitivity). Whereas, 100% of the patients with benign lesion will had negative results in radiological diagnosis (specificity) [Table/Fig-16]. Positive Predictive Value (PPV) indicated that if the patient's radiological diagnosis was malignant, there is a 100% chance that the patient really had malignancy,

whereas Negative Predictive Value (NPV) indicated that if the patient's radiological diagnosis was benign, there was a 87.1% chance that the patient really had a benign lesion.

Histopathological findings	Radiological findings		Validity of radiological findings	
	Benign	Malignant	Sensitivity=	PPV=100%
Benign	27	0	93.75%	NPV=87.1%
Malignant	4	60	Specificity=100%	

[Table/Fig-16]: Sensitivity, specificity, PPV, and NPV of radiological findings (based on 91 patients).

DISCUSSION

Cartilagenous tumours form the second largest group of primary bone tumours. The presentation of cartilagenous tumours differs according to site, location, and age group. Subclassifying the cartilagenous tumours as benign, malignant, and locally aggressive (intermediate) is important since treatment protocols differ for each category [4].

Benign Cartilagenous Tumours Osteochondroma

Osteochondroma is the most common benign tumour of the bone [2]. In the present study, osteochondromas and chondroblastomas were the most common benign tumours. According to the literature review, the most common site of involvement of osteochondromas are in the lower extremities [9], which is also the same in the present study, with the femur being the most common site with six cases. [60%] 15% of osteochondromas occur as multiple lesions in the context of hereditary multiple osteochondromas [10]. The percentage of solitary osteochondromas undergoing malignant transformation is 1-2%, while for multiple osteochondromas the risk of transformation is between 1% and 25% [11-13]. One [10%] of the 10 cases in the current study presented in multiple sites and the femoral lesion of the same patient had undergone malignant transformation. Two of the 10 cases had a cartilagenous cap thickness of more than 2 cm [3.5 and 3.2 cm]. Cap thickness greater than 2 cm is a high-risk indicator for transformation [13]. Radiologically, there is a stalk-like extension and the cortex and medulla are continuous with the underlying bone [14]. In the index study, nine cases were diagnosed radiologically as osteochondroma and 1 case was diagnosed as a benign cartilagenous lesion with no evidence of bone expansion, cortical thickening, or destruction. This case had a sessile architecture with absent stalk formation. There was 100% concordance between radiology and histopathology. In their retrospective study Bernard et al., had found that Computed Tomography (CT) imaging had a sensitivity and specificity of 100% and 95% in distinguishing chondrosarcoma [15], which mirrors in the present study. One of the differential diagnoses to be considered for osteochondroma is paraosteal osteochondromatous proliferation, also called Nora's lesion [2]. Histologically, Nora's lesion shows hypercellular cartilage with atypia. All the osteochondromas in our study had organised bland hyaline cartilage, and hence diagnosis was straightforward after radiological correlation.

Chondroblastoma

Chondroblastoma is rare and accounts for less than 1% of all primary bone tumours. However, in the present study, it was the most common along with osteochondroma. The literature review shows the average age range is 19 to 23 years [16], which is the same as in the present study with the exception of three cases in which two were above 30 years and one was 56 years old. The outcome is the same in adults and children, with the exception that the most common sites in adults are small tubular bones like the talus and calcaneum, as opposed to long tubular bones in children [17,18]. However, in the index study the most common site involved was temporal bone. Chondroblastoma presents as a solitary lesion.

All cases in this study were solitary lesions. Chondroblastoma is commonly associated with secondary aneurysmal bone cyst [16] and is the most common cartilagenous neoplasm to be associated with secondary aneurysmal bone cyst [19]. Five cases (50%) in the current study were presented with secondary aneurysmal bone cyst. Malignant transformation in chondroblastomas is rare, with only three cases reported in the literature so far [20]. One of the temporal bone chondroblastomas had multiple recurrences at the same site and is symptom-free now. The typical radiological finding in chondroblastomas is a radiolucent lesion with well-defined borders and a sclerotic rim [3]. In the present study, seven cases were diagnosed radiologically as chondroblastoma, correlating with the younger age of these patients. Two cases were diagnosed as benign cartilagenous lesion. One case was diagnosed as an aneurysmal bone cyst, the reason being a large cyst in radiology with a small cartilagenous component. All cases were diagnosed as benign radiologically, and there was 100% concordance.

All cases histologically showed classical round chondroblasts in a background of chondroid matrix, and hence the histopathological diagnosis was straightforward.

Enchondroma

Enchondroma is a medullary bone lesion that arises from the diaphyseal shaft. The most common site is the small bones of the hands [21]. The sites of the lesion in the present study were the humerus, hand, and foot, with one case each.

Radiologically, enchondromas are well demarcated and central in location [3]. In the present study, two of the cases were diagnosed as enchondroma, considering the location in the metatarsal and metacarpal, respectively. One was diagnosed as a benign chondromatous lesion, probably an osteochondroma, considering the location in the humerus. However, no stalk was visualised, and probably a sessile type was considered. Hence, all cases were diagnosed as benign, and hence there was 100% concordance between radiology and histopathology. In their study, Vidoni et al., found that out of 9 chondroblastomas diagnosed by imaging, 8 had concordant histological diagnosis. One case was diagnosed histologically as an osteoblastoma [22]. Histologically, the closest differential diagnosis for enchondroma is low-grade chondrosarcoma. Because enchondromas can also show increased cellularity and atypia, especially in the small bones of the hand and feet, bone permeation is the definitive feature for diagnosing a lesion as chondrosarcoma [23]. One of the three cases, which was a needle biopsy in the present study, showed atypical features such as myxoid change and increased cellularity. Cortical destruction or permeation of bone spicules was absent. It was difficult to categorise in needle biopsies and radiological correlation was essential for proper categorisation.

Chondromyxoid Fibroma

Chondromyxoid fibroma represents less than 1 % of all tumours of bone [24]. It has a wide age range, from 3 to 70 years [24]. The long bones are most commonly affected, with the tibia being the most common site [25], which is in correlation with the present study, with one case in the tibia and the other in the fibula.

Radiologically, chondromyxoid fibroma is an expansile lytic lesion with internal septations and sharply demarcated borders [3]. In the current study, both the cases radiologically showed an eccentric defect with thinned out cortex, sclerotic borders, and absent cortical destruction, and hence were diagnosed as benign cartilagenous lesions with a differential diagnosis of chondromyxoid fibroma. There was 100% concordance between radiology and histopathology. It is difficult to differentiate chondromyxoid fibroma from chondrosarcoma in small biopsies, since chondromyxoid fibroma can show a haphazard arrangement. Altering hypocellular and hypercellular areas seen in excision specimens can be missed in small biopsies. One case was excision, and the diagnosis was straightforward. The second case

was difficult to diagnose on needle biopsy because of nuclear atypia and haphazard arrangement. Subsequent excision biopsy proved it to be a chondromyxoid fibroma.

Synovial Chondromatosis

Synovial chondromatosis is rare and affects the third to fifth decade of life [25]. The most common site is the knee [26], which is in concurrence with the present study. Radiologically, the involved joint shows calcified bodies and can cause marginal bone erosion. Non-calcified bodies are usually visualised on a CT scan [26]. In this study, one lesion that presented in the knee joint had joint distention and intra-articular bodies with varying mineralization radiologically and hence was diagnosed as synovial chondromatosis. The other case was localised in the tibia with associated joint effusion and arthritis. A diagnosis of benign cartilagenous lesion with joint effusion was given. Malignancy was ruled out. Histology of both cases showed lobules of hypercellular hyaline cartilage and clustering of chondrocytes. There was 100% concordance between radiology and histopathology.

Malignant Cartilagenous Tumours

Chondrosarcoma-Conventional Type

Conventional chondrosarcoma occurs in older patients with a peak incidence between the 5th and 7th decades [27]. However, the mean age group of conventional chondrosarcomas in this study was 46 years, with seven (9.58%) cases younger than 25 years. Some authors suggest that chondrosarcomas at a younger age tend to have a worse prognosis compared to adults [28]. Other authors, however, claim that there is no difference in prognosis between adults and younger patients [29,30]. In the present study, none of the cases under 25 years of age were diagnosed as grade III. Conventional chondrosarcoma can involve any bone, with the most common site of involvement being the femur, followed by the humerus, which is in concurrence with this study. Histologically, all cases had bone permeation, which is the pathognomic feature for diagnosing chondrosarcoma. Radiologically, conventional chondrosarcoma shows a mixed lytic and sclerotic pattern with ring and arc type of calcification. Differentiating between atypical borderline lesions and malignant tumours is the most trickiest with both pathologists and radiologists having high inter-observer variability [7]. These are the five cases that had discordance between radiological and histopathological diagnosis.

Case 1: The patient was a 50-year-old male who presented with a painful swelling in the femur. Radiology revealed a predominant cystic component with an eccentrically located radiolucent lesion with non sclerotic margins. Based on the age, site and cystic component, a radiological diagnosis of giant cell tumour was given. The histology sections showed an extensive cystic component and a minor malignant moderate grade cartilagenous component and was diagnosed as grade II chondrosarcoma.

Case 2: The patient was a 23-year-old male who presented with a lesion in the femur. Radiology revealed a hyperattenuating large solid mass with cortical destruction and a probable diagnosis of primitive neuroectodermal tumour was given. Literature shows that a large solid mass with aggressive bone destruction is the classical presentation of the Ewing/PNET family of tumours [31]. The histology sections showed entirely atypical cartilagenous islands and was diagnosed as grade II chondrosarcoma. No round cell component was noted.

Case 3: The patient was a 56-year-old female who presented with a lesion in the lower femur. Imaging showed an expansile lesion involving bone and an adjacent soft tissue component. A probable diagnosis of tumour with neural origin was given. Histology was given as grade II chondrosarcoma. No neural component was noted in the sections studied.

Case 4: The patient was a 49-year-old female who presented with a lesion in the scapula. Radiology showed a cartilagenous lesion with

thinned out, mild endosteal scalloping and intact cortex. No cortical destruction or extension into adjacent soft tissue was noted. Hence, a diagnosis of chondroma was given radiologically. Histologically, most of the islands were benign, with a single focus exhibiting higher grade cartilage being noted, hence it was diagnosed as grade II chondrosarcoma. Increased tumour length was considered as a parameter to distinguish grade I chondrosarcoma from enchondroma [32]. Recent research, however, indicates that tumour length is insignificant in distinguishing enchondroma from grade I chondrosarcoma [33].

Case 5: The patient was a 58-year-old male who presented with a swelling in the humerus. Radiologically, a well-defined lesion with chondroid calcification and an intact cortex was noted. Similar to case 4, it was diagnosed as a benign cartilaginous lesion, but histologically turned out to be a grade II chondrosarcoma with evidence of adjacent bone permeation. In their retrospective study, Miwa et al., found that endosteal scalloping and cortical defect had high sensitivity (96.7% and 86.7% respectively). Whereas, periosteal reaction and extraskelatal mass involvement had very high specificity [100%] in diagnosing atypical cartilaginous tumour/chondrosarcoma [34].

Chondrosarcomas are graded based on cellularity, pleomorphism, and necrosis. In the present study grade I, grade II, and grade III were 32.87%, 52.53%, and 9.58% respectively. Aggerholm-Pedersen N et al., claim that grade I was more common than grades II and III (46%, 29%, and 25%, respectively) [35]. Within conventional chondrosarcomas, grade I had an 89 % five year survival rate compared to 57 % for grade II and grade III [27].

Five cases (6.09%) in the present study were secondary chondrosarcomas, which is less compared to other studies in which secondary chondrosarcomas made up to 15 % of conventional chondrosarcomas [27]. Three of the secondary chondrosarcomas had an osteochondromatous precursor component. As shown in various studies, solitary osteochondroma is the most common preexisting benign lesion [36,37].

Dedifferentiated Chondrosarcoma

Dedifferentiated chondrosarcoma is a distinct subtype of chondrosarcoma showing a cartilaginous tumour with an abrupt transition to a higher-grade non cartilaginous tumour. The age of presentation is a decade older than conventional chondrosarcomas [21]. However, in the present study, only one patient was older than sixty years, with the remaining patients under 50 years. The most common sites of involvement are the femur and pelvis [38]. Out of the four cases in the current study, one was in the femur and the other three in the pelvis. The most common dedifferentiating malignant component is a high-grade spindle cell sarcoma, mostly an undifferentiated high-grade sarcoma [21]. However, in some studies, the most common dedifferentiated component is osteosarcoma [39], which is in concurrence with the present study, which had three out of four cases with an osteosarcoma component. The other case had an undifferentiated spindle cell sarcoma. Radiologically dedifferentiated chondrosarcoma shows a cartilaginous neoplasm with an associated aggressive lytic component invading into the adjacent soft tissues [40]. In the present study, radiologically, three cases (75%) were diagnosed as malignant chondrosarcoma. Histologically, all the cases were diagnosed as dedifferentiated chondrosarcoma, with the percent of dedifferentiated areas being 11%, 16%, and 24%, respectively. One case (25%) was diagnosed radiologically as osteosarcoma. This case histologically had a dedifferentiated component of osteosarcoma. The percentage of the dedifferentiated osteosarcoma component was 43%. The percent of dedifferentiated component ranges from 2-98% [41]. However, the associated cartilaginous component was low grade. With the above findings and the age of the patient being 69 years, a diagnosis of dedifferentiated chondrosarcoma

with an osteosarcoma component was given. There was 100 % concordance between radiology and histopathology.

Mesenchymal Chondrosarcoma

Mesenchymal chondrosarcoma has an age range of 10-20 years. In the present study, two of the three patients were younger than 10 years. One patient presented at the age of 65 years. The most common site of involvement is the craniofacial region, especially the mandible and maxilla [27]. In the current study, two cases of mesenchymal chondrosarcoma were in the skull and the other in the femur. In the current study, all three cases were diagnosed as malignant chondrosarcoma both radiologically and by histology. There was 100% concordance between histopathology and radiology.

Clear Cell Chondrosarcoma

Clear cell chondrosarcoma has a very good prognosis with >80% 5-year survival, and dedifferentiated chondrosarcoma has a very bad prognosis with 10% five year survival [27]. Clear cell chondrosarcoma involves the long bones, which is the same in the present study, with the femur and humerus being the sites involved in the two cases. Radiologically, both cases were diagnosed as chondrosarcoma with cortical expansion and destruction. A histopathological diagnosis of clear cell chondrosarcoma was made since the major component in the tumour had clear or ground glass cytoplasm. Because neither case had any additional conventional chondrosarcoma components, the diagnosis was simple. There was 100% concordance between radiology and histopathology.

There is a low reliability for the grading of cartilaginous lesions in long bones, even among specialised and experienced pathologists and radiologists [10]. Slightly improved agreement was observed for lesions that had MRI imaging available compared to plain radiographs and computed tomography scans alone. [10]. The positive predictive value and negative predictive value in the present study were 0.93, and 1.00 respectively. Feldman et al., [PPV-1.00 NPV-0.95], Jesus Garcia et al., [PPV 0.95, NPV 0.94] had similar predictive values of the current study [42,43].

Limitation(s)

Even though histopathology is the gold standard for diagnosing cartilaginous tumours, the limitations of the study were that tests like immunohistochemistry and molecular genetic testing were not performed.

CONCLUSION(S)

Benign histological diagnoses in the study had no discordance with radiological findings. However, a few malignant histological diagnoses were classified as benign lesions whenever radiologically there was an associated large cyst or absence of cortical destruction or extracortical expansion. For core needle biopsies with suspicious atypical areas, the radiological correlation was the key to clinching the diagnosis. The utility of core needle biopsies in dedifferentiated sarcomas to represent the entire spectrum is questionable, and hence radiological correlation is mandatory. Prospectively, we believe that combined radiological and histomorphological efforts might play a significant role in subtyping the cartilaginous tumours, which may help to refine treatment protocols.

REFERENCES

- [1] Mohammed A, Sani MA, Hezekiah IA, Enoch AA. Primary bone tumours and tumour-like lesions in children in Zaria, Nigeria. *Afr J Paediatr Surg.* 2010;7(1):16-18.
- [2] Bukhari MH, Qamar S, Shamsi FB, Bambal K, Bedi M, Noaty M. Facts Sheets of Cartilage Tumors. *Classifications and Differential Diagnosis- Review Article.* *APMC.* 2016;10(4):172-87.
- [3] Suster D, Hung YP, Nielsen GP. Differential Diagnosis of Cartilaginous Lesions of Bone. *Arch Pathol Lab Med.* 2020;144(1):71-82.
- [4] Wells ME, Childs BR, Eckhoff MD, Rajani R, Potter BK, Polfer EM. Atypical Cartilaginous Tumors: Trends in Management. *J Am Acad Orthop Surg Glob Res Rev.* 2021;5(12): e21.00277.

- [5] Rozeman LB, Cleton-Jansen AM, Hogendoorn PC. Pathology of primary malignant bone and cartilage tumours. *Int Orthop*. 2006;30(6):437-44.
- [6] Sugiyama H, Omonishi K, Yonehara S, Ozasa K, Kajihara H, Tsuya T, et al. Characteristics of Benign and Malignant Bone Tumors Registered in the Hiroshima Tumor Tissue Registry, 1973-2012. *JB JS Open Access*. 2018; 3(2):e0064.
- [7] Skeletal Lesions Interobserver Correlation among Expert Diagnosticians (SLICED) Study Group. Reliability of histopathologic and radiologic grading of cartilaginous neoplasms in long bones. *J Bone Joint Surg Am*. 2007;89(10):2113-23.
- [8] WHO Classification of Tumours Editorial Board. Soft tissue and bone tumours. Lyon (France): International Agency for Research on Cancer; 2020. (WHO classification of tumours series, 5th ed.; vol. 3). <https://publications.iarc.fr/588>.
- [9] Bovée JV. Multiple osteochondromas. *Orphanet J Rare Dis*. 2008;3:3.
- [10] Kitsoulis P, Galani V, Stefanaki K, Paraskevas G, Karatzias G, Agnantis NJ, et al. Osteochondromas: Review of the clinical, radiological and pathological features. *In Vivo*. 2008;22(5):633-46.
- [11] Canella P, Gardini F, Boriani S. Exostosis: development, evolution and relationship to malignant degeneration. *Ital J Orthop Traumatol*. 1981;7(3):293-98.
- [12] Garrison RC, Unni KK, McLeod RA, Pritchard DJ, Dahlin DC. Chondrosarcoma arising in osteochondroma. *Cancer*. 1982;49(9):1890-97.
- [13] Peterson HA. Multiple hereditary osteochondromata. *Clin Orthop Relat Res*. 1989;239:222-30.
- [14] Uhl M, Herget G, Kurz P. Chondrogene Knochentumoren: Pathologie und Radiomorphologie [Cartilage tumors: Pathology and radiomorphology]. *Radiologe*. 2016;56(6):476-88.
- [15] Bernard SA, Murphey MD, Flemming DJ, Kransdorf MJ. Improved differentiation of benign osteochondromas from secondary chondrosarcomas with standardized measurement of cartilage cap at CT and MR imaging. *Radiology*. 2010;255(3):857-65.
- [16] Chen W, DiFrancesco LM. Chondroblastoma: An Update. *Arch Pathol Lab Med*. 2017;141:867-71.
- [17] Angelini A, Hassani M, Mavrogenis AF, Trovarelli G, Romagnoli C, Berizzi A, et al. Chondroblastoma in adult age. *Eur J Orthop Surg Traumatol*. 2017;27(6):843-49.
- [18] Xu H, Nugent D, Monforte HL, Binitie OT, Ding Y, Letson GD, et al. Chondroblastoma of bone in the extremities: a multicenter retrospective study. *J Bone Joint Surg Am*. 2015;97(11):925-31.
- [19] Sasaki H, Nagano S, Shimada H, Yokouchi M, Setoguchi T, Ishidou Y, et al. Diagnosing and discriminating between primary and secondary aneurysmal bone cysts. *Oncol Lett*. 2017;13(4):2290-96.
- [20] Narhari P, Haseeb A, Lee S, Singh VA. Spontaneous Conventional Osteosarcoma Transformation of a Chondroblastoma: A Case Report and Literature Review. *Indian J Orthop*. 2018;52(1):87-90.
- [21] Qasem SA, DeYoung BR. Cartilage-forming tumors. *Semin Diagn Pathol*. 2014;31(1):10-20.
- [22] Vidoni A, Pressney I, Saifuddin A. Paediatric bone lesions: diagnostic accuracy of imaging correlation and CT-guided needle biopsy for differentiating benign from malignant lesions. *Br J Radiol*. 2021;94(1120): 20201234.
- [23] Weiner SD. Enchondroma and chondrosarcoma of bone: clinical, radiologic, and histologic differentiation. *Instr Course Lect*. 2004;53:645-49.
- [24] Wu CT, Inwards CY, O'Laughlin S, Rock MG, Beabout JW, Unni KK. Chondromyxoid fibroma of bone: a clinicopathologic review of 278 cases. *Hum Pathol*. 1998;29(5):438-46.
- [25] Evans S, Boffano M, Chaudhry S, Jeys L, Grimer R. Synovial chondrosarcoma arising in synovial chondromatosis. *Sarcoma*. 2014;2014:647939.
- [26] Hermann G, Klein MJ, Abdelwahab IF, Kenan S. Synovial chondrosarcoma arising in synovial chondromatosis of the right hip. *Skeletal Radiol*. 1997;26:366-9.
- [27] Kim MJ, Cho KJ, Ayala AG, Ro JY. Chondrosarcoma: with updates on molecular genetics. *Sarcoma*. 2011;2011:405437.
- [28] Huvos AG, Marcove RC. Chondrosarcoma in the young. A clinicopathologic analysis of 79 patients younger than 21 years of age. *Am J Surg Pathol*. 1987;11(12):930-42.
- [29] Gambarotti M, Righi A, Picci P, Bertoni F, Manfrini M, Donati DM, et al. Paediatric chondrosarcomas: A retrospective review of 17 cases. *Histopathology*. 2016;68(7):1073-78.
- [30] Young CL, Sim FH, Unni KK, McLeod RA. Chondrosarcoma of bone in children. *Cancer* 1990;66(7):1641-48.
- [31] Murphey MD, Senchak LT, Mambalam PK, Logie CI, Klassen-Fischer MK, Kransdorf MJ. From the radiologic pathology archives: ewing sarcoma family of tumors: radiologic-pathologic correlation. *Radiographics*. 2013;33(3):803-31.
- [32] Wang XL, De Beuckeleer LH, De Schepper AM, Van Marck E. Low-grade chondrosarcomas: A retrospective review of 17 cases. *Eur Radiol*. 2001;11(6):1054-57.
- [33] Choi WH, Han EJ, Chang KB, Joo MW. Quantitative SPECT/CT for differentiating between enchondroma and grade I chondrosarcoma. *Sci Rep*. 2020;10(1):10587.
- [34] Miwa S, Yamamoto N, Hayashi K, Takeuchi A, Igarashi K, Tada K, et al. A Radiological Scoring System for Differentiation between Enchondroma and Chondrosarcoma. *Cancers (Basel)*. 2021;13(14):3558.
- [35] Aggerholm-Pedersen N, Maretty-Nielsen K, Baerentzen S, Jørgensen PH, Hansen BH, Baad-Hansen T et al. Chondrosarcoma: the impact of comorbidity-30 years of experience from a population-based database including 199 consecutive chondrosarcoma patients. *Orthop Res Rev*. 2019;11:109-16.
- [36] Ahmed AR, Tan TS, Unni KK, Collins MS, Wenger DE, Sim FH: Secondary chondrosarcoma in osteochondroma: Report of 107 patients. *Clin Orthop Relat Res* 2003;411:193-206.
- [37] Coley BL, Higinbotham NL: Secondary chondrosarcoma. *Ann Surg* 1954;139(5):547-59.
- [38] Mitchell AD, Ayoub K, Mangham DC, Grimer RJ, Carter SR, Tillman RM. Experience in the treatment of dedifferentiated chondrosarcoma. *J Bone Joint Surg Br*. 2000;82(1):55-61.
- [39] Huang J, Zhang HZ, Zheng L, Zhou J, Jiang ZM. Clinicopathologic diagnosis of dedifferentiated chondrosarcoma. *Zhonghua Bing Li Xue Za Zhi*. 2009;38(12):820-23.
- [40] Biery G, Feydy A, Larousserie F, Pluot E, Guerini H, Campagna R, et al. Chondrosarcomes dédifférenciés: revue iconographique radio-pathologique [Dedifferentiated chondrosarcoma: Radiologic-pathologic correlation]. *J Radiol*. 2010;91:271-9.
- [41] Staals EL, Bacchini P, Bertoni F. Dedifferentiated central chondrosarcoma. *Cancer*. 2006;106(12):2682-91.
- [42] Feldman F, Vanheertum R, Saxena C. 18Fluoro-deoxyglucose positron emission tomography evaluation of benign versus malignant osteochondromas: preliminary observations. *J Comput Assist Tomogr*. 2006;30(5):858-64.
- [43] Korukian M, de Carvalho Campos Neto G, Wagner J. Is PET-CT an accurate method for the differential diagnosis between chondroma and chondrosarcoma? *Springerplus*. 2016;5:236.

PARTICULARS OF CONTRIBUTORS:

1. Professor and Head, Department of Pathology, Regional Cancer Centre, Trivandrum, Kerala, India.
2. Assistant Professor, Department of Pathology, SRM Institute of Science and Technology, Kattankulathur, Tamil Nadu, India.
3. Assistant Professor, Department of Pathology, Regional Cancer Centre, Trivandrum, Kerala, India.
4. Professor and Head, Department of Radiology, Regional Cancer Centre, Trivandrum, Kerala, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Balaji Radhakrishnan,
68 E/4 RV Street Alagesan Nagar, Chengalpattu-603001, Tamil Nadu, India.
E-mail: balajir11@srmist.edu.in

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Apr 27, 2022
- Manual Googling: Sep 12, 2022
- iThenticate Software: Sep 22, 2022 (6%)

ETYMOLOGY: Author OriginDate of Submission: **Apr 26, 2022**Date of Peer Review: **May 23, 2022**Date of Acceptance: **Oct 12, 2022**Date of Publishing: **Nov 01, 2022**