Original Article ISSN (O):2395-2822; ISSN (P):2395-2814

A Retrospective Study of Histopathology and Clinical Correlation of Primary Benign Bone tumours at Thoothukudi Medical College, India.

Saranya K[1], P. Kannan[2]

[1]Assistant Professor. Department of Pathology, Thoothukudi Medical College.
[2]Professor and Head, Department of Pathology, Thoothukudi Medical College.

Received: March 2019
Accepted: March 2019

ABSTRACT

Background: The study was conducted to understand the clinical algorithm of benign bone tumours. Correlation was done by clinical presentation with radiological features and histopathology features. The osteogenic tumours are considered as one group because their common characteristic feature is the production of an osteoid or bone matrix by the tumour cells. The cartilaginous tumours have the characteristic feature of production of cartilage matrix. AIM: We have reported 62 cases of bone tumours during the study period of 5 years in the Department of Pathology, Thoothukudi Medical College, India. The cases were thoroughly studied by histopathology and 28 cases were diagnosed as benign tumours among which 8 cases were benign osteoid producing and 20 cases were diagnosed as benign cartilage producing tumours conclusively. The Histopathology diagnosis was correlated with the Radiological features. **Methods:** We have reported 62 cases of bone tumours during the study period of 5 years in the Department of Pathology, among which 28 cases were diagnosed as benign bone tumours. A total of 8 cases were osteoid producing and 20 cases were cartilage producing tumours conclusively. All the relevant clinical data of the patients were searched from the ward records. The data was stored in the Department computer server was very much useful in the study. The initial step in the assessment of patients with bone tumours is a good medical history, including age, gender, type and duration of symptoms, localization of the mass, and presence of a history of trauma. CT scan was useful in osteoid lesions. MRI Scan played a crucial role in cartilage producing tumours. Tests to assess general health included a complete blood count , differential count , tests for serum electrolytes including calcium, magnesium, phosphate, liver function studies, blood group typing, a coagulation profile, tests for hepatitis and human immunodeficiency virus infection were taken and recorded. **Results:** The total number of benign bone tumours reported during the 5 years period was 28 cases,. In benign bone tumours osteochondroma was the most common neoplasm. CT scan established the best choice in studying cortical lesions and nidus in osteoid osteoma. CT can identify the calcification of cartilage. In cases of cartilage producing tumours, the T2 weighted MRI with high signal intensity with a lobulated outline made a useful role. MRI can delineate the medullary extent. Multinucleated giant cells were seen in sections of chondroblastoma. Histopathology provided the final conclusive diagnosis. **Conclusion:** Benign bone tumours frequently pose a diagnostic challenge for general surgical pathologists. Accurate pathologic diagnosis requires careful clinical, radiological and histopathological correlation. The most common benign bone tumour occurring in children is osteochondromas, representing 10 to 15% of all bone tumours and 20 to 50% of all benign bone tumours.

Keywords: Benign bone tumours, Radiograph, CT, MRI and H&E Stain.

INTRODUCTION

Inadequate investigations have resulted in erroneous diagnosis of benign lesions as malignant, resulting in unnecessary surgical procedures. Osteoid osteoma arises from long bones of the limbs presenting with pain.[1] Osteoblastoma is a rare tumour, with a locally aggressive behaviour. Osteochondroma is the most common benign tumour. Hyaline cartilage cap is the continuity of this lesion with the underlying native bone cortex and medullary canal that is pathognomonic of osteochondroma. Müller suspected osteochondromas to arise from erroneous differentiation of cells in the periosteum. Genetic linkage analysis has located three etiological genes for osteochondroma HME-EXT1 (8q24.1),[2] EXT2 (11p11-p12),[3,4] and EXT3 (19p).[5] The Knudson theory's application to osteochondroma pathogenesis has been strengthened by noted EXT gene losses and mutations in chondrosarcomas arising from osteochondromas.[6-9] Loss of functional EXT1 or EXT2 in a chondrocyte alters its ability to attach heparan sulfate to the proteins intended for its in the cell surface and its immediate extracellular milieu.[10-12] FGF-R3 causes cell cycle exit by

Name & Address of Corresponding Author
Dr. P. Kannan
428, Main Road,
Near Old Bus Stand,
Kovilpatti, Thoothukudi District,
Tamilnadu,
India.

activating the transcription factor STAT1, which induces expression of p21.[13] In osteoid osteoma currently percutanous radiofrequency ablation is being used under CT guidance is being used with increasing frequency.[14] Osteoid osteoma resolves spontaneously over time and can be treated conservatively with NSAIDs,[15] they account for 10% of all benign bone lesions and there is a male predilection.[16] Osteoblastoma are located in the spine or major bones of the lower extremity,[17,18] According to Dorfman and Weiss,[19] aggressive osteoblastoma are diagnosed microscopically by the presence of wider or more irregular trabaculae, osteoid trabeculae are bordered by epithelioid-appearing osteoblasts . Importantly, up to 3 percent of patients with HME will eventually develop a chondrosarcoma in the cartilaginous cap of the lesion.[20-23] The supposition that accelerated chondrocyte differentiation and early ossification could create a local excess of bone.[24,25]

Aim

We have reported 62 cases of bone tumours during the study period of 5 years in the Department of Pathology, Thoothukudi Medical College, India. The cases were thoroughly studied by histopathology and 28 cases were diagnosed as various types of benign bone tumours, 8 cases were osteoid producing tumours and 20 cases were cartilage producing benign bone tumours conclusively. The histopathology diagnosis was correlated with the radiological features.

MATERIALS AND METHODS

We have reported 62 cases of bone tumours during the study period of 5 years in the Department of Pathology, among which 28 cases were diagnosed as benign bone tumours conclusively. Among the 28 cases, 8 cases were benign osteoid tumours and 20 cases were benign cartilage producing tumours. The five basic parameters of importance in the diagnosis are the age of the patient, bone involved, specific area within the bone, radiographic appearance, and microscopic appearance. The data was stored in the Department computer server was very much useful in the retrospective histopathology and radiology correlation study.

RESULTS

This retrospective study covered a total number of 62 cases reported, among which 28 cases were diagnosed by histopathology as various types of benign tumours. 8 cases were osteoid producing tumours and 20 cases were cartilage producing benign bone tumours conclusively at Thoothukudi Medical College, India.

The details of age, sex and location of various benign bone tumours were studied. Osteochondroma was the most common tumour reported with growth from the cortex away from the joint.

Table 1: Various types of benign bone tumours reported at the Department of Pathology, with bones involved and the age group involved

Tumour	Number of cases	Age group/Sex	Site of lesion
Osteoid osteoma	6	The age group involved was between 12-23 years. 4 were males and 2 were females.	Five lesions were found in the lower end of femur and one in fibula. Intense pain is the most prominent symptom.
Osteoblastoma	2	Two cases were reported. The presenting symptom was pain and the age group involved was between 12-23 years.	One lesion was found in L3 vertebra and one in fibula. .
Chondroma	2	Two cases were reported. The presenting symptom was soft tissue swelling and the age group involved was between 18-28 years.	Two lesions were reported from phalanges.
Osteochondroma	14	Fourteen cases were reported. The presenting symptom was soft tissue swelling and vague pain and the presenting age group was between 8-12 years.	Nine cases were male patients and five were female patients. Six cases were from femur, five from humerus, one from tibia, one from pubic ramus and one from fibula.
Chondroblastoma	2	Two cases were reported. The presenting symptom was soft tissue swelling and the involved age group was between 12-18 years.	One lesion involved lower end of femur and one case involved upper end of fibula.
Chondromyxoid fibroma	2	Two cases were reported. The presenting symptom was pain and the age group involved was between14-22 years.	Two lesions were from upper end of tibia.
Total	28		

Table 2: Bones involved in the study of benign tumours of bone at Thoothukudi Medical College, India.

Tumour	Femur	Humerus	Tibia	Fibula	Vertebra & pubic ramus	Others
Osteoid osteoma	5			1		
Osteoblastoma				1	1	
Chondroma						2
Osteochondroma	6	5	1	1	1	
Chondroblastoma	1			1		
Chondromyxoid fibroma			2			
Total	12	5	3	4	2	2

Table 3: correlation study between radiology and histopathology of various types of benignbone tumours

Tumour	Radiographic Findings	Histopathological Findings
Osteoid osteoma	CT Scan shows an area of central translucency measuring less than 1.5 cm in diameter, in cortex surrounded by dense sclerosis .The reactive new bone is dense. MRI shows nidus as a low signal intensity with sclerotic bone with high signal intensity.	Sections studied show a nidus with a fibrovascular core, plump osteoblasts are surrounding the anastomosing bone with dense sclerotic bone.
Osteoblastoma	X-ray shows an area of translucency measuring more than 2 cm. In this case measuring 5 cm in diameter. The margins are irregular. Cortical expansion and thinning was noted.	Sections studied show a nidus with plump osteoblasts rimming the broad irregular bone trabaculae.
Chondroma	X-Ray of both hands show an area of translucency expanding the cortex and with a popcorn calcification distally.	Sections studied show areas of cartilaginous tissue in lobules with areas of calcifications.
Osteochondroma	X-Ray shows a pedunculated growth from femur measuring 6 cms with the growth seen drifting away from knee joint.	Sections studied show a cartilaginous cap overlying broad bands of bone trabaculae.
Chondroblastoma	X-Ray femur showing an area of translucency with calcification.	Sections studied show highly cellular areas of mononuclear cells with chicken-wire calcification.
Chondromyxoid fibroma	T2 Weighted MRI of lower femur shows a high signal intensity lesion in the metaphysis with cortex is spared.	Section studied shows areas of chondroid , myxoid and fibrous areas . Other section studied shows a hypocellular area in the centre surrounded by areas of osteoclast type of giant cells and hypercellular fibrous areas in the periphery. .

The long bones are frequently involved in most of the benign tumours of bone and were around knee joint showing a high frequency of involvement. Chondroma is one benign cartilage producing tumour showing involvement of distal small bones of hand and foot.

The correlation was done with histopathological features with radiographic findings. The various radiological patterns in benign osteoid tumours is a nidus with a central translucent area with surrounding bone sclerosis and in benign cartilage producing lesions is an area of translucency surrounded by calcifications. Histopathologically benign osteoid tumours showed a highly vascularised area with immature osteoid present. The cartilage producing tumours showed cartilage production, calcifications were seen and a few cases showed giant cells surrounding them.

Osteoid Osteoma

Six cases were reported. The age group was between 12-23 years of age. Most osteoid osteomas occur in long tubular bones of the limbs, proximal femur but any bone may be involved. Five lesions were found in the lower end of femur and one in fibula. Intense pain was the most prominent symptom. Radiographically, the typical finding is a radiolucent central nidus that is not larger than 1.5 cm.. Lesions of long bones are usually metaphyseal. An osteoid osteoma is composed of three concentric parts:

1. Nidus
   - Meshwork of dilated vessels, osteoblasts, osteoid and woven bone.
   - May have a central region of mineralisation.
2. Fibrovascular rim.
3. Surrounding reactive sclerosis.

The pain associated with osteoid osteoma is characteristically more intense at night is due to the effect on nerves and vessels by osteoblast-produced prostaglandin E2, COX1 and COX2. The word nidus literally means "nest". The treatment of choice is surgical removal of nidus and sorrounding tissue. Six cases of osteoid osteoma were repoted .They were surgically removed with adequate margin .The pain relief after treatment is so dramatic that the patient realises on recovery from anesthesia that the lesion has been removed .

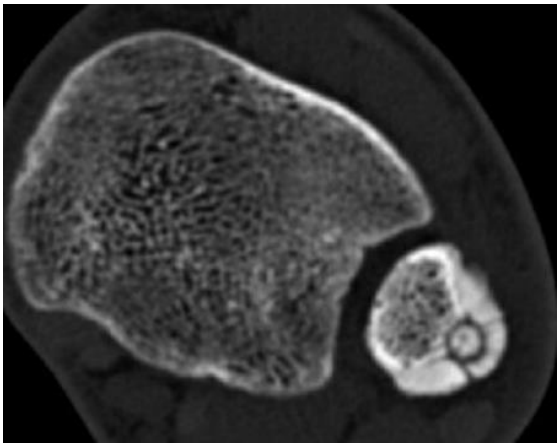

Figure 1: CT Scan shows an area of central translucency measuring less than 1.5 cm in diameter, in cortex surrounded by dense sclerosis

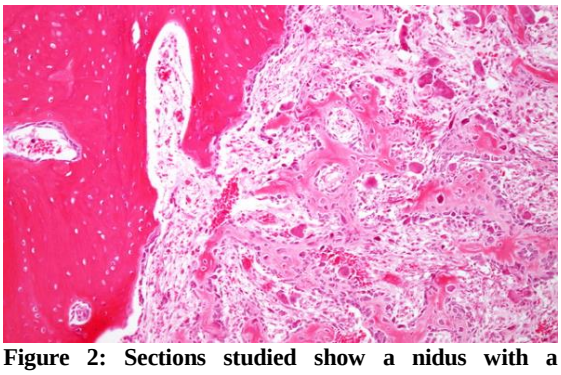

Figure 2: Sections studied show a nidus with a fibrovascular core, plump osteoblasts are surrounding the anastomosing bone with dense sclerotic bone

The CT Scan typically shows the typical nidus and the histopathological sections confirm a nidus with

interlacing woven bone within a vascularised connective tissue, the study correlating perfectly. MRI shows nidus as a low signal intensity with surrounding dense bone. CT scan guided RFA can be performed for ablation of the nidus in femur in future. Dr. Bhavin Jankharia is a skilled Radiologist in providing RFA Therapy in India.

Osteoblastoma

Two cases were reported .The presenting symptom was pain and the age group was between 12-23 years of age. One lesion was found in L3 vertebra and one in fibula. Osteoblastoma is distinguished from the osteoid osteoma by the larger size of the nidus more than 2 cms, the absence of a surrounding area of reactive bone formative, and the lack of intense pain. The majority of osteoblastomas enlarge slowly, with consequent remodelling of bone around the lesion. Two cases underwent tumour tissue curretted and bone grafting was done.

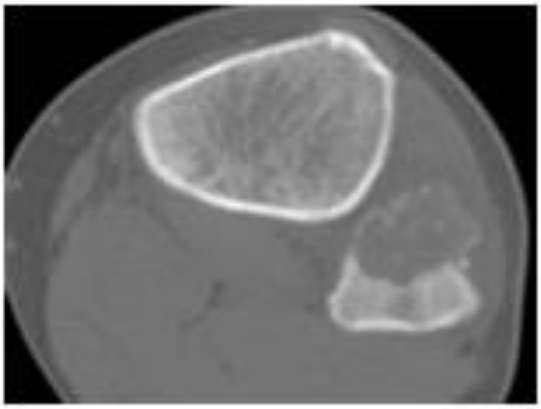

Figure 3: X-ray shows an area of translucency measuring more than 2 cm. In this case measuring 5 cm in diameter. The margins are irregular. Cortical expansion and thinning was noted.

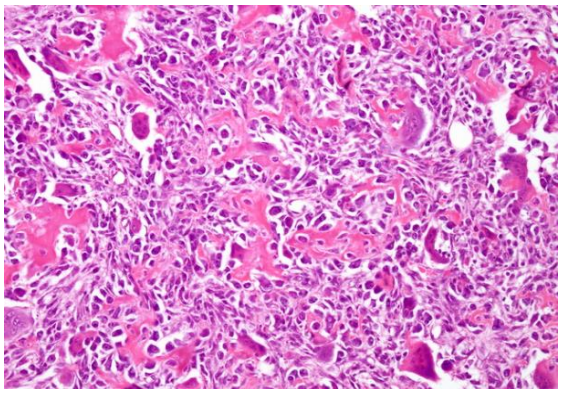

Figure 4: Sections studied show a nidus with plump osteoblasts rimming the broad irregular bone trabeculae

CT scan shows mixed lytic-sclerotic lesion in vertebra L3 in one case and a lytic mass lesion in fibula expanding the cortex .The tumour tissue was curretted and bone reconstruction was made. The histopathology section shows interlacing network of wide and broad osteoid woven bone rimmed by osteoblasts. The correlation study holds good here.

Chondroma

Chondroma is a common benign cartilaginous tumor that occurs most frequently in the small bones of the hands and feet, particularly the proximal phalanges. They begin in the spongiosa of the bone, from which they expand and thin out the cortex. The tumors are notoriously insensitive to therapy. Cartilage tumours have a tendency to be aggressive with each surgical interference. The T2 weighted MRI shows high signal intensity with a lobulated outline. MRI can delineate the medullary extent. CT can identify the calcification of cartilage. About 30% of chondromas are multiple. Ollier's disease and Maffucci's syndrome have an increased risk of developing chondrosarcoma. It is named after Louis Leopold Ollier. Microscopically, chondromas are composed of mature lobules of hyaline cartilage. Foci of myxoid degeneration, calcification, and endochondral ossification are common. The majority of enchondromas remain asymptomatic and require no treatment. If necessary, a curettage and bone grafting can be performed at a later time.

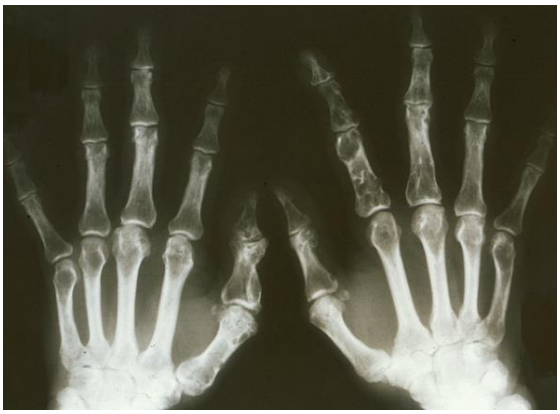

Figure 5: X-Ray of both hands show an area of translucency expanding the cortex and with a popcorn calcification distally

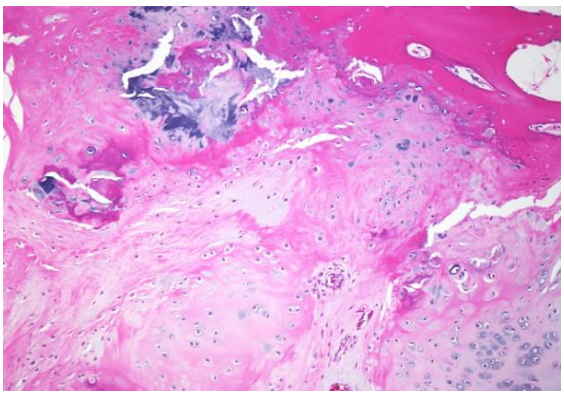

Figure 6: Sections studied show areas of cartilaginous tissue in lobules with areas of calcifications

Two cases were reported. The presenting symptom was soft tissue swelling and the age group was

between 18-28 years. Two lesions were reported from phalanges. X-Ray of both hands show an area of translucency expanding the cortex and with a popcorn calcification distally, another case showing a lesion in the right index finger showing the same features. For the two cases curettage and bone grafting were performed. Sections studied show areas of cartilaginous tissue in lobules with areas of calcification. The radiographic findings correlated with histopathology findings.

Osteochondroma

Osteochondroma is the most frequent benign bone tumor. The most common locations are the metaphyses of the lower femur, upper tibia, upper humerus, and pelvis. The radiographic appearance of osteochondroma is the tumours grow out in a direction opposite to the adjacent joint. The most common symptom related to osteochondroma is a nontender painless mass, osseous deformity, fracture, vascular compromise, neurologic sequelae, overlying bursa formation, and malignant transformation. The average age of the patient at onset is approximately 10 years. The bulk of the lesion is made up of mature bone trabeculae located beneath the cartilaginous cap and containing normal bone marrow. The three-dimensional imaging CT shows cortical and marrow continuity of the lesion and parent bone in osteochondromas. Growth of osteochondroma continues till skeletal maturation is complete. Fourteen cases were reported with H/O soft tissue swelling and vague pain. Nine cases were male patients and five cases were female patients .Six cases were from femur, five from humerus, one from tibia, one from pubic ramus and one from fibula. The presenting age group was between 8-12 years of age.

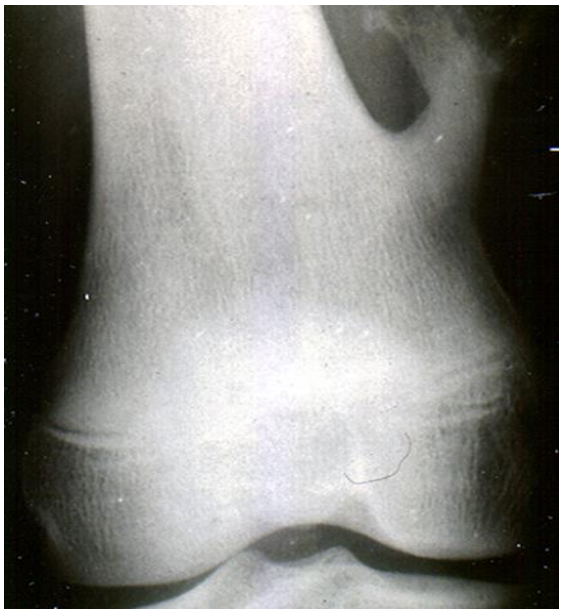

Figure 7: X-Ray shows a pedunculated growth from femur measuring 6 cms with the growth seen drifting away from knee joint

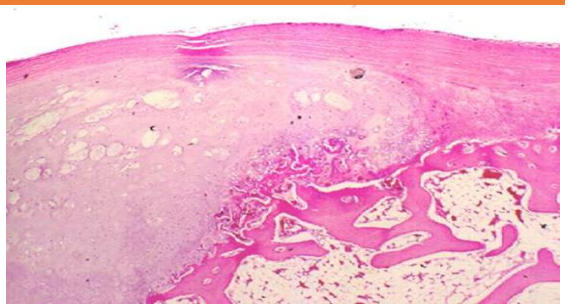

Figure 8: Sections studied show a cartilaginous cap overlying broad bands of bone trabeculae

Treatment: Most cases needed no absolute indication for surgery except for cosmetic reasons and complications. Fourteen cases underwent surgery. Larger symptomatic lesions were resected at their base where there is continuity to underlying bone. Pedunculated lesions are more easily removed. Sections studied show a cartilaginous cap overlying broad bands of bone trabaculae. In all the cases the Radiographic findings correlated with Histopathology findings.

Chondroblastoma

Chondroblastoma is also referred to as Codman tumours, arises in the epiphysis or apophysis of a long bone in young patients. In 1931, this lesion was described by Ernest Armory Codman an American. 50 % of chondroblastoma occur predominantly in males under 20 years of age. Clinical presentation includes joint pain, muscle wasting, tenderness, and swelling as a local mass. It usually arises in the distal end of the femur, proximal end of the humerus, and proximal end of the tibia. MRI shows, T1: lesion itself is of low to intermediate signal, T2/STIR: lesion is of intermediate to high signal. Microscopically the presence of small zones of focal calcification are present with cellular areas of mononuclear cells. These zones range from a network of thin lines ("chicken wire") to obvious deposits surrounded by giant cells. Helpful features which suggest a clear cell chondrosarcoma include: older age, larger mass, absent adjacent bone edema, high T2 signal in MRI. Two cases were reported. One lesion involved lower end of femur and one upper end of fibula.

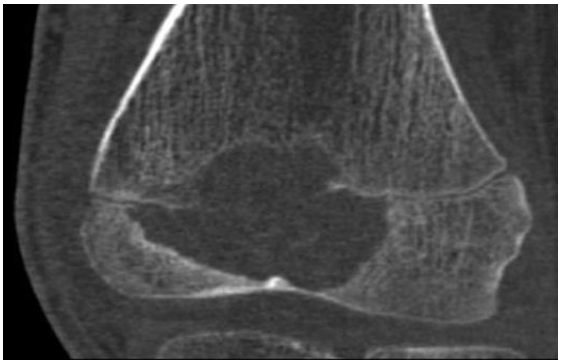

Figure 9: X-Ray femur showing an area of translucency with calcification.

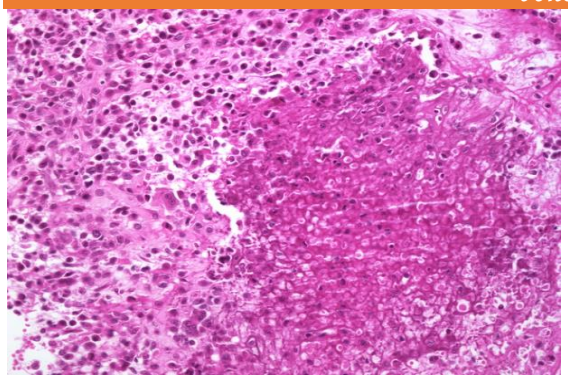

Figure 10: Sections studied show highly cellular areas of mononuclear cells with chicken-wire calcification.

The two cases were treated with curettage and packing of the resulting cavity with bone cement. X-Ray femur showing an area of translucency with calcification .X-Ray right fibula showing an area of translucency with calcification. Sections studied show highly cellular areas of mononuclear cells with chicken-wire calcification. Radiofrequency ablation has also been used currently for therapy. The Radiographic findings correlated with Histopathological section findings.

Chondromyxoid Fibroma

Chondromyxoid fibroma of bone is a benign tumor of cartilaginous origin. Most chondromyxoid fibromas are located in the metaphyseal region of long bones (60%). The tumour consists of chondroid, myxomatous areas with giant cells. It usually occurs in a long bone around knee joint of a young adult. Radiographically, a radiolucent, eccentric space occupying lesion is seen in the metaphysis. Cortex is expanded. Grossly, it is solid and yellowish white or tan tissue, replaces bone, and thins the cortex. Microscopically, it comprises hypocellular lobules with a myxochondroid appearance, separated by intersecting bands of highly cellular tissue composed of fibroblast-like spindle cells and osteoclast type of giant cells

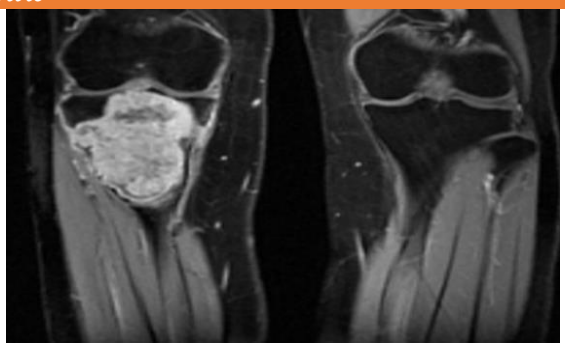

Figure 11: T2 Weighted MRI of lower femur shows a high signal intensity lesion in the metaphysis with cortex is spared.

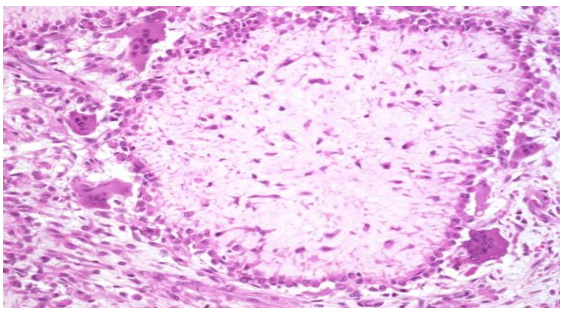

Figure 12: Section studied shows areas of chondroid, myxoid and fibrous areas. Other section studied shows a hypocellular area in the centre surrounded by areas of osteoclast type of giant cells and hypercellular fibrous areas in the periphery.

X-Ray right tibia shows a translucent eccentric lesion with well-defined margins sparing the cortex. T2 Weighted MRI of lower femur shows a high signal intensity lesion in the metaphysis with cortex is spared. Two cases underwent en bloc excision and bone grafting. Section studied shows areas of chondroid, myxoid and fibrous areas. Other section studied shows a hypocellular area in the centre surrounded by areas of osteoclast type of giant cells and hypercellular fibrous areas in the periphery. Radiographic features correlated with Histopathology findings.

Table 4: Final Outcome of the Study of Benign Bone Tumours

Tumour	Surgery Done	Cure rate	Follow up
Osteoid osteoma	Six cases underwent surgery. The nidus was surgically removed with a margin .	100 %	Two cases are attending follow up.
Osteoblastoma	Two cases underwent tumour tissue curretted and bone grafting was done.	100 %	No cases reported for follow up.
Chondroma	Two cases underwent curettage and bone grafting	100 %	One case reported for follow up.
Osteochondroma	Fourteen cases underwent surgery. Larger symptomatic lesions were resected at their base where there is continuity to underlying bone. Pedunculated lesions were more easily removed.	100 %	Two cases reported for follow up
Chondroblastoma	Curettement with bone cement filling was done for the two cases	100 %	No cases reported for follow up.
Chondromyxoid fibroma	Two cases underwent en bloc excision and bone grafting was done.	100 %	One case reported for follow up
Total	Twenty eight cases underwent surgery.		Six cases turned for follow up.

None of the benign osteogenic and cartilaginous tumours turned malignant after careful study and follow up after treatment so far

DISCUSSION

The presentation of chondromyxoid fibroma is interesting as it occurs in the second and third

decades, with 75% of cases occurring before the age of 30 years.[26-28] The tumour comprises of a variable combination of chondroid, myxoid, and fibrous tissue components organised in a pseudolobulated architecture.[29] In osteoid osteoma the pain relief after treatment is so dramatic that the patient realises on recovery from anesthesia that the lesion has been removed . In future noninvasive procedure like CT guided radiofrequency ablation in osteoid osteoma, osteoblastoma and chondroblastoma may have a promising role. Treatment of osteoid osteomas with RFA has been extremely successful, with negligible complications.[30,31] Osteochondroma was the most common type of tumour, occurred commonly in male children. The peak incidence was in the second decade and commonest site was the lower extremity, particularly in the femur. Giant cells were found considerably in chondroblastoma and chondromyxoid fibroma leading to a suspicion of giant cell tumour. Enchondromas have similar histopathological appearance of low grade chondrosarcoma. In these cases imaging modality provided the final diagnosis. Highly cellular chondroid tumours have high signal intensity in T2 weighted MRI. Gadolinum enhanced images helps to differentiate between viable tumour, reactive oedema and necrosis and guide the biopsy site. Twenty eight cases underwent surgery. Six cases turned for follow up. The cure rate was 100 % with the team approach of Radiologists, Clinicians and Pathologists.

CONCLUSION

The Histopathology is the final tool for the diagnosis of various types of benign tumours of bone both osteoid producing and cartilage producing tumours. The study also explains the pain in diagnosing benign and malignant cartilaginous tumours located peripherally in the bone that is a challenging task in histopathology reporting. Histopathology provides the final verdict for further treatment of the patient. The study provides the importance of other medical faculty the Surgeon and Radiologist to work as a team for a successful outcome. We correlated the Histopathological findings with Radiological findings. This resulted in perfect correlation between the Histopathology study and Radiology study

REFERENCES

1. Unni KK, Inwards CY, Research MF. Dahlin's bone tumors, general aspects and data on 10,165 cases. Lippincott Williams & Wilkins. (2009) ISBN:0781762421.
2. Ludecke HJ, et al. Molecular dissection of a contiguous gene syndrome: localization of the genes involved in the Langer-Giedion syndrome. Hum Mol Genet. 1995;4:31–36.
3. Ligon AH, et al. Gene for multiple exostoses (EXT2) maps to 11(p11.2p12) and is deleted in patients with a contiguous gene syndrome. Am J Med Genet. 1998;75:538–540.
4. Wuyts W, et al. Refinement of the multiple exostoses locus (EXT2) to a 3-cM interval on chromosome 11. Am J Hum Genet. 1995;57:382–387.
5. Le Merrer M, et al. A gene for hereditary multiple exostoses maps to chromosome 19p. Hum Mol Genet. 1994;3:717–722.
6. Bovee JV, et al. EXT-mutation analysis and loss of heterozygosity in sporadic and hereditary osteochondromas and secondary chondrosarcomas. Am J Hum Genet. 1999;65:689–698.
7. Hecht JT, et al. Hereditary multiple exostosis and chondrosarcoma: linkage to chromosome II and loss of heterozygosity for EXT-linked markers on chromosomes II and 8. Am J Hum Genet. 1995;56:1125–1131.
8. Hecht JT, et al. Hereditary multiple exostoses (EXT): mutational studies of familial EXT1 cases and EXT-associated malignancies. Am J Hum Genet. 1997;60:80–86
9. Raskind WH, et al. Loss of heterozygosity in chondrosarcomas for markers linked to hereditary multiple exostoses loci on chromosomes 8 and 11. Am J Hum Genet. 1995;56:1132–1139.
10. Lin X, et al. Disruption of gastrulation and heparan sulfate biosynthesis in EXT1-deficient mice. Dev Biol. 2000;224:299–311
11. McCormick C, Duncan G, Tufaro F. Herpes simplex virus: discovering the link between heparan sulphate and hereditary bone tumours. Rev Med Virol. 2000;10:373–384. [
12. McCormick C, et al. The putative tumour suppressor EXT1 alters the expression of cell-surface heparan sulfate. Nat Genet. 1998;19:158–161.
13. Su WC, et al. Activation of Stat1 by mutant fibroblast growth-factor receptor in thanatophoric dysplasia type II dwarfism. Nature. 1997;386:288–292 .
14. Unni KK, Inwards CY, Research MF. Dahlin's bone tumors, general aspects and data on 10,165 cases. Lippincott Williams & Wilkins. (2009)
15. Greenspan A, Jundt G, Remagen W. Differential diagnosis in orthopaedic oncology. Lippincott Williams & Wilkins. (2006) ISBN:0781779308.
16. Feletar M, Hall S. Osteoid osteoma: a case for conservative management. Rheumatology (Oxford). 2002;41 (5): 585-6.
17. Lucas DR, Unni KK, McLeod RA, O'Connor MI, Sim FH: Osteoblastoma. Clinicopathological study of 306 cases Human Pathology 25:117-134, 1994.
18. McLeod RA, Dahlin DC, Beabout JW: The spectrum of osteoblastoma. Am J Roentgenology 126:321-335, 1976.
19. deSantos LA, Murray JA, Finklestein JB, Spjut HJ, Ayala AG: The radiographic spectrum of periosteal osteosarcoma. Radiology 127:123-129, 1978.
20. Hennekam RC. Hereditary multiple exostoses. J Med Genet. 1991;28:262–266 ,
21. Schmale GA, Conrad EU, 3rd, Raskind WH. The natural history of hereditary multiple exostoses. J Bone Joint Surg. (Am) 1994;76:986–992.
22. Voutsinas S, Wynne-Davies R. The infrequency of malignant disease in diaphyseal aclasis and neurofibromatosis. J Med Genet. 1983;20:345–349.
23. Wicklund CL, et al. Natural history study of hereditary multiple exostoses . Am J Med Genet. 1995;55:43–46.
24. Chung UI, et al. The parathyroid hormone/parathyroid hormone-related peptide receptor coordinates endochondral bone development by directly controlling chondrocyte differentiation. Proc Natl Acad Sci USA. 1998;95:13030–13035.]
25. Chung UI, et al. Indian hedgehog couples chondrogenesis to osteogenesis in endochondral bone development. J Clin Invest. 2001;107:295–304.
26. Grainger RG, Allison D, Adam A et-al. Grainger's and Allison's Diagnostic Radiology, A Textbook of Medical Imaging. (2008) ISBN:0443101639.

27. Unni KK, Inwards CY, Research MF. Dahlin's bone tumors, general aspects and data on 10,165 cases. Lippincott Williams & Wilkins. (2009) ISBN:0781762421 .
28. Hefti F, Brunner R, Hasler CC et-al. Pediatric Orthopedics in Practice. Springer Verlag. (2007) ISBN:3540699635 .
29. Mitchell M, Sartoris DJ, Resnick D. Case report 713. Chondromyxoid fibroma of the third metatarsal. Skeletal Radiol. 1992;21 (4): 252-5.
30. Woertler K, Vestring T, Boettner F, Winkelmann W, Heindel W, Lindner N. Osteoid osteoma: CT-guided percutaneous radiofrequency ablation and follow-up in 47 patients. J Vasc Interv Radiol. 2001;12:717–722 .
31. Rosenthal D I, Hornicek F J, Torriani M, Gebhardt M C, Mankin H J. Osteoid osteoma: percutaneous treatment with radiofrequency energy. Radiology. 2003;229:171–175.

How to cite this article: Saranya K, Kannan P. A Retrospective Study of Histopathology and Clinical Correlation of Primary Benign Bone tumours at Thoothukudi Medical College, India. Ann. Int. Med. Den. Res. 2019; 5(3):PT12-PT19.

Source of Support: Nil, **Conflict of Interest:** None declared