A STUDY OF AGREEMENT BETWEEN CLINICORADIOLOGICAL AND HISTOPATHOLOGICAL DIAGNOSIS OF BONE TUMOURS AND TUMOUR – LIKE LESIONS WITH FNAC STUDY IN SELECTED CASES

DISSERTATION SUBMITTED FOR

M.D., BRANCH – III

PATHOLOGY

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CERTIFICATE FROM THE GUIDE

This is to certify that this dissertation titled **"A STUDY OF AGREEMENT BETWEEN CLINICORADIOLOGICAL AND HISTOPATHOLOGICAL DIAGNOSIS OF BONE TUMOURS AND TUMOUR – LIKE LESIONS WITH FNAC STUDY IN SELECTED CASES"** is the bonafide record of work done by **DR. G. SHUBHA** submitted in partial fulfilment of the requirement for the award of **M.D Degree in Pathology** and carried out by her during the period May 2012 to July 2014 under my direct supervision and guidance.

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DECLARATION BY THE CANDIDATE

I, Dr. G.SHUBHA, solemnly declare that this dissertation titled **"A STUDY OF AGREEMENT BETWEEN CLINICORADIOLOGICAL AND HISTOPATHOLOGICAL DIAGNOSIS OF BONE TUMOURS AND TUMOUR – LIKE LESIONS WITH FNAC STUDY IN SELECTED CASES"** is a bonafide record of work done by me at Department of Pathology, Madurai Medical College and Government Rajaji Hospital, Madurai during the period from May 2012 to July 2014.

I also declare that this bonafide work or a part of this work was not submitted by me or any other for any reward, degree and diploma to any university, board either in India or abroad.

This dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University, towards the partial fulfilment of requirement for the reward of M.D. Degree in **PATHOLOGY.**

Place: Madurai

Date: DR. G.SHUBHA

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ABSTRACT

BACKGROUND

Bone tumours and tumour-like lesions are rare. However, they cause significant morbidity and mortality. Histopathological examination of bone tumours is considered to be a challenging field in pathology and final diagnosis should be given only after review of clinical and radiological findings. FNAC (Fine Needle Aspiration Cytology) evaluation of bone tumours is a safe, simple and cost-effective procedure that is minimally disruptive to bone. In this era of neo-adjuvant chemotherapy and limb salvage surgeries, FNAC is proving to be a valuable tool in preliminary diagnosis of bone tumours. This study aims at elaborating the various bone tumours and analysing the age and gender distribution of these tumours. The agreement between clinico-radiological and histopathological diagnosis of bone tumours has been studied. An attempt has been made to study the FNAC findings of bone tumours. Immunohistochemical markers have been used to confirm diagnosis in challenging bone tumours.

METHODS

The study was carried out in the Department Of Pathology, Madurai Medical College, Madurai, during the period from May 2012 to July 2014 on 90 specimens of bone tumours and tumour-like lesions received in the department after exclusion of specimens with leukaemic infiltration of marrow. After adequate fixation and decalcification, representative bits were taken, processed and stained with Haematoxlyin and Eosin. The cases were classified based on WHO classification ,2002. Cohen's Kappa value was calculated to test the strength of agreement between clinico-radiological and histopathological diagnosis. FNAC was performed on 15 bone tumours and slides stained with H&E after fixation. The observations were compared with other studies and inferences drawn. The provisional histopathological diagnosis of two bone tumours was confirmed by immunohistochemical markers.

RESULTS

Bone tumours and tumour-like lesions formed only 1.03% of all diagnosed neoplasms received in the department during the study period. Benign bone tumours formed 58.9% of the study material and 36.7% were malignant bone tumours. Among the malignant tumours, 66.7% were primary bone malignancies and 33.3% cases were metastatic deposits. Cartilage tumours formed the major category constituting 43.3%. Osteosarcoma was the most common primary bone malignancy (50%) while osteochondroma was the

commonest benign tumour (66%). The incidence of tumours was maximum during second decade of life (45.6%). Osteosarcoma and osteoid osteoma showed predilection for males. Bone tumours were most commonly encountered around the knee joint (23.3%). Metastasis occurred most commonly in the femur (36.4%). 85 cases showed agreement between clinicoradiological and histopathological diagnosis. In 5 cases, the histopathological diagnosis was not in agreement with clinicoradiological diagnosis. Cohen's Kappa value was 0.943 which showed excellent agreement between clinicoradiological and histopathological diagnosis.

Out of the 12 adequate FNAC smears, categorisation was correctly done in 10 cases. However, in 2 cases of suspected osteosarcoma, a cytological diagnosis of sarcoma, not otherwise specified was given due to lack of osteiod. These two cases were later confirmed by histopathology to be osteosarcoma.

IHC was used to confirm a provisional histopathological diagnosis of primary bone lymphoma using CD 45 immunostain. Also, a provisional histopathological diagnosis of metastatic deposits of follicular thyroid carcinoma to skull with occult primary was confirmed by TTF -1 and Thyroglobulin immunomarkers.

CONCLUSION

There is very good agreement between clinico – radiological and histopathological diagnosis in bone tumours. However, many benign bone tumours and tumour - like lesions mimic malignant lesions radiologically. Hence, histopathological confirmation of radiological diagnosis should always be done before definitive treatment. A close co – ordination between the orthopaedician, radiologist and pathologist is the best approach to treat a patient with bone tumours.

Cytology can serve as a good tool for rendering quick and cost effective diagnosis for further management. However, the results of FNAC should be cautiously interpreted and when in doubt, histopathological confirmation should be obtained before treatment.

Immunohistochemistry has its own role in bone tumour diagnosis. It can be a valuable tool in categorising small round cell tumours and determining sites of occult primary in case of metastasis to bone.

KEY WORDS

Bone tumours, tumour-like lesions, osteosarcoma, FNAC (Fine Needle Aspiration Cytology), Radiology, Immunohistochemistry.

INTRODUCTION

Bone is a highly specialized connective tissue engineered by nature to perform a variety of important functions. Bones and joints together provide the stability needed for movement, protect internal organs and determine a person's build and stature. This dynamic tissue is essential for mineral homeostasis and also houses the blood forming bone marrow.

Primary tumours of the bone are rare[1]. They account for less than one percent of the overall human tumour burden. The morbidity and mortality associated with them is however, very significant. Bone tumours are diverse in their gross and morphologic features. They may present as relatively benign lesions of no clinical significance to highly aggressive and rapidly fatal tumours. Every age group is affected but the peak incidence[2] usually occurs in the second decade of life. Diagnosis should be made at the earliest and appropriate therapy instituted rapidly so that affected patients enjoy a good quality of life in this era of limb salvage surgeries.

Bone tumours often pose diagnostic challenges. Low incidence of these tumours and the resulting limited experience in dealing with them adds to the diagnostic difficulties. The key to their accurate diagnosis is utilization of an integrated approach[3] involving clinical, radiological and histopathological findings.

Fine Needle Aspiration Cytology (FNAC) is turning out to be a useful alternative to open biopsies in diagnosis of bone lesions. It is safe, simple, highly economical and a relatively painless procedure which can be performed at the bedside or in the out- patient department. It has the advantage over biopsy of being less disruptive[4] to bone, permitting multiple sampling and leaving no scar. With the development of neo-adjuvant chemotherapy and new orthopaedic surgical techniques like limb salvage procedures, there has been an enhancement in the role of FNAC in management of metastatic as well as primary malignant bone tumours.

Immunohistochemical study for the diagnosis of bone tumors has to be scheduled after an appropriate analysis of clinical data, radiological findings and results of histological sections. Immunohistochemistry (IHC) plays a significant role in accurate diagnosis of certain groups of bone tumours. Small cell osteosarcomas may be confused with other small round cell tumours[5] and here, IHC may serve as the deciding factor. Metastatic tumours can also be categorized by IHC.

This study aims at elaborating the wide range of bone tumours and tumour-like lesions. The agreement between clinico - radiological and histopathological diagnosis has been studied in detail. An attempt has been made to study the FNAC findings of bone tumours. Immunohistochemical markers have been used to diagnose challenging bone tumours.

AIM OF THE STUDY

1. To study the distribution of various bone tumours and tumour - like lesions during the period from May 2012 to July 2014.
2. To analyse the age and sex distribution of bone tumours and tumour - like lesions.
3. To elaborate the spectrum of bone tumours and tumour – like lesions by histopathological examination.
4. To establish the statistical significance by testing the strength of agreement between histopathological and clinico-radiological diagnosis by Cohen's kappa value.
5. To study the FNAC (Fine Needle Aspiration Cytology) findings of selected bone tumours.
6. To study the usefulness of immunohistochemical markers in categorising diagnostically challenging bone tumours.

REVIEW OF LITERATURE

EMBRYOLOGY

The skeletal system develops from paraxial mesoderm[6], lateral plate (parietal layer) mesoderm and neural crest. Paraxial mesoderm forms somites. The ventromedial part of somites called sclerotome gives rise to the connective tissue of the embryo called mesenchyme. These mesenchymal[7] cells migrate and differentiate to form fibroblasts, chondroblasts and osteoblasts.

The parietal layer of lateral plate mesoderm forms bones of pelvic and shoulder girdles, limbs and sternum. Neural crest cells also differentiate into mesenchyme and in the region of head, participate in the formation of skull and facial bones. Bones of the cranial vault and base of skull are also formed from occipital somites and somitomeres.

If mesenchyme differentiates directly into bone, the process is called **intramembranous[8] ossification** (**Fig.1**). Flat bones of the skull may develop in this manner. In most other bones, mesenchymal cells first form cartilage models that ossify later, a process called **enchondral ossification**.

MACROSCOPIC ANATOMY OF BONE (Fig.2)

Human skeletal system has 206 bones. The skeleton is divided into two regions: **the axial skeleton** (skull, vertebrae, ribs, sternum, hyoid) and the **peripheral skeleton (**the limbs and pelvis).

Living bone is white. The texture of **compact bone** is dense like ivory and that of **cancellous or spongy bone** is honeycombed. The hard thin outer shell is called compact bone or **cortex**. The marrow cavity is housed inside the cortex and contains hematopoietic elements, fat and spicules of bone called trabecular or spongy bone.

Based on their general shape, bones are classified as long, short, flat, irregular and sesamoid bones.

Topographically, **long bone** is divided into three regions: **diaphysis**, **epiphysis** and **metaphysis**. Diaphysis is the shaft; epiphysis is the region at the ends of the bone and is partially covered by articular cartilage. At the junction of epiphysis and diaphysis lies the metaphysis. It is the epicentre for many bone tumours. Epiphyseal plate is seen occupying the junction of metaphysis and epiphysis in growing bones. Enchondral ossification occurs at the epiphyseal plate. When the bone has reached its adult length, the epiphysis closes by becoming completely ossified. The epiphyseal plate is considered of paramount importance in bone pathology because it is by far the commonest site of occurrence of most primary bone tumours.

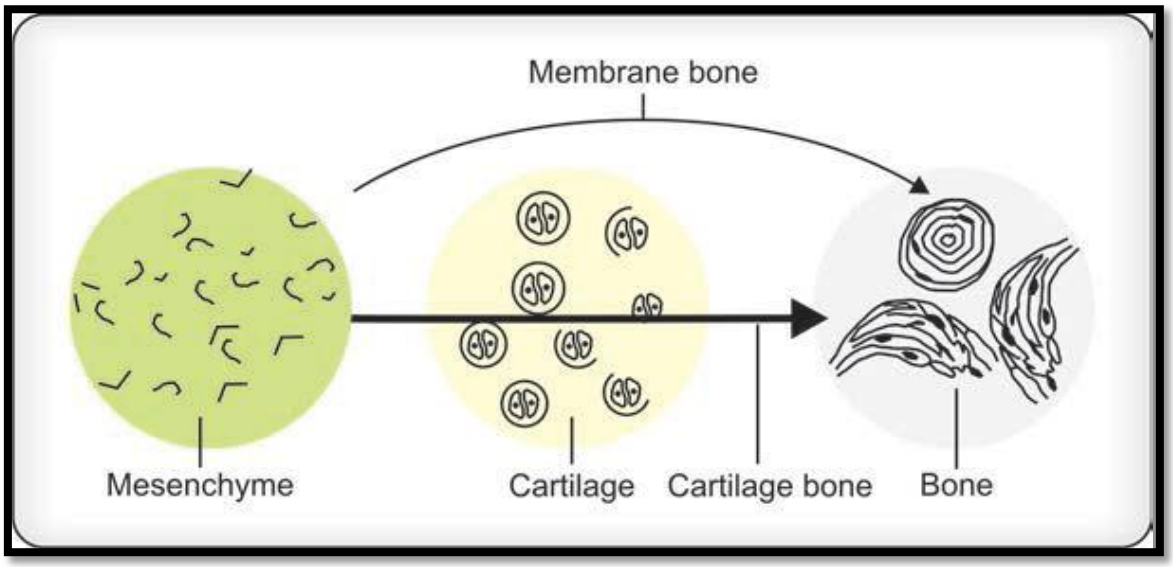


Fig.1 – Development of bone

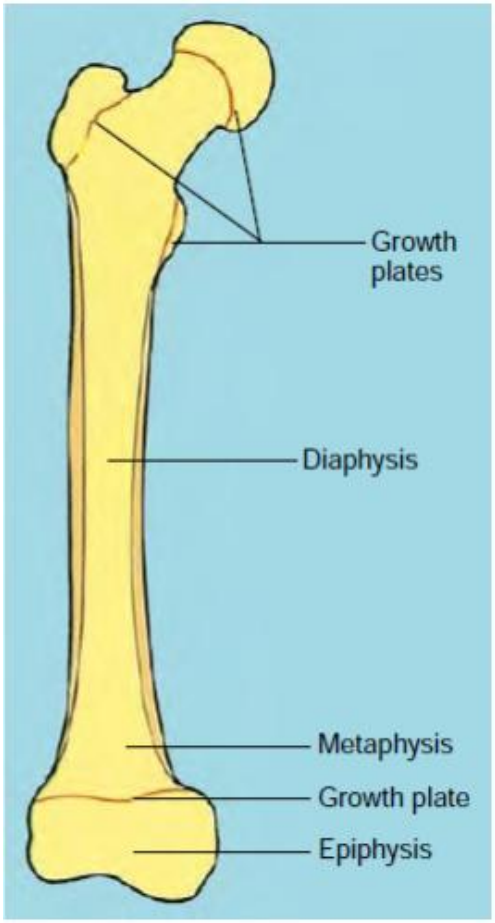


Fig. 2 – Macroscopic anatomy of Long Bone

Short bones are roughly cuboidal in shape. They are chiefly composed of cancellous bone with a thin cortical shell. Examples of short bones are scaphoid, lunate, talus and calcaneum – bones of hand and foot.

Flat bones consist of thin inner and outer layers of compact bone, the tables . The tables are separated by a layer of cancellous bone, the diploe. Bones of the vault of the skull , frontal and parietal bones and scapula are examples of flat bones.

In long and short bones, bone marrow occupies the marrow cavity. In flat and irregular bones, the interstices of cancellous bone contain bone marrow. The marrow can be red haematopoietic or of yellow adipose type according to the age and site.

Periosteum and **endosteum** are fibrous layers that line the external and internal surfaces of bone respectively.

Vascular supply[9] –

The shaft of long bones is penetrated by **diaphyseal nutrient arteries**. They enter the shaft obliquely through nutrient foramina that lead to nutrient canals. Nutrient arteries divide into ascending and descending branches in the medullary cavity. Metaphyseal arteries are direct branches of neighbouring systemic vessels. Epiphyseal arteries are derived as branches from vascular plexus formed on non – articular surfaces of bone.

Innervation –

Richly innervated structures of the skeletal system include

- Periosteum
- Articular extremities of long bones, vertebrae and larger flat bones

The perivascular spaces of haversian canals contain axons which accompany nutrient vessels into bone marrow.

HISTOLOGY

The microscopic examination of bone dates back to the earliest days of microscopy. Full and accurate descriptions of all human bones have been elucidated in classical books like Osteologia Nova[10] and Osteographia.

Bone is composed of an extracellular mineralised matrix and different types of cells including osteoblasts, osteocytes, osteoclasts, marrow and components of the periosteum and endosteum.

Bone matrix consists of a ground substance with embedded **collagen (Fig.3)** fibres. The ground substance is composed of glycosaminoglycans, proteoglycans and water. Osteocalcin and osteonectin are two special glycoproteins present in large quantities. The inorganic ions present are chiefly calcium and phosphorus. They are present as needle shaped crystals of hydroxyapatite ($Ca_{10}[PO_4]_6[OH]_2$).

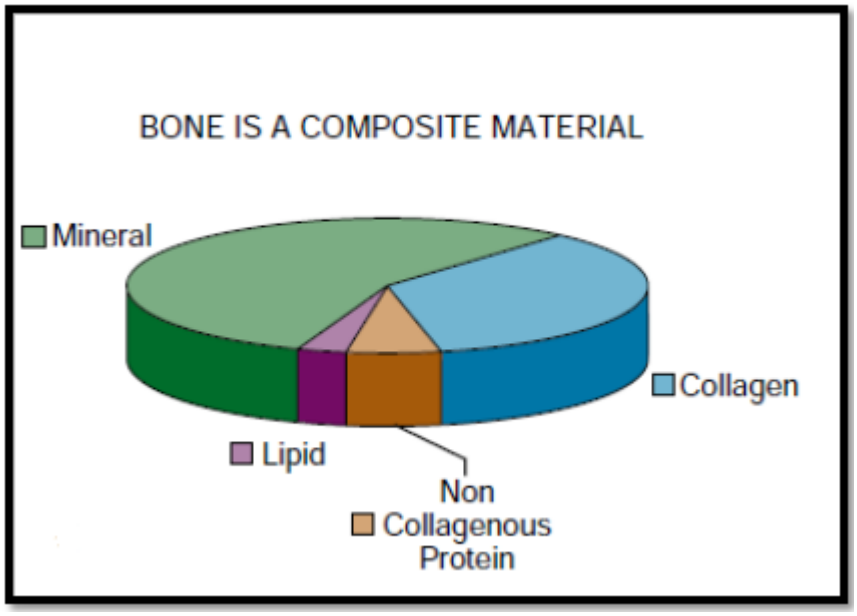


Fig. 3 – Composition of Bone

Osteoblasts (Fig. 4) lay down organic matrix of bone including collagen and are also responsible for calcification of the matrix. They have basophilic cytoplasm and ovoid euchromatic nucleus. Cytoplasmic basophilia is due to abundant rough endoplasmic reticulum. **Osteocytes (Fig. 4)** are formed when osteoblasts become imprisoned in the matrix during bone formation. In contrast to osteoblasts, osteocytes have eosinophilic cytoplasm due to negligible secretory activity and less endoplasmic reticulum. **Osteoclasts (Fig. 5)** arise from mononuclear macrophage precursors and are large cells 20 – 100 micrometer in diameter located in resorption bays called **lacunae of Howship**. They have numerous nuclei and their chief function is bone resorption.

Fig. 4 – Osteoblasts and Osteocytes

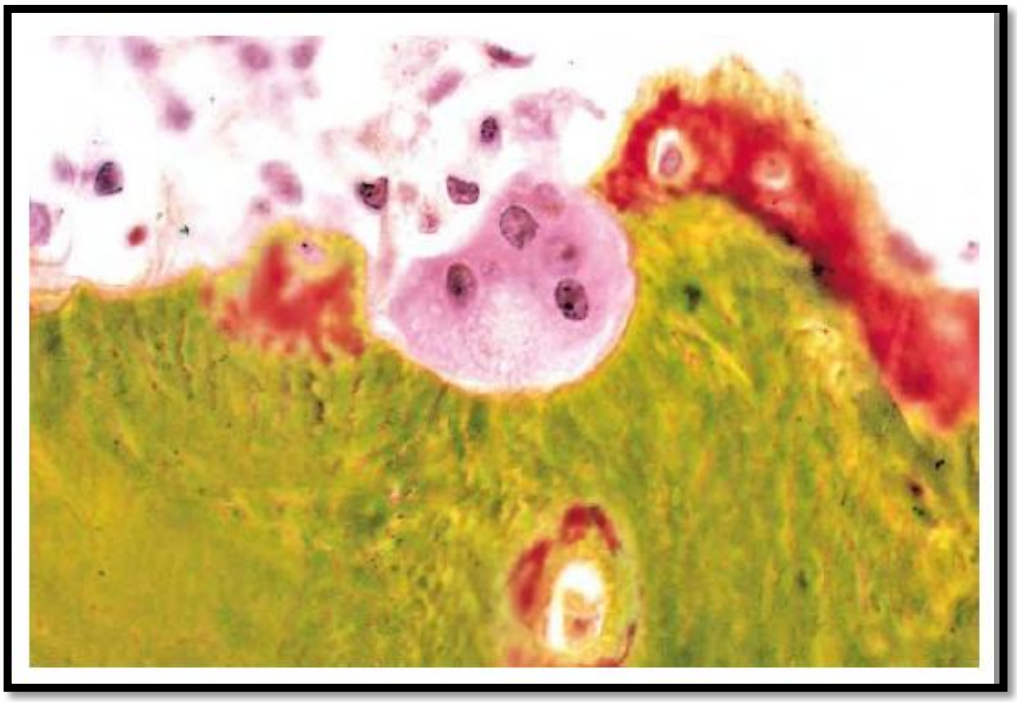


Fig. 5 - Osteoclast in a Howship's lacuna. Goldner stain.

The junction between the original resorbed surface and new bone is called **cement line**. It is sharp and basophilic with routine staining.

Lamellar bone that makes up almost the entire osseous skeleton is organised concentrically as cylinders around neurovascular channels **(Haversian canals)**. **Volkmann's canals**[10] are vascular channels connecting Haversian canals to each other and to vessels in the periosteum.

The **periosteum** has two layers - the outer fibrous layer , the inner cellular layer.

In young bones, the inner cellular layer has numerous osteoblasts whereas osteoprogenitor cells are present in the cellular layer in adults. Numerous nerve fibres are present in the periosteum. Perforating collagen fibres called **Sharpey's fibres** attach the periosteum to the surface of the bone. Neoplastic processes or physical tearing forces may detach the periosteum from the bone cortex due to damage to sharpey's fibres. New bone formation that occurs between the raised periosteum and cortical layer of bone may lead to radiological changes.

CLINICO-RADIOLOGICAL EVALUATION

CLINICAL ASPECTS

A detailed history and thorough physical examination are a pre - requisite for diagnosing bone tumours. Patients may present with a wide range of symptoms that do not prompt the clinician to a correct diagnosis.

Pain, swelling, limitation of movement and fracture on trivial trauma are the commonest presenting symptoms.

Pain – The first symptom of nearly all malignant bone tumours is pain[11]. It begins as a tearing neuralgia like pain which later becomes constant and gnawing. As the disease progresses, the pain may become agonizing requiring treatment with opiates. A tumour impinging on nerve trunks may cause radiating pain.

Swelling – Swelling is the next significant symptom in bone tumours. In benign neoplasms, the patient may be living with the swelling for many years. For a bone tumour to present as swelling, it should either have an extra - osseous component or the tumour should expand the bone.

Rapidly developing swellings are usually malignant. Tumours may be bony hard or have soft areas. The consistency of the tumour ought to be noted. Secondary changes in skin like stretching of skin with prominent veins, warmth and denudation of overlying epithelium may occur. An assessment of mobility of skin and subcutaneous tissue overlying the tumour should be made. Malignant lesions present with lesser mobility of underlying structures due to rapid growth of tumours.

Limitation of movement – Lesions close to the joint may cause limitation of mobility. This is seen with osteoblastomas, chondroblastomas, giant cell tumours and sarcomas.

Pathological fracture – Fracture may occur with no prior symptoms as in juvenile cysts and non-ossifying fibromas. Metastatic osteolytic lesions are usually associated with pathological fractures. Less common is the likelihood of primary bone tumours presenting with fractures.

General symptoms – Fever and loss of weight and appetite are symptoms associated with malignant tumours.

Fig.6 depicts the site predilection of bone tumours.

Fig.7 shows common lesions affecting different bones.

Table 1. shows the peak age predilection of bone tumours.

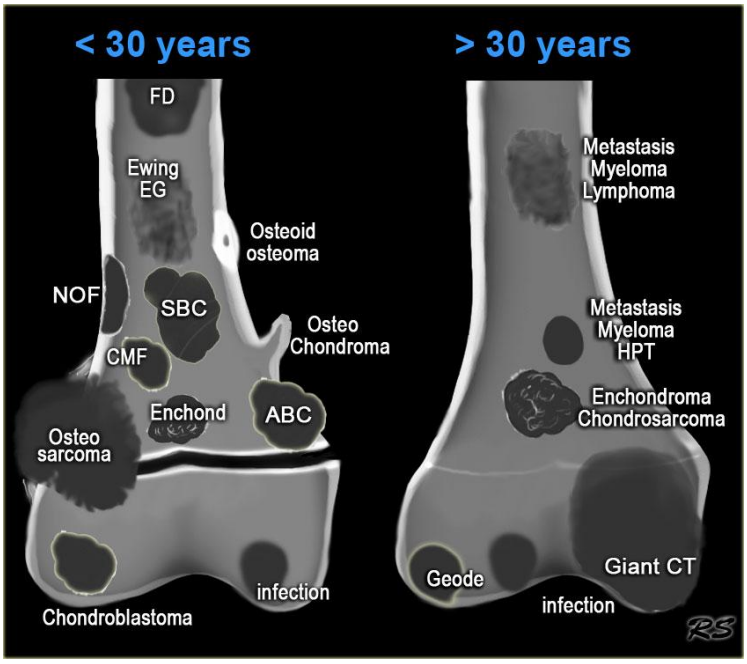


Fig6. – Site predilection of bone lesions

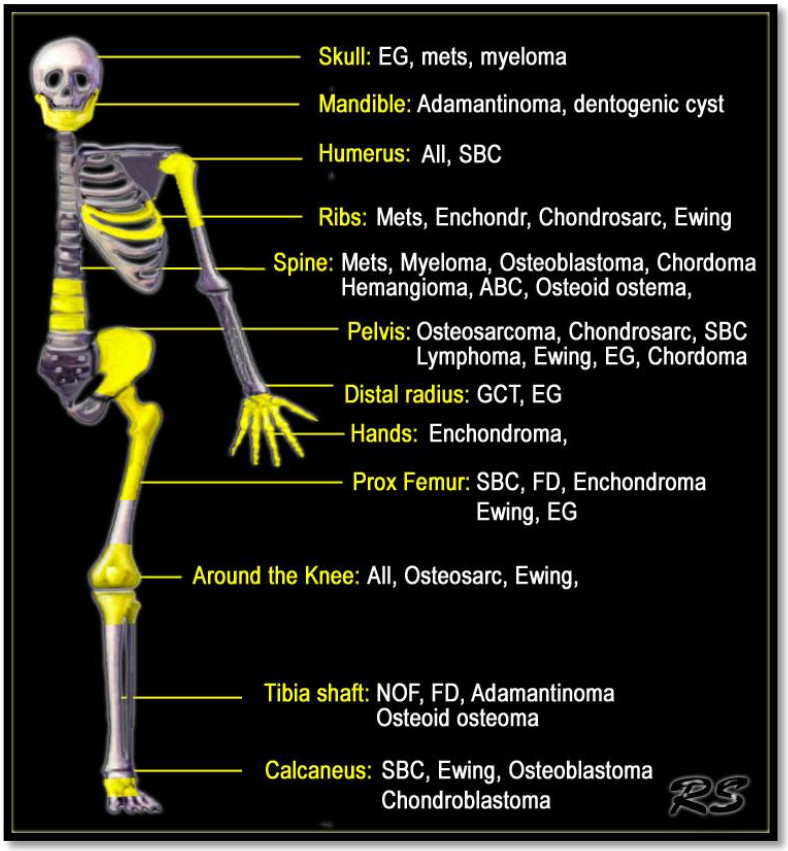


Fig7. Common lesions affecting different bones

Table 1 - Peak age predilection of bone lesions[14]

Age(yr)	Benign	Malignant
<20	➢ Enchondroma ➢ Chondromyxoid fibroma ➢ Chondroblastoma ➢ Osteoid osteoma ➢ Osteoblastoma ➢ Langerhans cell histiocytosis ➢ ABC ➢ Simple bone cyst ➢ Fibrous dysplasia	➢ Leukemia ➢ Ewing sarcoma ➢ Osteosarcoma (conventional, telangiectatic) ➢ Metastatic disease from Neuroblastoma, Retinoblastoma, Rhabdomyosarcoma and Hodgkin lymphoma
20-40	➢ Enchondroma ➢ Chondromyxoid fibroma ➢ Osteoblastoma ➢ Osteoid osteoma ➢ GCT ➢ Fibrous Dysplasia	➢ Osteosarcoma (parosteal) ➢ Adamantinoma
>40	➢ Chondrosarcoma ➢ Osteosarcoma secondary to Paget disease ➢ MFH ➢ Lymphoma ➢ Fibrous dysplasia	➢ Metastatic disease ➢ Myeloma

RADIOLOGICAL ASPECTS

Conventional radiographs are considered a gold standard for initial assessment of suspected bone lesions[12]. They provide most crucial information about the nature, progression, location and aggressiveness of bone lesions. The CT scan is an effective tool in visualising the anatomical location of the tumour, disruption of overlying cortex and calcifications within the tumour. MRI[13] helps in demonstrating abnormalities of bone marrow and illustrating soft tissue reactions to cancerous growths. Bone scintigraphy is a highly sensitive technique in detection of suspected bone metastases in the skeleton.

The following points are to be considered while reading an x-ray - age, location (type of bone, cortex/medulla, epiphysis/ metaphysis/ diaphysis), unifocal/multifocal, margins, periosteal reaction, matrix calcification, soft tissue shadows and fracture.

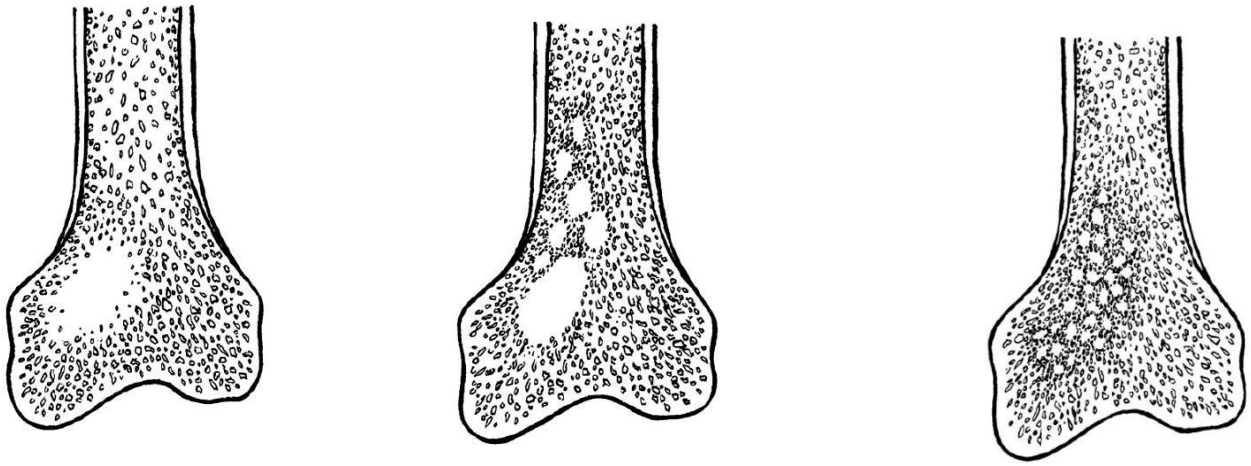
In order to reach a correct diagnosis, following specific signs must be considered –

1. Patterns of bone destruction (**Table 2**) and configuration of margin.
2. Penetration of cortex.
3. Presence of sclerotic rim.
4. Presence and extent of expanded cortical shell.

Table 2: Patterns of bone destruction[15]

Type I		**Geographic pattern**
	IA	Normal area separated from lytic regions by a sclerotic rim.
	IB	Absence of sclerosis. Lesion is well limited with distinct separation from normal bone.
	IC	Less sharp limit between the normal and lytic area
Type II		Moth-eaten pattern. Multiple lytic areas separated by bone not yet destroyed denotes aggressive pattern of tumour progression
Type III		Permeative pattern. A lesion growing aggressively and rapidly presents with a blurring or fuzzy transition.

The patterns of bone destruction have been depicted in Fig. 8.



Type 1 Type 2 Type 3

Fig. 8 Patterns of bone destruction

Matrix mineralisation (Fig.9) can affect radiographic opacity of a lesion. Matrix refers to type of tumour tissue like osteoid, chondral or fibrous. Calcification of matrix is called mineralisation. Uncalcified matrix is radiolucent.

Calcification of chondral tissue may produce the following types of mineralization –

1. Punctate / stippled
2. Flocculent
3. Arc / ring like

Bone forming tumours produce fluffy, amorphous or cloud like mineralization. This may cause different types of radiographic appearance –

4. Solid

5. Cloud

6. Ivory

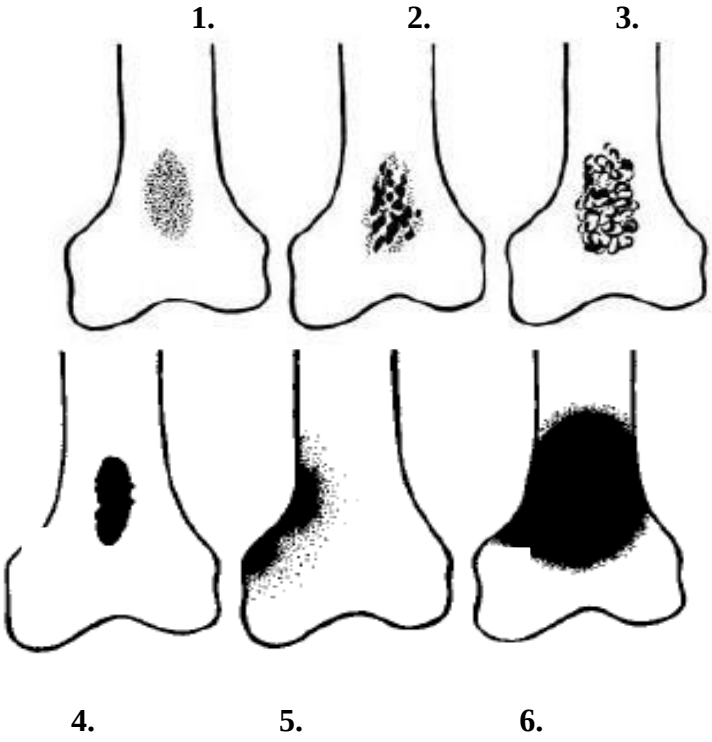


Fig. 9 Matrix mineralisation

Periosteal reaction[15] is an important radiographic feature that helps characterise a bone lesion (**Fig.10**).

1. Solid or unilamellated periosteal reaction is a non aggressive appearance.

2. Multilamellated or ‘onion skin’ appearance is suggestive of an intermediate aggressive process.

3. Spiculated , ‘hair on end’ or ‘sunburst’ pattern is a very aggressive appearance highly suggestive of malignancy.

4. Codman triangle refers to elevation of periosteum away from the cortex.

An angle is formed at the meeting point of elevated periosteum with the bone.

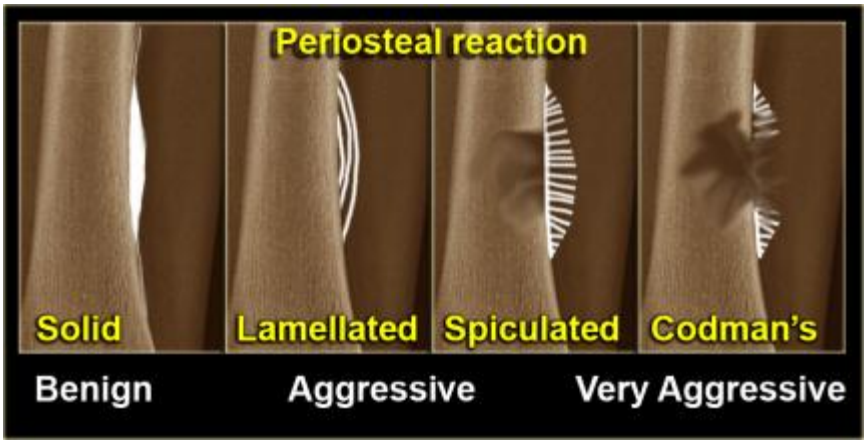


Fig. 10 Periosteal reaction

If cortex is disrupted and soft tissues are involved, it usually indicates that the tumour is aggressive.

Cortical destruction may be of “ballooning” type. The endosteal cortical bone is destroyed and there is simultaneous laying down of new bone on the outside. This results in ballooning of the affected area and formation of a neocortex.

This '**neocortex**' can be smooth and uninterrupted, but in more aggressive lesions like GCT, it may be focally interrupted.

The following tumours may show multiple lesions – chondromas, osteochondromas, Langerhans cell histiocytosis and metastases.

Osteolytic lesions can be classified as well defined or ill – defined by looking at the zone of transition between it and the adjacent normal bone. A small zone of transition results in a sharp, well – defined border and is a sign of slow growth. An ill – defined border with broad zone of transition is indicative of aggressive growth. Infections may mimic malignancy due to aggressive growth patterns.

Radiological picture of metastatic bone tumours[16] –

Predominantly lytic – Lung, Kidney, Melanoma, Colon.

Predominantly blastic – Prostate, Breast.

Mixed lytic and blastic - This is the commonest appearance.

PATHOLOGY

The WHO classification of Bone tumours (2002) has been given in

Annexure I.

CARTILAGE TUMOURS

OSTEOCHONDROMA

Osteochondroma accounts for around 35% of benign bone tumours. It is the most frequently encountered benign tumour. The tumour occurs predominantly in the first two decades of life. Rare cases in infants and newborns[17] have been reported. Osteochondromas have an osseous stalk capped by cartilage. The stalk is in continuation with the underlying bone.

Though majority of these tumours (85%) are solitary[18], 15% of them arise in a setting of hereditary multiple exostoses, an autosomal dominant disorder. Germ line mutations in tumour suppressor genes EXT 1 or EXT 2 are found in 90% of patients with hereditary multiple exostoses. The EXT 1 and EXT 2 proteins are important in the biosynthesis of heparin sulphate proteoglycans which are multifunctional proteins involved in several growth signalling pathways in the normal epiphyseal growth plate. Reduced expression of these proteins in osteochondromas is associated with disordered cellular distribution of these proteoglycans. Defective enchondral ossification that ensues, leads to formation of osteochondromas.

The tumour grows in size as the patient grows. Once epiphyses close, it becomes quiescent. Rarely, radiation therapy in children has led to the development of osteochondromas. Chondrosarcomatous change occurs in less than 1% of patients with multiple hereditary exostoses.

Patients maybe asymptomatic and present with a long standing painless mass that may either be ignored by the patient or be of cosmetic significance. If the tumour impinges on a nearby nerve, it may lead to pain. Cases have been reported where bursae form over an osteochondroma leading to pain. Infrequently, the stalk of the lesion may become infracted or fractured. An overlying vessel may show pseudoaneurysm formation due to pressure. However, increasing pain is an indication of malignant transformation and should be considered seriously.

Lower end of femur and upper end of tibia are the commonest sites of occurrence, though flat bones, ileum and scapulae may be involved in 5% of cases.

Radiologically (Fig.13,14) , the lesion may be sessile or pedunculated. Osteochondromas appear as a protruberance from the bone shaft in a juxta-epiphyseal location and are contiguous with the adjacent cortical bone. The lesion usually points away from the adjacent joint. Irregular calcification is often seen. Excessive cartilage type fluffy calcification is an indication of malignant process.

On macroscopic examination (Fig.12) , the lesion is usually an irregular bony mass with a bluish-gray cartilaginous cap. The lesion has a rim of cortical bone in its base and central cancellous bone which is in continuation with the shaft. The cap varies in thickness. A thick (> 2 cm) or irregular cap may be suggestive of malignancy.

On histopathology (Fig.15), the tumour has three layers - perichondrium, cartilage and bone. The chondrocytes within the cartilage cap are clustered superficially, and towards the transition zone, they resemble the growth plate. Organisation into chords and enchondral ossification occurs.

CHONDROMAS

Chondromas are benign cartilaginous neoplasms that can be centrally located in the bone (enchondromas) or eccentric (periosteal chondroma). This group of tumours shares many histologic features. Chondromas usually occur sporadically but enchondromatosis (Ollier's disease) usually manifests as a congenital tumour syndrome.

ENCHONDROMA

They are relatively common benign intramedullary cartilaginous neoplasms which most often occur in the short tubular bones[19] of hands and feet of adults. The lesions are usually asymptomatic. An enlarging lesion may fracture and cause pain.

Radiologically, they produce a localised central region of rarefaction. Unless a fracture has occurred, the cortex is intact. Calcification may appear as fine, punctate stippling.

Gross examination reveals bluish grey lobules of firm translucent tissue.

Microscopically (Fig.16), enchondromas show minute chondrocytes placed in lacunae. The nuclei are round and not well delineated in low power examination. Lesions of small bones differ from those in large bone by:

- Increase in cellularity.
- Clustering of chondrocytes.
- Some amount of myxoid change.
- Increase in nuclear size.
- Binucleation.

However, if cortex is breached or bone is entrapped, it is suggestive of chondrosarcoma.

JUXTACORTICAL (PERIOSTEAL) CHONDROMA

This tumour is located on the metaphyseal cortex. **On imaging studies**, a scalloped cortical defect with a sclerotic margin is seen. Typically, the lesion has overhanging edges. Juxtacortical chondroma is a periosteum covered, well – circumscribed lesion partially embedded in cortical bone. **On cut surface**, it is greyish white, or bluish and lobulated. Proliferating chondrocytes showing minimal pleomorphism and nuclear abnormalities are seen on **microscopic examination**. Limited extension into adjacent cortex may be seen. Penetration through cortex into medullary cavity however suggests a juxtacortical chondrosarcoma. The tumour is treated by enbloc resection.

ENCHONDROMATOSIS (OLLIER'S DISEASE)

This developmental disorder was discovered by the father of French orthopaedic surgery – Louis Xavier Edouard Leopold (Ollier).

It is caused by failure of normal enchondral ossification. Multiple cartilaginous masses are seen in the metaphysis and nearby areas of shafts and flat bones during childhood. Predominantly unilateral involvement is seen along with bone deformity. Some studies have implicated a gene encoding for a receptor of parathyroid hormone (PTH) and PTH-related peptide (PTHR1)[20] to be associated with Ollier disease.

When Ollier disease is associated with soft tissue angiomas, it is called **Maffucci's syndrome**.

Chondrosarcoma may develop in 25% of patients by forty years of age in Ollier disease . In Maffuci's syndrome, the risk of malignant transformation is even higher.

CHONDROBLASTOMA

This is a benign tumour that originates from cartilage and shows predilection for the epiphyseal region. It occurs mostly in patients under 25 years of age. Around one-fourth of cases in long bones reported by Kurt[21] and associates involved an apophysis, either greater trochanter of femur or the greater tuberosity of the humerus. The presenting complaint usually is pain, sometimes longstanding.

Rare lesions can metastasize. They are probably passively transported to the lung as surgical removal of the metastatic lesions gives complete cure.

Radiologically, the lesion is lytic. Margins however are well defined and sclerotic. The lesion is centered in the epiphysis.

In a case series reported by Kurt[21] and associates, 97 % of chondroblastomas of long bone were either entirely epiphyseal or had an epiphyseal component. Majority of cases do not show matrix production. The lesion may secondarily degenerate into an aneurysmal bone cyst. **On macroscopic examination**, these lesions are circumscribed and variegated with blue gray areas representing cartilaginous regions and chalky gritty areas representing calcified zones.

Microscopically, a variety of histopathological appearances may be seen due to variations in matrix and cell types. The basic proliferating cell is said to be a **chondroblast**. It is oval in shape with distinct cytoplasmic borders. The nucleus is oval and has a longitudinal groove in the middle that gives rise to a **coffee-bean appearance**. Osteoclasts are unevenly distributed in the sections and chondroid material is seen in the background. **Chicken wire calcification** is seen in many cases. Brown granular pigment, positive with iron stain is present in approximately one-fourth of all cases. These pigments are commonly seen in tumours of skull bones and may indeed be very prominent.

The treatment consists of simple curettage with or without bone grafting. In a case series reported by Turcotte[22] and co-authors, 9 out of 64 patients treated with curettage had recurrence

CHONDROMYXOID FIBROMA

An infrequently occurring benign bone tumour, chondromyxoid fibroma occurs in patients mostly in their twenties or thirties.

It occurs eccentrically in the metaphysis of lower femur or upper tibia or in short tubular bones of foot.

Radiography shows an eccentric, well – demarcated lucent defect with a thin, well – defined scalloped border of sclerotic bone.

Gross examination of the intact specimen shows a well demarcated lesion covered by a thin rim of bone or periosteum. On cut surface, it appears as a firm, lobulated, grayish white mass. Small cystic foci and haemorrhage may be seen.

A lobulated pattern with sparsely cellular lobules alternating with more cellular zones is seen on **microscopy** (**Fig. 17)**. Spindle and stellate cells without distinct cytoplasmic borders are seen in the sparsely cellular lobules. They are arranged in a myxoid matrix. Running between these lobules are highly cellular fibrous septae with scattered multinucleated giant cells. As recurrences are common after curettage, enbloc excision is done.

CHONDROSARCOMA

Chondrosarcoma is a malignant neoplasm in which tumour cells form chondroid matrix. Osteoid production is not a feature of this tumour. Adults in their fifth and sixth decades are most commonly affected. The most frequent sites are pelvis, the medullary cavity of femur, humerus and ribs. Persistent mild pain and local swelling are the initial complaints.

The tumour is classified into primary or secondary based on whether it arises de novo from normal bone or develops by malignant transformation in osteochondromas and enchondromas.

PRIMARY CHONDROSARCOMA

Primary chondrosarcoma accounts for one fifth of all malignant bone tumours. Among all primary bone tumours, it is the third most frequent tumour. The tumour arises centrally in a previously normal bone.

The **radiograph** is nearly always helpful and often affords almost pathognomonic evidence of chondrosarcoma. Chondrosarcomas tend to be large. In a study by Bjornsson[23] and co-workers, the mean size of the tumours of the 180 cases for which radiographs were available was 9.5cm. In long bones, the tumour presents as a metaphyseal or diaphyseal fusiform expansion. Cortex is many a times thickened. Radiolucent areas with ring like opacities are seen. The tumour shows minimal periosteal reaction.

Macroscopically (Fig.20), the tumour is translucent and blue grey due to presence of hyaline cartilage. Lobular growth pattern may be apparent with cystic, myxoid and chalky white areas. Cortical erosion with soft tissue extension is seen more commonly in tumours of flat bones.

Microscopically (Fig.21&22), blue gray cartilage matrix production is evident at low magnification. Lobules of cartilage of varying shapes and sizes are seen either separated by fibrous bands or permeating bony trabeculae.

The criteria that differentiate low –grade chondrosarcoma from chondroma are very subtle. Mirra[24] and co-authors proposed several histologic criteria to make this distinction.

Enchondromas tend to form well-circumscribed nodules that may be surrounded by bony trabeculae. Chondrosarcomas tend to permeate, filling the marrow cavity and entrapping bony trabeculae. This permeative quality is the most important feature distinguishing chondrosarcoma from enchondromas **(Fig.18).** Chondromas tend to have a solid chondroid matrix. The matrix stains blue and has a smooth, unbroken appearance under low power. Chondrosarcomas tend to show a myxoid change in the matrix. This manifest as partial dissolution of matrix into strings and chords. Foci of necrosis manifesting as lacunae containing pink-staining cells without blue-staining nuclei is a worrisome feature.

As a rule, cartilaginous tumours of the sternum are malignant. The features suggested by Lichtenstein and Jaffe[25] are very helpful to diagnose chondrosarcoma when viable fields are studied. These include many cells with plump nuclei, more than occasional cell with two such nuclei, and especially, giant cells with large nuclei or multiple nuclei or clumps of chromatin.

Grading predicts histologic behaviour and prognosis in chondrosarcoma. They are graded mainly based on **cellularity** of neoplasm and **cytologic atypia**. Mitotic activity being uncommon, is not used in grading chondrosarcomas.

Table – 3 GRADING OF CHONDROSARCOMAS[26]

Grade 1	More cellular than enchondromas; nuclei small; high chromatin density.
Grade 2	Cellularity increased; medium sized regular nuclei; loose chromatin structure.
Grade 3	Extreme cellularity; large bizarre nuclei; binucleate forms; small foci of spindling at the periphery of the lobule.

SECONDARY CHONDROSARCOMA

This tumour is marked by the occurrence of chondrosarcoma in a benign lesion like osteochondroma or enchondroma. There is 2% risk of malignant transformation in osteochondromas. Patients with Ollier disease and Maffucci syndrome have a 25-30 % risk of developing chondrosarcoma. Patients frequently present with sudden pain or increase in size of the swelling. **Roentgenogram** shows irregular mineralisation and thicker cartilage cap as evidence of malignant transformation in osteochondromas. Destructive permeation of bone and appearance of soft tissue mass suggest malignancy in a chondroma. **Macroscopic appearance** of a greater than 2cm cartilage cap thickness with lobulations and cystic cavities may be suggestive of malignant transformation.

Microscopically, secondary chondrosarcomas are usually low grade tumours invading the surrounding tissues and showing marked myxoid change in matrix.

DEDIFFERENTIATED CHONDROSARCOMA

This is a term used for lesions in which a high-grade, non-chondromatous sarcoma (Osteosarcoma, Malignant fibrous histiocytoma, Rhabdomyosarcoma) arises in a patient harbouring a benign cartilage neoplasm. Majority of patients are of elderly age group in their fifth decade of life. The distribution of these tumours parallels that of conventional chondrosarcomas.

On imaging, these tumours are usually large and show aggressive, destructive changes. Characteristically, the lesions have a bimorphic pattern, with an area of low-grade tumour juxtaposed to an area of more aggressive destructive change.

Grossly and microscopically, the tumour shows areas representing the chondrosarcoma and the other sarcoma component. In three fourths of cases, the chondrosarcoma component is of grade 1. The tumour has to be differentiated from chondroblastic osteosarcoma. The cartilage cells are of high grade in chondroblastic osteosarcoma.

MESENCHYMAL CHONDROSARCOMA

This is an uncommon malignant neoplasm seen most commonly in patients in their twenties and thirties. The tumour shows a predilection for maxilla, mandible and ribs though any bone may be affected.

The characteristic **microscopic feature** of this tumour is its biphasic pattern. Small, uniform, round to spindle shaped cells showing perivascular arrangement resulting in hemangiopericytoma - like pattern are seen.

Focal areas of cartilaginous or chondroid matrix are seen admixed in lobular pattern with the cellular areas. This tumour predominantly metastasizes to lungs.

CLEAR CELL CHONDROSARCOMA

This is a rare malignant, slow growing tumour composed of malignant chondrocytes having abundant clear cytoplasm. Males are affected more commonly. Patients are usually in their third or fourth decade of life.

Radiologically, the tumour is well circumscribed and shows mixed lucent and sclerotic defects with a thin sclerotic border and scattered calcifications.

Microscopically, the tumour cells have abundant clear, vacuolated cytoplasm containing PAS positive glycogen seen infiltrating woven bone and lying between heavily calcified cartilage matrix. The giant cells and chondroid matrix help to differentiate it from metastatic renal cell carcinoma.

FNAC in chondrosarcoma shows –

- Predominantly tissue fragments in low-grade (grades 1 and 2) tumours. Single cells may dominate in high grade sarcomas.
- Abundant eosinophilic vacuolated cytoplasm.
- Chondromyxoid material.

OSTEOGENIC TUMOURS

OSTEOID OSTEOMA

These are relatively common, solitary, benign, small (less than 1 cm in diameter) lesions. Children and adolescents are most commonly affected and boys are affected twice as commonly as girls.

Nocturnal pain which is usually relieved by aspirin is the most characteristic clinical presentation. Local swelling, tenderness and leukocytosis may be present.

The typical site of involvement is the cortex of a long bone. **Radiology (Fig.23)** shows a central lucent zone (nidus), with the surrounding bone showing sclerosis and marked periosteal new bone formation.

Localization of the lesion at surgery is difficult and may be aided by preoperative technetium (^{99}Tc) isotope injection. The overlying cortical bone may get a pinkish hue due to periosteal reaction and increased vascularity.

Microscopically (Fig.25), these tumours are characterised by a maze of small spicules of immature bone. They are lined by prominent osteoblasts and there are many osteoclasts. Intervening stroma is sparsely cellular with many vascular spaces in mature lesions.

OSTEOBLASTOMA

This tumour has been called as giant osteoid osteoma. The tumour most often affects males in their third decade. Pain, often progressive, is the most frequent complaint.

Yoshikawa[27] and co-authors reported two examples of osteoblastoma associated with osteomalacia. Mirra[28] and co-authors described a case of osteoblastoma associated with severe systemic toxicity. Axial skeleton is preferentially involved with the posterior elements of spine being commonly affected. **The radiographic features** of osteoblastoma are often nonspecific. In reviewing the radiographs of 116 cases of appendicular osteoblastomas, Lucas[29] and co-authors found that 65% of the tumours were located within the cortex and other 35% in the medullary canal. **Whole gross specimens** are rarely seen because the average lesion is removed by curettage. The lesions are reasonably well circumscribed. The tumour is haemorrhagic, granular and friable because of its vascularity and osteoid component which shows variable calcification. **On microscopic examination (Fig.26)**, a vascular spindle cell stroma with abundant irregular spicules of mineralised bone and osteoid are seen. Osteoblasts and multinucleated giant cells are readily evident on bone surfaces. The differentiation of osteoid osteoma and osteoblastoma is rather difficult. However, tissue pattern appears less regular in osteoblastoma than osteoid osteoma. Sometimes secondary changes like aneurysmal bone cyst and fracture may occur.

OSTEOSARCOMA (OSTEOGENIC SARCOMA)

Osteosarcoma is the commonest non haematopoietic primary malignant skeletal neoplasm which accounts for about 20 % of all primary malignant bone tumours. Malignant cells produce osteoid but the pluripotential nature of the

tumour cell is evident in the fibrous and cartilaginous matrix present in many of these tumours.

Conventional osteosarcoma is predominantly a disease of the young occurring in patients under 20 years of age. When these tumours occur above the age of 40 years, the possibility of Paget's disease or post radiation sarcoma should always be considered. Males are affected more commonly.

The most common sites of involvement are the metaphyseal part of long bones and nearly one half occur in the region surrounding the knee. 91% of tumours affect the metaphysis and about 9% affect the diaphysis. With increasing age, involvement of jaws, pelvis, skull and spine increase. Huvos[30] noted that in the Memorial Sloan – Kettering Cancer Centre group of older patients with osteosarcoma, the axial skeleton was the most common site.

A deep boring to severe pain with or without swelling **(Fig.27&28)** is the most common presenting symptom. A sudden increase in pain is attributable to intralesional haemorrhage. Pathological fracture may occur in 5 -10 % of patients. Cheng[31] and co-authors reported a case of osteosarcoma associated with oncogenic osteomalacia. An increased level of alkaline phosphatase, which occurs in about half the patients, reflects osteoblastic activity.

The tumour exhibits marked variation in overall **radiological features (Fig.29 &30)**. It may be purely osteoblastic or osteolytic though a mixed blastic-lytic appearance is most common. Cortical destruction and tumour extension into soft tissue are present.

Non – contiguous intramedullary **skip metastases** growths called may occur. Periosteal elevation with reactive new bone formation **(Codman's triangle)** tends to occur. Mcleod and Berquist[32] emphasized that although the use of plain radiographs is the standard means for diagnosing osteosarcoma, computed tomograms and magnetic resonance images are far superior in delineating the extent of the disease. Gillespy[33] and co-authors also emphasised the superiority of magnetic resonance imaging studies for preoperative staging of osteosarcoma.

Macroscopic appearance (Fig.19) may vary from extremely soft, fleshy masses through firm, fibrous tumours with foci of irregular ossification and various amounts of chondroid material, to a densely sclerotic type. Cortical disruption ith soft tissue mass are usually present. Tumour is usually centered around the metaphysis.

Microscopically there is tremendous variation in the appearance of the tumour. Lichtenstein[34] tersely stated the essential criteria for diagnosis as –

1. The presence of a frankly sarcomatous stroma.
2. The direct formation of tumour osteoid and bone by this malignant connective tissue.

The sarcomatous tumour cells show high degree of anaplasia and pleomorphism. They may be plasmacytoid, epithelioid, oval, small cell type, clear cell type or spindle shaped. Malignant osteoid appears as a dense eosinophilic amorphous material between tumour cells. Osteoid is curvilinear with arborisation. The thinnest form of osteoid is called filigree osteoid **(Fig.35)**.

CONVENTIONAL OSTEOSARCOMA

Type of matrix helps to subdivide osteosarcoma into – osteoblastic (50%), chondroblastic (25%) and fibroblastic (25%).

Osteoblastic osteosarcoma (Fig.35)

The matrix predominantly is bone or osteoid. It can be thin, arborising filigree osteoid or thick, dense sclerotic osteoid.

Chondroblastic osteosarcoma

Chrondroid elements predominantly malignant hyaline cartilage are admixed with non – chondroid elements.

Fibroblastic osteosarcoma (Fig.36)

The tumour cells are spindle-shaped and may be arranged in herringbone pattern. Matrix production is seen only focally. Some of these tumours have a rich vascular pattern and may even resemble a hemangiopericytoma.

TELANGIECTATIC OSTEOSARCOMA (Fig.37)

Following criteria are followed for diagnosing a telangiectatic osteosarcoma:

1) **Radiography** – The lesion is purely lytic. Sclerosis if appreciable rules out the diagnosis.
2) **Grossly**, the tumour resembles a bag of blood. Flesh like or sclerotic appearance is not seen.
3) **Microscopically**, spaces are separated by septa as in an aneurysmal bone cyst. The cells that line the septa are cytologically malignant. Osteoid production is minimal.

The prognosis of this tumour was considered to be very poor compared to conventional osteosarcoma. However, Bertoni[35] and co-authors from Bologna, reporting on 41 patients with telangiectatic osteosarcoma, found no significant difference in prognosis.

SMALL CELL OSTEOSARCOMA

This is a microscopically distinct variant of osteosarcoma comprising of small round cells but showing at least focal osteoid production. Ewing's sarcoma, mesenchymal chondrosarcoma and lymphoma should be considered in the differential diagnosis. Reticulin stain may be used to differentiate small cell osteosarcoma from Ewing sarcoma. Reticulin is seen to stain around the individual tumour cells in small cell osteosarcoma. However, in Ewing sarcoma reticulin is scant. Neoplastic osteoid is characteristically absent in Ewing tumour. Mesenchymal chondrosarcoma may also be considered in the differential diagnosis. It has a predilection for axial skeleton. Though small cells are seen, there is a component of low grade cartilage. Cartilage if present in small cell osteosarcoma, presents with malignant looking, high grade differentiation. Lymphoma panel of IHC markers helps to distinguish small cell osteosarcoma from lymphoma.

LOW GRADE CENTRAL OSTEOSARCOMA

This tumour usually occurs in individuals who are older than those affected by the conventional high grade tumours.

On imaging studies, the lesions may be sclerotic mimicking large bone islands or resemble foci of solitary fibrous dysplasia. Microscopically, these tumours have a fibrous stroma with bland looking foci of bone formation. They mimic conventional surface (parosteal) lesion or fibrous dysplasia. The clinching points favouring diagnosis are the identification of the invasive character of the lesion, typified by the presence of islands of residual lamellar bone within the lesion and evidence of malignant tumour bone plastered onto and surrounding these islands of residual bone . This tumour has a more indolent clinical progression. Local recurrences are however high.

SECONDARY OSTEOSARCOMA

These tumours occur in bones which are already affected by some pathology. Paget disease of bone, irradiation for a prior tumour, infarction of bone, prosthetic implant in the joint, and tumour like-lesions (fibrous dysplasia) are suggested etiologies.

Paget osteosarcoma constitutes one fifth of all osteosarcomas in patients beyond the third decade of life. Two – thirds of sarcomatous change occurs in large limb bones and one-third in flat bones. Skull involvement is seen in 10-17% of all Paget osteosarcomas. Multifocal osteosarcomas may be seen in 17% of patients with polyostotic Paget disease. Patients present with change in pain pattern, increase in size of swelling or pathological fracture. Elevation of alkaline phosphatase levels above those seen in Paget disease is usual.

Radiological studies reveal underlying features of Paget disease with superimposed tumours exhibiting lytic pattern more often than blastic or sclerotic appearance. Histpathologically, Paget osteosarcomas are high grade sarcomas mostly of osteoblastic or fibroblastic type. The prognosis for these patients is poor especially for those in pelvic girdle and skull.

Post radiation osteosarcoma constitutes 3.4-5.5% of all osteosarcomas. The risk of osteosarcoma developing in an irradiated bone is 0.03-0.8%. The greatest risk of sarcoma is seen in children treated with high dose radiotherapy and chemotherapy. Pelvis and shoulder girdle are the commonest sites of involvement. The latent period is usually long (median of 11 years) but may be as short as two years. The criteria for diagnosis are, a tumour developing in the path of radiation beam in a previously normal bone or region of benign tumour or non bone forming malignancy. There should be a symptom free latent period. **Radiologically**, the tumours are densely sclerotic or lytic with a soft tissue mass. 50% cases show features of radiation osteitis (trabecular coarsening and lytic areas in the cortex). **On microscopy**, the tumours are usually of high grade with histological changes of radiation osteitis.

PAROSTEAL OSTEOSARCOMA

This is a low grade osteosarcoma arising from the surface of the bone. It has also been called juxtacortical osteosarcoma. The surface of distal posterior femur is the most common site of involvement. A slight female preponderance has been noted.

X-Ray shows a heavily mineralised mass with a broad base, attached to the cortex with a tendency to encircle the bone. **On macroscopic examination**, the tumour presents as a cortex based mass that is hard with lobations. The occasional presence of a cartilage cap may suggest the diagnosis of osteochondroma. Invasion of surrounding soft tissues and bone marrow is seen. **Microscopic features** show a stroma with low cellularity with bony trabeculae that are well formed. Parallel arrangement of bony trabeculae may simulate normal bone. Osteoblastic rimming of bony trabeculae may or may not be seen. The hypocellular intertrabecular stroma shows minimal atypia. Cartilaginous differentiation may be evident in 50 % of tumours. Prognosis of these tumours is generally good with a high (>90%) five year survival rate.

PERIOSTEAL OSTEOSARCOMA

This tumour has been variably named as juxtacortical chondrosarcoma by Schajowicz and cortical osteosarcoma by Jaffe.

This tumour accounts for less than 2% of all osteosarcomas.

The peak incidence occurs at second and third decades with a slight male preponderance. The most common location of this tumour is the mid portion of femur followed by mid portion of tibia. The most common presenting complaint is a painless mass or swelling of long duration. Tenderness develops later in the course of the disease.

Radiologically, the tumour displays non homogenous, calcified spiculations disposed perpendicular to the cortex and giving a sun burst appearance. **Macroscopically**, the tumour arises from the bone surface and involves part or entire circumference of the bone. **Histopathological examination** shows that although chondroid differentiation may dominate, condensation of nuclei in the periphery of the lobules and production of trabeculae of bone in the centre supports the diagnosis of osteosarcoma.

HIGH GRADE SURFACE OSTEOSARCOMA

Very rarely, a highly anaplastic osteosarcoma occurs predominantly on the surface of the bone. This tumour has to be differentiated from the very well differentiated parosteal osteosarcoma and the moderately differentiated periosteal osteosarcoma. Patients are usually males in their second decade of life. Distal femur is the most frequent location of this tumour. The **radiological appearance** is that of a partially mineralised mass arising from the bone surface and extending into the soft tissues. Microscopic foci of medullary involvement may be seen. Large areas of medullary tumour are against this diagnosis. **Macroscopic examination** shows the tumour attached to the surface with erosion of underlying cortex. All tumours have soft areas that help distinguish them from parosteal osteosarcomas. **Histopathological spectrum** is similar to that seen in conventional osteosarcomas with high grade spindle cells and lace like osteoid. These features help to distinguish it from parosteal osteosarcomas.

The **FNAC (Fig.34)** criteria for diagnosis are –

- Pleomorphic spindle and rounded cells.
- Tumour cells more or less resembling osteoblasts.
- Multinucleated tumour cells.
- Mitotic Figures.
- Clumps of amorphous, faintly eosinophilic material in between cell clusters (osteoid).

FIBROGENIC TUMOURS

DESMOPLASTIC FIBROMA

Desmoplastic fibroma is one of the rarest of bone tumours and may be considered to be an intraosseous counterpart of the much more common desmoid tumour of soft tissues. Gebhardt[36] and co-authors found 85 cases in their review of literature. Also Kwon[37] and co-authors found 47 cases of desmoplastic fibromas of jawbones reported in the literature.

This is a locally aggressive non-metastasising lesion. Cytologically, typical fibroblasts are seen arranged in a collagenized stroma. Mean age of occurrence is by fourth decade and patients may have pain, swelling or fracture as their complaints. Metaphysis of long bones is most frequently involved.

The **radiographs** show purely lucent defect in the bone. Slight to moderate expansion of the bone may be seen.

Lobulated and well defined margins are seen. As described by Crim[38] and co-authors, there is a striking tendency for uneven bone destruction, leaving behind intact ridges of bone and producing a pseudo-trabecular appearance. **On macroscopy**, the tumour is gray and whorled. **Microscopically**, desmoplastic fibromas are composed of spindle cells with abundant collagen production. Bone entrapment may be seen. Soft tissue extension is also common. A prominent vascular component may be seen. Mitotic figures are usually absent. The chief differential diagnosis is fibrosarcoma which has nuclear atypia and increased cellularity.

FIBROSARCOMA

It is a malignant spindle cell neoplasm which produces moderate to sparse collagen matrix. No other matrix differentiation is seen either in the primary lesion or in the secondary deposits. Adults between 20 to 60 years of age are affected and metaphyseal ends of long bones especially around the knee are the commonest site. Patients may present with pain, swelling or pathological fracture. Predisposing factors like Paget's disease, fibrous dysplasia, irradiated giant cell tumour, bone infarct or long standing osteomyelitis are found in one quarter of patients.

Radiographically, the tumour appears lucent with a moth-eaten pattern. Tumour margins are irregular. Cortical destruction and soft tissue extension are commonly seen. Periosteal new bone formation may be minimal.

Taconis[39] and Van Rijssel found that the radiographic features of fibrosarcoma and malignant fibrous histiocytoma are essentially the same.

Fibrosarcoma in the bone has the same **histopathologic** features as its soft tissue counterpart. However, sections may show that it has invaded and destroyed the bone especially near the periphery of the tumour. There is wide variation in the degree of differentiation in the component fibroblasts and in the amount of collagen produced. The shape of the nuclei vary from long and slender to oval. Cells are organised in a herringbone pattern.

Fibrosarcomas are graded **(Table 4)** on the basis of cytologic features of the tumour cells and cellularity of the lesion. Cellularity is inversely proportional to collagen produced.

Table 4 - GRADING OF FIBROSARCOMAS

GRADE	FEATURES
1	Abundant collagen, spindle cells are separated from each other, nuclei elongated with tapered ends, mitotic figures uncommon.
2	Increased cellularity, nuclei more atypical, mitotic activity more prominent.
3	Darkly stained spindle cells in herringbone pattern, little collagen production, mitotic figures abundant, necrotic areas seen.
4	No matrix, cells packed closely together. Mitotic figures and necrotic areas very prominent.

Leiomyosarcoma, synovial sarcoma, malignant peripheral nerve sheath tumour, metastatic carcinoma and metastatic melanoma may also demonstrate a spindle cell pattern and should be considered in the differential diagnosis. Appropriate immunohistochemical studies are essential to arrive at the correct diagnosis.

FIBROHISTIOCYTIC TUMOURS

BENIGN FIBROUS HISTIOCYTOMA OF BONE

This is a very rare benign bone tumour. Females tend to get affected more frequently than males. Most of the patients have no findings attributable to their tumour. The most common sites of involvement are long bones. **X-ray** examination reveals a well defined zone of rarefaction. **Macroscopically**, the tumour is firm and grey white with yellowish areas. **On microscopic examination**, the fibrogenic quality may be manifested by interlacing bundles of cells. Benign giant cells are present in variable numbers but they may be sparse. Some of the nuclei are indented or grooved, and this histiocytic quality may be associated with lipid production. Matsuno[40] has referred to the problem of differentiating benign fibrous histiocytoma from giant cell tumour when the lesions occur at the ends of long bones.

MALIGNANT FIBROUS HISTIOCYTOMA

This is an uncommon bone tumour with most cases seen in males between fifty to seventy years of age. The commonest sites of occurrence are the lower extremities particularly femur, followed by tibia.

Around 20 % of these tumours may be considered secondary to a variety of causes like Paget disease, radiation therapy, bone infarct and total hip arthroplasty. Troop[41] and co-authors have reported a case of malignant fibrous histiocytoma at the site of previous hip replacement. A similar case was reported by Hagg[42] and Adler. **Grossly**, the tumour appears as a lobulated, fleshy, grey white mass. **Microscopically**, the tumour has variable presentation. Most tumours have a storiform pleomorphic pattern. Some may show a myxoid or predominantly giant cell pattern. Plump spindle cells are seen arranged in a matted pattern of short fascicles. Interspersed focal areas of large atypical cells, multinucleate giant cells and typical and atypical mitotic figures are seen. This tumour is largely a diagnosis of exclusion after various immunohistochemical markers have been studied to rule out other entities.

EWING SARCOMA

This is a small round cell malignant neoplasm of bone accounting for 6-8 % of primary malignant bone tumours. This tumour was earlier subject to high controversy as to whether all Ewing sarcoma were actually metastatic neuroblastomas.

Essentially a tumour of childhood, most patients are younger than 20 years of age. Boys are affected more commonly than girls. The most common sites involved are diaphysis of long bones. Ribs and pelvic bones may also be commonly affected.

Patients report with pain and tenderness of several weeks duration in the affected bones. Most patients have a palpable tender mass and some have dilated veins over the tumour. An initial diagnosis of osteomyelitis may be suggested by fever, anemia, leukocytosis and elevated erythrocyte sedimentation rate. The radiologic and microscopic appearance of the tumour may also mimic osteomyelitis.

Ewing tumour tends to be extensive, sometimes involving the entire shaft of a long bone. More bone is usually found to be pathologically involved than found in the radiograph.

Radiologically (Fig.38), lytic destruction is the most common finding. There may however be regions of density due to stimulation of new bone formation. As the tumour bursts through the cortex, it raises the periosteum gradually. This elevation produces characteristic multiple layers of subperiosteal reactive new bone which produces the **onion peel appearance** of Ewing tumour. Radiating spicules from the cortex of an affected bone are not uncommon, a fact that complicates the differentiation from osteosarcoma. This differentiation may be especially difficult in flat bones like ilium. Edeiken[43] has stressed that saucerisation of the exterior surface of the cortex is an early and characteristic sign of tumours presenting subperiosteally.

Macroscopically, the tumour has a poorly demarcated, grayish white appearance with areas of haemorrhage, cystic degeneration and necrosis.

Microscopic examination (Fig.39) shows homogenous, densely packed small cells with regular nuclei and finely granular nuclear chromatin. 1- 2 small nucleoli may be seen. The cell walls are indistinct and cytoplasm is delicate and lace like. Areas of haemorrhage and necrosis are usually seen. Most tumours show positivity for CD99 **(Fig.39)** antibody and vimentin. A microscopic differential diagnosis of osteomyelitis, eosinophilic granuloma and other small round cell tumours should be considered. Occasionally, the cells of the tumour contain nuclei that have a somewhat larger and less regular shape than those of a typical Ewing tumour. This has been named as atypical or large cell variant of Ewing tumour. Prognosis is similar to classical Ewing tumour.

CD 99 is an immunostain that recognises a product of the MIC – 2 gene and has become a sensitive marker to diagnose Ewing sarcoma. The **t(11;22) chromosomal translocation** which results in EWS-FLI 1 fusion can be detected by molecular methods and may serve as a useful adjunctive test in diagnosis of Ewing sarcoma.

Patients with Ewing sarcoma present with early metastasis to lung and other bones but with aggressive chemotherapy and radiotherapy, the outlook has greatly improved.

The criteria for diagnosis by **FNAC** are –

- Clusters of loosely cohesive cells.
- Two cell types – large pale cells with abundant cytoplasm and small dark cells with scanty cytoplasm.
- Rounded or irregular bland nuclei; small nucleoli.
- Occasional rosette like structures.

HAEMATOPOIETIC TUMOURS

PLASMA CELL MYELOMA

Myeloma, a tumour of hematopoietic derivation is the most common primary neoplasm of the bone. The neoplasm is composed of plasma cells that show various degrees of differentiation. The tumour predominantly occurs in the sixth and seventh decades of life. Less than 7% of cases occur in the first four decades of life. The disease process consists of osteolytic lesions, bone pain, hypercalcemia and monoclonal gammopathy. Commonly involved bones include those that have haematological marrow in adults especially, vertebrae, ribs, skull, pelvis and scapula. In a review of the cases of 46 patients from Mayo Clinic files who had solitary plasmacytoma of bone, Frassica[44] and co-authors found that 54 % lesions involved the vertebral column. Bone pain, pathological fracture, anaemia and hypercalcemia are the most common presenting symptoms.

The radiographic features result from the replacement of osseous structures by myelomatous masses. **Radiologically (Fig.40)**, there are sharply demarcated punched out areas of lytic lesions not surrounded by a sclerotic zone. Expansion of the affected bones may produce a "ballooned out" appearance especially in the ribs. Variable osteoporosis and pathological fracture may be seen. **Grossly**, the myelomatous masses are soft, pink, or gray and friable, similar to currant jelly. **Histopathological examination (Fig.41)** shows sheets of closely packed round to oval plasma cells with little intercellular substance. The cells have abundant cytoplasm that tends to be granular and basophilic. The cell outlines are distinct with a characteristically round or oval eccentric nucleus. Two or even three nuclei may be observed in each cell. Well differentiated tumours show plasma cells with prominent clumping of chromatin producing a cart wheel appearance. With decreasing differentiation, nucleoli become enlarged and clumping of chromatin becomes less pronounced. Myelomas may become extremely vascular and show amyloid deposits.

When in doubt whether the plasma cells are a part of neoplastic or inflammatory process, a monoclonal staining pattern for kappa or lambda will establish a diagnosis of malignancy. Neoplastic and non-neoplastic plasma cells usually express CD 138 **(Fig.42)**.

The **FNAC** diagnostic criteria are –

- Many plasma cells
- Single cell presentation

MALIGNANT LYMPHOMA

Parker[45] and Jackson, in 1939, first described malignant lymphoma of bone. A neoplasm composed of malignant lymphoid cells, this tumour accounts for about 7% of all bone malignancies. In the series reported by Ostrowski[46] and co-authors in 1986 involving 422 patients with malignant lymphoma of bone, the tumours were considered to be primary in 179 cases. Older adults are most often affected with a slight male preponderance. Portions of bone with persistent red marrow are commonly involved with femur being the most common bone affected followed by ilium. Bone pain is the most frequent symptom. The **radiological features** of lymphoma are non-specific. Wilson and Pugh[47], who studied the Mayo clinic series of lymphomas, concluded that the radiographic findings varied so much that they could not be regarded as characteristic.

Diaphyseal involvement is common in long bones. **Grossly**, the tumour tends to involve and destroy large portions of the bone. The process is poorly demarcated and there is a wide area of transition from normal bone. The tumour may be very sclerotic or purely lytic. Cortical destruction with a large soft tissue mass is common. **Histopathologically (Fig.43)**, the majority of malignant lymphomas of bone are diffuse large B – cell lymphomas rather than follicular or small lymphocytic type. Most lymphomas of bone show a mixed cell infiltrate – that is there is considerable difference in the sizes and shapes of tumour cells.

Indeed, this feature is very helpful in differentiating lymphoma from Ewing tumour, the tumour cells of which show little variation in size and shape. Most lymphomas have a diffuse growth pattern. The tumour tends to permeate between normal structures like medullary bone and marrow fat. Dosoretz[48] and co-authors have suggested that patients with tumours composed predominantly of large cleaved cells have a better prognosis than patients with tumours composed of non cleaved cells. Pettit[49] and co-authors found that primary bone lymphoma has an unusually high incidence of large cleaved and multilobated cells. Immunohistochemical stains and occasionally molecular studies, are necessary for typing lymphomas of bone. Most of the times, the diagnosis can be made with a limited number of stains including the B – cell marker CD 20, the T – cell marker CD 3, and CD 45 **(Fig.44)**. In the study of Ostrowski[46] and co-authors, the 5 year survival for patients with primary lymphoma of bone was 58%.

GIANT CELL TUMOUR

Giant cell tumour of bone is a distinctive neoplasm of undifferentiated cells. The multinucleated giant cells apparently result from fusion of the proliferating mononuclear cells, and although they are a constant and prominent part of these tumours, the giant cells are probably of less significance than mononuclear cells. If the stromal cells of a tumour that has many giant cells are malignant throughout, the tumour probably has no relationship to GCT.

The clinical correlative studies reported by Troup[50] and co-workers in 1960 have fortified this concept.

GCT constitutes 4-5 % of all primary bone tumours and about one fifth of all benign bone tumours. Most giant cell tumours are found at the ends (epiphysis) of long bones. Just less than half of these tumours occur around the knee joint, the distal femur being the most common single location. In the axial skeleton, sacrum is the commonest site. Small bones of the hands and feet are rarely involved **(Fig.47&49)**. Skeletally mature individuals in their third and fourth decades of life are commonly affected. Female to male ratio is 1.5:1. The presenting complaints may be pain, swelling or pathological fracture. **Radiograph (Fig.45&48)** reveals a well-defined defect in epiphysis that is eccentrically located and extends to the subchondral bone end plate of the articular surface. There is usually no sclerosis around the lesion. Gee[51] and Pugh summarized the radiographic features of GCT. Campanacci[52] and co-authors have developed a grading system for GCT based on radiographic appearance but they were not able to correlate the different stages with clinical outcome. **Grossly (Fig.46)**, the tumour appears homogenous with a tan colour and moderately firm consistency. Some tumours have foci of haemorrhage and necrosis. **Microscopic features (Fig.51)** include a background of proliferating, homogenous mononuclear cells admixed with an evenly dispersed population of multinucleated giant cells. The mononuclear cells are round to ovoid in shape with relatively large nuclei and inconspicuous nucleoli.

Some areas may show spindling out of cells simulating benign fibrous histiocytoma. Reactive bone formation has been observed at periphery of the tumour. Occasional tumour may show involutional changes with lipid-filled histiocytes. The chances of local recurrence after curettage are 50 %. The treatment of choice therefore is surgical excision.

The **FNAC (Fig.50)** criteria for diagnosis are –

- Abundant material.
- A double population of cells – mononuclear spindle cells and giant cells of osteoclastic type.
- Giant cells attached to the periphery of the clustered spindle cells.

MALIGNANCY IN GIANT CELL TUMOUR

Malignancy in a giant cell tumour may be primary when a high grade sarcoma arises in a GCT or secondary when malignancy arises in a previously documented site of GCT. Evidence is increasing that radiation may trigger malignant transformation of giant cell tumours. Rock[53] and co-authors reported on 19 cases of secondary malignant giant cell tumours and found a survival rate of 32 % at a mean of 9.6 years.

NOTOCHORDAL TUMOURS

CHORDOMA

This slow growing tumour arises from remnants of the notochord. Therefore, in most cases it occurs in the midline of the axial skeleton. The sacrococcygeal region accounts for half the cases . The tumour may also be found in the base of the skull and vertebral column. Males are affected more frequently than women. The average age at diagnosis of sacral lesions is 55 years whereas that for spheno-occipital lesions is somewhat younger. The clinical symptoms depend on the location of the tumour. Pain is a nearly constant feature of sacrococcygeal chordoma, and it characteristically occurs at the tip of the spinal column. Constipation is also a common complaint. Spheno – occipital chordoma may cause symptoms referable to any of the cranial nerves. The **radiologic (Fig.52)** hallmark of chordoma is bone destruction. MRI greatly aids in localisation of the tumour. Focal calcifications are seen in half of the patients. In a study of 14 cases of chordomas of the spine, de Bruine[54] and Kroon found that 64% were sclerotic and the rest purely lytic. **Grossly**, these are soft encapsulated tumours with a bluish gray colour and extensive gelatinous translucent areas. Lobulations may be apparent on cut surface. Recurrences often produce multiple nodules in the region of previous surgical excision. Metastasis is usually through haematogenous route. The process may develop in an unusual location, including the skin.

Su[55] and co-authors reported involvement of the skin in 19 of 207 chordomas studied. **Microscopically (Fig.53)**, the tumour is separated into lobules by fibrous septae. The tumour cells are arranged in cords and sheets. Cells have eosinophilic cytoplasm associated with both extra and intracellular mucin. The vacuoles in cells may be very prominent producing **physaliphorous cells**. Chondroid chordoma is a term coined by Heffelfinger[56] and co-authors for neoplasms at the base of the brain that have features of both chordoma and chondrosarcoma. Positivity for both S-100 **(Fig.55)** protein and epithelial markers **(Fig.54)** is seen. Radical excision of the tumour along with radiation therapy should be offered to patients. Fuch[57] and co-authors reported on 52 patients with sacral chordomas of whom 23 had local recurrence.

The **FNAC**[58] diagnostic criteria are –

- Abundant myxoid ground substance encircling tumour cells.
- Large cells with abundant bubbly cytoplasm (physaliphorous cells).
- Clusters of medium sized epithelial – like cells.
- Rounded nuclei, moderate anisokaryosis , bland chromatin.

VASCULAR TUMOURS

HEMANGIOMA

These are relatively common, benign vaso formative neoplasms of endothelial origin. Vertebral bodies are the commonest sites followed by craniofacial skeleton and metaphyses of long bones.

Most tumours are clinically asymptomatic. **Radiologically**, well demarcated lucent masses containing coarse trabeculations are seen. **Macroscopic** appearance is that of a dark red mass. **Microscopically**, the tumour may be a capillary or cavernous hemangioma composed of thin walled blood vessels lined by single layer of endothelial cells. The vessels permeate the marrow and surround pre-existing trabeculae.

ANGIOSARCOMA

This rare malignant vascular tumour accounts for less than 1 % of all bone tumours. Age distribution of these tumours has a wide range from second to eighth decades of life. Long tubular bones of extremities and spine are commonly affected. Multicentricity is a common feature of these tumours. They present as painful lesions. **Radiologically**, these are purely lytic lesions. Clustering of multifocal lesions in a single anatomic location suggests the diagnosis of angiosarcoma. **Macroscopically**, the tumours are firm in consistency and bloody with absence of necrosis. The **histological feature** of angiosarcoma is tumour cells forming vascular spaces.

SMOOTH MUSCLE TUMOURS

LEIOMYOMA AND LEIOMYOSARCOMA

Leiomyoma of bone is an extremely rare tumour with predilection for facial bones, especially mandible. Tibia is a common site in the extragnathic skeleton.

Roentgenograms show radiolytic, often multilocular lesions. The lesions are firm gray tan on **gross examination** and similar to leiomyomas elsewhere on **histological examination**. Leiomyosarcoma of bone is extremely rare and metastasis from a leiomyosarcoma especially in the uterus has to be ruled out before making a diagnosis.

LIPOGENIC TUMOURS

LIPOMAS AND LIPOSARCOMAS

Lipomas are rare tumours and incidental findings on radiological examination. The calcaneus is frequently involved. **X-ray** shows a well circumscribed lucent area with central calcification.

Liposarcoma is a very rare occurrence in the bone and very few cases have been documented so far in literature.

NEURAL TUMOURS

NEURILEMMOMA

Schwannomas are very uncommon tumours with mandible and sacrum being affected more often. In a review of literature in 1992, Turk[59] and co-authors found 79 examples of intra - osseous schwannomas.

ADAMANTINOMA

This tumour is a very rare, low grade, malignant, biphasic tumour. The anterior diaphysis of tibia is involved in 90% of cases. The prolonged clinical course of many patients indicates the slow growth of the tumour.

Pain is the most common symptom. The duration of symptoms before diagnosis varies from a few months to 50 years. In the series reported by Keeney[60] and co-authors, approximately one- third of patients had symptoms for more than 5 years. **Radiological examination** shows a well circumscribed, lobulated osteolytic, cortical lesion with intralesional opacities. **Grossly**, the tumours have lobulated contours, are grey white and vary in consistency from firm and fibrous to soft and brain like. **Histopathology** reveals small epithelial islands in a fibrous stroma.

METASTATIC MALIGNANCY

After lungs and liver, metastatic deposits occur commonly in bones. **Carcinomatous deposits** are the most common malignant tumours seen in the human skeleton. Patients affected are usually in their fourth to sixth decade of life. 93% of all deposits originate from common cancers like those of breast, prostate, lung, kidney and thyroid. Metastatic deposits in bone are rare in children; commonest primaries being – neuroblastoma, rhabdomyosarcoma and clear cell sarcoma of kidney. The commonly favoured sites of metastatic deposits in bone are the lumbar spine[61] and proximal femur. In general, bones with persistent red marrow are affected. Small bones of hands and feet are almost never involved. The commonest presenting symptoms are pain, swelling or fracture.

Radiological examination (Table 5) (Fig.56&60) reveals lytic, blastic or mixed patterns. While prostatic deposits are osteoblastic, thyroid **(Fig.56 - 59)** and kidney deposits are purely lytic. Deposits from lung and breast **(Fig.62)** are irregularly lytic but may be osteoblastic. Vertebral deposits are difficult to detect using plain X-Ray. The **macroscopic appearance** varies depending on the primary tumour; osteoblastic metastases from breast are greyish white and firm as against soft haemorrhagic metastases from renal cell carcinoma.

Table 5 Radiological appearance of metastatic deposits from different primary sites

Radiological appearance	Primary malignancy
Lytic	Thyroid and kidney
Blastic	Prostate
Lytic and blastic	Lung and breast

The diagnostic criteria for **FNAC (Fig.61)** are –

- Foreign cell population.
- Cell clusters; acinar or gland like structures.
- Cells meeting criteria for malignancy.

MISCELLANEOUS LESIONS

ANEURYSMAL BONE CYST

This is a solitary, expansile lesion of unknown etiology. Usually, it is eccentric in location. Patients are most commonly under 20 years of age with swelling or pain as their presenting complaint. Most commonly involved bones are long bones or spine. Vertebral arches are usually affected. **Radiologically (Fig.64 & 65)**, the tumour presents as a lucent lesion in the shaft of the bone with trabeculated appearance. Periphery of the lesion is indistinct. MRI is helpful in demonstrating loculated pattern with fluid levels. **Histologically (Fig.67)**, cystic spaces of various sizes filled with blood but without endothelial lining are seen. Fibrous septae containing giant cells and foci of immature bone are seen between the blood filled spaces. Haemosiderin laden cells and chronic inflammatory cells are also seen. 50%[62] of aneurysmal bone cysts may occur secondary to osteoblastoma, chondroblastoma and fibrous dysplasia.

Multiple sections should be studied to rule out telangiectatic osteosarcoma which may be radiographically and microscopically similar.

SIMPLE CYST

A benign, solitary cystic defect in the metaphyseal region of long bones, simple cysts are more common in children and young adolescents. Males are most often affected.

Proximal humerus is the usual site of this lesion which usually presents with pathological fracture. On **x-ray**, the lesion appears as a well-defined lucent area with a thin sclerotic margin. **Macroscopic examination** shows a fluid filled cyst covered by a thin fibrous membrane. **Microscopic examination** shows a fibrous membrane lining the cyst. Secondary changes may occur after fracture through the cyst and present as haemorrhage, hemosiderin deposits, granulation tissue, cholesterol clefts, calcification, fibrin or reactive new bone formation.

FIBROUS DYSPLASIA

Fibrous dysplasia is a relatively common (5-7% of benign bone tumours)[63] , slow growing, hamartomatous, solitary lesion which contains bone and fibrous tissue. Femur, tibia, skull, facial bones and ribs are most commonly affected. The lesion usually affects children and adolescents and most of the times, it remains relatively unchanged throughout life. Polyostotic involvement may be seen in 25 % of affected cases. Deformity may occur if repeated minor fractures occur in the affected bone. The commonly affected bones are femur, tibia, skull or ribs.The classic '**Shepherd's Crook**' deformity occurs in the upper end of femur. The lesion is usually asymptomatic. The **radiological appearance** is that of a well defined lesion with ground glass appearance due to finely scattered bone islands. **Grossly**, there is fusiform expansion of bone with thinning of cortex and replacement of bone by a firm whitish tissue of gritty consistency.

Microscopically, irregular foci of woven bony trabeculae are seen in a cellular fibrous stroma. The bony trabeculae are characteristically arranged in Chinese letter pattern. Cartilage if present in the lesion may either be intrinsic to the lesion or secondary to fracture.

OSTEOFIBROUS DYSPLASIA

This lesion was originally described by Kempson[64] in 1966 who believed it was an aggressive condition and named it ossifying fibroma. Campanacci[65] thought it was a benign lesion and called it osteofibrous dysplasia.

The lesion has a tendency to involve the tibia, more often the cortex. Most patients are affected in the first two decades of life. **Radiographs (Fig.68)** show multiple lucencies involving the anterior cortex of tibia with intervening sclerosis. **Macroscopically**, the tumour is solid with whitish or yellowish colour and soft or gritty texture. The lesion is composed of spindle cell proliferation that may have a storiform pattern. Bony trabeculae show prominent osteoblastic rimming **(Fig.69)**. The lesion tends to mature towards the periphery and seems to merge with cortical bone giving rise to zonation phenomenon.

LANGERHANS CELL HISTIOCYTOSIS

This disease is a neoplastic proliferation of Langerhans cells. It is a rare disorder and accounts for less than 1% of all bone lesions. Males are affected twice as commonly as females.

60 % of cases occur under the age of 10 years though any age group may be affected. The skull, femur, pelvis, mandible and ribs are most commonly affected sites. Pain and swelling are the most common symptoms. **Radiologic examination** shows bony defects that are discretely defined and lytic. In the skull, there may be a "hole in a hole" appearance because of differential destruction of the two tables. Periosteal new bone formation may be seen. The involved tissue is soft and red in colour on **macroscopic examination**. **Microscopically**, the lesion is composed of nests of Langerhans cells admixed with inflammatory cells, predominantly eosinophils and also lymphocytes, neutrophils and plasma cells. In 1967, Enriquez[66] and co-workers , in a study of 116 patients with LCH at Mayo Clinic, found patients younger than 3 years, those with more than 3 bones involved, those with haemorrhagic manifestations and those with spelnomegaly all had ominous prognosis.

The diagnostic criteria for **FNAC** are –

- Large histiocytes with vescicular nuclei of irregular shape
- Variable number of eosinophils
- Giant cells of histiocytic type

MATERIALS AND METHODS

This is a prospective study undertaken in the Department of Pathology, Madurai Medical College, Madurai during the period from May 2012 to July 2014. The Government Rajaji Hospital, Madurai is a tertiary health care centre catering to the population of Madurai as well as referrals from neighbouring districts. The surgical specimens and biopsy materials are processed and histopathological diagnosis is made in the Department of Pathology, Madurai Medical College, Madurai.

INCLUSION CRITERIA

Patients of all ages and both sexes with biopsy proven bone tumours and tumour like lesions were included in this study.

FNAC was performed on selected patients with clinico – radiological suspicion of bone tumours and tumour – like lesions. Patients were selected based on convenience sampling.

EXCLUSION CRITERIA

Patients with leukaemic infiltration of bone marrow were excluded from the study.

We received a total of 29,291specimens for histopathological examination during the study period. Out of these specimens, 8762 were neoplastic (both benign and malignant) lesions.

Among the 8762 neoplastic lesions, 90 specimens were bone tumours and tumour like lesions.

The study material included these 90 specimens (**AnnexureVI A**).

The detailed clinical history and general and local examination findings of the patients were recorded in the proforma sheet (**Annexure II**). The radiological investigations like X-ray, CT scan and MRI were photographed and details of clinico – radiological diagnosis noted in the proforma sheet.

The specimens were received in 10% neutral buffered formalin. Gross examination was done and dimensions of the received specimen were documented. The type of specimen whether biopsy/curettage, resection or amputation was noted. In case of resection or amputation specimens, the tumour site (epiphysis, metaphysis, diaphysis), medullary cavity involvement, joint involvement and soft tissue extension were recorded.

Biopsy or curettage specimens were segregated as soft tissue and hard tissue. Soft tissue was submitted for processing and hard tissue was sent for decalcification.

Representative bits were taken from the resection and amputation specimens and submitted for processing. Decalcification was done using 10% aqueous solution of hydrochloric acid for hard tissues. After decalcification end point test, tissues were submitted for further processing.

Tissue processing was done using automated tissue processor and sections of 3-5 microns were cut manually using a microtome. Staining was done with routine haematoxylin and eosin stain. (**Annexure III**) Slides were then examined under the light microscope.

FNAC PROCEDURE

FNAC was done on 15 patients with clinico – radiological suspicion of bone tumours. Patients were selected based on convenience sampling after getting written informed consent. 10 or 20 cc syringes and 18-22 gauge needles were used and a maximum of three passes were tried. FNAC was performed under strict aseptic precautions and local anaesthesia was given when required. Slides were fixed in isopropyl alcohol and stained with Haematoxylin and Eosin. Slides were examined under the light microscope and results were recorded in the master chart. **(Annexure VI B)**.

IMMUNOHISTOCHEMISTRY

In diagnostically challenging cases, where accurate diagnosis could not be arrived at by light microscopic examination of Hematoxylin and Eosin stained sections, specific immunohistochemical marker analysis was done.

STATISTICAL ANALYSIS

Cohen's Kappa value was calculated to test the strength of agreement between Clinico – radiological diagnosis and histopathological diagnosis.

The observations were then compared with other studies and inferences drawn.

OBSERVATIONS AND RESULTS

This prospective study included 90 specimens of various benign and malignant bone tumours and tumour – like lesions. The total number of neoplasms diagnosed during the same study period in the Department Of Pathology of our college was 8762. Thus, bone tumours and tumour – like lesions constituted only 1.03 % of all neoplasms.

The various benign tumours diagnosed were osteochondroma, enchondroma, chondromyxoid fibroma, osteoid osteoma, osteoblastoma and giant cell tumours.

The malignant tumours diagnosed were chondrosarcoma, osteosarcoma, Ewing sarcoma, Plasma cell myeloma, malignant lymphoma, malignancy in giant cell tumour, chordoma and metastatic deposits.

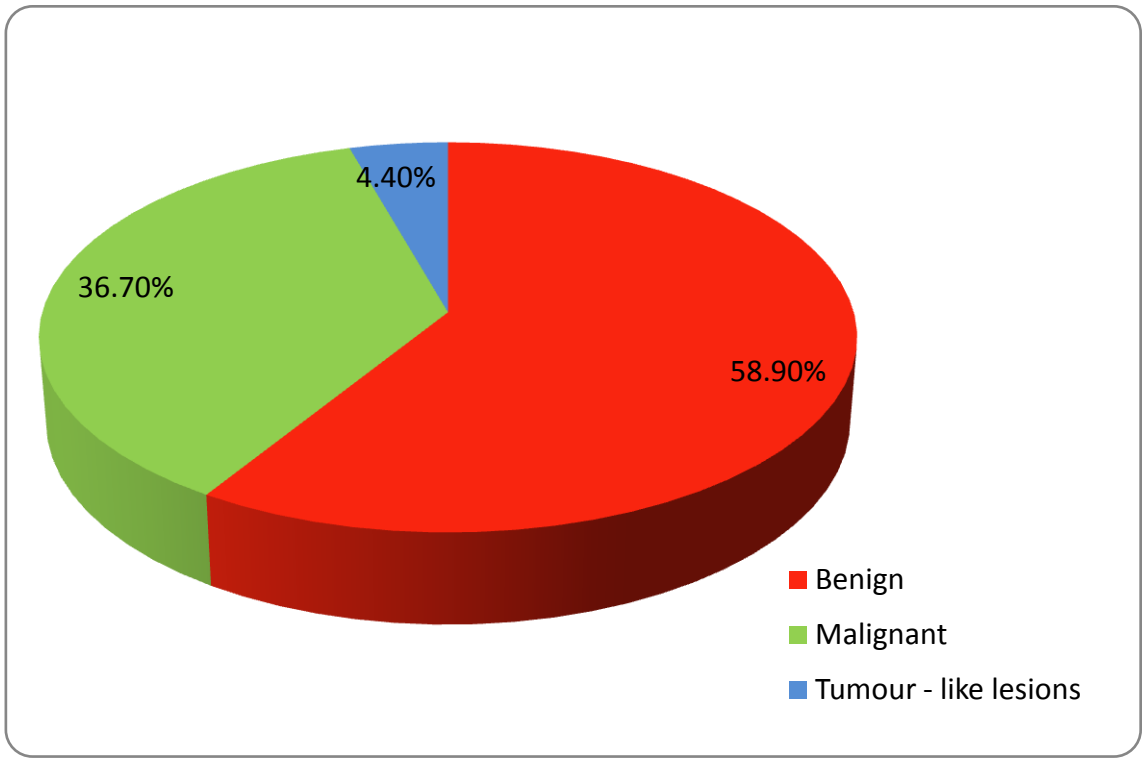
Only 4 cases of tumour – like lesions were received and included aneurysmal bone cyst and osteofibrous dysplasia.

The distribution of bone lesions in our study is shown in Table 6 and Chart 1.

Table 6 - Distribution of bone lesions

Category	Frequency	Percentage
Benign	53	58.9%
Malignant	33	36.7%
Tumour – like lesions	4	4.4%
Total	90	100%

Chart 1 – Distribution of Bone lesions



Benign tumours accounted for more than half the percentage of lesions (58.9%). Malignant tumours constituted 36.7% of the samples received. Tumour – like lesions were the least frequent constituting only 4.4% of all cases.

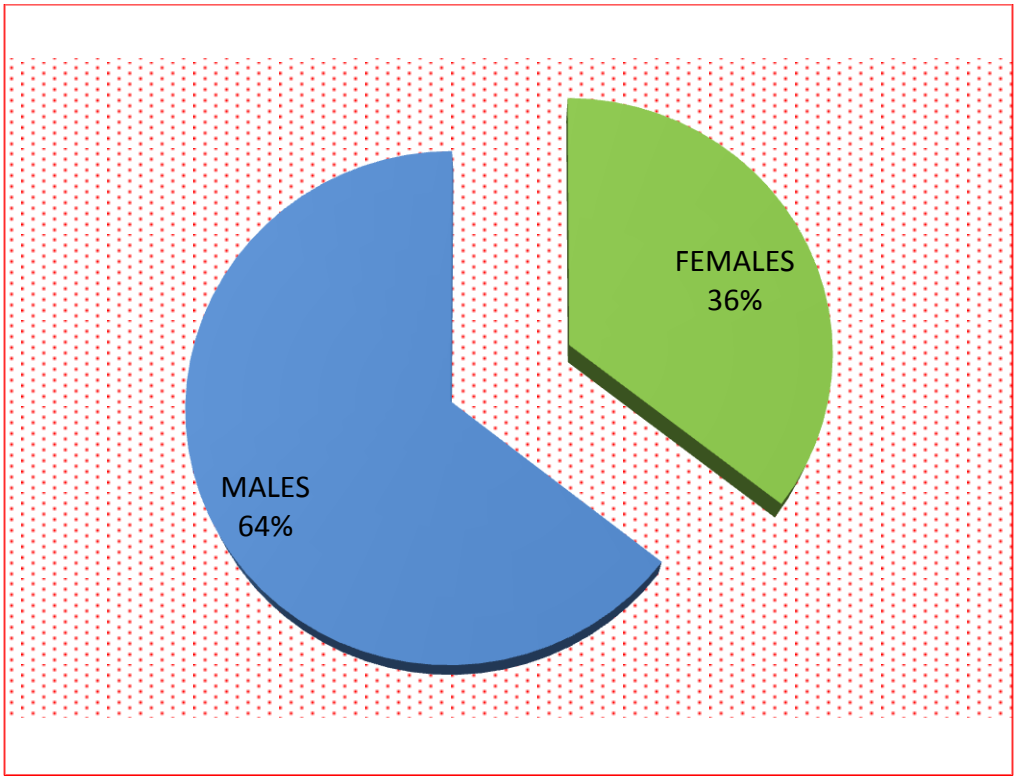
The gender distribution of the cases has been shown in Table 7 and Chart 2.

Table 7 - Gender distribution of the cases

Gender	Frequency	Percentage
Female	32	36
Male	58	64
Total	90	100

Male to female ratio : **1.78:1**

Chart 2 - Gender distribution of cases



The greater majority of patients were males constituting 64% of the total cases.

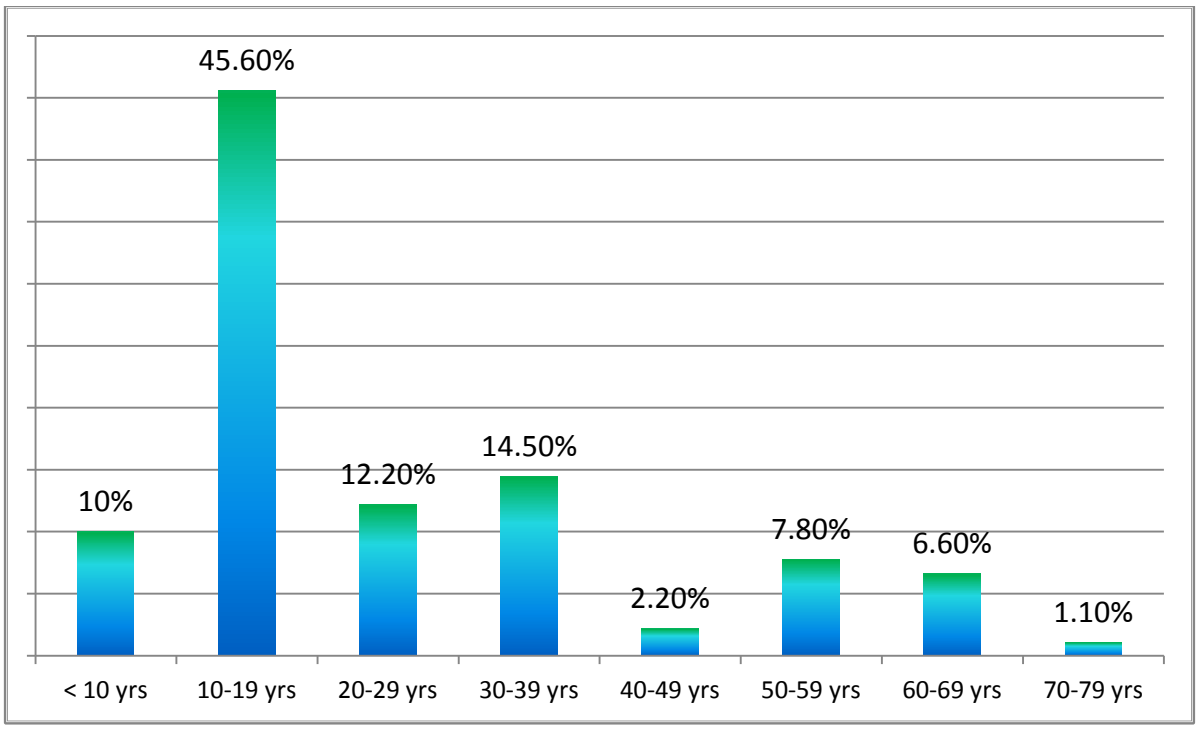
Just above one third of patients (36%) were females.

The age distribution of cases received has been shown in Table 8 and Chart 3.

Table 8 - Age distribution of cases

Age in years	Frequency	Percentage
< 10	9	10
10-19	41	45.6
20-29	11	12.2
30-39	13	14.5
40-49	2	2.2
50-59	7	7.8
60-69	6	6.6
70-79	1	1.1
Total	90	100

Chart 3 - Age distribution of cases



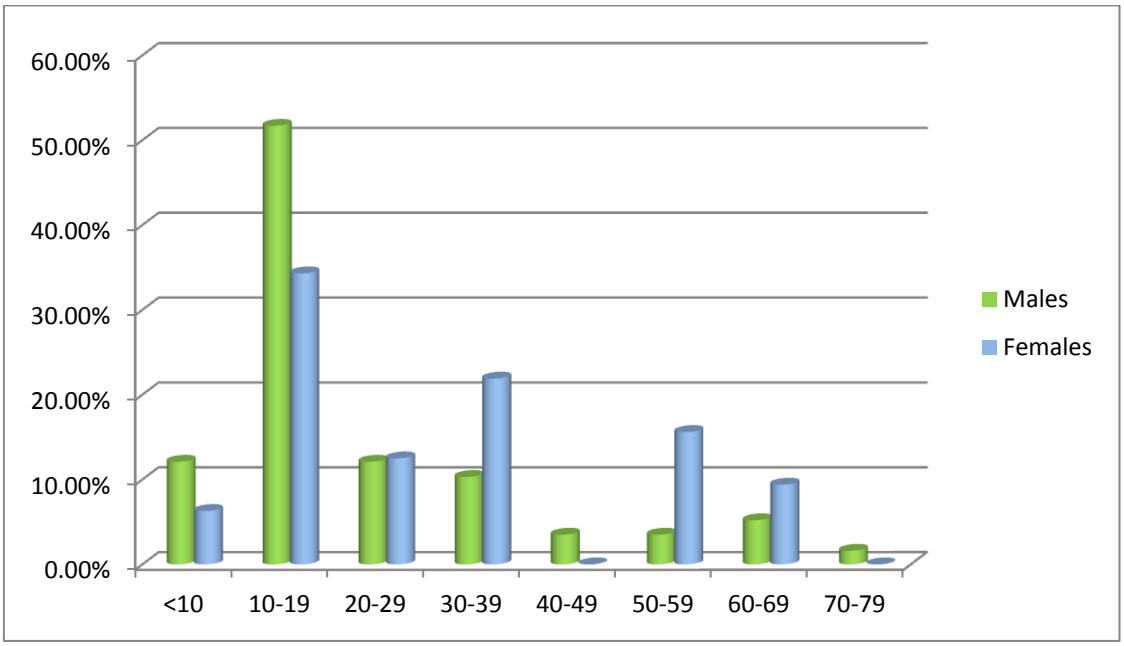
Majority of the patients were in their second decade (45.6%). Patients in their third and fourth decades constituted 12.2% and 14.5% of the cases respectively. Children below 10 years were seen to form 10% of the total sample. The youngest patient was 5 years old and the oldest was 70 years old.

The combined age and gender distribution of cases has been represented in Table 9 and Chart 4.

Table 9 - Age and gender distribution of cases

Age in Yrs	Gender				Total	
	Male		Female			
<10	7	12.1%	2	6.3%	9	10%
10-19	30	51.7%	11	34.3%	41	45.6%
20-29	7	12.1%	4	12.5%	11	12.2%
30-39	6	10.3%	7	21.9%	13	14.5%
40-49	2	3.5%	0	0%	2	2.2%
50-59	2	3.5%	5	15.6%	7	7.8%
60-69	3	5.2%	3	9.4%	6	6.6%
70-79	1	1.6%	0	0%	1	1.1%
Total	58	100%	32	100%	90%	100%

Chart 4 - Age and gender distribution of cases



The second decade was the commonest age – group of bone lesions in males as well as females.

The gender distribution of bone tumours and tumour like lesions has been shown in Table 10 .

Table 10 – Gender distribution of bone tumours and tumour - like lesions

Categories	Gender				Total	
	Male		Female			
Osteochondroma	28	48.3%	7	21.9%	35	38.9%
Enchondroma	0	0%	1	3.1%	1	1.1%
Chondromyxoid fibroma	0	0%	1	3.1%	1	1.1%
Chondrosarcoma	0	0%	2	6.3%	2	2.3%
Osteoid osteoma	4	6.9%	0	0%	4	4.4%
Osteoblastoma	1	1.7%	0	0%	1	1.1%
Osteosarcoma	8	13.8	3	9.4%	11	12.2
Ewing sarcoma	2	3.4%	2	6.3%	4	4.4%
Plasma cell myeloma	1	1.7%	1	3.1%	2	2.3%
Malignant lymphoma	1	1.7%	0	0%	1	1.1%
GCT	7	12.1%	4	12.5%	11	12.2%
Malignancy in GCT	1	1.7%	0	0%	1	1.2 %
Chordoma	0	0%	1	3.1%	1	1.1%
Metastatic malignancy	3	5.3%	8	25%	11	12.2%
ABC	2	3.4%	1	3.1%	3	3.3%
Osteofibrous dysplasia	0	0%	1	3.1%	1	1.1%
Total	58	100%	32	100%	90	100%

The most common tumour in males and females was osteochondroma constituting 48.3% of cases in males and 21.9% in females.

There were 4 cases of osteoid osteoma and all were seen in males.

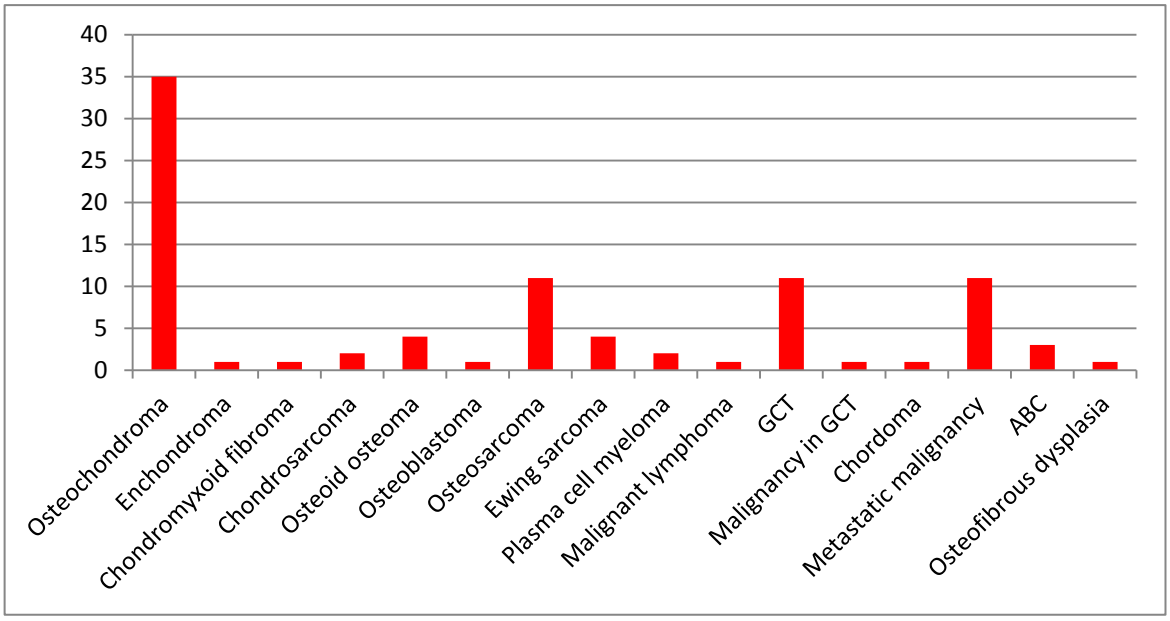
Metastatic deposits showed a predilection for females in this study constituting 25% of all cases in females as against only 5.3% of all cases in males.

Distribution of cases based on histopathologic diagnosis has been shown in Table 11 and Chart 6.

Table 11- Distribution of cases based on Histopathological diagnosis

S.No	Pathological diagnosis	Frequency	Percentage
1	**Osteochondroma**	35	38.9
2	**Enchondroma**	1	1.1
3	**Chondromyxoid fibroma**	1	1.1
4	**Chondrosarcoma**	2	2.3
5	**Osteoid osteoma**	4	4.4
6	**Osteoblastoma**	1	1.1
7	**Osteosarcoma**	11	12.2
8	**Ewing sarcoma**	4	4.4
9	**Plasma cell myeloma**	2	2.3
10	**Malignant lymphoma**	1	1.1
11	**GCT**	11	12.2
12	**Malignancy in GCT**	1	1.2
13	**Chordoma**	1	1.1
14	**Metastatic malignancy**	11	12.2
15	**ABC**	3	3.3
16	**Osteofibrous dysplasia**	1	1.1
	Total	**90**	**100**

Chart 6 - Distribution of cases based on Histopathological diagnosis



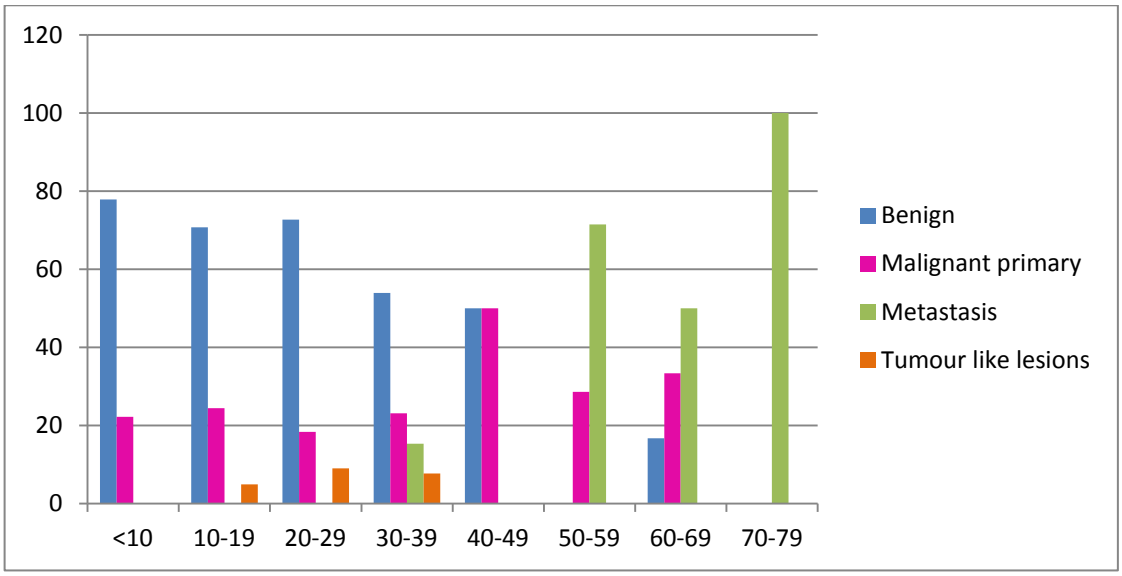
The commonest tumour encountered in this study was osteochondroma (38.9%). Giant cell tumours, metastatic malignancy and osteosarcomas were the other common tumours amounting to 12.2% each.

The age distribution of the cases based on behaviour of bone lesions is given in Table 12 and Chart 7 .

Table 12 - Age distribution of cases based on behaviour of bone lesions

Age in Yrs	Tumour				Total
	Benign	Malignant primary	Metastasis	Tumour like lesions	
<10	7	2	0	0	9
	77.8%	22.2%	0%	0%	100%
10-19	29	10	0	2	41
	70.7%	24.4%	0%	4.9%	100%
20-29	8	2	0	1	11
	72.7%	18.3%	0%	9%	100%
30-39	7	3	2	1	13
	53.9%	23.1%	15.3%	7.7	100%
40-49	1	1	0	0	2
	50%	50%	0%	0%	100%
50-59	0	2	5	0	7
	0%	28.6%	71.4%	0%	100%
60-69	1	2	3	0	6
	16.7%	33.3%	50%	0%	100%
70-79	0	0	1	0	1
	0%	0%	100%	0%	100%

Chart 7 - Age distribution of cases based on behaviour of bone lesions



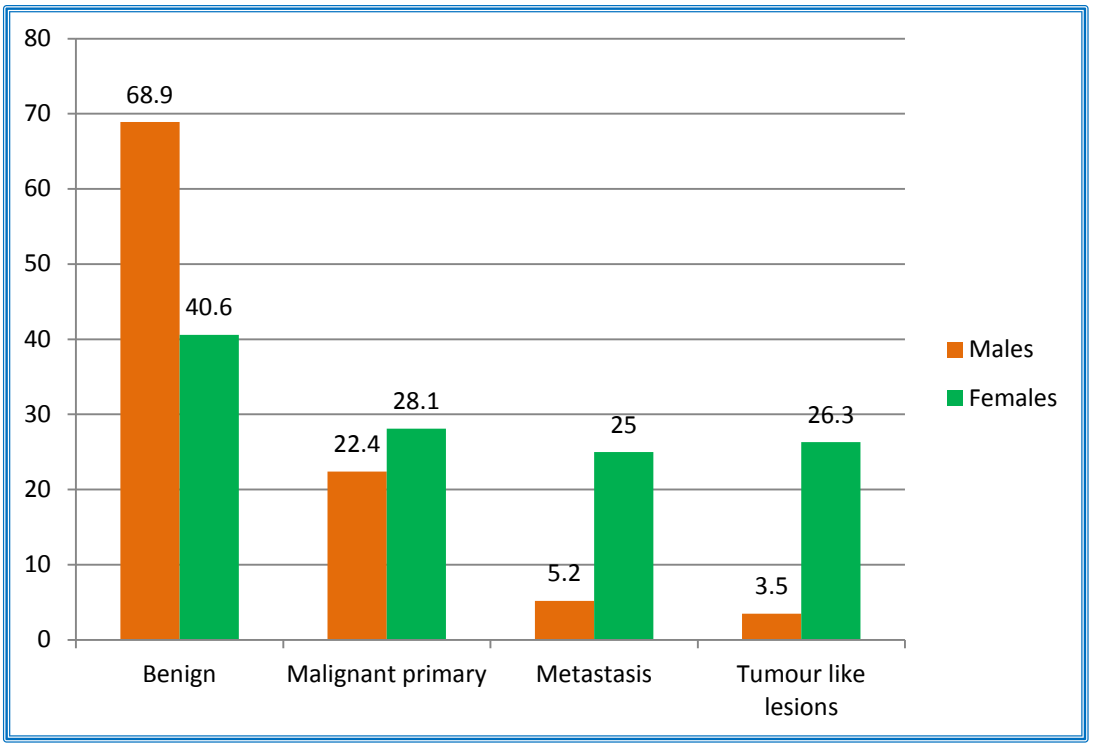
Benign tumours were nearly equally distributed in the first few decades of life. Metastatic malignancy was commonest in the fifth, sixth and seventh decades of life.

The gender distribution of cases based on behaviour of bone lesions has been depicted in Table 13 and Chart 8.

Table 13 - Gender distribution of cases based on behaviour of bone lesions

	Category				Total
	Benign	Malignant primary	Metastasis	Tumour like lesions	
Male	40	13	3	2	58
	68.9%	22.4%	5.2%	3.5%	100%
Female	13	9	8	2	32
	40.6%	28.1%	25%	6.3%	100%
Total	53	22	11	4	90
	58.9%	24.4%	12.2%	4.5%	100%

Chart 8 - Gender distribution of cases based on behaviour of bone lesions



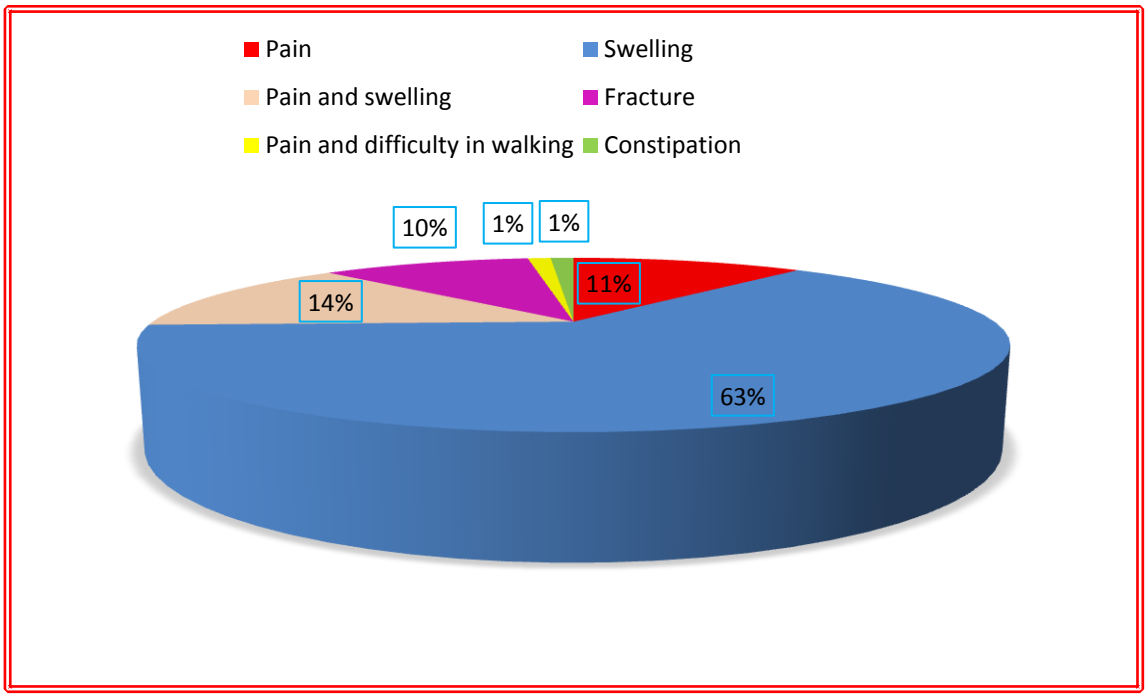
In our study, benign tumours were encountered more commonly in males. The percentage of females with a diagnosis of primary malignancy was 28.1% as against 22.4% of males. Metastatic malignancy was also more common in females (25%) as against only 5.2% in males.

The distribution of cases based on presenting symptoms has been shown in Table 14 and Chart 9 .

Table 14 - Distribution of presenting symptoms

Symptoms	Frequency	Percentage
Pain	10	11.1%
Swelling	57	63.3%
Pain and swelling	12	13.4%
Fracture	9	10%
Pain and difficulty in walking	1	1.1%
Constipation	1	1.1%
Total	90	100%

Chart 9 - Distribution of presenting symptoms



63% of the patients presented with swelling as their chief complaint.

Pain along with swelling was the next common complaint (14%).

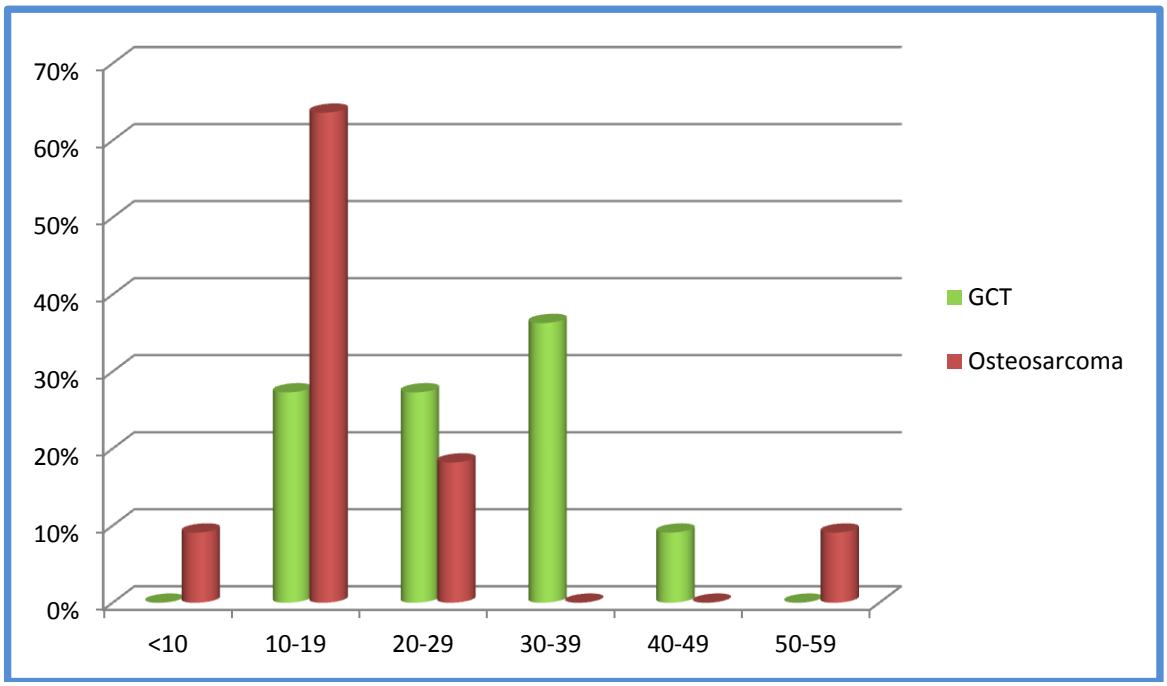
One patient with chordoma had constipation for 6 months. Another patient diagnosed with plasmacytoma of spine had pain with difficulty in walking.

The age distribution of giant cell tumours and osteosarcomas has been shown in Table 15 and Chart 10.

Table 15 - Age distribution of giant cell tumours and osteosarcomas

Age group (years)	GCT		Osteosarcoma	
<10	0	0%	1	9.1%
10-19	3	27.3%	7	63.6%
20-29	3	27.3%	2	18.2%
30-39	4	36.3%	0	0%
40-49	1	9.1%	0	0%
50-59	0	0%	1	9.1%
Total	11	100%	11	100%

Chart 10 - Age distribution of giant cell tumours and osteosarcomas



There was a clustering of cases of osteosarcoma in the second decade of life (63.6% of all osteosarcomas).

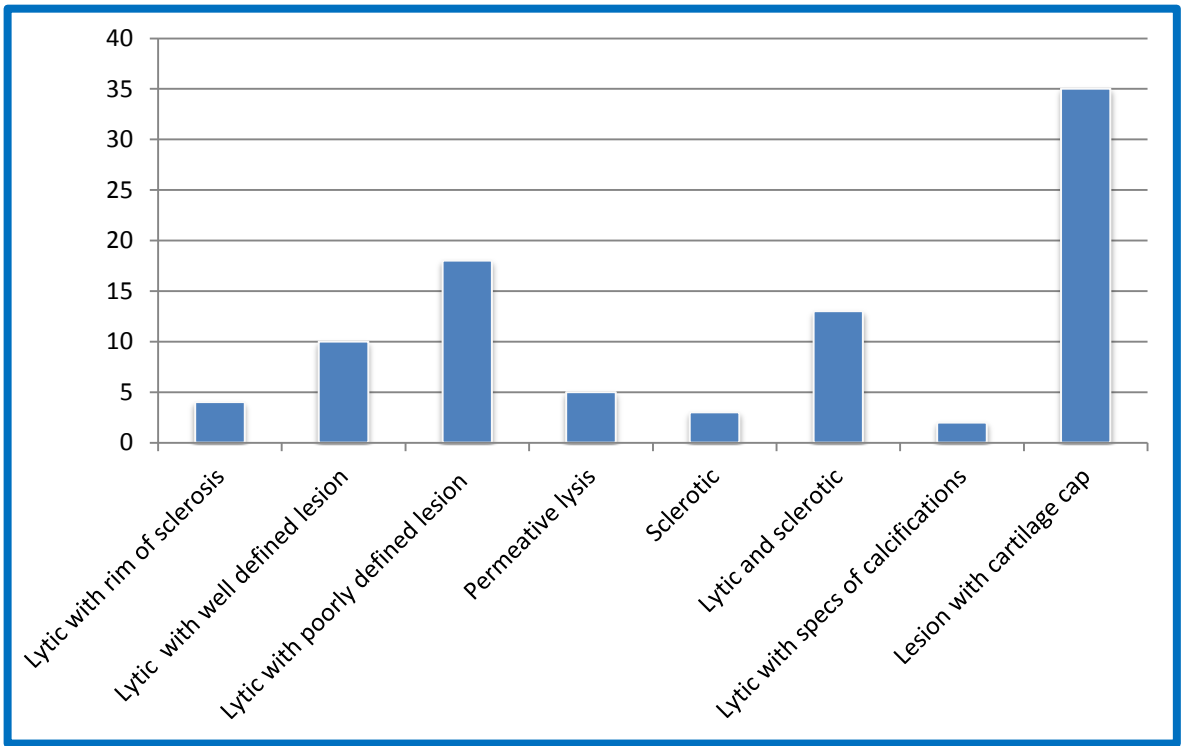
36.3% of giant cell tumours occurred in patients in the age group of 30-39 years.

The distribution of cases based on radiological findings has been shown in Table 16 and Chart 11.

Table 16 - Distribution of radiological findings of bone lesions

Radiological finding	Frequency	Percentage
Lytic with rim of sclerosis	4	4.4%
Lytic with well defined lesion	10	11.1%
Lytic with poorly defined lesion	18	20%
Permeative lysis	5	5.6%
Sclerotic	3	3.3%
Lytic and sclerotic	13	14.4%
Lytic with specs of calcifications	2	2.2%
Lesion with cartilage cap	35	38.9%
Total	90	100%

Chart 11 - Distribution of radiological findings of bone lesions



Among the lytic lesions, the commonest radiological finding was that of a poorly defined lytic lesion.

The distribution of cases based on radiological findings and behaviour of bone lesions is given in Table 17 .

Table 17 - Distribution of cases based on radiological findings and behaviour of bone lesions.

Radiologic finding	Tumour				Total
	Benign	Malignant primary	Metastasis	Tumour – like lesion	
Lytic with rim of sclerosis	1	0	0	3	4
Lytic with well defined lesion	9	0	0	1	10
Lytic with poorly defined lesion	5	5	8	0	18
Permeative lysis	0	5	0	0	5
Sclerotic	3	0	0	0	3
Lytic and sclerotic	0	10	3	0	13
Lytic with specs of calcificaion	0	2	0	0	2
Lesion with cartilage cap	35	0	0	0	35
Total	53	22	11	4	90

Among the primary malignant tumours, the commonest radiological appearance was of lytic and sclerotic type seen in ten cases. Poorly defined lytic lesions and permeative lysis were seen in five cases each.

Eight metastatic deposits produced poorly defined lytic lesions on radiograph while three had a lytic and sclerotic appearance.

Distribution of cases based on bone involved has been shown in Table 18 and Figure -11 .

Table 18 - Distribution of bone lesions based on bone involved.

Bone involved	Site	Frequency	Total	Percent
Humerus	Proximal	13	16	17.8%
	Shaft	3		
	Distal	0		
Radius	Distal	4	4	4.5%
Ulna	Distal	1	1	1.1%
Scapula		4	4	4.5%
Metacarpal		2	2	2.2%
Femur	Proximal	5	26	28.9%
	Shaft	7		
	Distal	14		
Tibia	Proximal	7	19	21.1
	Shaft	1		
	Distal	1		
Fibula	Proximal	3	4	4.4%
	Distal	1		
Ilium		5	5	5.6%
Phalanx		2	2	2.2%
Skull		1	1	1.1%
Spine	Vertebra	3	4	4.4%
	Sacrum	1		
Sternum		2	2	2.2%

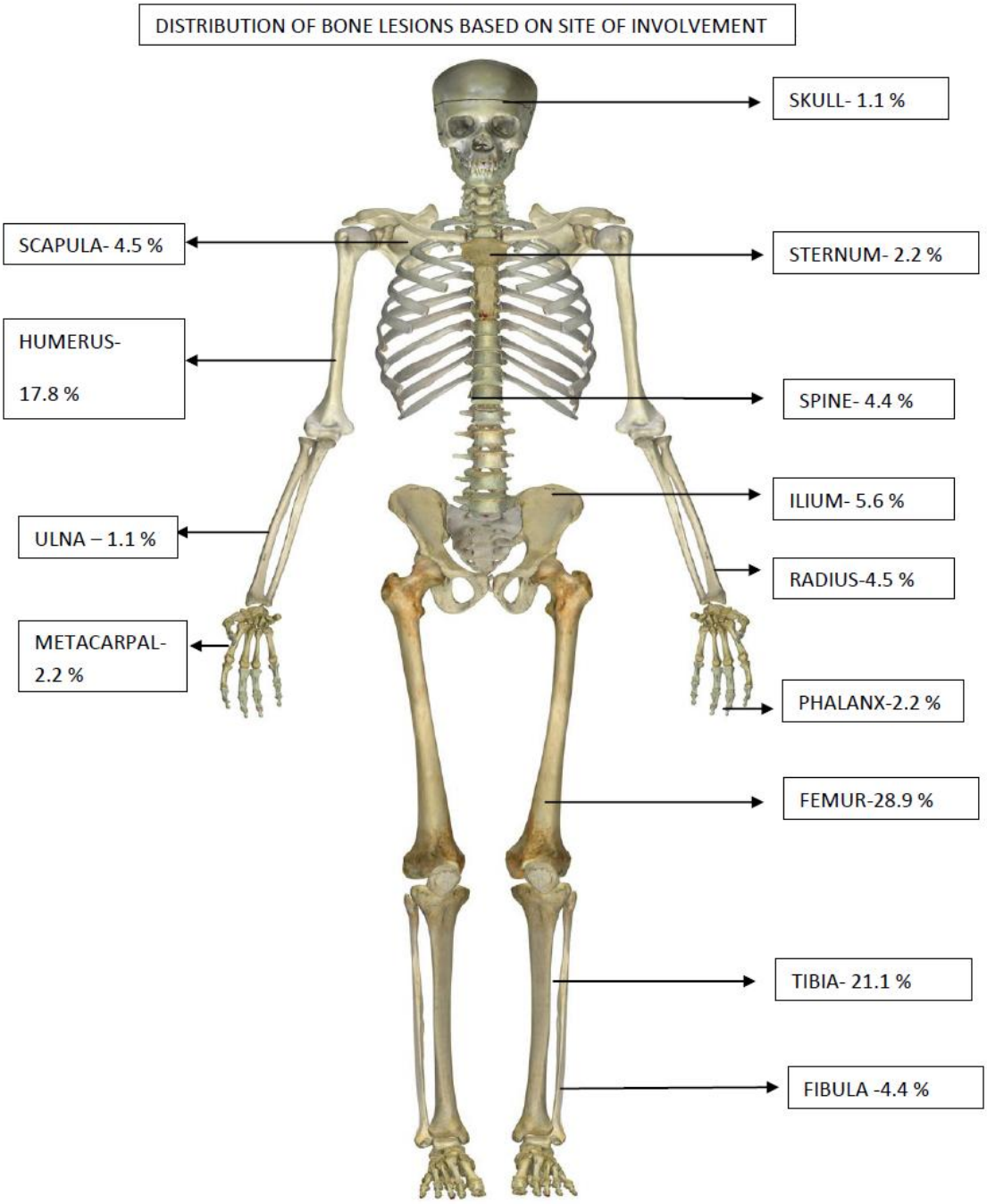
The commonest bones involved were femur, tibia and humerus with 28.9%, 21.1% and 17.8% cases respectively.

23.3% of the lesions occurred around the knee joint (distal femur and proximal tibia). Involvement of the axial skeleton occurred in 13.3% of the cases.

Small bone involvement was seen in 4.4% of the cases.

Figure.11 - Pictorial representation of bones involved by bone tumours and tumour – like lesions.

Fig.11

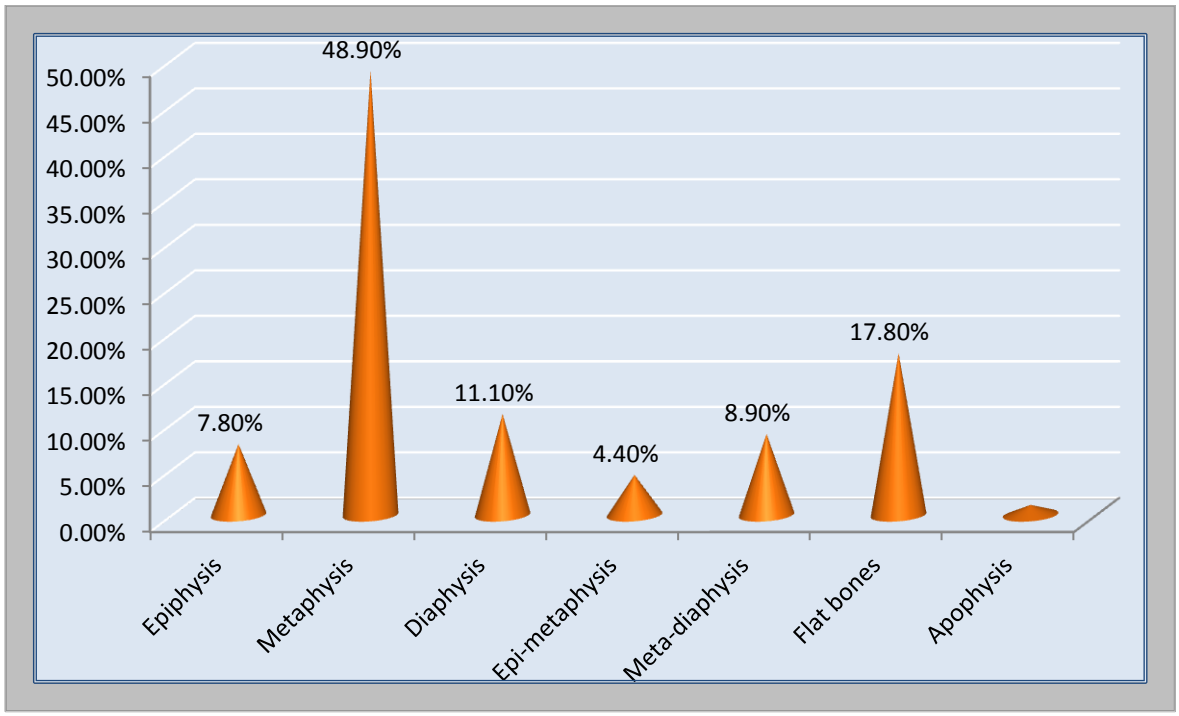


The distribution of bone lesions based on site of involvement is shown in Table 19 and Chart 12 .

Table 19 - Distribution of bone lesions based on site of involvement

Site involved	Frequency	Percent
Epiphysis	7	7.8%
Metaphysis	44	48.9%
Diaphysis	10	11.1%
Epi-metaphysis	4	4.4%
Meta-diaphysis	8	8.9%
Flat bones	16	17.8%
Apophysis	1	1.1%
Total	90	100%

Chart 12 - Distribution of bone lesions based on site of involvement



Nearly half (48.9%) of lesions were seen to occur in the metaphysis.

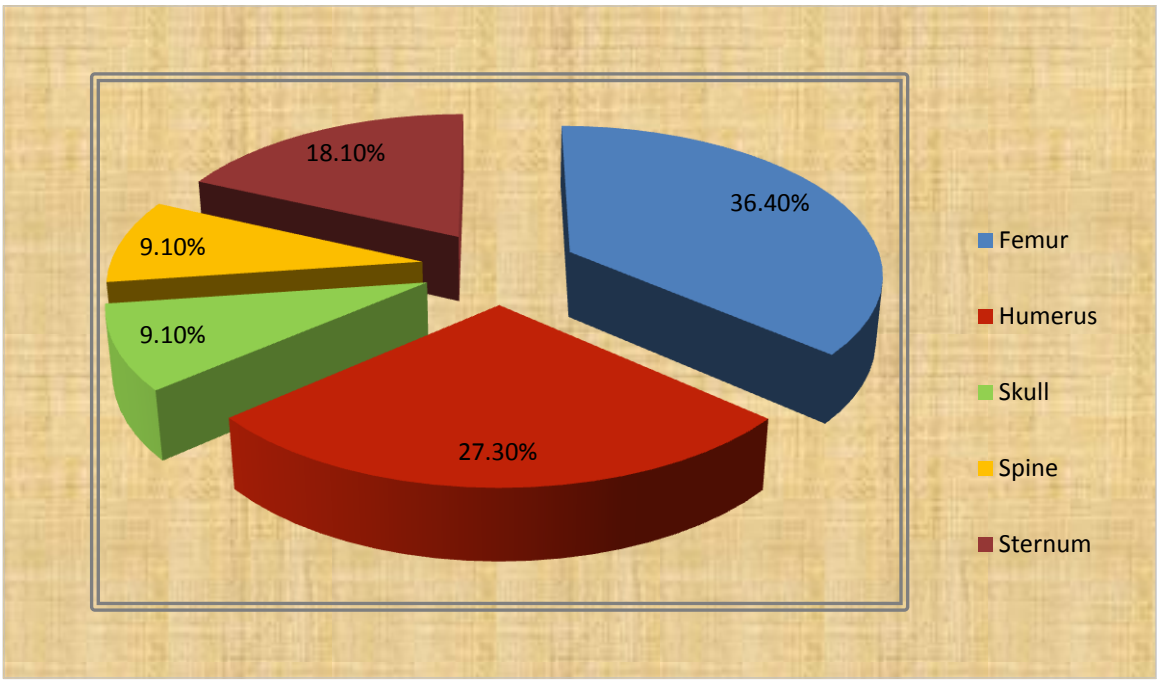
Flat bones were affected in 17.8 % of the cases.

The distribution of sites of metastatic deposits is shown in Table 20 and Chart 13.

Table 20 - Distribution of sites of metastatic deposits

Bone	Frequency	Percentage
Femur	4	36.4%
Humerus	3	27.3%
Skull	1	9.1%
Spine	1	9.1%
Sternum	2	18.1%
Total	11	100%

Chart 13 - Distribution of sites of metastatic deposits



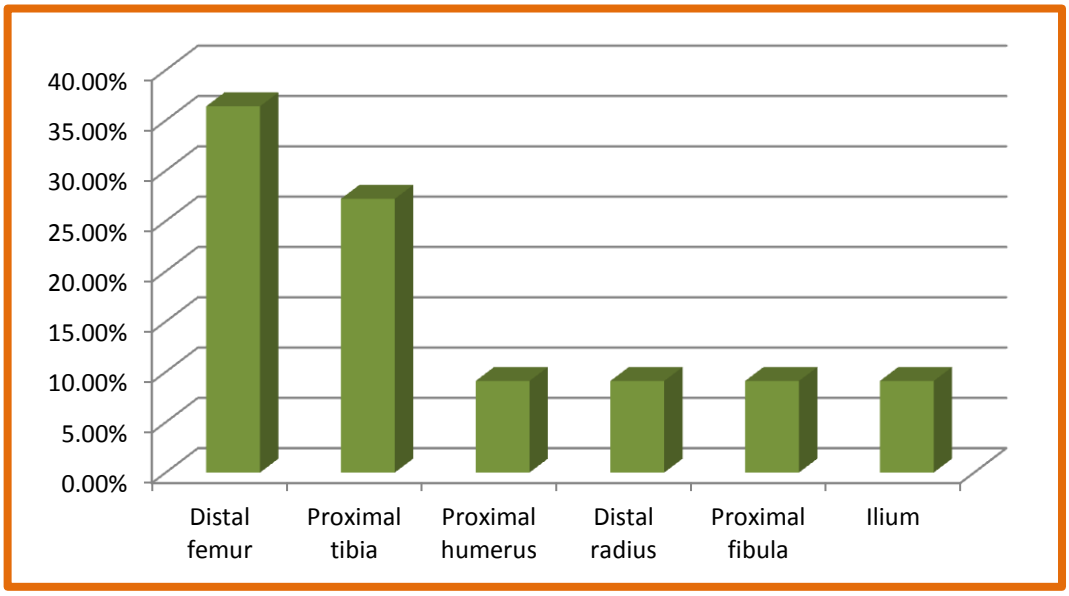
Femur was the most common bone involved by metastatic deposits (36.4%). Bones of the axial skeleton put together (Skull, Spine, Sternum) accounted for 36.3% of all metastatic deposits.

The distribution of sites of occurrence of osteosarcoma have been shown in Table 21 and Chart 14

Table 21 – Distribution of sites of occurrence of osteosarcoma

Bone	Frequency	Percentage
Distal femur	4	36.4%
Proximal tibia	3	27.2%
Proximal humerus	1	9.1%
Distal radius	1	9.1%
Proximal fibula	1	9.1%
Ilium	1	9.1%
Total	11	100%

Chart 14 - Distribution of sites of occurrence of osteosarcoma



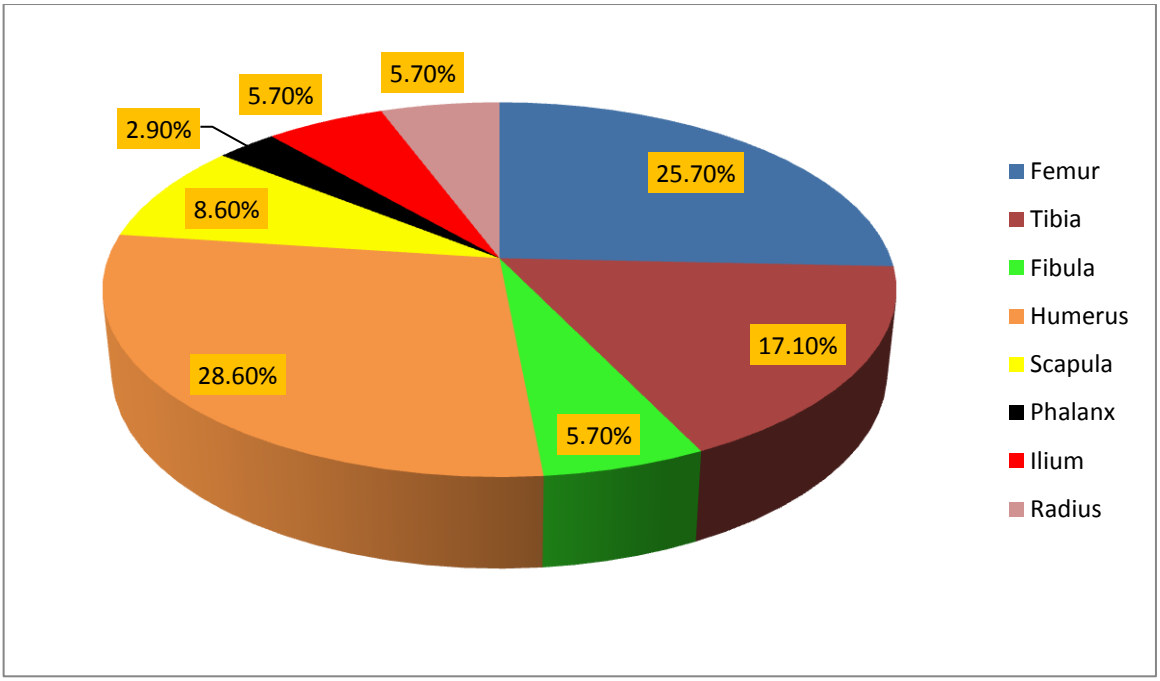
63.6 % of all osteosarcomas occurred around the knee joint (distal femur and proximal tibia). Distal end of femur was the bone most commonly involved by osteosarcoma (36.4%).

Distribution of sites of occurrence of osteochondromas is shown in Table 22 and Chart 15

Table 22 - Distribution of sites of occurrence of osteochondromas

Bone	Frequency	Percentage
Femur	9	25.7%
Tibia	6	17.1%
Fibula	2	5.7%
Humerus	10	28.6%
Scapula	3	8.6%
Phalanx	1	2.9%
Ilium	2	5.7%
Radius	2	5.7%
Total	35	100%

Chart 15 - Distribution of sites of occurrence of osteochondromas



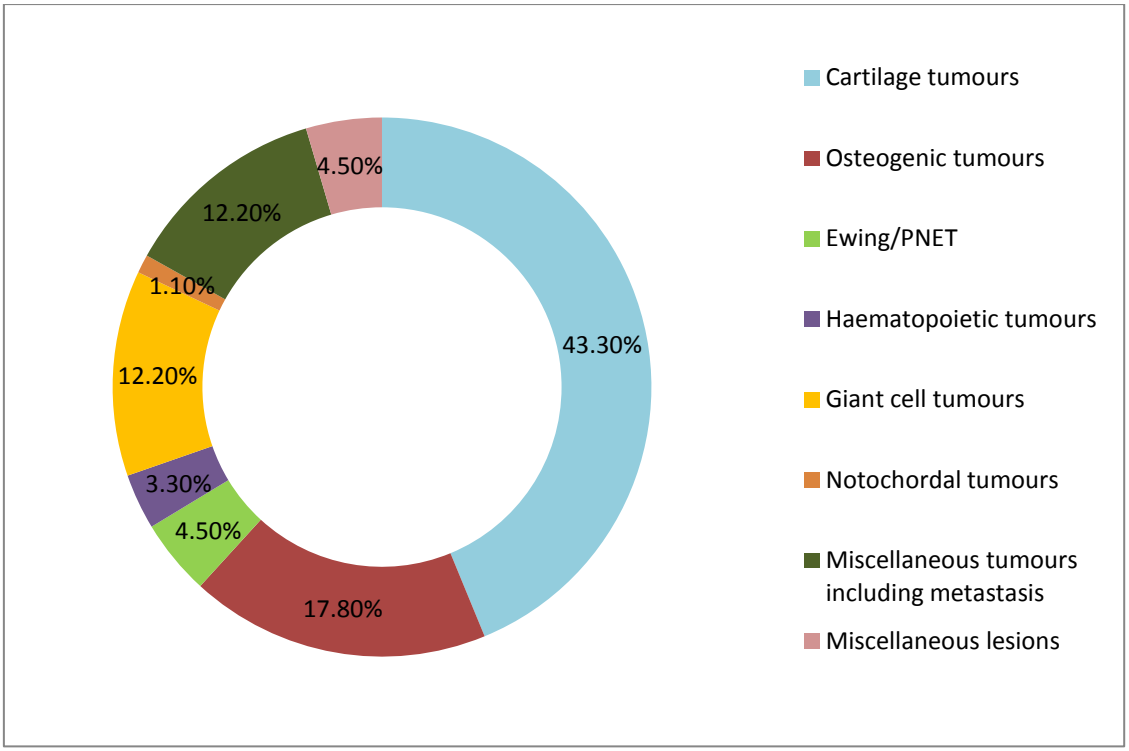
Osteochondromas showed involvement of many bones with humerus being most commonly involved (28.6%) followed closely by femur (25.7%).

The distribution of lesions based on WHO classification has been depicted in Table 23 and chart 16.

Table 23 - Distribution of cases based on WHO classification

WHO Category	Frequency	Percentage
Cartilage tumours	39	43.3
Osteogenic tumours	16	17.8
Ewing sarcoma /PNET	4	4.5
Haematopoietic tumours	3	3.3
GCT	12	13.3
Notochordal tumour	1	1.1
Miscellaneous tumours	11	12.2
Miscellaneous lesions	4	4.5
Total	90	100

Chart 16 - Distribution of cases based on WHO classification



Cartilage tumours constituted the single largest category (43.3%) followed by osteogenic tumours (18.9%).

The distribution of cases based on behaviour of lesions is tabulated in Table 24.

Table 24 - Distribution of cases based on behaviour of bone lesions

Category	Pathological diagnosis	Frequency	Percentage
Benign	Osteochondroma	35	66
	Chondroma	1	1.9
	Chondromyxoid fibroma	1	1.9
	Osteoid osteoma	4	7.5
	Osteoblastoma	1	1.9
	GCT	11	20.8
	Total	**53**	**100**
Malignant primary	Chondrosarcoma	2	9.1
	Osteosarcoma	11	50
	Ewing sarcoma	4	18.3
	Malignant lymphoma	1	4.5
	Malignancy in GCT	1	4.5
	Plasma cell myeloma	2	9.1
	Chordoma	1	4.5
	Total	**22**	**100**
Metastasis	Metastasis	11	100
Tumour like lesions	ABC	3	75
	Osteofibrous dysplasia	1	25
	Total	**4**	**100**

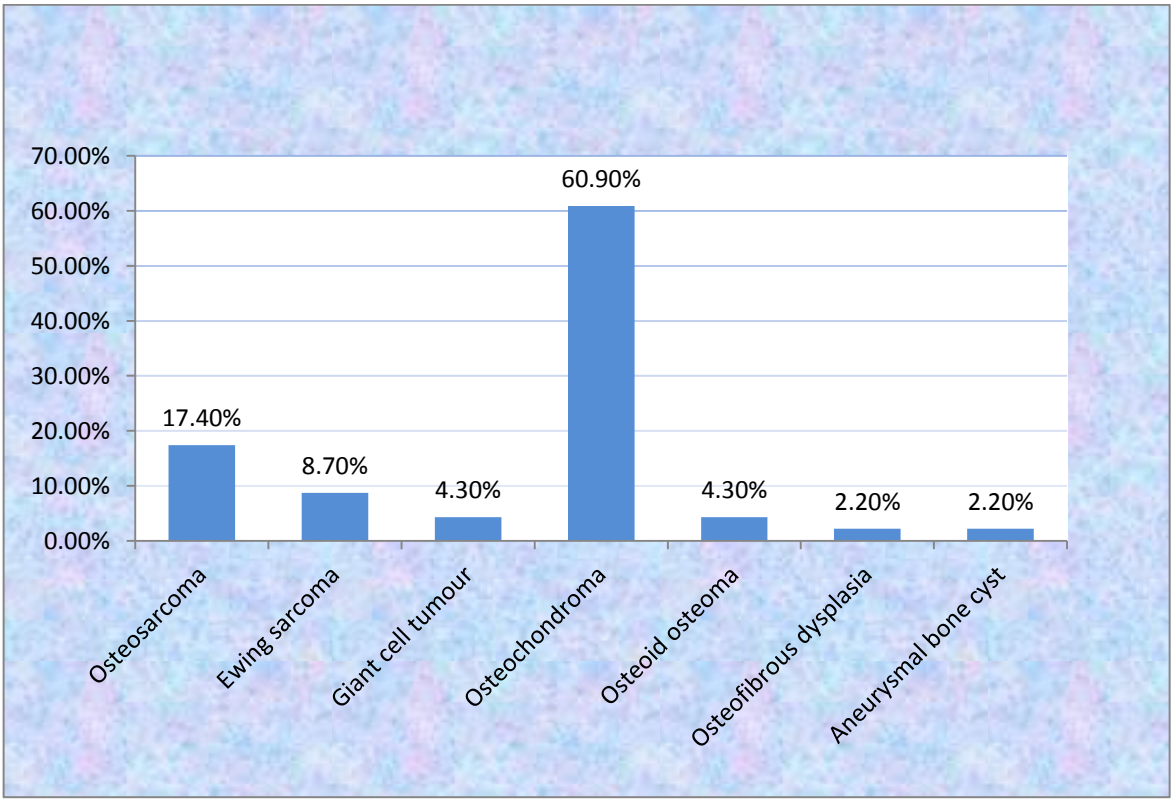
Osteochondroma was the commonest benign tumour constituting 66% of all benign tumours followed by giant cell tumour (20.8%). 50% of all primary malignant tumours were osteosarcomas. Ewing Sarcoma was the second most common primary malignant tumour amounting to 18.3% of cases.

Distribution of bone tumours in the paediatric age-group (0-18 years) has been shown in Table 25 and Chart 17.

Table 25 - Distribution of paediatric bone tumours

Bone tumour	Frequency	Percentage
Osteosarcoma	8	17.4%
Ewing sarcoma	4	8.7%
Giant cell tumour	2	4.3%
Osteochondroma	28	60.9%
Osteoid osteoma	2	4.3%
Osteofibrous dysplasia	1	2.2%
Aneurysmal bone cyst	1	2.2%
Total	46	100%

Chart 17 - Distribution of paediatric bone tumours



The commonest paediatric bone tumour was osteochondroma (60.9%). Osteosarcoma was the commonest primary malignancy in the paediatric age group (17.4%).

Clinico – radiological versus histopathological diagnosis has been tabulated in Table 26.

Table 26 - Clinico – Radiological versus Histopathological Diagnosis

	Histopathological Diagnosis																**Total**
Clinico radiological diagnosis	**Osteochondroma**	**Chondroma**	**CMF**	**Chondrosarcoma**	**Osteoid osteoma**	**Osteoblastoma**	**Osteosarcoma**	**Ewing Sarcoma**	**Plasma cell myeloma**	**Malignant lymphoma**	**GCT**	**Malignancy in GCT**	**Chordoma**	**Metastasis**	**ABC**	**Osteofibrous dysplasia**	
Osteochondroma	35																35
Chondroma		1									**1**						2
CMF			1														1
Chondrosarcoma				2													2
Osteoid osteoma					4												4
Osteoblastoma						1											1
Osteosarcoma							10										10
Ewing sarcoma							**1**	4									5
Plasma cell myeloma										**1**							1
Malignant lymphoma									**1**								1
GCT											11						11
Malignancy in GCT												1					1
Chordoma													1				1
Metastasis														11			11
ABC															3		3
Osteofibrous dysplasia																1	1
Pott's spine									**1**								1
																	90

Considering all bone lesions together, clinico - radiological diagnosis was confirmed by similar histopathological diagnosis in 85 out of the 90 cases (94.44%).

The histopathological diagnosis was not in agreement with clinico – radiological diagnosis in 5 out of the total of 90 cases.

The corresponding **Cohen's Kappa value calculated was 0.943**. This showed **excellent agreement** between clinico – radiological and histopathological diagnoses of bone tumours and tumour – like lesions in this study.

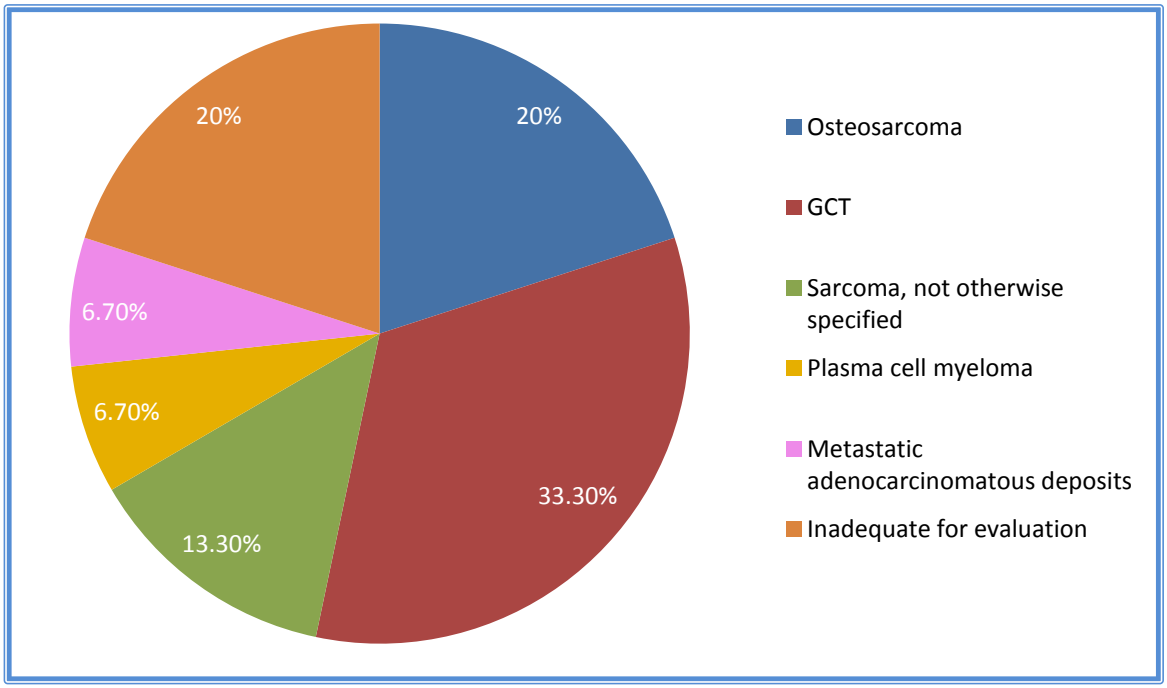
FNAC was performed in 15 cases of bone tumours.

The distribution of bone tumours based on the results of FNAC are shown in Table 27 and Chart 18.

Table 27 - Distribution of bone tumours based on results of FNAC

FNAC diagnostic categories	Frequency	Percentage
Osteosarcoma	3	20
GCT	5	33.3
Sarcoma, not otherwise specified	2	13.3
Plasma cell myeloma	1	6.7
Metastatic adenocarcinomatous deposits	1	6.7
Inadequate for evaluation	3	20
Total	15	100

Chart 18 - Distribution of bone tumours based on results of FNAC



Giant cell tumour was the commonest diagnosis made comprising 33.3% of all cases.

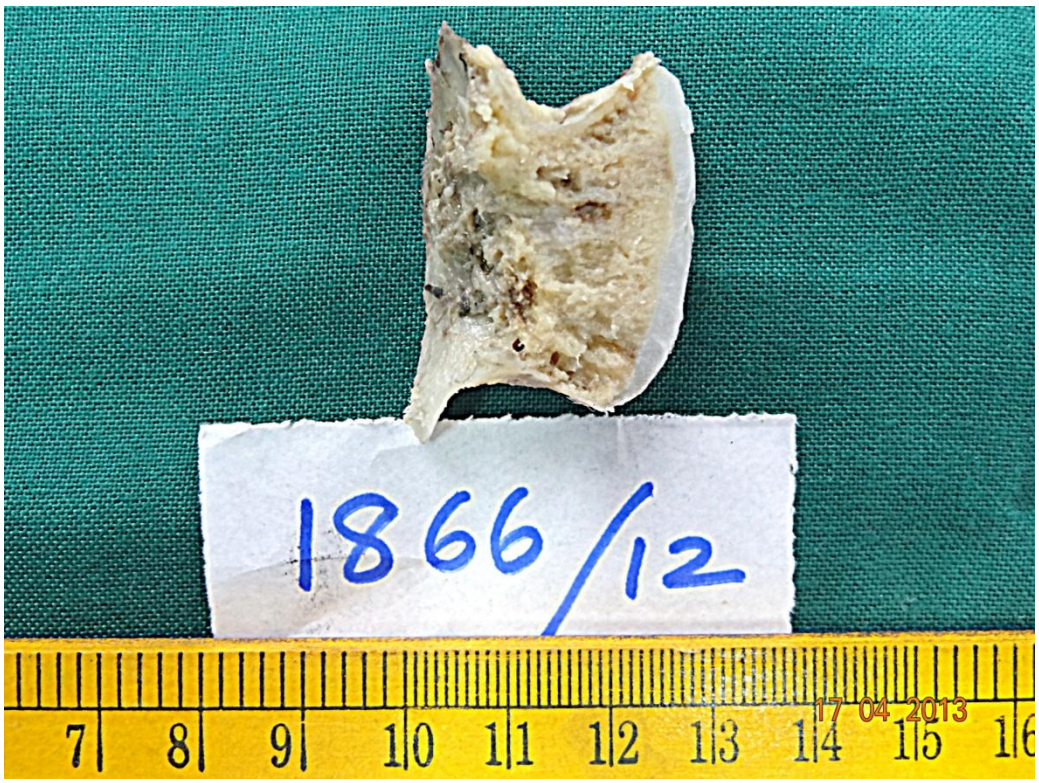


Fig.12 - Macroscopic appearance of osteochondroma – thin and smooth cartilage cap with underlying bone. Case 1866/12.

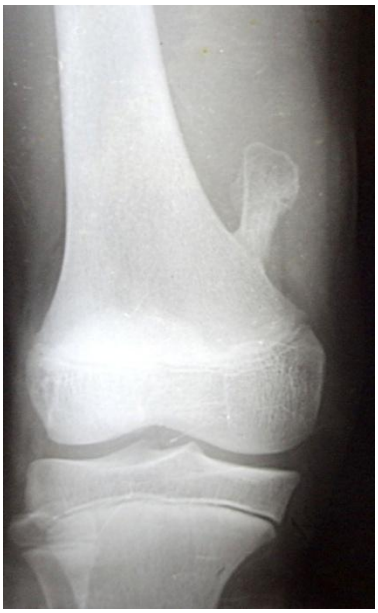


Fig.13- Anteroposterior radiograph of an osteochondroma involving right femur. Lesion characteristically pointing away from the joint. Case 152/14.

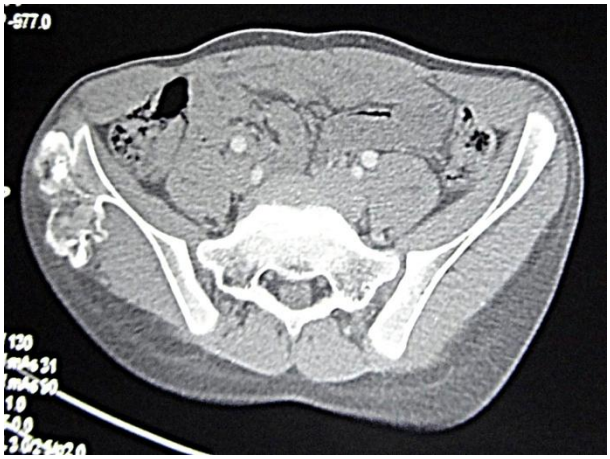


Fig.14 – Osteochondroma. Contrast enhanced axial CT section of pelvis showing an exophytic lobulated cortical mass arising from right iliac blade with medullary continuity. Case 1839/13.

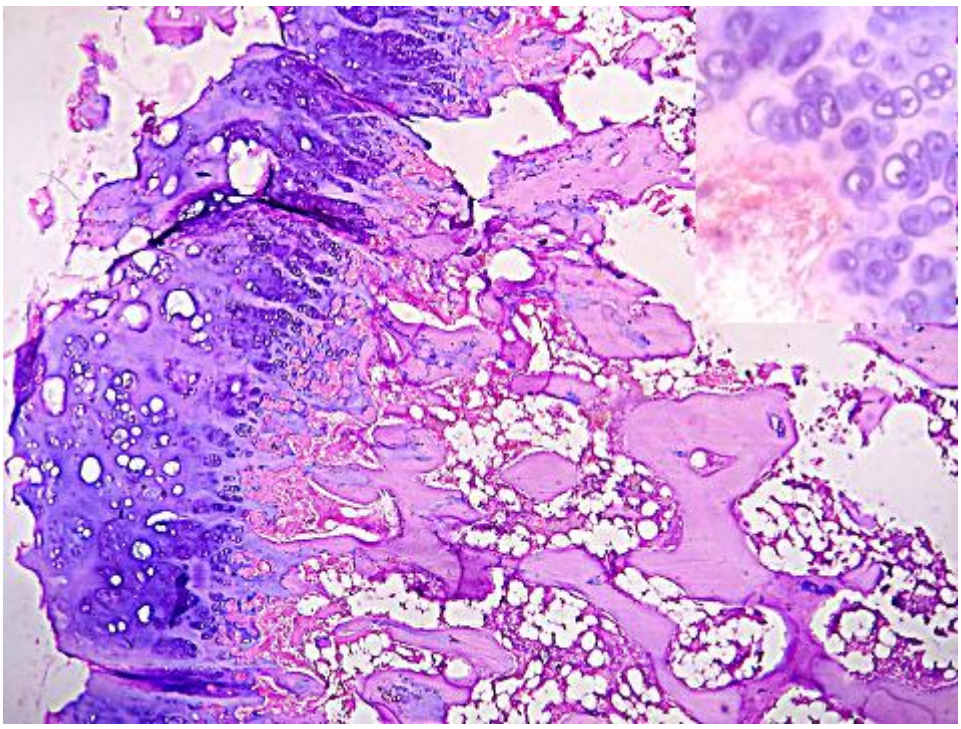


Fig.15 - Osteochondroma with cartilage cap. Chondrocytes have an orderly arrangement in the cartilage cap and there is maturation into trabecular bone. (H&E scanner view) Inset shows columnar arrangement of chondrocytes towards the base. (H&E x 400) Case 1866/12.

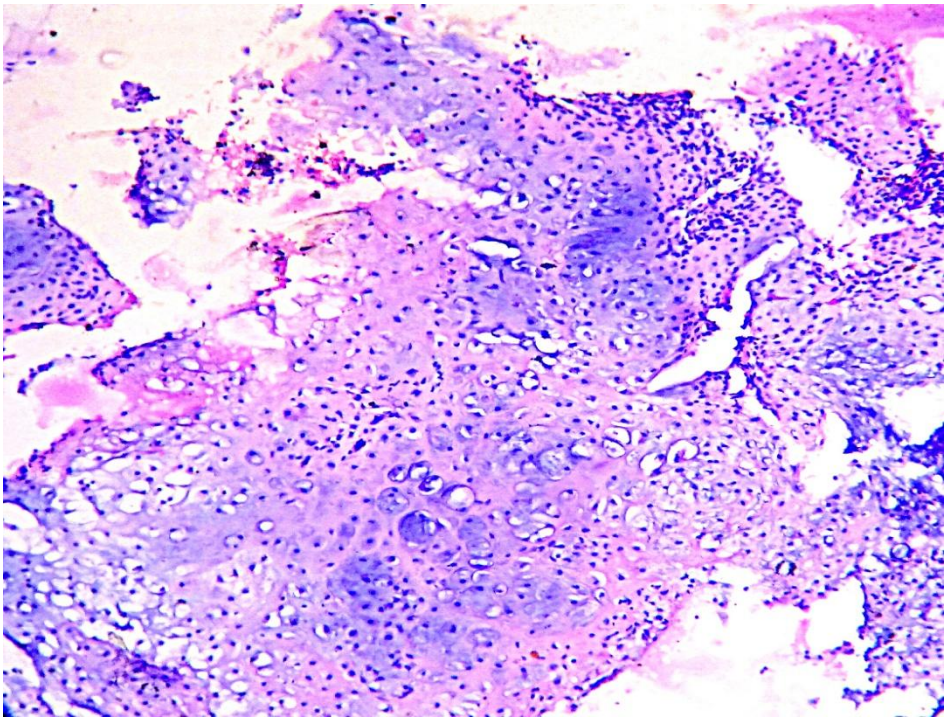


Fig.16 - Enchondroma with lobules of hypocellular cartilage. (H&E x 100) Case 5068/13.

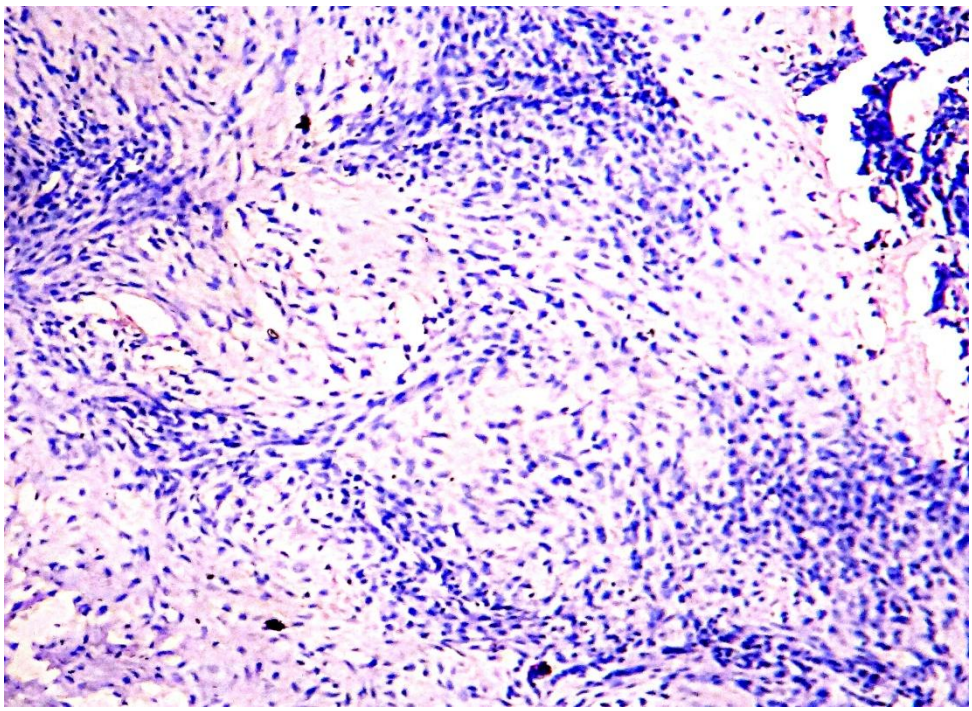


Fig. 17 - Chondromyxoid fibroma. Lobular pattern. Lobules have a hypocellular centre with condensation of tumour cells towards the periphery. (H&E x 100) Case 2637/13.

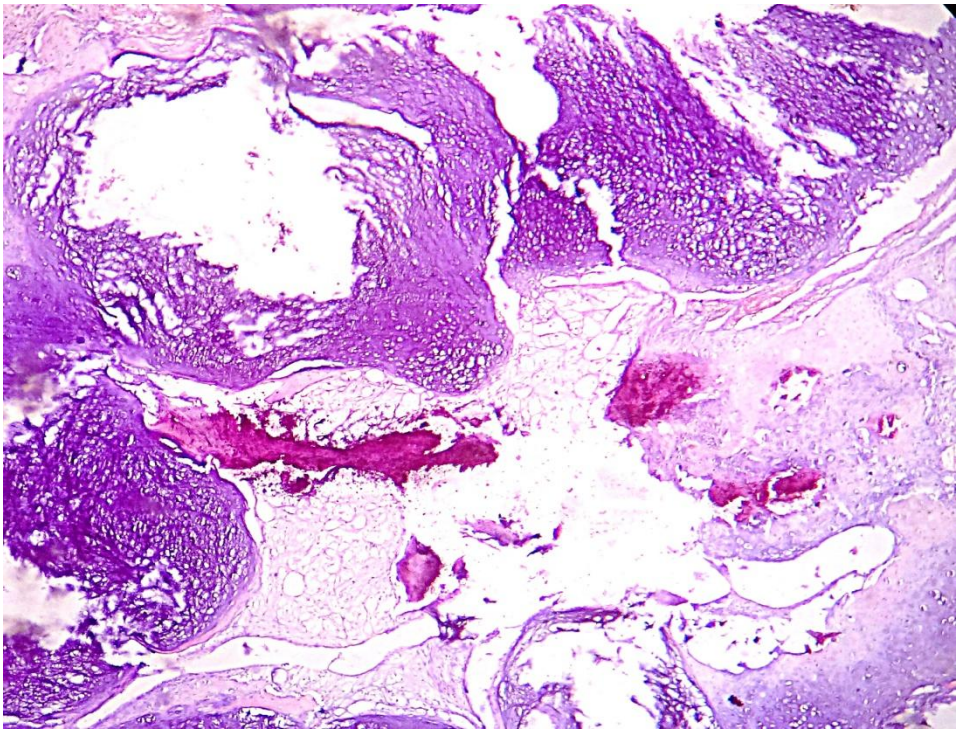


Fig . 18 - Chondrosarcoma of phalanx. Tumour invades pre-existing bone. (H&E Scanner view) Case 3954/12.

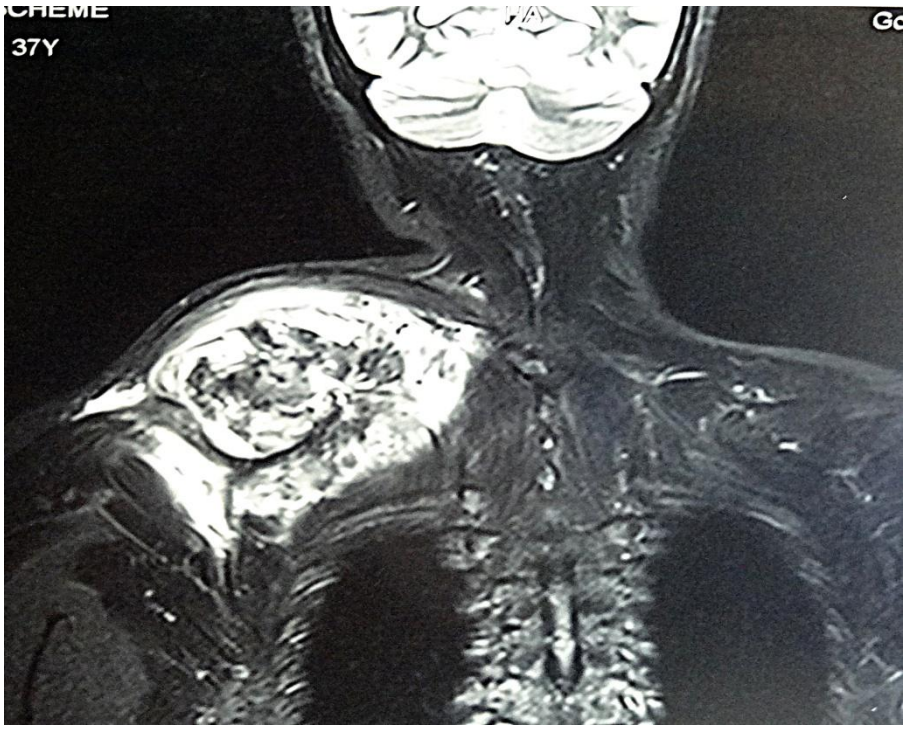


Fig.19 - Chondrosarcoma right scapula. MRI – T2 weighted fat saturated coronal image of right shoulder region showing heterogeneously hyperintense large mass with internal T2 hypointense areas. Case 2903/14.

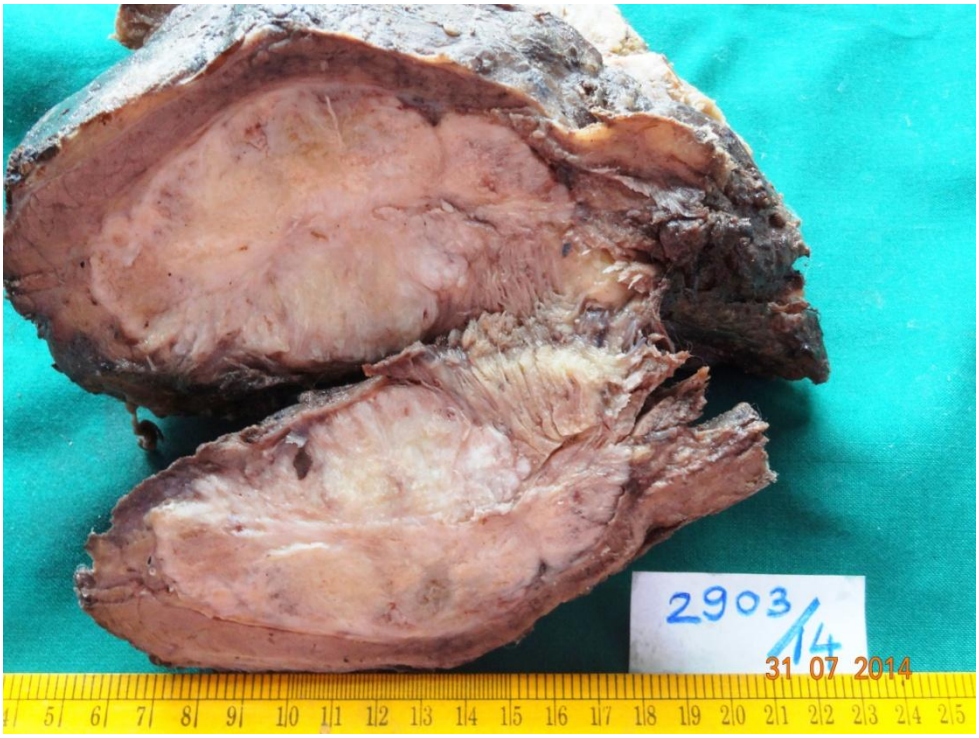


Fig.20 - Gross cut surface of chondrosarcoma. Resection specimen of scapula. Gray white lobulated tumour with degenerative myxoid change. Case 2903/14.

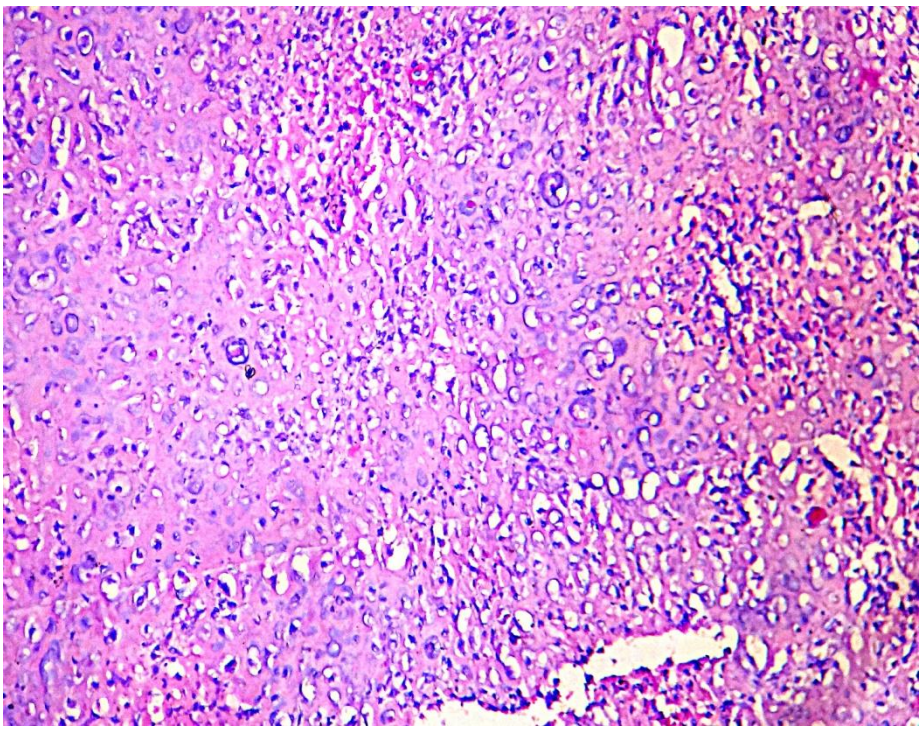


Fig.21 - Grade-II chondrosarcoma. Increased cellularity, nuclear enlargement and hyperchromasia. (H&E x 100) Case 2903/14.

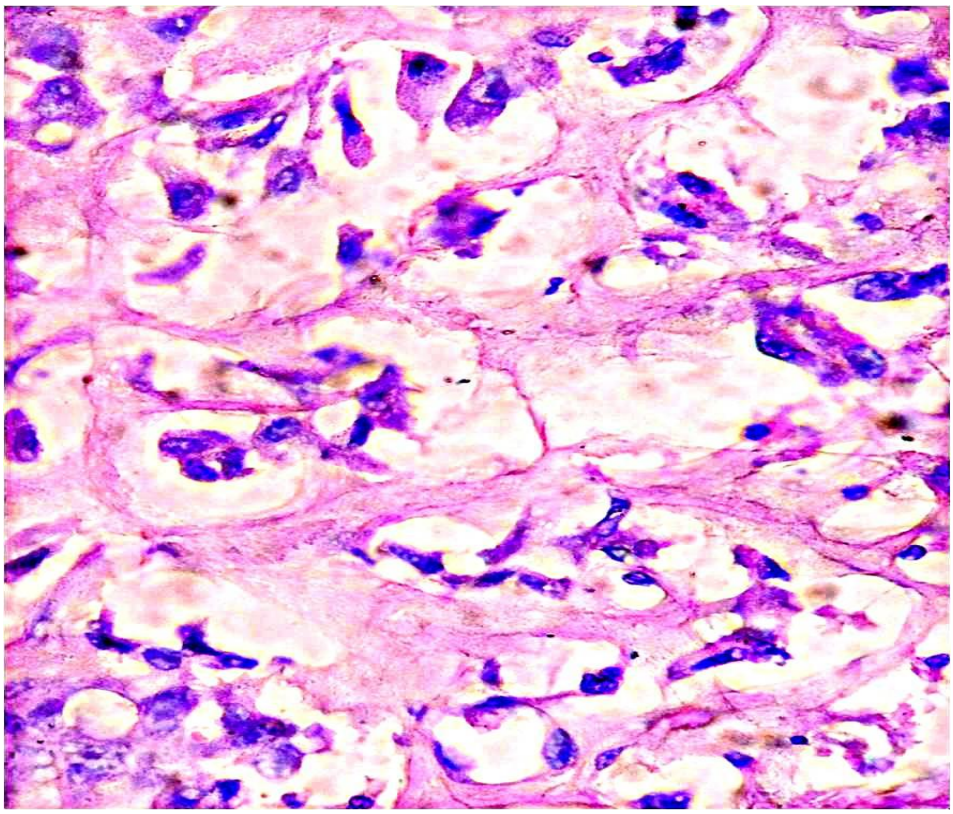


Fig.22 - Binucleated chondrocytes. Moderate nuclear atypia and pleomorphism in grade II chondrosarcoma. (H&E x 400) Case 2903/14.

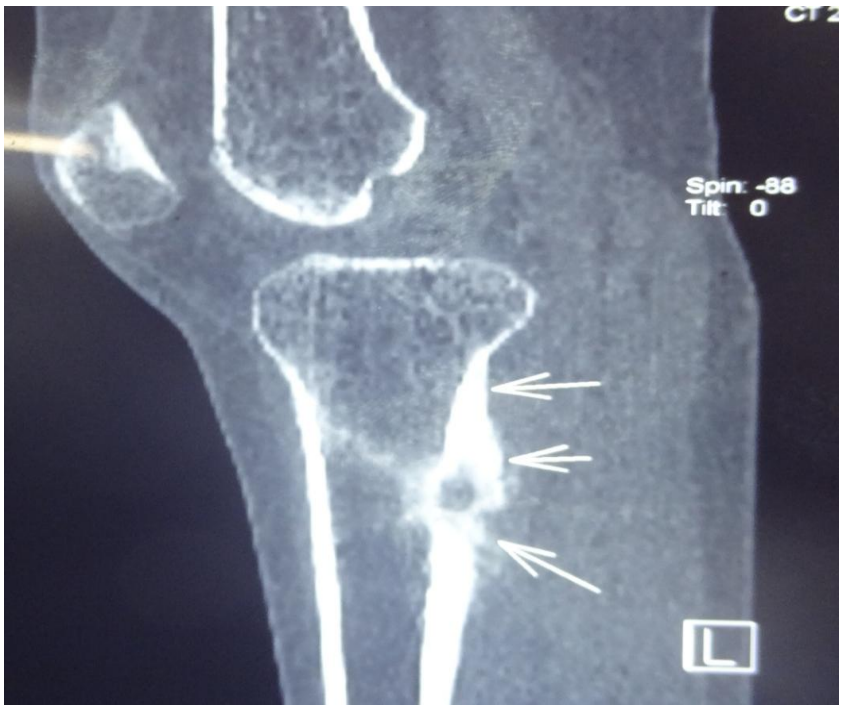


Fig.23 - CT scan left leg – upper part of shaft of tibia showing intracortical cystic lesion with internal nidus and surrounding reactive sclerosis. Case 2349/13.

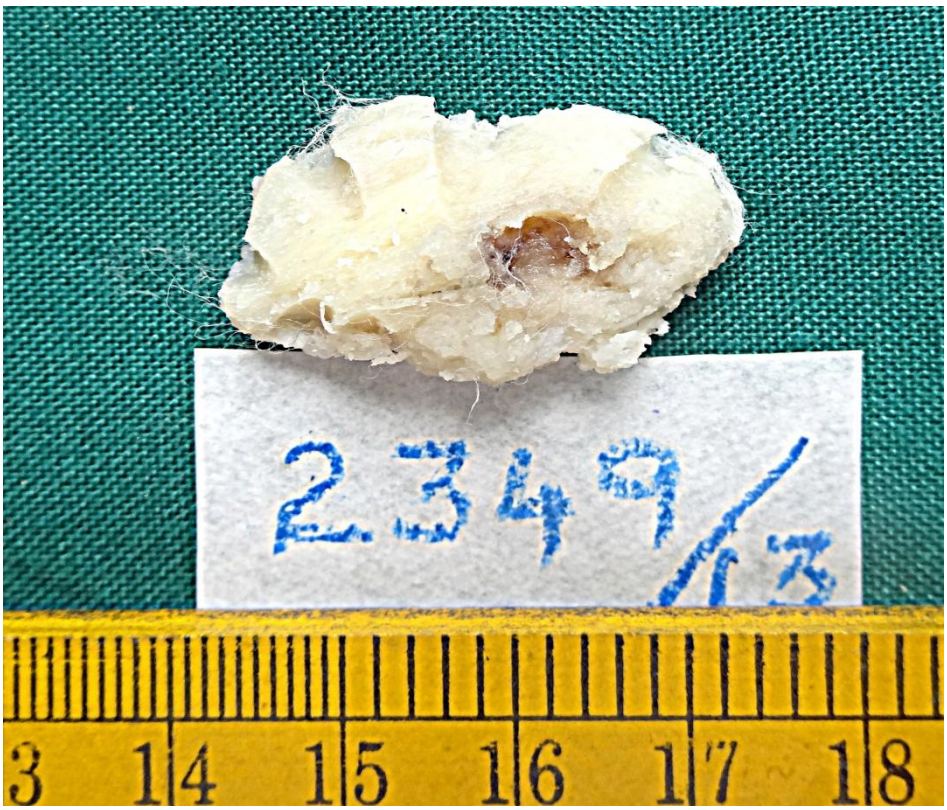


Fig.24 - Macroscopic appearance of osteoid osteoma. Nidus forming a circumscribed nodule surrounded by a thick shell of bone. Case 2349/13.

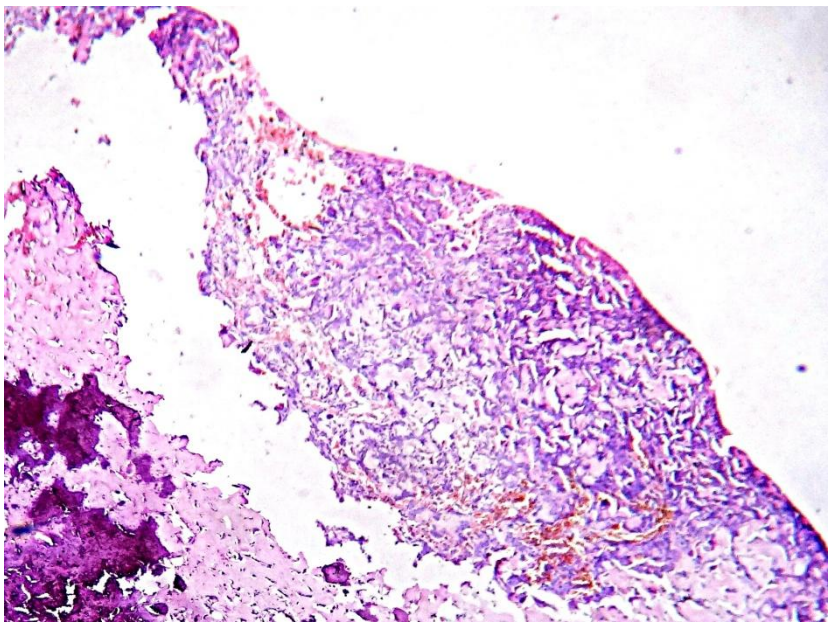


Fig.25 - Osteoid osteoma. Well circumscribed vascularised nidus surrounded by reactive bone. (H&E x 100) Case 2349/13.

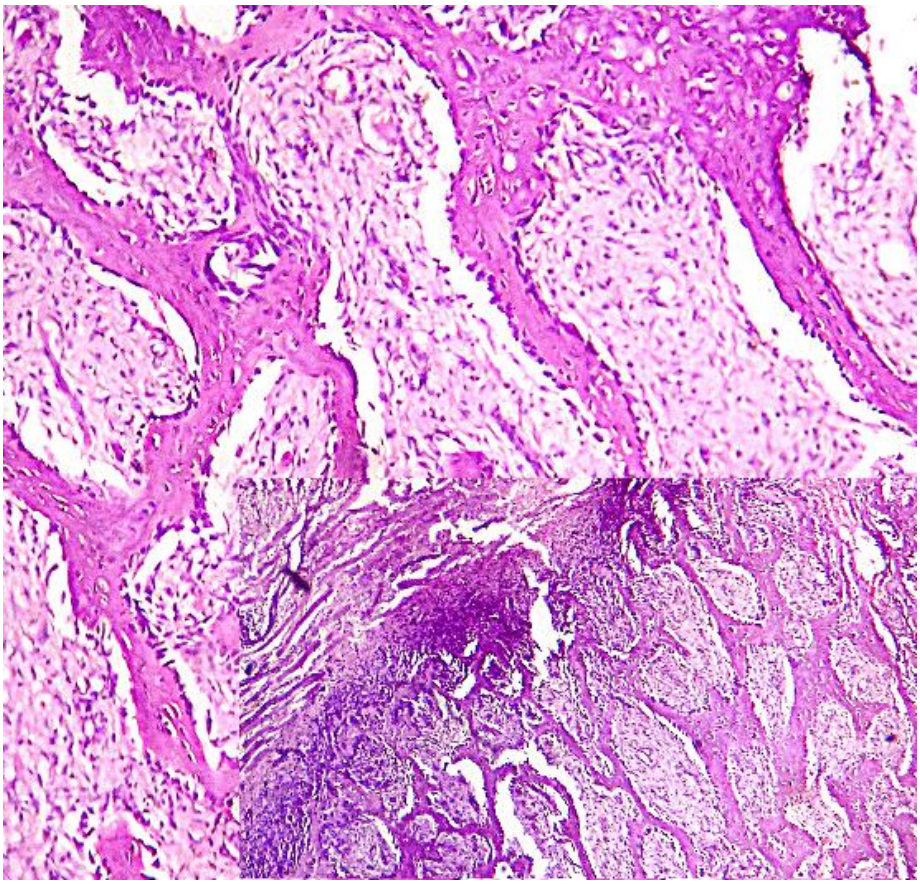


Fig.26 - Osteoblastoma. Anastamosing bony trabeculae in a loose fibrovascular stroma. (H&E x 400). Inset shows well circumscribed edge of the lesion. (H&E scanner view) Case 5048/13.

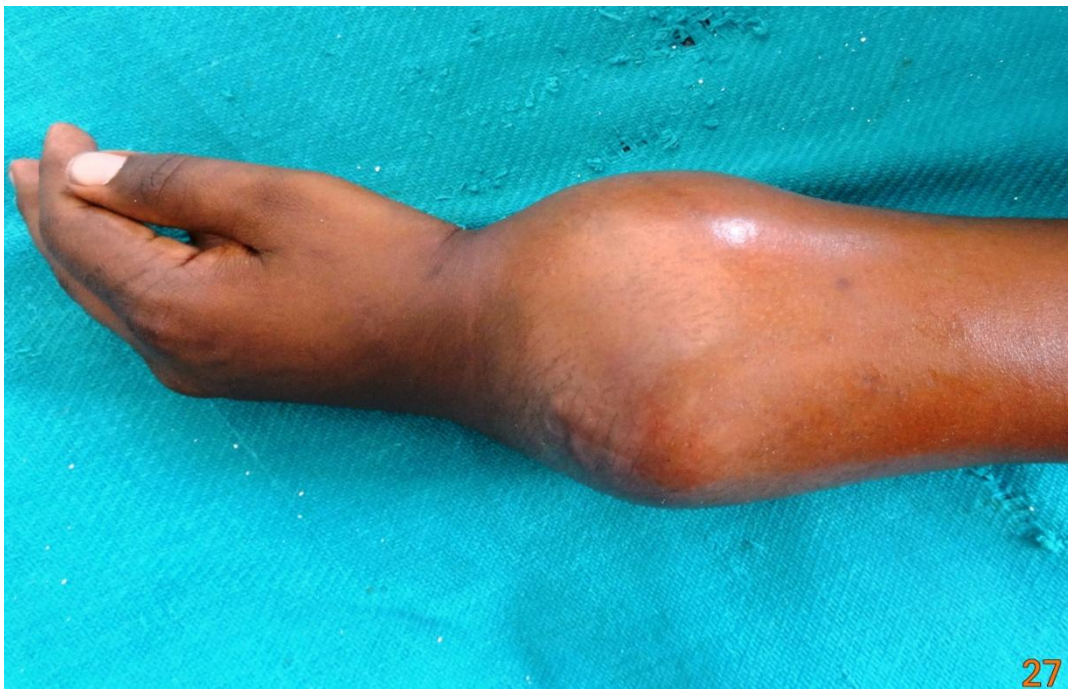


Fig.27 - Clinical presentation of osteosarcoma - distal end of radius in a 17 year old boy. Case 2472/13.

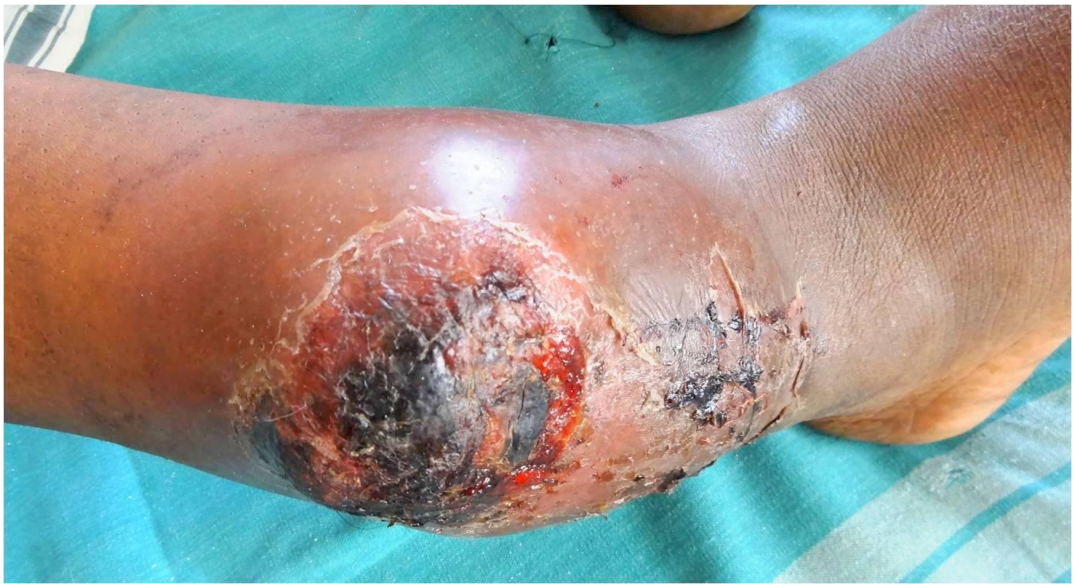


Fig.28 - Clinical presentation of osteosarcoma distal end of tibia with fibular involvement. Ulceration due to stretching of skin by the tumour. Case 3018/13.

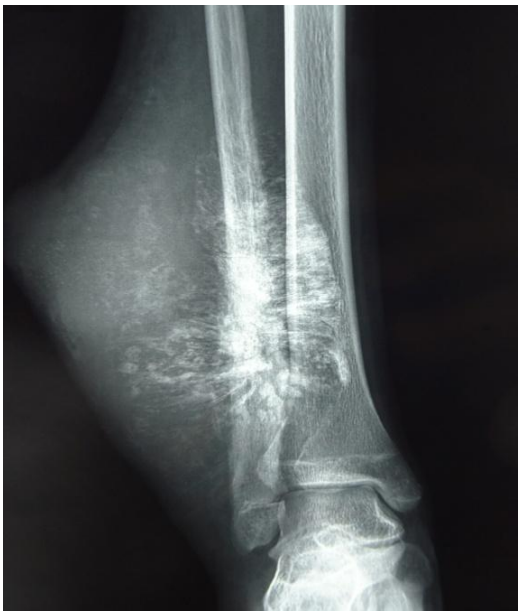


Fig.29 - Osteosarcoma distal tibia with fibular involvement. Plain radiograph. Mixed lytic – sclerotic mass with sunray type of periosteal reaction. Cloud like matrix mineralisation seen. Case 3018/13.

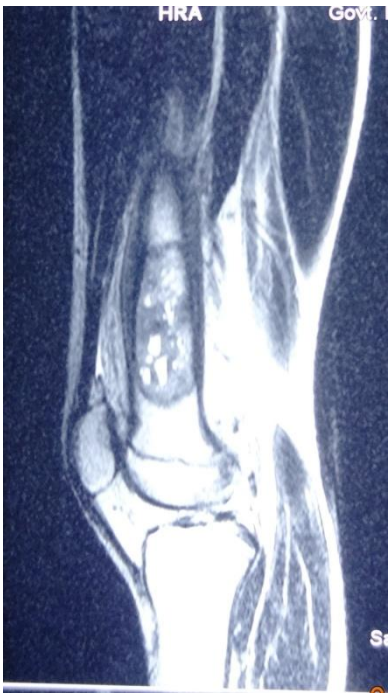


Fig.30 - Osteosarcoma distal femur. MRI T2 weighted image. Sagittal plane of knee joint. Case 1221/13.

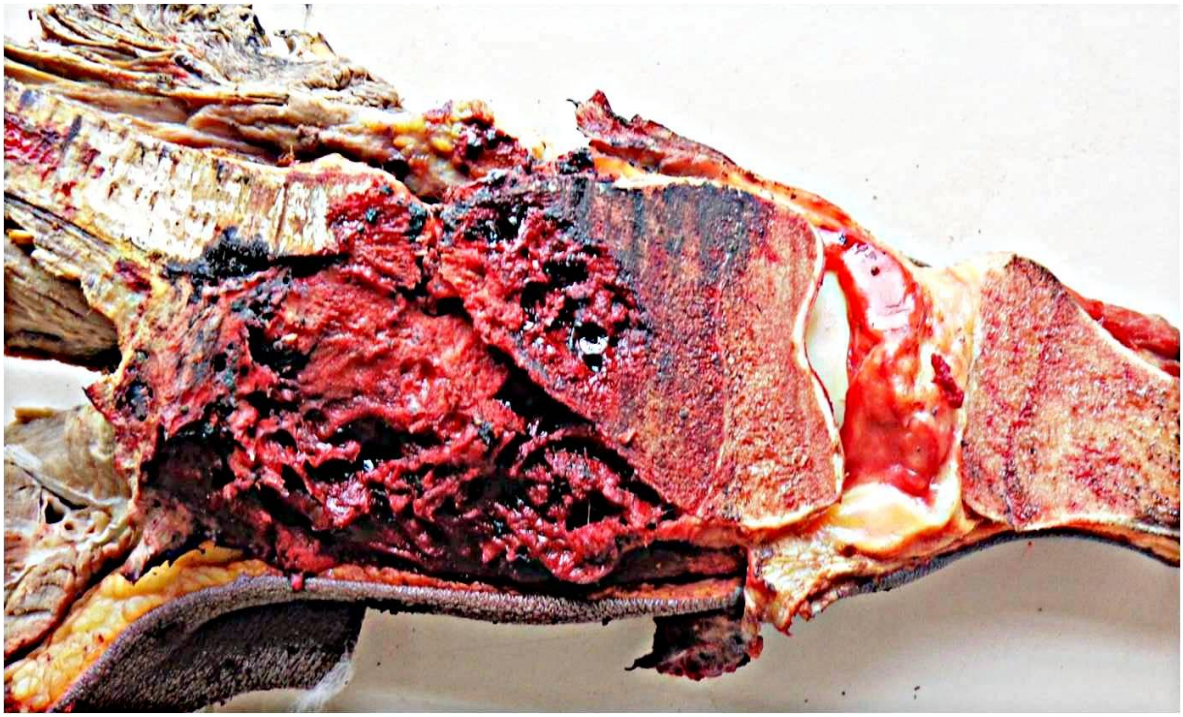


Fig.31- Macroscopic cut surface appearance of osteosarcoma in above knee amputation specimen. Tumour involving distal metadiaphyseal region of right femur with soft tissue extension. Case 1221/13.

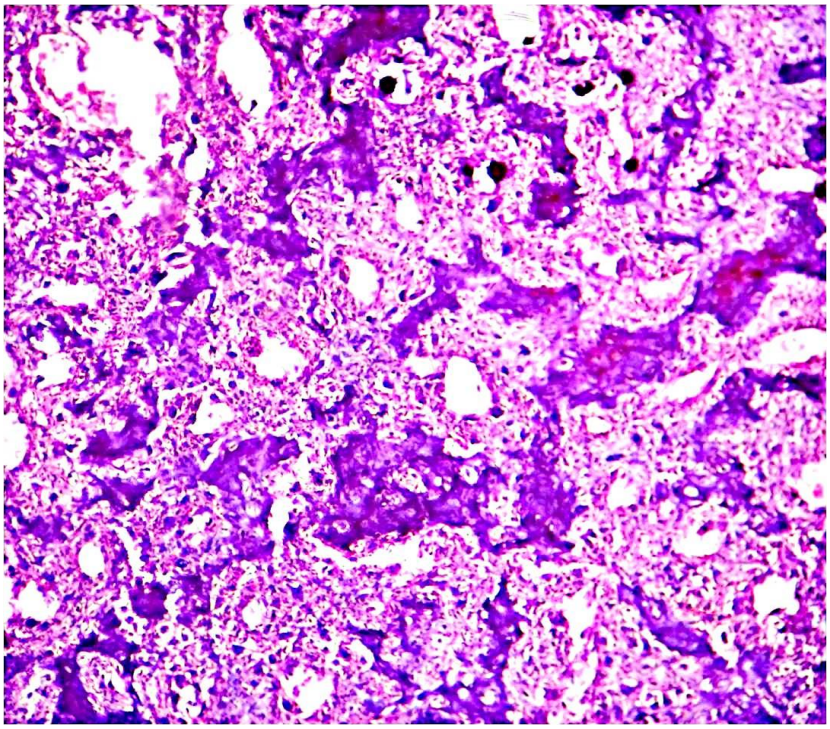


Fig. 32 - Osteosarcoma; malignant stromal cells with osteoid production. (H&E Scanner view) Case 1221/13.

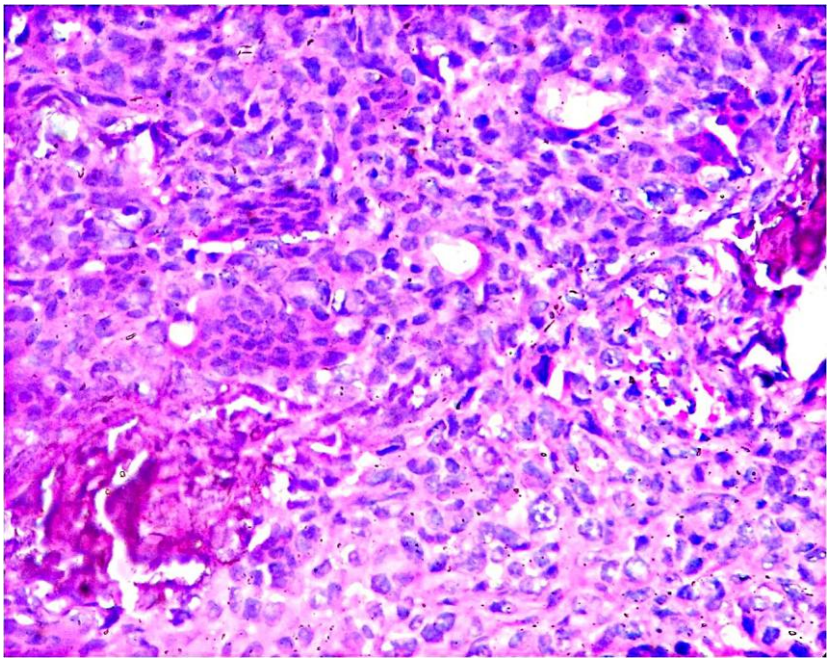


Fig.33 - Osteosarcoma with giant cells. The nuclei of malignant stromal cells are pleomorphic and vesicular as against benign looking nuclei of giant cells. (H&E x 400) Case 1221/13.

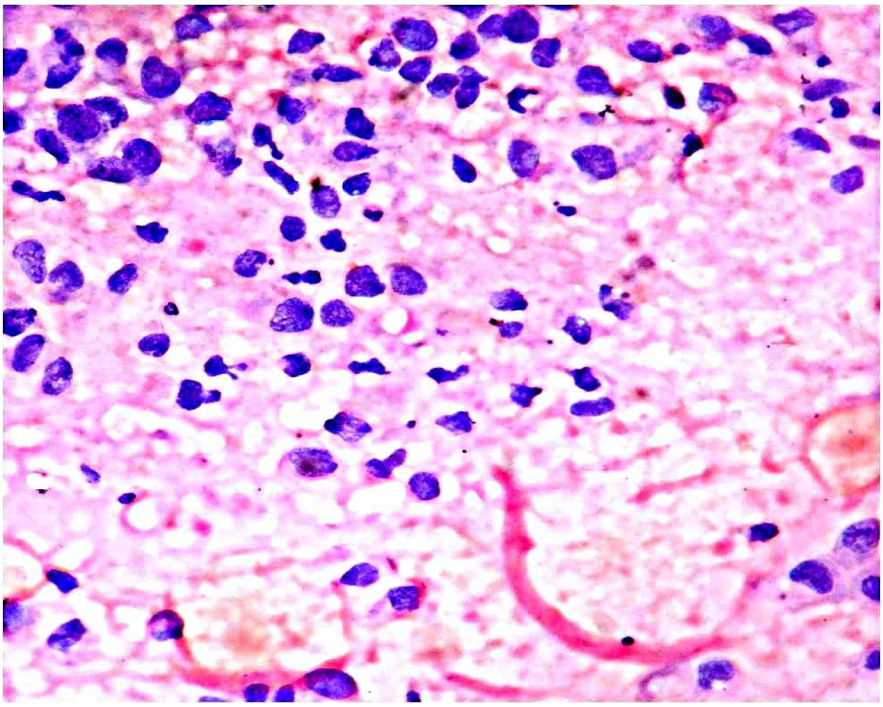


Fig .34 - FNAC. Scattered and small groups of pleomorphic sarcoma cells with strands of intercellular pink material consistent with osteoid. (H&E x 400) Case Cy 1461/13.

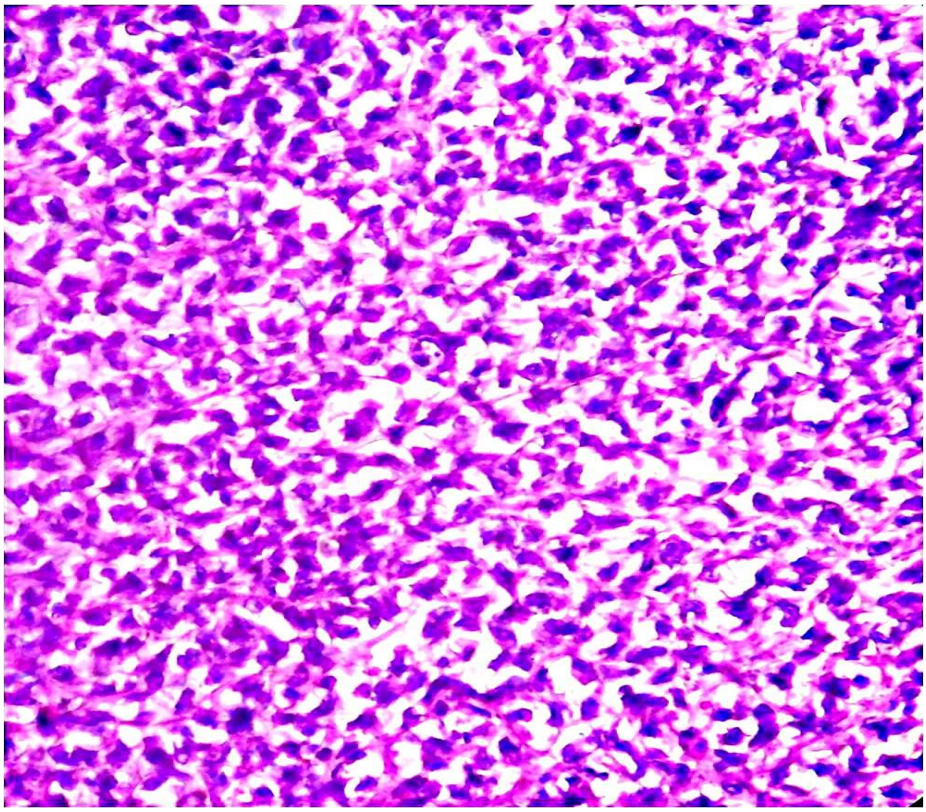


Fig.35 - Osteoblastic osteosarcoma. Malignant tumour cells with lace like filigree pattern osteoid. (H&E x 400) Case 4202/12.

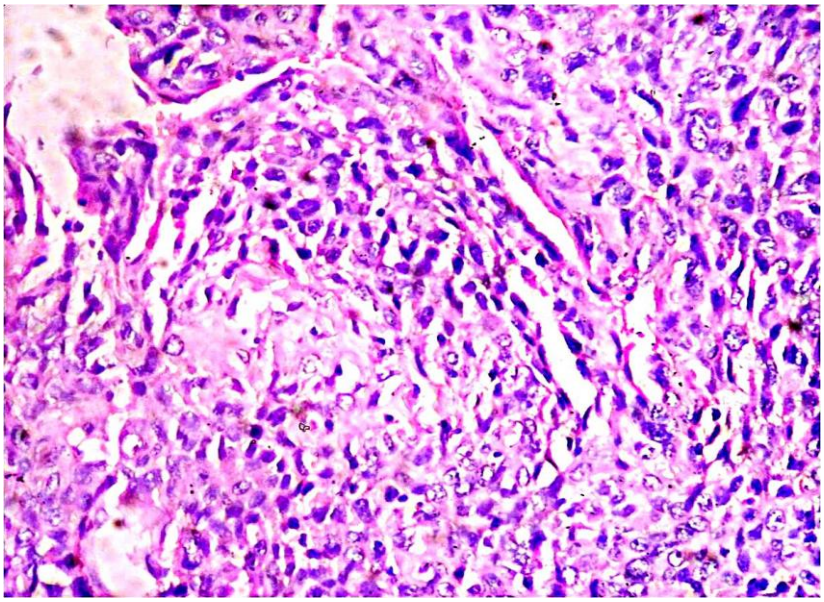


Fig.36 - Fibroblastic osteosarcoma. Malignant osteoid production is present between malignant spindle cells. (H&E x 400) Case 2473/13.

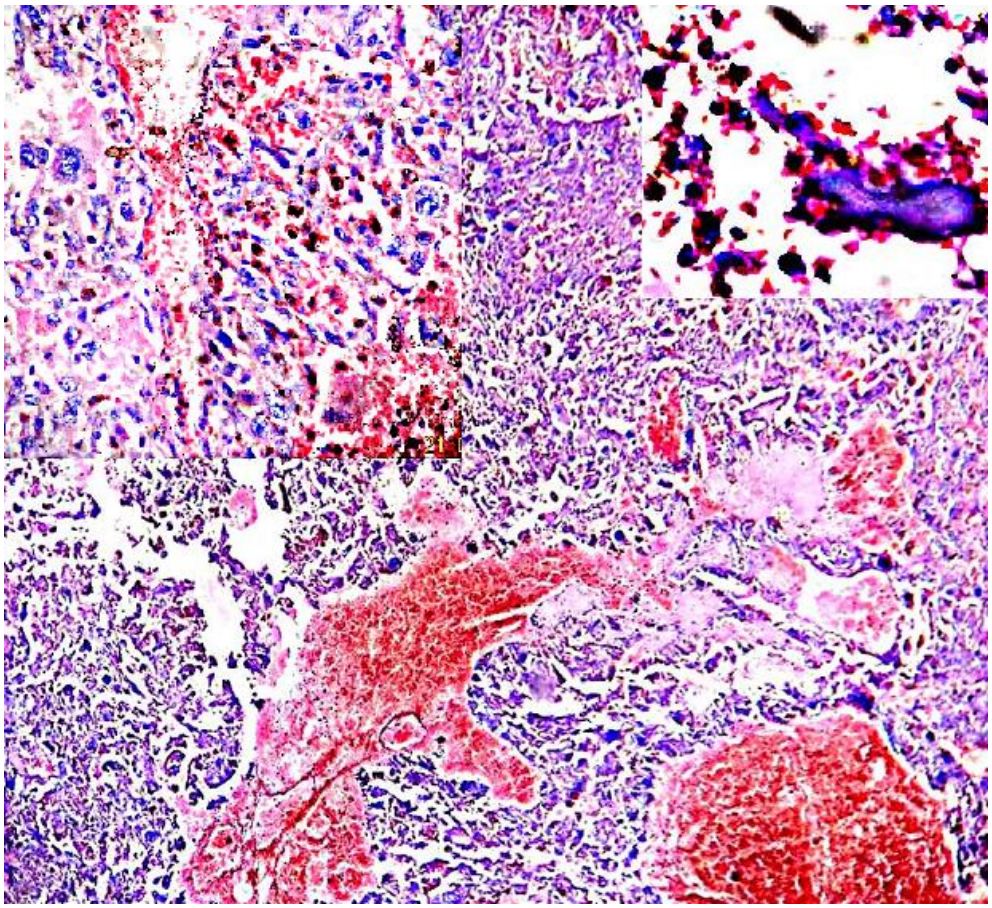


Fig.37- Telangiectatic osteosarcoma. This tumour occurred at the site of a biopsy proven GCT. Haemorrhagic spaces separated by septae. (H&E scanner view) Inset on the left shows malignant tumour cells lining the septae and on the right shows focal production of malignant osteoid. (H&E x 400) Case 2206/13.

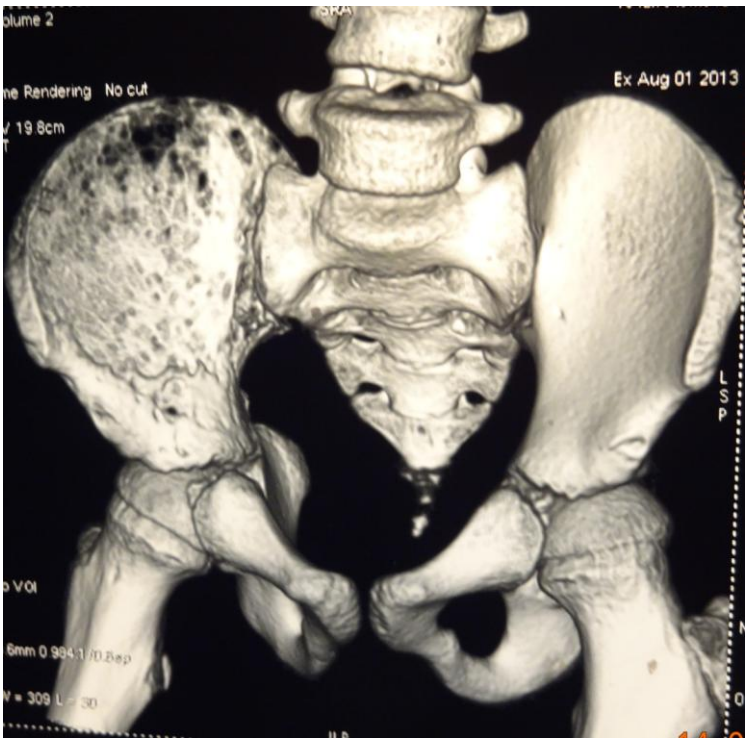


Fig.38 - Ewing sarcoma. MRI pelvis. Diffuse ill – defined permeative type of lytic lesion involving entire right iliac bone. Case 3231/13.

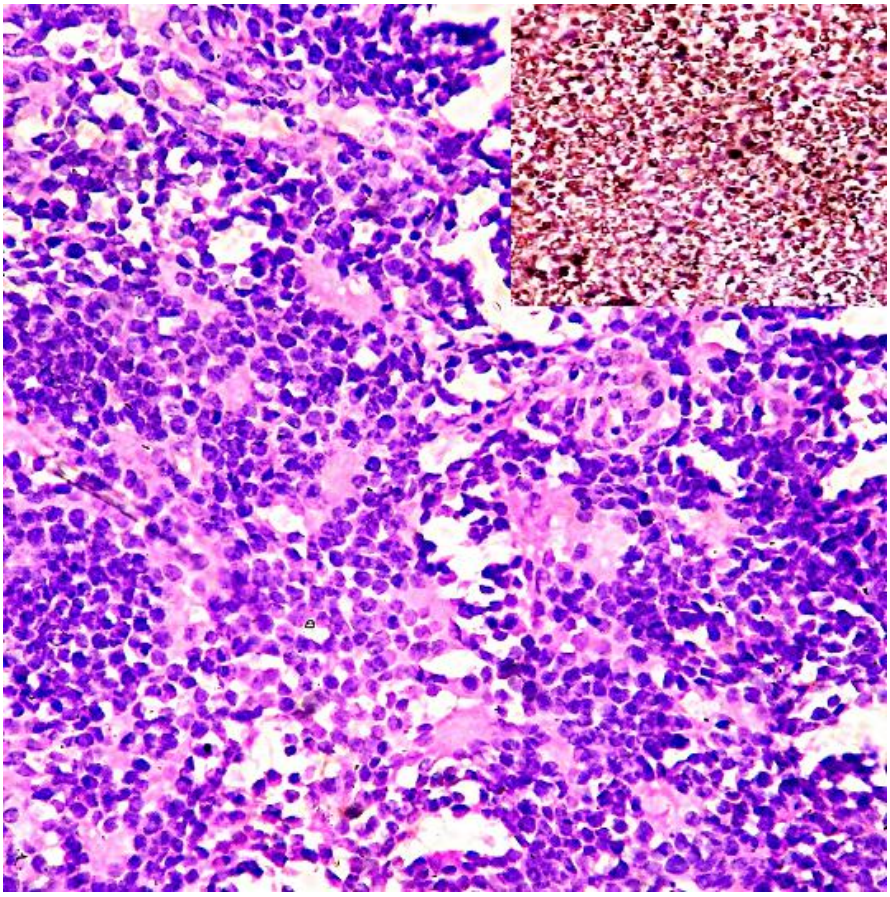


Fig.39 - Ewing sarcoma. Sheets of tumour cells with uniform round nuclei. Rosette formation seen. (H&E x400). Inset shows membrane positivity of tumour cells with CD99 immunostain. Case 3030/12.

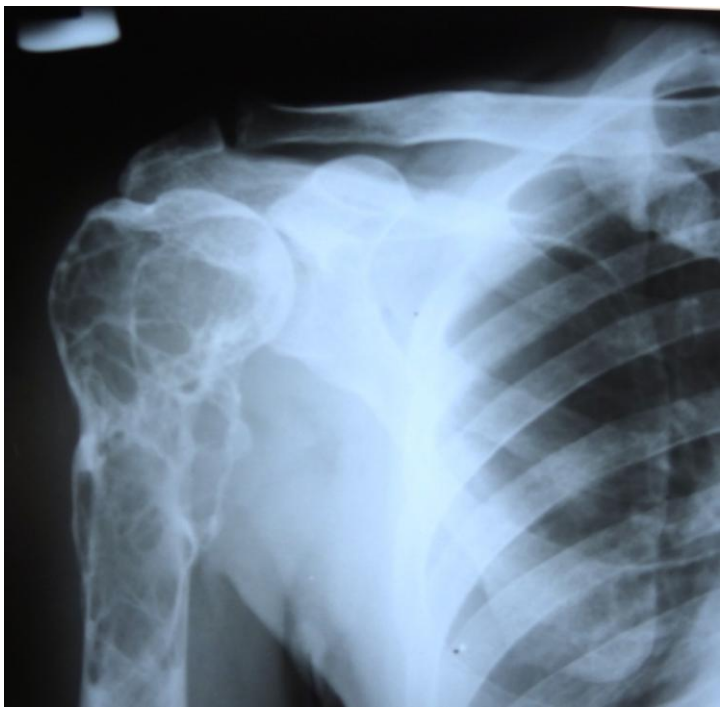


Fig.40 - Plasma cell myeloma of right humerus. X- Ray of right shoulder joint in AP view showing large expansile ill – marginated lytic lesion involving upper meta – diaphyseal region of humerus with apparent trabeculations. Case 5408/13.

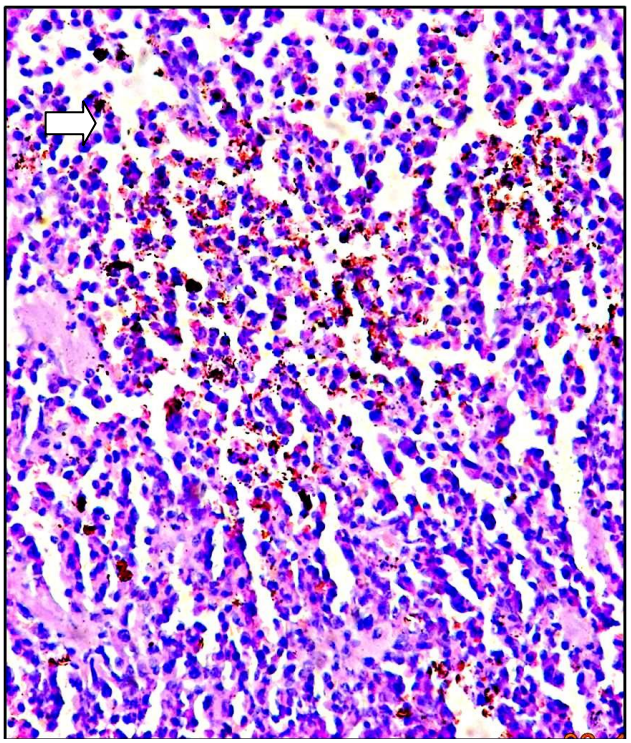


Fig. 41 – Plasma cell myeloma. Sheets of plasma cells. Arrow indicates binucleate plasma cell. Case 4061/13.

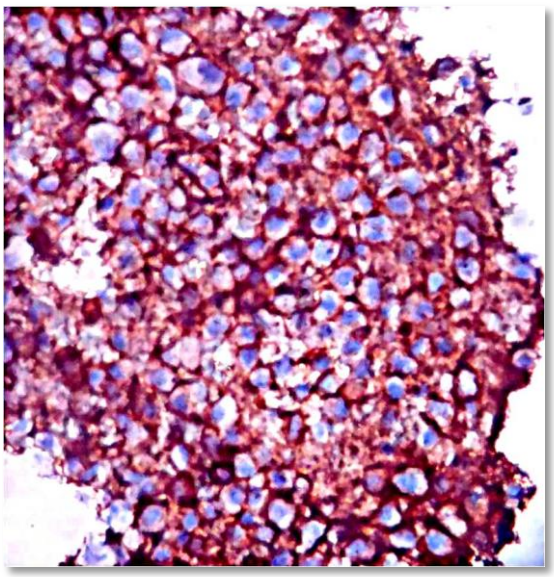


Fig.42 - CD 138 positive plasma cells. Case 4061/13.

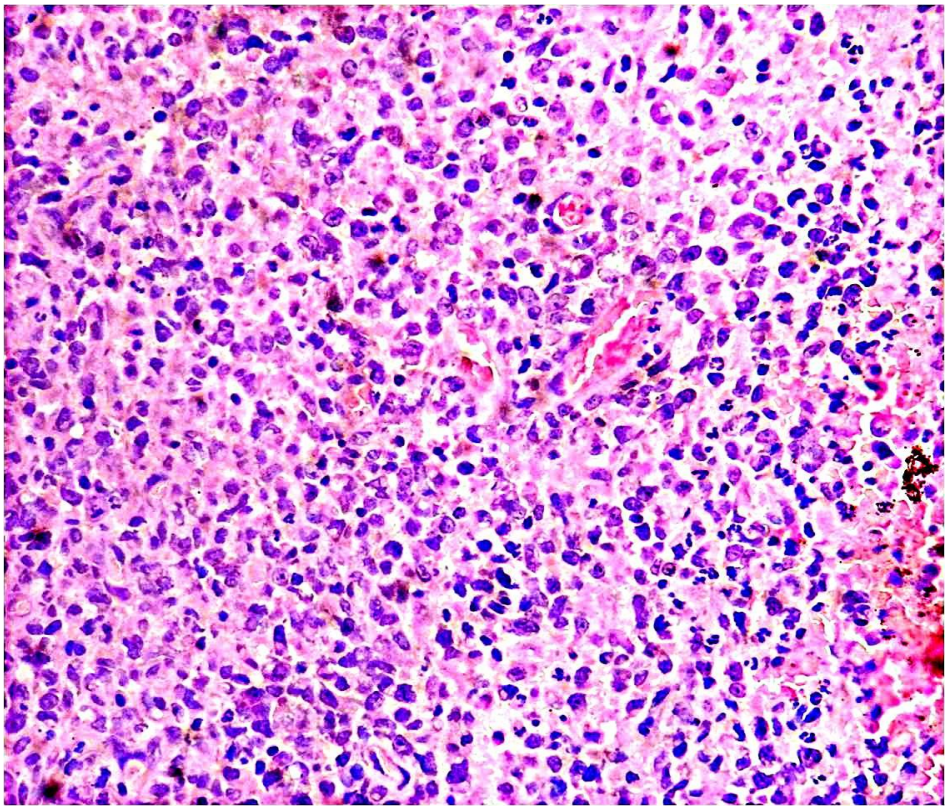


Fig.43 - Primary malignant lymphoma of bone. Polymorphic tumour cells with nuclear irregularities and prominent nucleoli. (H&E x 400) Case 186/14.

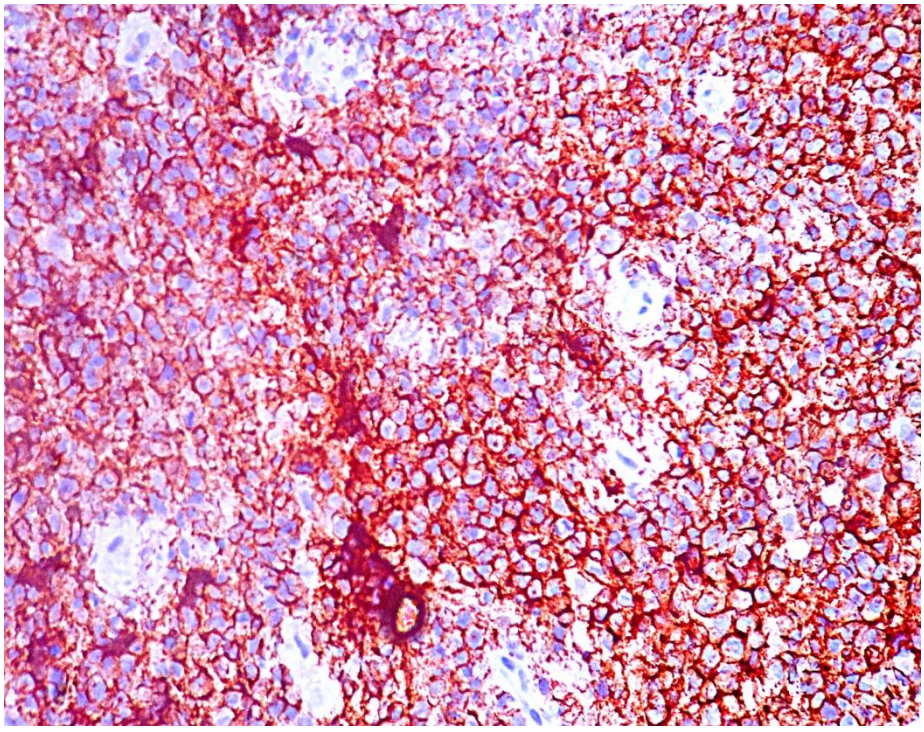


Fig.44 - Strong CD45 positivity of lymphoma cells. Case 186/14.

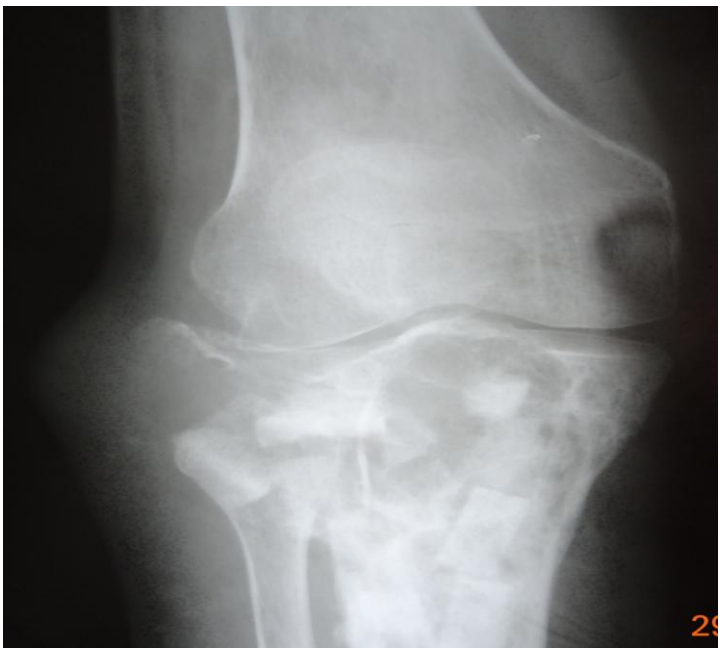


Fig.45 - Recurrent GCT of proximal tibia. Plain radiograph in AP view. Bone graft seen with evidence of recurrent expansile lytic lesion in proximal tibia. Case 1925/13.

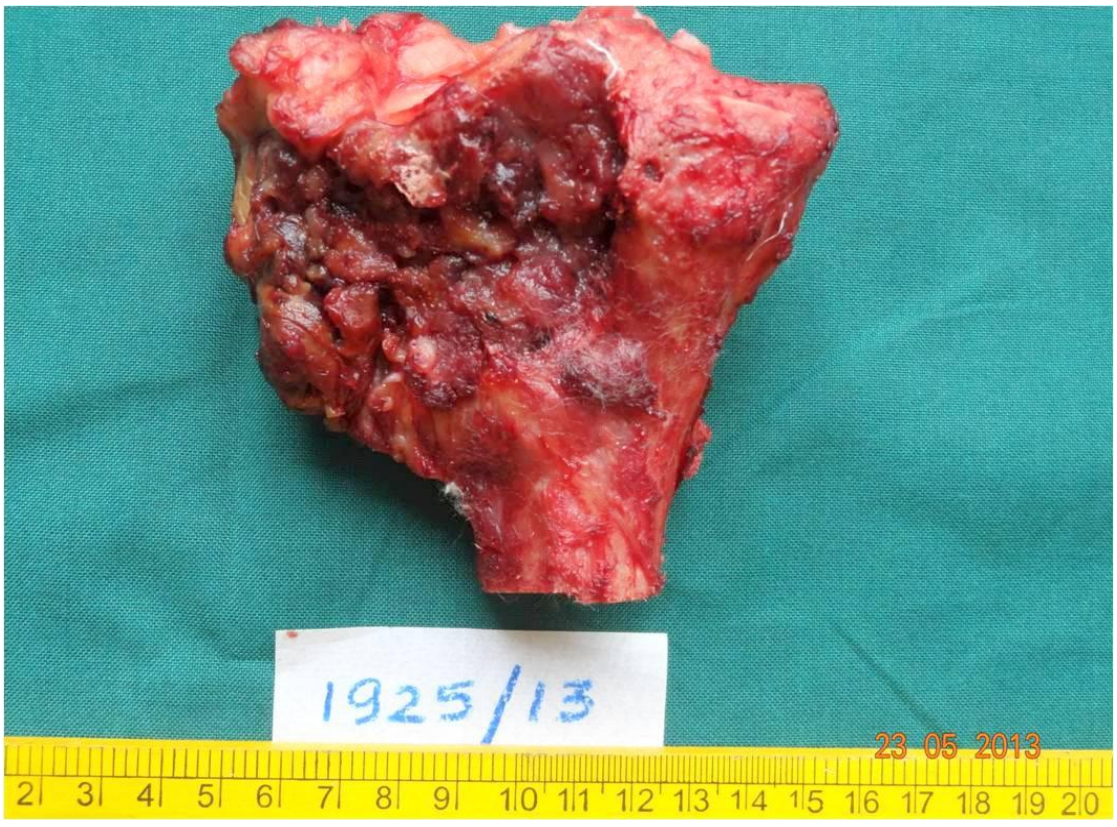


Fig.46 - Proximal tibial resection for recurrent GCT. Characteristic red brown tumour destroying the cortex. Case 1925/13.

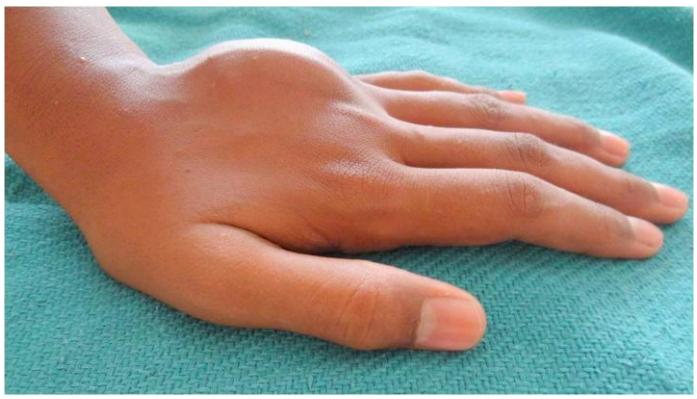


Fig.47 - Clinical presentation of GCT – 4th metacarpal. Case 4552/13.

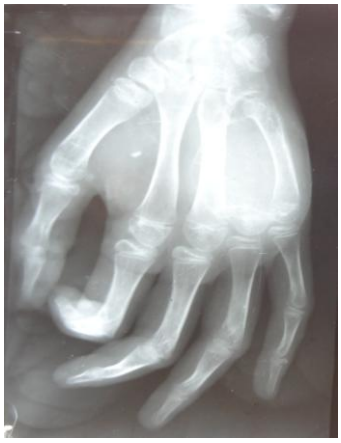


Fig.48 - Radiograph of hand in oblique view showing lytic lesion destroying the 4th metacarpal. Case 4552/13.

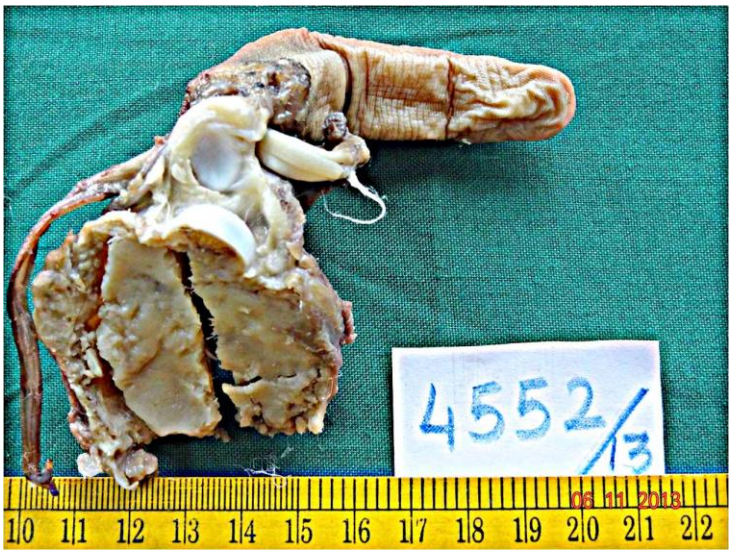


Fig.49 - Ray amputation specimen of GCT 4th metacarpal. Tumour extends into the epiphysis. Case 4552/13.

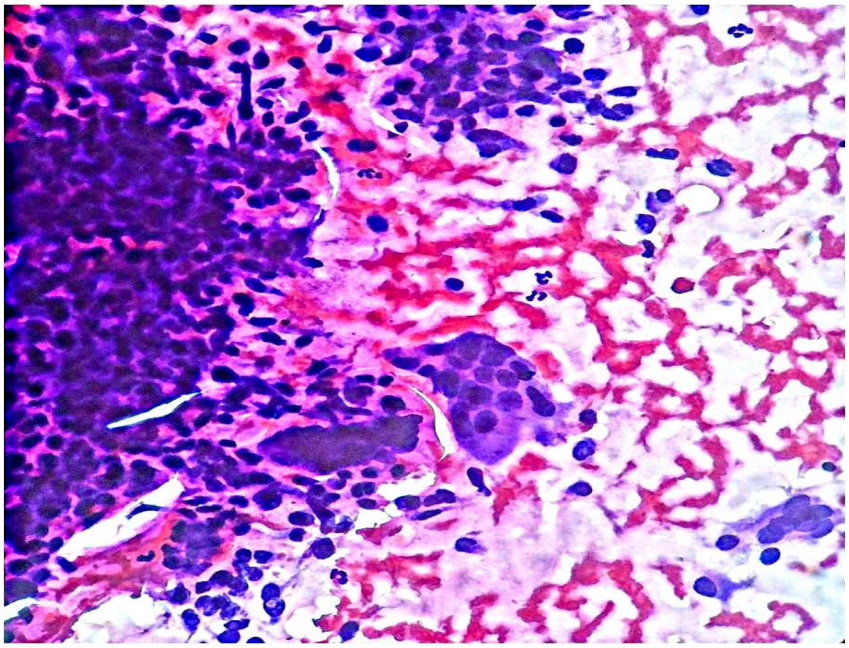


Fig.50 - FNAC from a case of GCT showing spindle shaped stromal cells and osteoclastic giant cells. (H&E x 400) Case Cy 756/13.

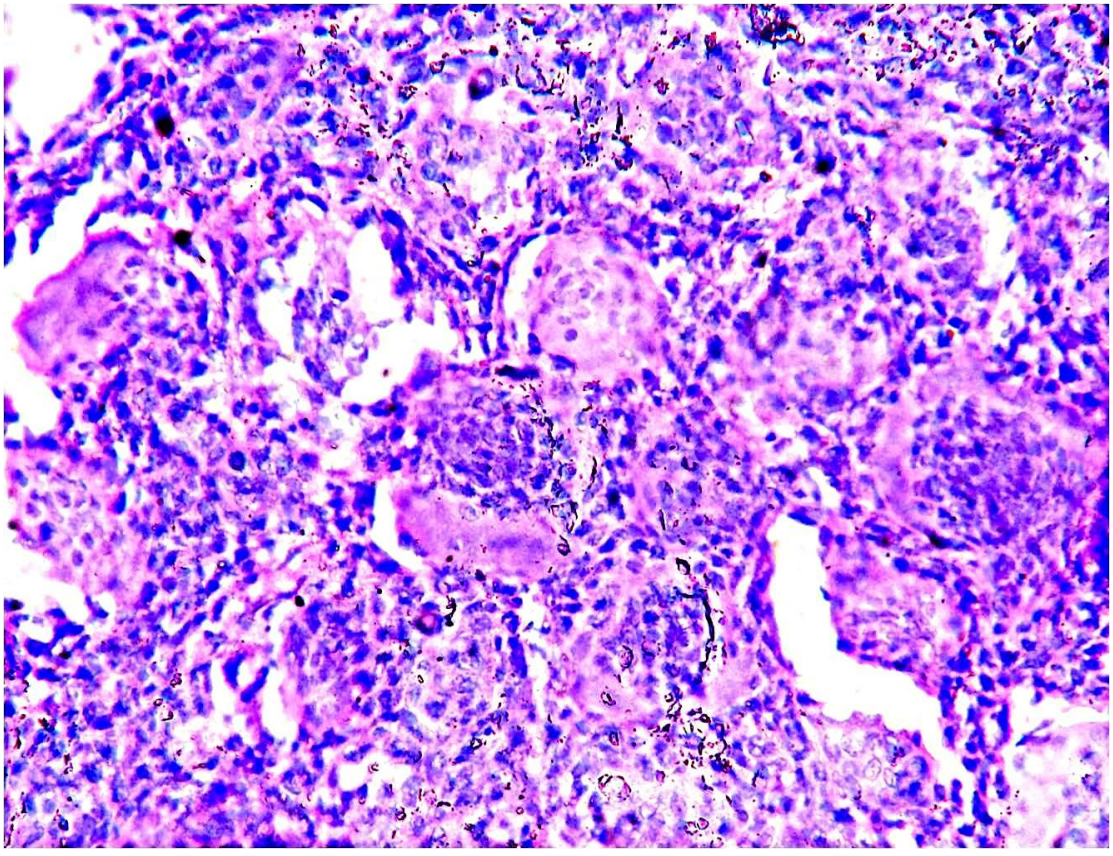


Fig .51 - GCT – Multi nucleated giant cells arranged uniformly in a background of mononuclear cells. Case 4552/13.

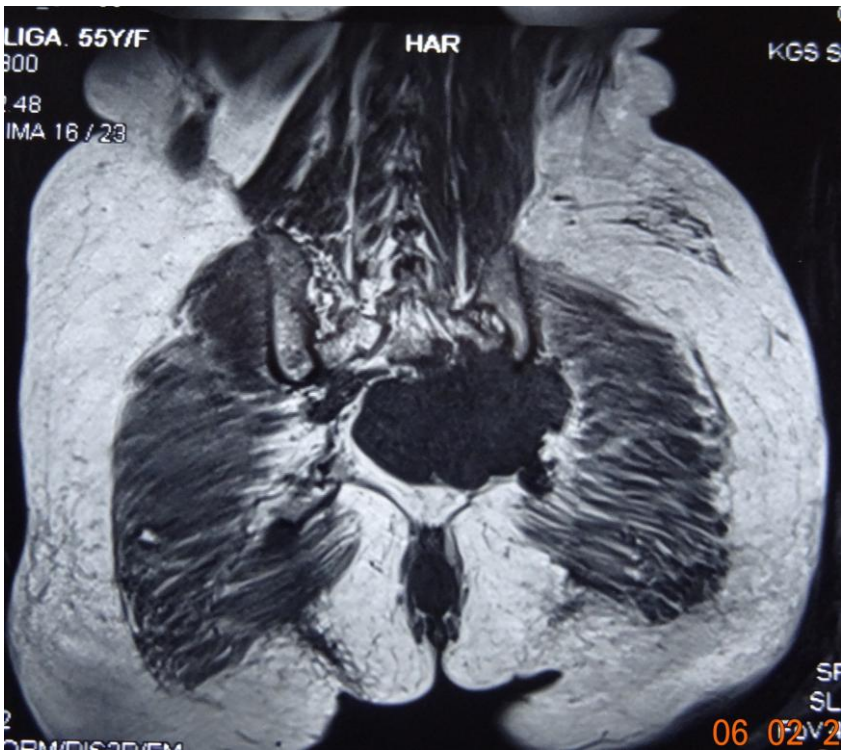


Fig.52 – Chordoma. TI weighted non – fat saturated MRI of pelvis in coronal view showing homogenously hypo intense lobulated lesion in sacral region. Case 480 /13.

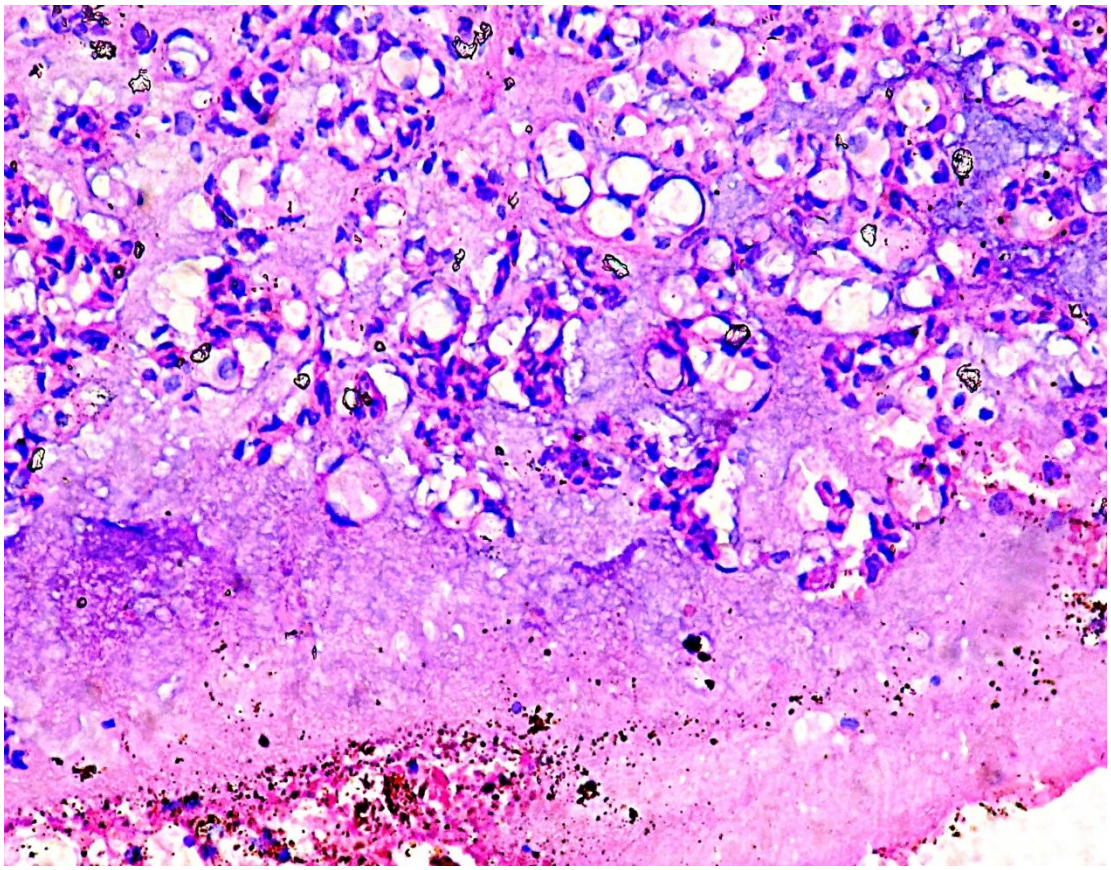


Fig.53 - Chordoma – cords and strands of tumour cells in a mucinous background. Physaliferous cells with abundant vacuolated cytoplasm seen. (H&E x 400) Case 480/13.

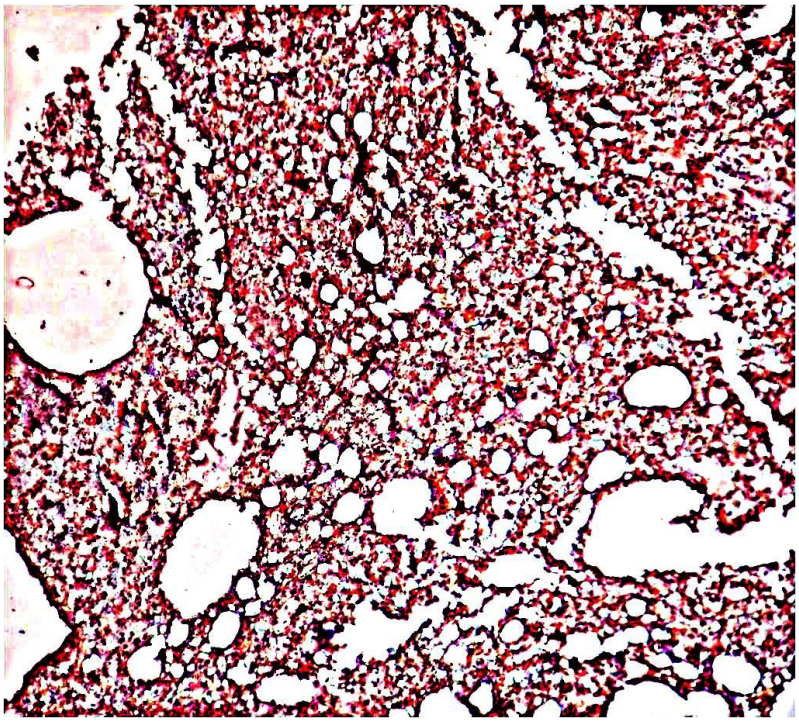


Fig.54 - Cytokeratin positivity in chordoma. Case 480/13.

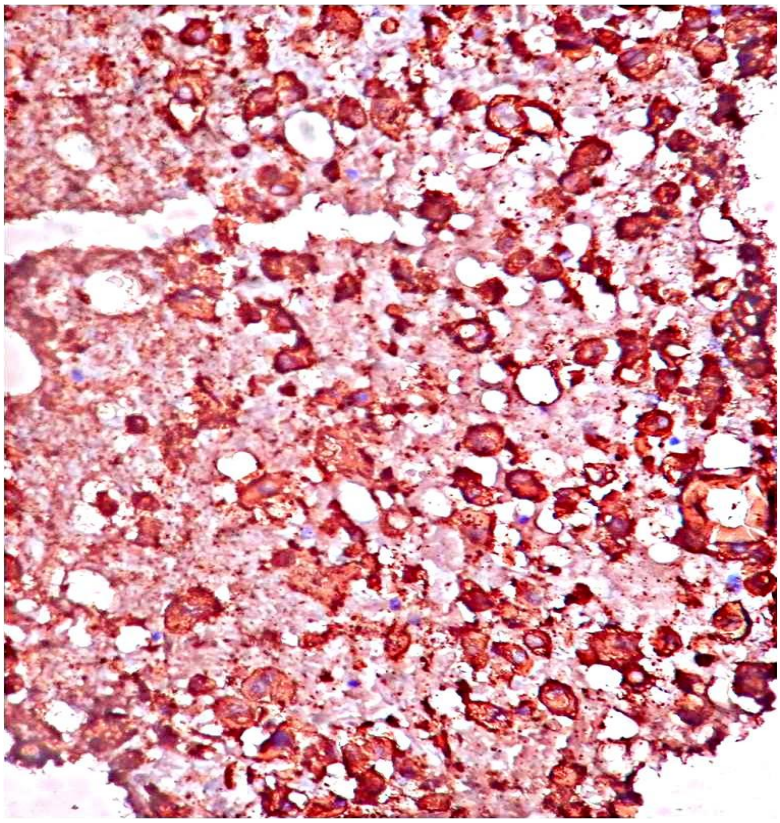


Fig.55 - Physaliferous cells positive for S - 100 immunostain. Case 480/13.

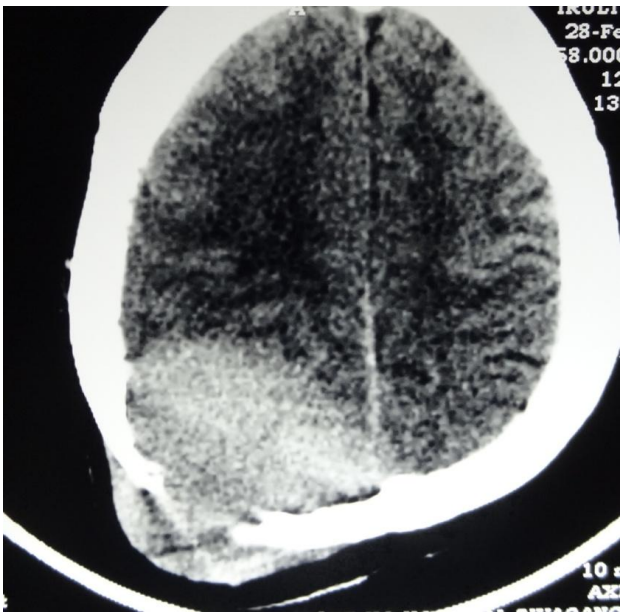


Fig.56 - Metastatic deposits in skull and brain from occult primary in thyroid. Axial contrast enhanced CT section of head showing lytic destructive lesion of right parietal bone with large homogenously enhancing associated soft tissue component both on scalp and intracranial extra axial region indenting underlying brain. Case 1321/13.

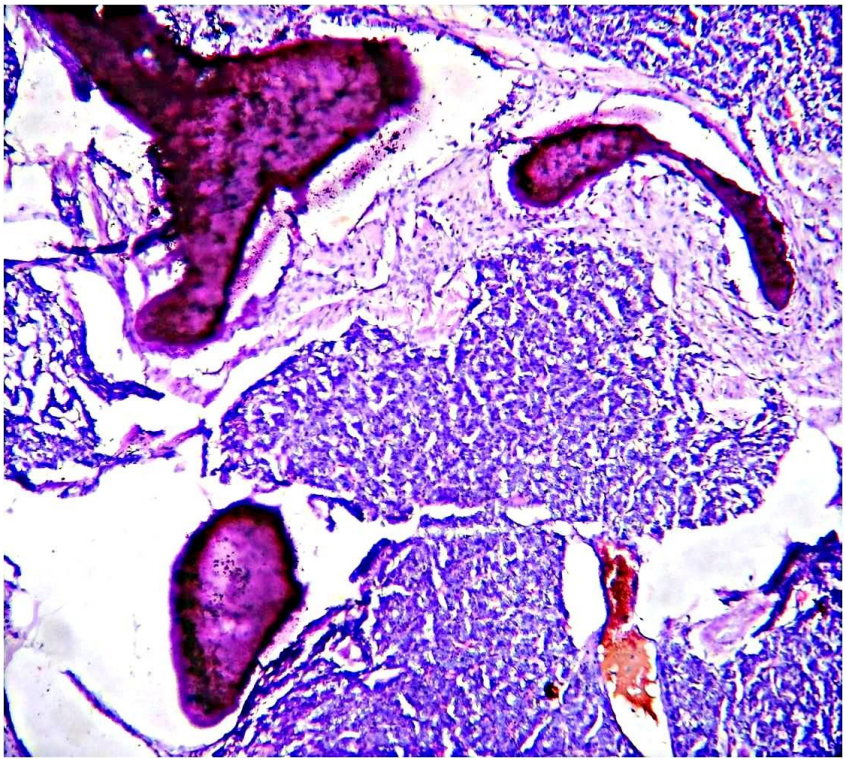


Fig.57 - Metastatic follicular carcinoma thyroid invading the skull bone and brain parenchyma. (H&E x 100) Case 1321/13.

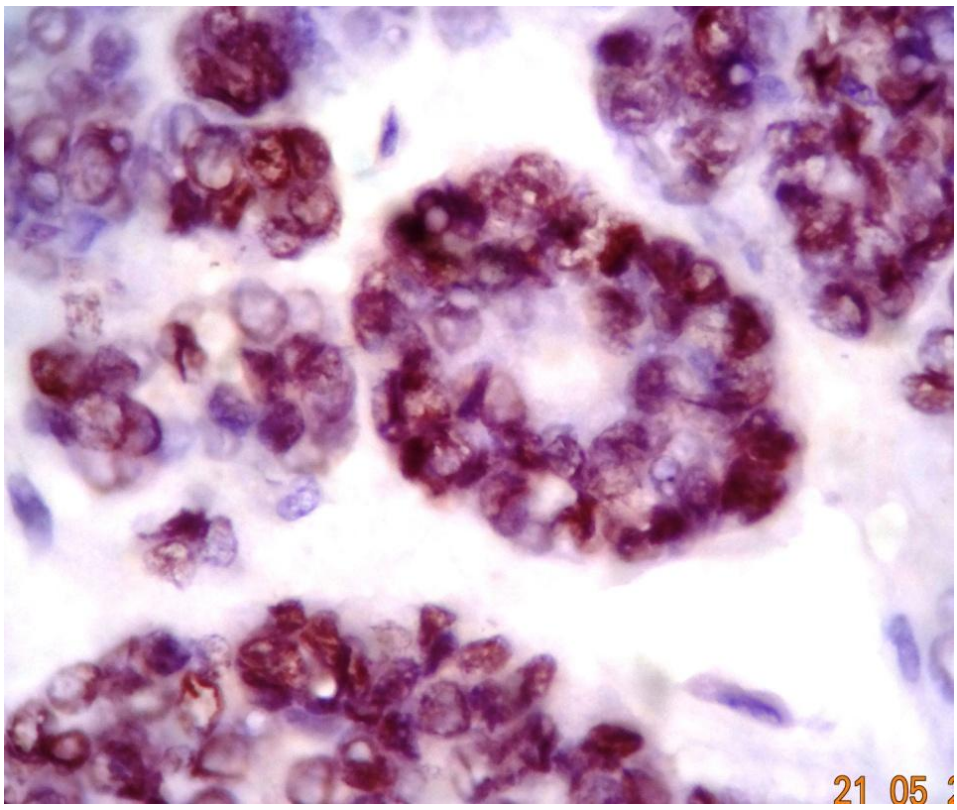


Fig .58 - TTF – 1 immunostain. Nuclear positivity of follicular cells in metastatic follicular carcinoma thyroid . Case 1321/13.

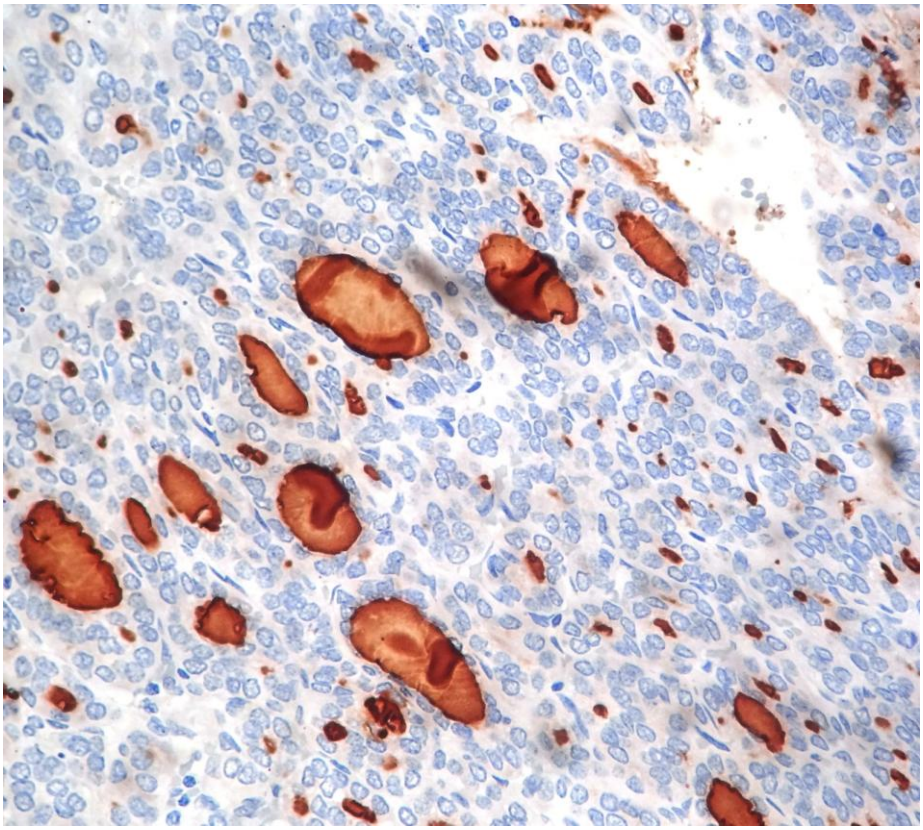


Fig.59 - Thyroglobulin immunostain. Colloid staining positive in metastatic follicular carcinoma thyroid. Case 1321/13.

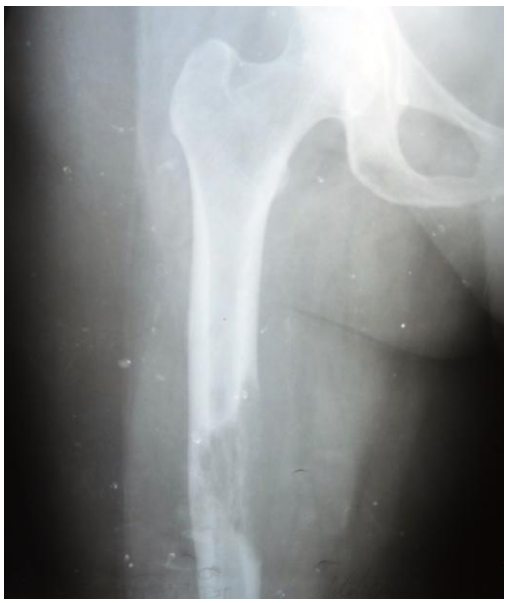


Fig.60 - Carcinomatous deposits in shaft of femur from a primary in the breast in a 39 year old female. X-ray upper thigh in AP view showing permeative lytic destructive lesion of mid – diaphysis of femur with cortical breach. Case 819/13.

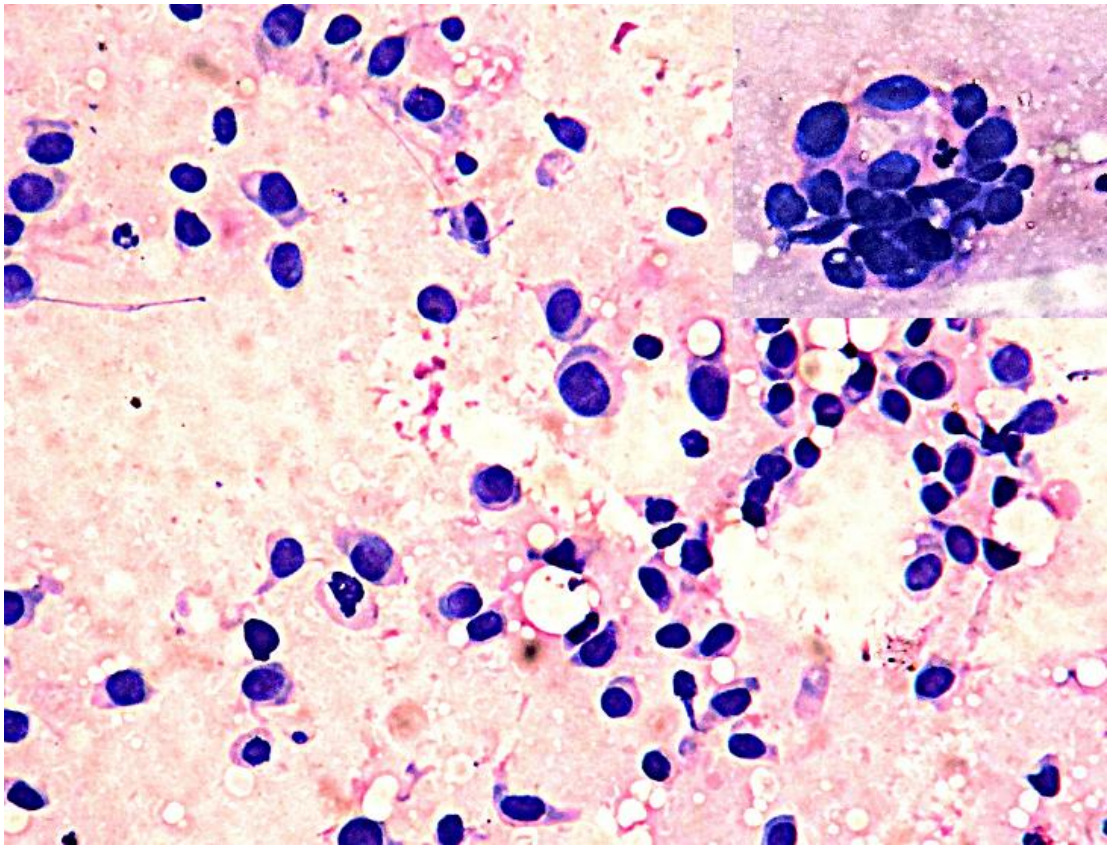


Fig.61 - FNAC from costo-chondral metastatic deposits of breast carcinoma. Scattered and clusters of pleomorphic tumour cells. Inset shows ductal pattern of arrangement of tumour cells. (H&E x 400) Case Cy 230/13.

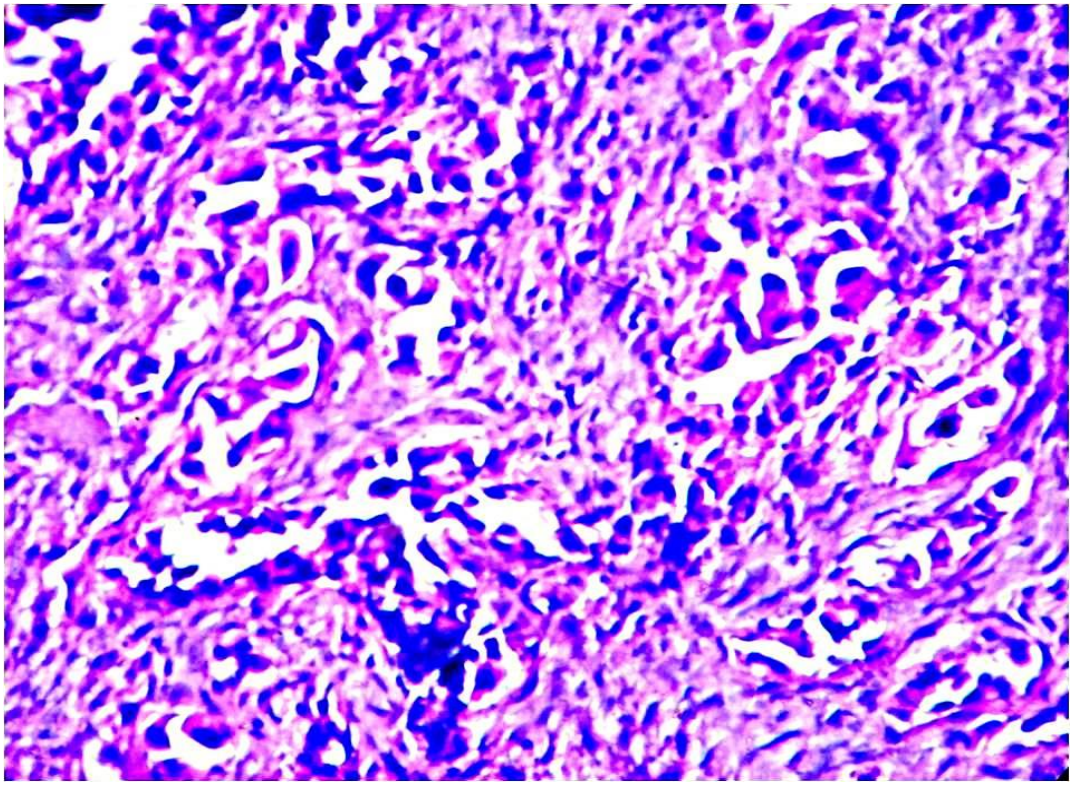


Fig.62 - Metastatic adenocarcinomatous deposits. Bony trabeculae infiltrated by nests and cords of pleomorphic tumour cells. (H&E x400) Case 819/13.

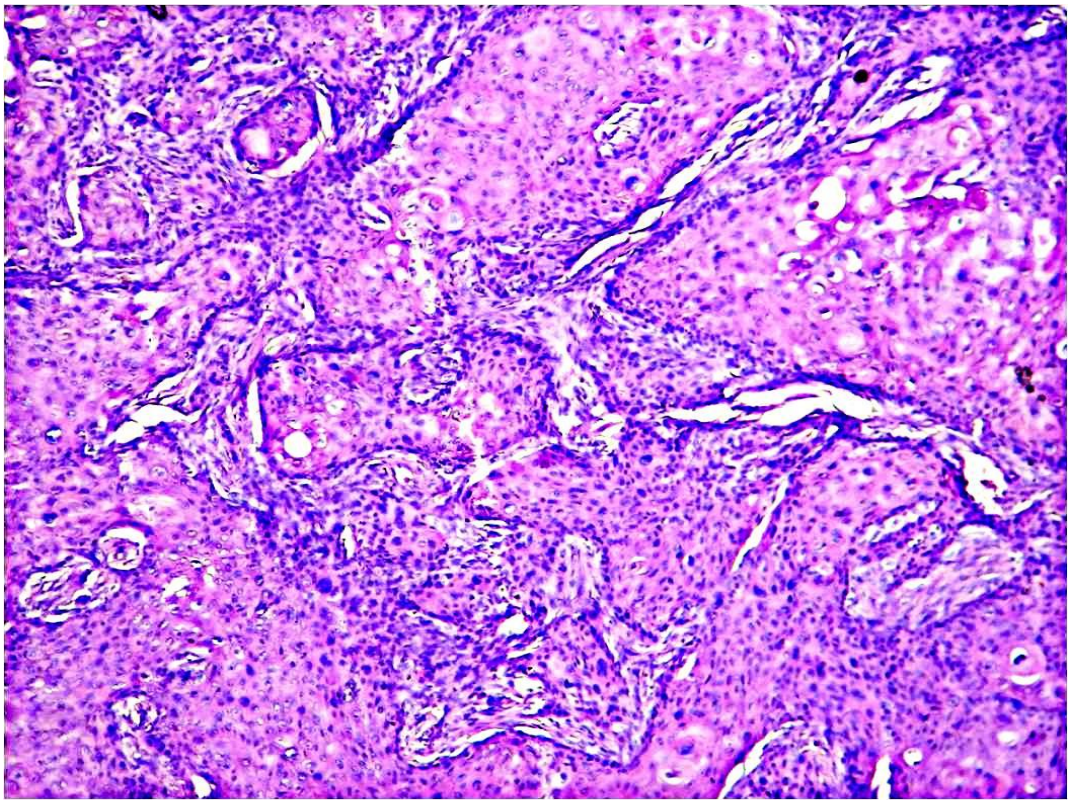


Fig.63 - Metastatic squamous cell carcinoma deposits in the sternum of a 60 year old woman. (H&E x 400) Case 370/13.

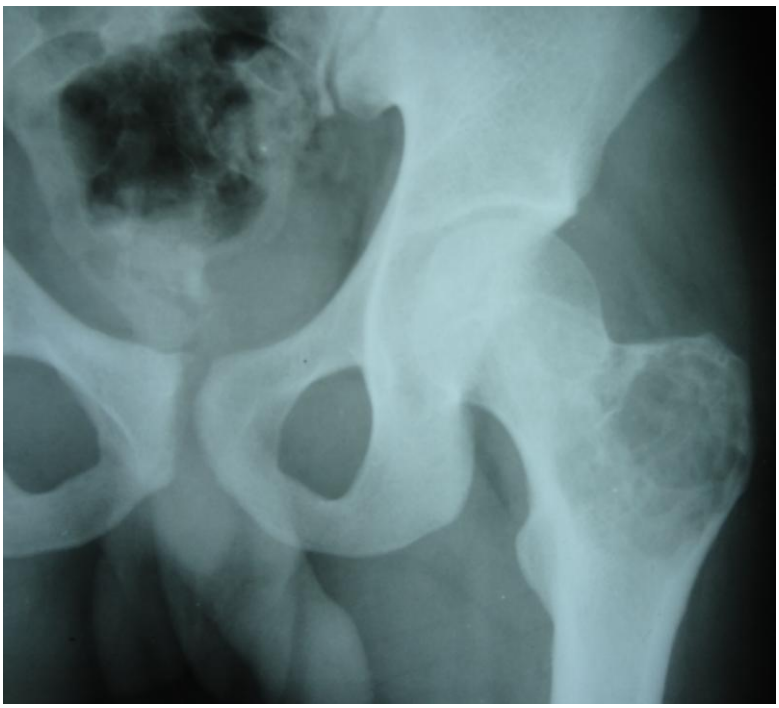


Fig.64 - Aneurysmal Bone Cyst. Plain radiograph. Lytic lesion in greater trochanter of femur. Thin sclerotic rim present. Case 5249/13.

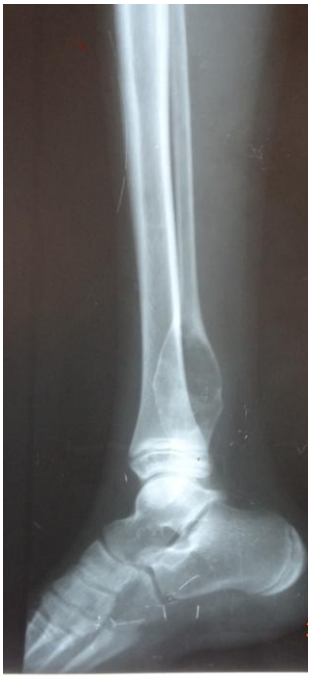


Fig.65 - Aneurysmal Bone Cyst of distal fibula. Plain radiograph, lateral view of lower leg revealing well circumscribed expansile radiolucent lesion in lower metaphysis of fibula with thin ballooned out intact cortex and faintly appreciable internal septations. Case 2035/13.

Fig.66 - Macroscopic appearance of distal fibular resection for ABC. Inset shows cut surface with internal sepate and haemorrhagic material. Case 2035/13.

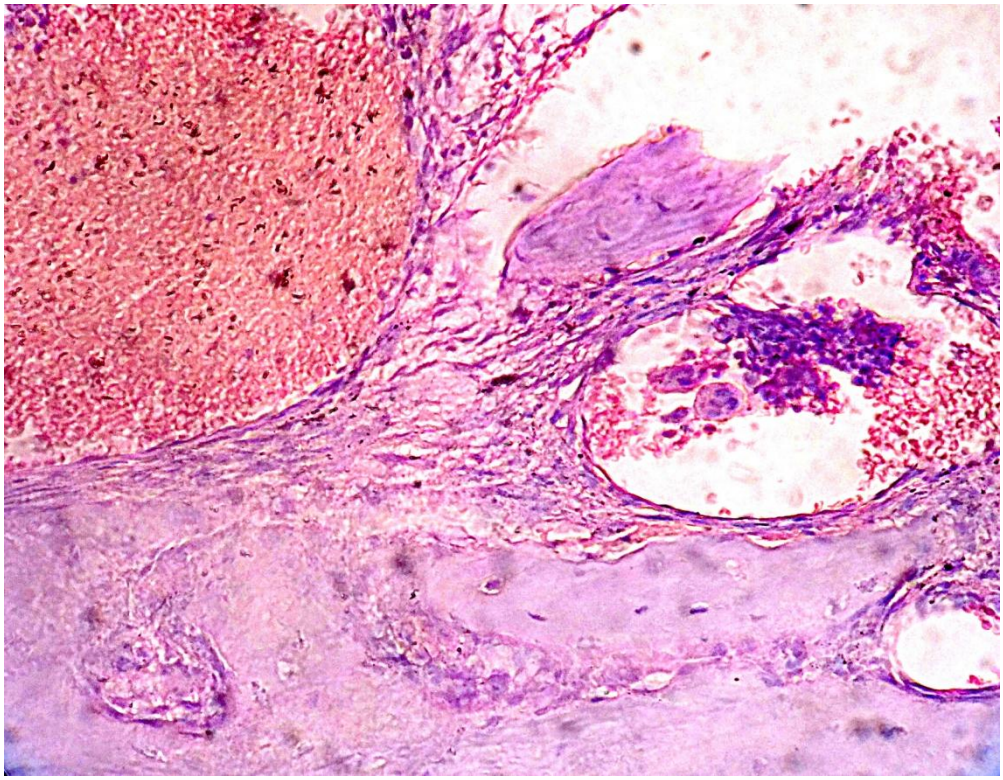


Fig.67 - Aneurysmal Bone Cyst. Cystic spaces separated by septae containing fibroblasts, benign giant cells and immature bone . (H&E x 400) Case 5249/13.

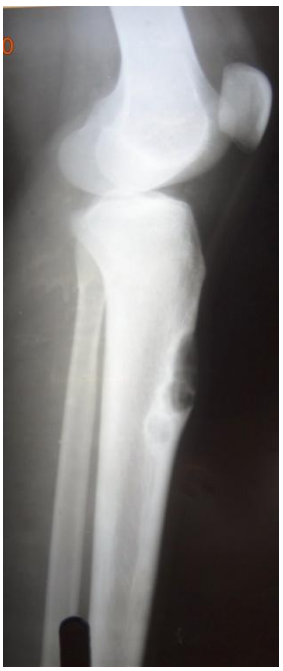


Fig.68 - Osteofibrous dysplasia. Plain radiograph, lateral view of knee joint showing well defined lytic cortical based lesion in the proximal diaphysis of tibia with sclerotic scalloped margins and fine intralesional dense septae. Case 1668/14.

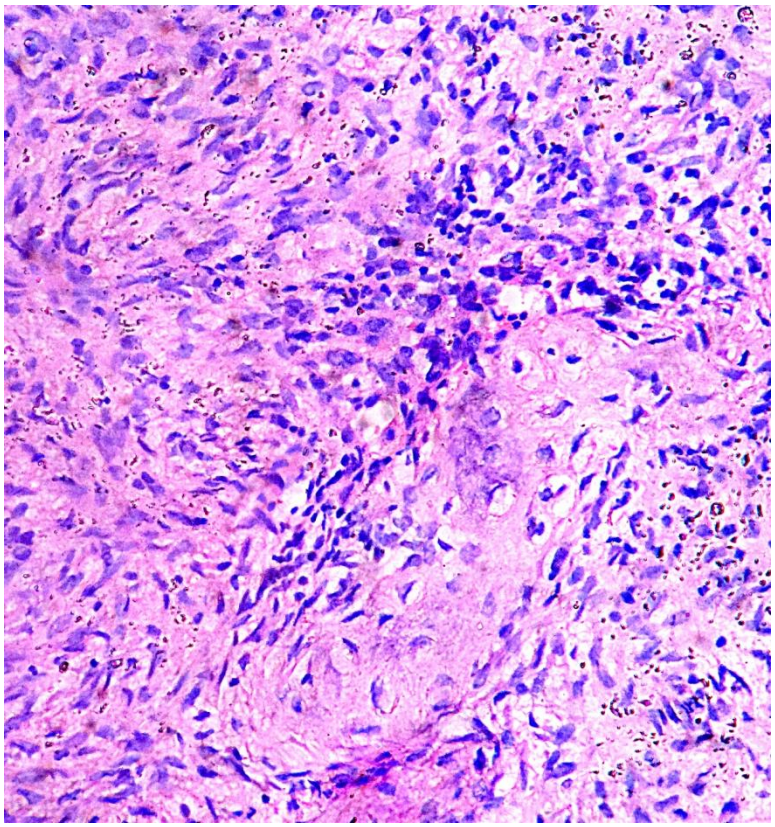


Fig.69 - Osteofibrous dysplasia. Immature bone trabeculae with osteoblastic rimming and surrounding fibrous stroma. (H&E x 400) Case 1668/14.

DISCUSSION

Histological examination of bone tumours is considered to be a challenging field in pathology. Bone tumours and tumour – like lesions are very rare. The low incidence of these tumours and the resulting limited experience in dealing with them adds to the diagnostic difficulties. Clinico – radiological evaluation of bone tumours and tumour – like lesions is an essential part of patient management. Histopathological diagnosis should be given after proper review of clinical and radiological findings. It is difficult to evaluate the precise incidence of bone tumours as many benign lesions may not be biopsied.

This present study had 90 bone tumours and tumour – like lesions. An attempt has been made to categorise the cases and study their histopathology. Age distribution and gender distribution of the cases have been studied. An attempt has also been made to evaluate the level of agreement between clinico - radiological and histopathological diagnosis of bone tumours and tumour – like lesions. FNAC study has been attempted in 15 cases of bone tumours. Immunohistochemical markers have been used to categorise the lesions in case of diagnostic difficulty.

I. BEHAVIOUR OF THE BONE LESION

1) The comparison of data from different studies for classification of bone lesions based on behaviour has been shown in Table 28.

Table 28 - Comparison of data from different studies done on classification of bone lesions based on behaviour

Study	Total cases	Benign		Malignant		Tumour – like lesions	
		No.	%	No.	%	No.	%
Nayar M.[67] (1979)	411	93	22.6	273	66.5%	45	10.9
Chitale A.R.[68] (1987)	1222	300	24.6	642	52.5	280	22.9
S.C. Peh [69] (1988)	209	-	-	188	90	21	10
Rao V.S.[70](1994)	523	235	44.9	206	39.4	82	15.7
Present study (2014)	90	53	58.9	33	36.7	4	4.4

In the present study, benign tumours were most commonly encountered constituting 58.9% of all lesions. These findings were similar to Rao V.S.[70] (44.9%).

Malignant tumours were second most common (36.7%) similar to the observations by Rao V.S.[70] (39.4%).

2) The comparative distribution of benign tumours has been shown in Table 29.

Table 29 - Comparative distribution of benign tumours

Bone tumour	Nayar M[67] (1979) n = 93		Rao V.S.[70] (1994) n = 235		Nidhi V [73] (2012) n = 154		Present study (2014) n = 53	
	No	%	No	%	No	%	No	%
Osteoid osteoma	3	4.9	15	6.4	5	3.3	4	7.51
Osteoblastoma	1	1.1	2	0.8	5	3.3	1	1.9
Osteochondroma	52	54.3	96	40.7	38	24.7	35	66
Chondroma	9	9.6	6	2.6	19	12.2	1	1.9
Chondroblastoma	8	8.6	13	5.6	5	3.3	0	0
CMF	5	5.4	6	2.6	4	2.5	1	1.9
Hemangioma	2	2.1	6	2.6	2	1.3	0	0
Desmoplastic fibroma	8	8.6	0	0	0	0	0	0
Neurofibroma	5	5.4	0	0	0	0	0	0
GCT	0	0	91	38.7	76	49.4	11	20.8
Total	93	100	235	100	154	100	53	100

The most common benign tumour encountered in the present study was osteochondroma (66%). This result matches with those of Nayar M. (54.3%) and Rao V.S.(40.7%).

Giant cell tumour was the second most common benign tumour in the present study (20.8%) similar to Rao V.S. (38.7%).

3) The comparative distribution of primary malignant bone tumours in different studies has been shown in Table 30.

Table 30 - Comparative distribution of primary malignant bone tumours

Bone tumour	Dorfman HD[74] (1994) n = 2627		Rao VS[70] (1994) n = 206		Katchy KC[75] (2005) n = 76		Present study (2014) n = 22	
	No	%	No	%	No	%	No	%
Osteosarcoma	922	35.9	94	45.7	16	21	11	50
Chondrosarcoma	677	25.8	35	17	6	7.9	2	9.1
Ewing sarcoma	420	16	40	19.4	23	30.3	4	18.3
Myeloma	0	0	12	5.8	19	25	2	9.1
Lymphoma	0	0	13	6.3	5	6.5	1	4.5
Angiosarcoma	36	1.4	1	0.4	0	0	0	0
MFH	149	5.7	0	0	0	0	0	0
Fibrosarcoma	0	0	7	3.4	0	0	0	0
Undifferentiated	32	1.2	0	0	0	0	0	0
Chordoma	221	8.4	4	12	3	3.9	1	4.5
Adamantinoma	6	5.2	0	0	0	0	0	0
Hemangiopericytoma	0	0	0	0	2	2.6	0	0
Malignant GCT	0	0	0	0	0	0	1	4.5
Sarcoma (not otherwise classified)	0	0	0	0	1	1.3	0	0
Total	2627	100	206	100	76	100	22	100

Osteosarcoma was the most common malignancy encountered in the present study (50%). This finding is in concurrence with Dorfman H.D (35.9%) and Rao V.S (45.7%).

The second most common malignancy in the present study was Ewing sarcoma (18.3%). A similar finding was reported by Rao V.S. (19.4%).

One case of malignancy in GCT was diagnosed. A 32 year male , with biopsy proven GCT, presented with pain and swelling in the right humerus for 3 months. He had been treated with curettage and plate fixation for GCT with fracture one year back. Radiology was suggestive of sarcomatous change. FNAC done on the lesion showed groups of malignant spindle cells in a haemorrhagic background. Biopsy from the tumour showed features of telangiectatic osteosarcoma. Subsequently, amputation specimen of right upper limb was received. Even after extensive sampling, giant cell tumour - like areas were not seen.

Hashimoto[76] K et al reported a similar case of malignancy in Giant cell tumour of tibia.

II. AGE DISTRIBUTION OF BONE LESIONS

The youngest patient in this study was a 5 year old boy with osteochondroma of scapula and the oldest was a 70 year old lady with metastatic adenocarcinomatous deposits in the femur.

1) The comparison of age distribution of bone lesions is shown in Table 31.

Table 31- Comparison of age distribution of bone lesions

Age Group	Nayar M.[67](1979)		Present study (2014)	
	Number	%	Number	%
1st decade	58	14.1	9	10
2nd decade	155	37.7	41	45.6
3rd decade	94	22.9	11	12.2
4th decade	59	14.3	13	14.5
5th decade	23	5.6	2	2.2
6th decade	15	3.6	7	7.8
7th decade	7	1.8	6	6.6
8th decade	0	0	1	1.1
Total	411	100	90	100

Majority of patients in the present study were in their second decade of life (45.6%). This finding is similar to Nayar M.[67] (1979) who reported 37.7% patients in the second decade.

The occurrence of bone tumours more commonly in the second decade of life probably suggests that adolescents and young adults are more susceptible to bone tumours due to local changes related to rapid growth of bones during adolescent growth spurt[71].

The age group commonly involved in osteosarcoma was second decade of life. In the present study, the average age of patients with metastatic bone tumour deposits was 53 years. This finding correlates well with Rhutso[77] et al and Sirikulchayanonta[78] et al who reported an average age of 50 years.

2) The comparison of distribution of bone tumours in the paediatric age group is shown in Table 32.

Table 32 - Comparison of distribution of bone tumours in the paediatric age group (0 – 18 years)

Bone lesions	Hendrik van den Berg[72] (2005)		Present study (2014)	
	Number	%	Number	%
ABC	101	6.9	1	2.2
Adamantinoma	13	0.9	0	0
Chondroblastoma	22	1.5	0	0
CMF	9	0.6	0	0
Chondroma	137	9.3	0	0
Chondrosarcoma	7	0.5	0	0
Ewing sarcoma	79	5.4	4	8.7
Fibrous dysplasia	85	5.8	0	0
Fibrous histiocytoma	2	0.1	0	0
Fibrosarcoma	5	0.3	0	0
Non-ossifying	48	3.3	0	0
Osteoblastoma	23	1.6	0	0
Osteochondroma	655	44.4	28	60.9
Osteosarcoma	126	8.5	8	17.4
GCT	20	1.4	2	4.3
Solitary bone cyst	54	3.7	0	0
Osteoid osteoma	88	6.0	2	4.3
Osteofibrous	0	0	1	2.2
Total	1474	100	46	100

The most common benign tumour in the paediatric age group in the present study was osteochondroma (60.9%) which is similar to the findings by Hendrik van den Berg[72] (2005).

Osteosarcoma was the most frequently occurring primary malignancy in the paediatric age group (17.4%) in the present study. This is consistent with the findings of Hendrik van den Berg[72] (2005). Ewing sarcoma was the second most common malignant tumour (8.7 %).

III. GENDER DISTRIBUTION OF BONE TUMOURS

1) In the present study, the ratio of male to female patients with bone tumours and tumour – like lesions was 1.78:1. This male preponderance observed is similar to that reported by Baena – Ocampo Ldel C[79].

2) Nearly 75% of all osteosarcomas in the present study occurred in males. This finding correlated well with the findings of Shah[80] S.H. et al.

3) All four cases of osteoid osteoma in the present study were seen in males. This male preponderance seen for the tumour is similar to that reported by Panagotis[81] et al (2:1 ratio).

IV. DISTRIBUTION OF BONE TUMOURS BY SITE OF INVOLVEMENT

1) The most common site of occurrence of bone tumours in the present study was the femur (28.9%) followed by tibia (21.1%).

Thus, the majority of bone tumours occurred around the knee joint. Rhusto[77] et al had similar findings with 30.6% tumours in femur and 29% in tibia.

2) Osteosarcoma showed a predilection for femur with 4 out of 11 cases (36.4%) occurring there. Tibia was the next common site (27.3%). The findings are in concordance with Rhusto et al.

3). 63.6% of all giant cell tumours occurred in the tibia in the present study. Similar preponderance for tibia was noted by Karun Jain[2] et al. There were two cases of recurrent giant cell tumours in this study. One was a 35 year female with recurrent GCT in the distal end of radius after 6 months of initial treatment with curettage. The second case was of a 37 year old male with recurrence of GCT in the proximal tibia after one year of treatment. Resection of proximal tibia with arthrodesis was the treatment given to him.

4). Small bone (metacarpal and phalanx) were involved in 4.4% cases. There was a case of GCT of 4th metacarpal of left hand in a 17 year male treated with ray amputation. Another case was of an enchondroma of third metacarpal of the left hand in a 21 year old female.

5). Flat bones along with sacrum and spine were involved in 17.7% of the cases. There were three cases of osteochondroma in the scapula and one case of chondrosarcoma.

6). Out of the 11 cases of metastatic deposits, 4 were found in the femur comprising 36.4% of the cases. Humerus was involved in 3 cases, sternum in 2 and skull and spine in one case each. Thus, femur was the most common bone with metastatic deposits in the present study. This result is in agreement with Karun Jain[2]. Axial skeleton was involved in 36.3% of all metastatic deposits.

V. CLINICORADIOLOGICAL AND HISTOPATHOLOGICAL AGREEMENT IN DIAGNOSIS OF BONE TUMOURS AND TUMOUR – LIKE LESIONS

Considering all bone lesions together, clinico - radiological diagnosis was confirmed by similar histopathological diagnosis in 85 out of the 90 cases (94.44%).

The histopathological diagnosis was not in agreement with clinico – radiological diagnosis in 5 out of the total of 90 cases.

The corresponding **Cohen's Kappa value calculated was 0.943**. This showed **excellent agreement** between clinico – radiological and histopathological diagnosis of bone tumours and tumour – like lesions in this study.

Comparison of Cohen's Kappa value has been shown in Table 33.

Table 33 - Comparison of Cohen's Kappa value

Study	No. of cases	No of cases with disagreement	Agreement percentage	Cohen's kappa value	Interpretation of Kappa value
Negash[3] et al (2009)	205	33	83.90%	0.82	Excellent agreement
Present study(2014)	90	5	94.44%	0.94	Excellent agreement

Thus, the agreement between clinico – radiological and histopathological diagnosis was similar to the study by Negash et al.

The 5 cases in the present study where clinico – radiological diagnosis and histopathological diagnosis were not in agreement were –

1) A 60 year male presented with swelling and pain in the proximal part of left upper limb for one year. MRI revealed a large expansile lesion over the left humerus in the meta – diaphysis extending to epiphysis. Cortical destruction and pathological fracture were noted. A clinico – radiological diagnosis of lymphoma was offered. The biopsy received in our department showed sheets of plasma cells with many binucleate forms. IHC by CD 138 marker showed strong membrane positivity. A diagnosis of plasma cell myeloma was offered and further biochemical investigations were suggested.

A similar case was reported by Ajit Mahale[82] et al where a lytic lesion of skull base with radiological differential diagnoses of lymphoma and plasmacytoma was finally reported as plasmacytoma by histopathological examination.

Ly JQ[83] et al also reported a case of plasmacytoma of proximal humerus in 2005.

2) A 45 year male presented with swelling and pain in the right side of hip for past 6 months. MRI pelvis showed an expansile bone lesion in the right iliac blade with bone destruction.

A clinico – radiological diagnosis of plasmacytoma was offered. Histopathological examination of the biopsy revealed polymorphic tumour cells with vesicular nucleus arranged in sheets. IHC marker analysis showed strong positivity of tumour cells for CD 45. As the patient had no evidence of disease elsewhere in the body, a final diagnosis of primary lymphoma of bone was made.

3) A 14 year old male presented with pain and swelling in left side of hip for past 3 months. MRI revealed a permeative lytic lesion of left iliac wing and a clinico – radiological diagnosis of Ewing sarcoma was made. However histopathology showed malignant sarcoma cells producing osteoid. A diagnosis of Osteosarcoma was made. Unni[85] K.K. reported that radiating spicules from the cortex of an affected bone may cause difficulty in differentiation of Ewing sarcoma from osteosarcoma especially in a flat bone like ilium.

4) 35 year patient with history of tuberculosis on treatment presented with sudden onset of backpain and difficulty in walking for one week. MRI showed bone and disc destruction at D7 – D8 level. A clinico – radiological diagnosis of tubercular spondylolisthesis was made. The biopsy material received showed sheets of plasma cells with many binucleate forms. A final diagnosis of plasmacytoma was made and further investigation was suggested.

5) 17 year old male patient presented with swelling and pain over dorsum of left hand for 3 months. X ray and MRI revealed an osteolytic lesion involving the left 4^{th} metacarpal with soft tissue extension. A clinico – radiological diagnosis of enchondroma was made. FNAC showed a double population of cells – mononuclear spindle cells and osteoclastic giant cells attached to the periphery of the spindle cell clusters. A provisional diagnosis of GCT was made which was confirmed by histopathology. Ray amputation was done as GCT of small bones has a high rate of recurrence.

Mohammad Shahid[84] et al reported a similar case where GCT of metacarpal was diagnosed as enchondroma by radiology.

The incidence of giant cell tumours in small bones is very less. Unni[85] et al reported an incidence of 1% and Averill[86] et al reported an incidence of 1.5% in their studies.

There is very good agreement between clinico – radiological and histopathological diagnosis in bone tumours and tumour – like lesions. However, discrepancies do exist and an integrated approach involving clinical, radiological and histopathological examination is the gold standard to diagnose bone lesions.

VI. FINE NEEDLE ASPIRATION CYTOLOGY OF BONE TUMOURS

FNAC was performed in 15 cases with clinico – radiological suspicion of bone tumours. The clinical details and radiological findings were reviewed.

The most common diagnosis was giant cell tumour which was diagnosed correctly in all 5 cases with suspicion of GCT. Rana Sherwani[87] et al also reported GCT to be the most common diagnosis by FNAC in their study.

The most common malignant tumour in our study to be diagnosed by FNAC was osteosarcoma. In 5 cases with clinico – radiological suspicion of osteosarcoma, a categorical diagnosis of osteosarcoma was made based on sarcomatous cells and pink amorphous intercellular material consistent with osteoid in 3 cases (60%). This finding is similar to that reported by Wahane[87] et al (63.6%). However, in 2 cases only malignant sarcomatous cells were seen without osteoid. Hence, they were diagnosed as sarcoma, not otherwise specified. Histopathological analysis of biopsy however was diagnostic of osteosarcoma.

A 32 year old patient with history of breast cancer treated 2 years back had presented with swelling in the costochondral junction and FNAC revealed malignant tumour cells arranged in ductal pattern. A diagnosis of metastatic deposits was made.

A 60 year old man with a clinico – radiological diagnosis of lymphoma of humerus was diagnosed as plasma cell lesion by FNAC showing scattered plasma cells with few a binucleate forms. The finding was later confirmed by histopathology.

Out of the 15 cases, 3 samples were inadequate for evaluation. This constituted 20 % of the cases. Handa[89] et al reported a similar percentage of inadequacy (18.2 %).

Sudipta[90]et al reported a very low percentage of inadequate samples (13.7%) and attributed it to repeated attempt of aspiration in difficult cases. They also recommended clinico - radiological correlation to determine the suitable area for aspiration.

Excluding the cases with inadequate sampling, in the present study accurate diagnosis could be given in 10 out of the 12 cases by FNAC (83.3%).

In this era of neoadjuvant chemotherapy and limb salvage surgeries, FNAC can prove to be of great value in diagnosing bone tumours. This is especially true when FNAC diagnosis correlates with clinico – radiological diagnosis.

It can be a cost effective tool obviating the need for open biopsies. However, in cases where cytopathological diagnosis is debatable and not in concurrence with radiology, FNAC cannot substitute histopathological examination.

VII. BONE TUMOUR DIAGNOSIS – THE ROLE OF IHC

In the present study, there were two cases where IHC helped in confirming the histopathological findings.

1). A 50 year female presented to the neurosurgery department with history of swelling in the right side of head and headache for 2 months. MRI revealed a large mass in the right parietal lobe with destruction of the overlying skull bone. A clinico – radiological diagnosis of metastatic deposit involving skull and brain was made. There was no evidence of primary tumour anywhere. Biopsy received showed tumour cells arranged in follicular pattern invading the skull bone and brain parenchyma. At places eosinophilic material resembling colloid was seen. A diagnosis of metastatic deposits was made with a suggestion of primary tumour in thyroid - follicular carcinoma thyroid. IHC analysis revealed malignant follicular cells showing strong nuclear positivity for TTF - 1 (Thyroid transcription factor – 1). Colloid stained strongly with thyroglobulin. On closer examination of the thyroid by ultrasonogram, a small nodule in the thyroid was found which on histopathology showed follicular carcinoma thyroid.

2). The second case was a 45 year old male with tumour of right iliac blade and clinico – radiological diagnosis of plasmacytoma. However, the provisional histopathological diagnosis of lymphoma was confirmed by IHC with CD 45 marker.

IHC is used in bone tumours mainly to differentiate primary tumour from metastatic deposits and to diagnose the primary tumour in case of occult primary. The role of IHC in bone tumours has been discussed by Gao[5] et al and Ushigome[91] et al. Categorisation of small round cell tumours where histopathology is not confirmative, is also an area where IHC plays a major role.

SUMMARY

In the present prospective study of 90 bone tumours and tumour – like lesions evaluated by histopathological examination, Fine Needle Aspiration Cytology and immunohistochemistry, the following results were obtained,

- Bone tumours and tumour - like lesions constituted only 1.03 % of all diagnosed neoplasms during the study period.
- Out of the 90 cases, 86 cases (95.6%) were bone tumours and only 4 cases (4.4%) were tumour-like lesions.
- 53 cases (58.9%) were benign tumours and 33 cases (36.7%) were malignant tumours.
- Among the malignant tumours, 22 cases (66.7%) were primary malignancies of the bone and 11 cases (33.3%) were metastatic deposits.
- Cartilage tumours were the most common constituting 43.3% followed by osteogenic tumours 17.8%. Giant cell tumours and metastatic malignancies constituted 12.2% each.
- Osteochondroma was the most frequently encountered benign tumour constituting 66% followed by Giant cell tumour 20.8%.
- Among the primary malignant tumours of bone, osteosarcoma was the most common (50%) followed by Ewing sarcoma (18.3%). Plasma cell

myeloma and chondrosarcoma constituted 9.7 % each. There was one case each of malignancy in GCT, chordoma and malignant lymphoma.

- Commonest presenting symptom was swelling (63.3%) followed by pain and swelling (13.4%).
- The incidence of bone tumours was maximum in second decade of life (45.6%).
- 51.1% cases were in the paediatric age group (0-18 years).
- Osteochondroma was the most common benign bone tumour in paediatric age group also (60.9%).
- Osteosarcoma was the most common malignant tumour in the paediatric age group (17.4%) followed by Ewing sarcoma (8.7%).
- Bone tumours commonly occurred around the knee joint (23.3%).
- The most common site for bone tumours was the femur (28.9%) followed by tibia (21.1%).
- Involvement of the axial skeleton occurred in 13.3% of the cases.
- Small bone involvement was seen in 4.4% of the cases.
- Osteochondromas occurred in the humerus most commonly (28.6%).

- Osteosarcomas occurred commonly in the distal femur (36.4%) followed by proximal tibia (27.3%) .
- Tibia was the bone most commonly involved by giant cell tumour (63.6).
- Femur was the commonest site of metastatic deposits (36.4%).
- 27.2% of metastatic deposits occurred in the humerus.
- Flat bones including sacrum and spine were the site of metastatic deposits in 17.7% of the cases.
- The average age of patients with metastatic deposits was 53 years.
- Aneurysmal bone cyst was the commonest tumour – like lesion (75%).
- Osteosarcomas (75%) and osteoid osteomas (100%) showed male preponderance.
- Metaphysis was the commonest site involved by bone tumours (48.9%).
- The commonest radiological picture of bone tumours among lytic lesions was of a lytic and poorly defined lesion (20%).
- 85 cases showed agreement between clinico – radiological and histopathological diagnosis. Only 5 cases were in disagreement. The corresponding Cohen's Kappa value was 0.943 which showed excellent agreement between clinico – radiological and histopathological diagnosis.

- FNAC was done in 15 cases of bone tumours out of which three smears were inadequate.
- GCT was the commonest diagnosis given by FNAC (33.3%).
- Categorical diagnosis was correctly rendered in 10 out of 12 cases (83.3%) in which smears were adequate for evaluation.
- Immunohistochemistry was useful in confirming a diagnosis of primary malignant lymphoma of bone and a case of metastatic skull deposits of follicular carcinoma thyroid with occult primary.

CONCLUSION

Histological examination of bone tumours is considered to be a challenging field in pathology. Bone tumours and tumour – like lesions are very rare. The low incidence of these tumours and the resulting limited experience in dealing with them adds to the diagnostic difficulties.

Clinico – radiological evaluation of bone tumours and tumour – like lesions is an essential part of patient management. Histopathological diagnosis should be given after proper review of clinical and radiological findings.

There is very good agreement between clinico – radiological and histopathological diagnosis in bone tumours. However, many benign bone tumours and tumour - like lesions mimic malignant lesions radiologically. Hence, histopathological confirmation of radiological diagnosis should be always done before definitive treatment.

A close co – ordination between the orthopaedician, radiologist and pathologist is the best approach to treat a patient with bone tumours.

In this era of neoadjuvant chemotherapy and limb salvage surgeries, Fine Needle Aspiration Cytology can serve as a good tool for rendering quick and cost effective diagnosis for further management. However, the results of FNAC should be cautiously interpreted and when in doubt, histopathological confirmation should be obtained before treatment.

Immunohistochemistry has its own valuable role in bone tumour diagnosis. It can be a valuable tool in categorising small round cell tumours and determining sites of occult primary in case of metastasis to bone.

Neoplasms of bone are being studied with several new modalities including flow cytometry and cytogenetics[85]. These techniques may prove to be very important in future especially in predicting response to treatment.

ANNEXURE - I

WHO HISTOLOGICAL CLASSIFICATION OF BONE TUMOURS (2002)	
CARTILAGE TUMOURS	**OSTEOGENIC TUMOURS**
OSTEOCHONDROMA	OSTEOID OSTEOMA
CHONDROMA	OSTEOBLASTOMA
ENCHONDROMA	OSTEOSARCOMA
PERIOSTEAL CHONDROMA	*CONVENTIONAL*
MULTIPLE CHONDROMATOSIS	CHONDROBLASTIC
CHONDROBLASTOMA	FIBROBLASTIC
CHONDROMYXOID FIBROMA	OSTEOBLASTIC
CHONDROSARCOMA	*TELANGIECTATIC*
CENTRAL, PRIMARY, SECONDARY	*SMALL CELL*
PERIPHERAL	*LOW GRADE CENTRAL*
DEDIFFERENTIATED	*SECONDARY*
MESENCHYMAL	*PAROSTEAL*
CLEAR CELL	*PERIOSTEAL*
FIBROGENIC TUMOURS	*HIGH GRADE SURFACE*
DESMOLASTIC FIBROMA	**EWING SARCOMA/PRIMITIVE NEUROECTODERMAL TUMOUR**
FIBROSARCOMA	
FIBROHISTIOCYTIC TUMOURS	EWING SARCOMA
BENIGN FIBROUS HISTIOCYTOMA	**NOTOCHORDAL TUMOURS**
MALIGNANT FIBROUS HISTIOCYTOMA	CHORDOMA

HEMATOPOIETIC TUMOURS	**NEURAL TUMOURS**
PLASMA CELL MYELOMA	NEURILEMMOMA
MALIGNANT LYMPHOMA, NOS	**MISCELLANEOUS TUMOURS**
GIANT CELL TUMOUR	ADAMANTINOMA
GIANT CELL TUMOUR	METASTATIC MALIGNANCY
MALIGNANCY IN GCT	**MISCELLANEOUS LESIONS**
VASCULAR TUMOURS	ANEURYSMAL BONE CYST
HEMANGIOMA	SIMPLE CYST
ANGIOSARCOMA	FIBROUS DYSPLASIA
SMOOTH MUSCLE TUMOURS	OSTEOFIBROUS DYSPLASIA
LEIOMYOMA	LANGERHANS CELL HISTIOCYTOSIS
LEIOMYOSARCOMA	ERDHEIM – CHESTER DISEASE
LIPOGENIC TUMOURS	CHEST WALL HAMARTOMA
LIPOMA	**JOINT LESIONS**
LIPOSARCOMA	SYNOVIAL CHONDROMATOSIS

ANNEXURE - II

PROFORMA

A STUDY OF AGREEMENT BETWEEN CLINICORADIOLOGICAL AND HISTOPATHOLOGICAL DIAGNOSIS OF BONE TUMOURS AND TUMOUR-LIKE LESIONS WITH FNAC STUDY IN SELECTED CASES

1. Name
2. Age
3. Sex
4. Ip/Op number
5. Occupation
6. Address
7. Phone number
8. Socioeconomic status
9. Presenting complaints
10. H/o presenting complaints

11. Past history/ Personal history
12. Family history
13. General physical examination
14. Systemic examination
    - CVS
    - RS
    - Per abdomen
    - CNS
15. Lymph nodes
16. Local examination
17. Investigations: Hb % TC DC ESR
18. Relevant Biochemical findings

19. Radiological Findings

X RAY

MRI

CT

- Location – epiphysis, metaphysis, diaphysis, apophysis
- Location – centric, eccentric , juxtacortical
- Periosteal reaction
- Cortical destruction
- Matrix
- Monostotic or polyostotic
- Soft tissue extension
- Any other comments

CLINICO - RADIOLOGICAL IMPRESSION

20. Grossing notes Biopsy number

- Type of specimen – biopsy/ curettage, resection, amputation
- Tumour site – epiphysis, metaphysis , diaphysis, apophysis, medullary cavity, joint involvement, soft tissue extension
- Tumour size
- External surface appearance
- Cut surface appearance

21. Microscopic examination

HISTOPATHOLOGICAL IMPRESSION

22. FNAC diagnosis

ANCILLARY INVESTIGATIONS

23. IHC

FINAL DIAGNOSIS

ANNEXURE – III

Haematoxylin and Eosin staining method

1. Sections were dewaxed with xylene for 20 minutes.

2. Sections were hydrated through descending concentrations (absolute alcohol, 90%, 70%, 50%) of ethanol to water solutions.

3. Sections were rinsed in distilled water.

4. Sections were placed in Ehrlich haematoxylin stain for 20-30 minutes.

5. Sections were rinsed with water.

6. Differentiation was done by immersing the sections in 1% acid alcohol for 10 seconds.

7. Sections were rinsed with water.

8. Blueing was done by keeping the sections in scott's tap water for 2-10 minutes.

9. Counterstaining was done with 1% aqueous eosin for 1-3 minutes.

10. Sections were rinsed with water.

11. Sections were dehydrated through increasing concentrations of ethanol solutions (50%,70%, 95%, absolute alcohol) and cleared with xylene.

12. Sections were mounted with DPX .

ANNEXURE - IV

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ANNEXURE - V

KEY TO MASTER CHART

GENDER

Male – M

Female – F

COMPLAINTS

Swelling – 1

Pain – 2

Swelling and pain – 3

Fracture – 4

Constipation – 5

Pain and difficulty in walking – 6

NUMBER OF SWELLINGS

Single – 1

Multiple – 2

LATERALITY

Right – R

Left – L

SITE

Apophysis – 1

Diaphysis – 2

Epi – metaphysis – 3

Epiphysis – 4

Flat bone – 5

Meta - diaphysis – 6

Metaphysis – 7

BONE

Proximal femur – 1

Shaft of femur – 2

Distal femur – 3

Proximal fibula – 4

Distal fibula – 5

Proximal humerus – 6

Shaft of humerus – 7

Ilium – 8

Metacarpal – 9

Phalanx – 10

Distal radius – 11

Sacrum – 12

Scapula – 13

Skull – 14

Spine – 15

Sternum – 16

Proximal tibia – 17

Shaft of tibia – 18

Distal tibia – 19

Ulna – 20

MACROSCOPY

Amputation – 1

Biopsy – 2

Curettage – 3

Resection – 4

RADIOLOGICAL FINDINGS

Lytic lesion with rim of sclerosis – 1

Lytic lesion with well – defined margins – 2

Lytic lesion with ill – defined margins – 3

Permeative lytic lesion – 4

Sclerotic lesion – 5

Lytic and sclerotic lesion – 6

Lytic lesion with specks of calcification – 7

Pedunculated or sessile lesion with cartilage cap; cortex and marrow in continuity with bone of origin - 8

CLINICO – RADIOLOGICAL DIAGNOSIS / HISTOPATHOLOGICAL DIAGNOSIS/ FNAC DIAGNOSIS

ABC – 1

Chondromyxoid fibroma – 2

Chondrosarcoma – 3

Chordoma – 4

Enchondroma – 5

Ewing Sarcoma – 6

GCT – 7

Malignant GCT – 8

Malignant Lymphoma – 9

Metastatic deposits – 10

Metastatic Adenocarcinoma deposits – 10A

Metastatic Squamous cell carcinoma deposits – 10B

Metastatic Thyroid carcinoma deposits – 10C

Osteoblastoma – 11

Osteochondroma – 12

Osteofibrous Dysplasia – 13

Osteoid osteoma – 14

Osteosarcoma – 15

Plasmacytoma – 16

Pott's Spine – 17

Recurrent GCT - 18

Sarcoma, not otherwise specified – 19

Inadequate for evaluation - 20

NA – Not Applicable

HPE NO – Histopathological Examination Number

Histopath – Histopathological

ANNEXURE – VI A : MASTER CHART

S.NO	AGE	SEX	IP/OP NO	COMPLAINTS	NO OF SWELLINGS	LATERALITY	SITE	BONE	MACROSCOPY	RADIOLOGICAL FINDINGS	CLINICO - RADIOLOGICAL DIAGNOSIS	HPE NO	HISTOPATH DIAGNOSIS
1	17	F	4441	1	2	R	7	3	4	8	12	229/12	12
2	10	M	6031	1	1	R	7	10	4	8	12	271/12	12
3	13	F	26754	1	1	L	7	3	4	8	12	439/12	12
4	70	M	4319	4	NA	L	2	3	2	6	10	579/12	10A
5	12	M	11274	1	1	L	7	4	4	8	12	621/12	12
6	7	F	9241	3	1	R	7	17	2	6	15	669/12	15
7	11	F	9526	1	1	R	7	6	4	8	12	722/12	12
8	15	M	18742	3	1	L	7	3	2	6	15	1082/12	15
9	52	M	20571	4	NA	R	2	7	2	6	10	1202/12	10A
10	10	M	23456	1	1	R	7	3	4	8	12	1283/12	12
11	12	F	26778	1	1	L	7	17	4	8	12	1527/12	12
12	15	M	32136	1	1	R	7	6	4	8	12	1716/12	12
13	18	M	32544	1	1	L	7	4	2	6	15	1721/12	15
14	23	M	26944	1	1	R	7	1	4	8	12	1758/12	12
15	8	M	33682	1	2	L	7	17	4	8	12	1779/12	12
16	10	M	51	1	1	L	7	6	4	8	12	1866/12	12
17	18	M	32195	1	1	R	3	17	2	*3*	7	1875/12	7
18	8	M	54	1	1	R	7	6	4	8	12	1920/12	12
19	25	M	8912	1	1	R	7	6	4	8	12	1928/12	12
20	9	M	36151	1	1	L	7	11	4	8	12	2039/12	12
21	18	M	562	1	1	L	7	3	4	8	12	2045/12	12
22	16	M	38070	1	1	R	7	6	4	8	12	2148/12	12
23	9	M	86	1	1	R	7	6	4	8	12	2253/12	12
24	40	M	57321	1	1	R	4	17	2	3	7	2306/12	7
25	15	M	25345	1	1	R	7	3	4	8	12	2321/12	12
26	15	F	52843	1	1	L	6	1	2	4	6	3030/12	6
27	12	F	124	1	1	L	7	3	4	8	12	3131/12	12
28	19	M	189	1	1	L	7	17	4	8	12	3374/12	12
29	30	M	569770	2	NA	L	2	2	4	5	14	3585/12	14

S.NO	AGE	SEX	IP/OP NO	COMPLAINTS	NO OF SWELLINGS	LATERALITY	SITE	BONE	MACROSCOPY	RADIOLOGICAL FINDINGS	CLINICO - RADIOLOGICAL DIAGNOSIS	HPE NO	HISTOPATH DIAGNOSIS
30	35	F	197	1	1	R	4	11	3	3	7	3645/12	7
31	65	F	74733	3	1	R	6	10	4	7	3	3954/12	3
32	30	M	72183	2	NA	L	3	3	3	1	1	4083/12	1
33	14	M	68156	1	1	R	2	2	2	4	6	4199/12	6
34	13	F	673974	3	1	R	7	17	1	6	15	4202/12	15
35	14	F	97098	1	2	R	7	6	4	8	12	22/13	12
36	15	M	52	2	NA	NA	5	15	4	5	14	343/13	14
37	55	F	53	5	NA	NA	5	12	2	3	4	480/13	4
38	32	F	71008	1	1	R	5	16	2	3	10	495/13	10A
39	60	M	8680	4	NA	L	2	7	2	3	10	705/13	10B
40	39	F	10783	4	NA	R	2	2	2	3	10	819/13	10A
41	15	M	119	3	1	R	7	3	1	6	15	1221/13	15
42	59	F	18363	2	NA	NA	5	15	2	3	10	1267/13	10C
43	50	F	14641	2	NA	NA	5	14	2	3	10	1321/13	10C
44	60	F	20528	3	NA	NA	5	16	2	3	10	1370/13	10B
45	16	M	13840	1	1	L	7	4	4	8	12	1569/13	12
46	13	M	31163	1	1	R	5	8	4	8	12	1839/13	12
47	37	M	242	1	1	L	6	17	4	3	7	1925/13	7
48	9	M	57200625	1	1	R	7	17	4	8	12	2033/13	12
49	11	F	321	1	1	R	7	5	4	1	1	2035/13	1
50	32	M	326	1	1	R	6	6	1	3	8	2206/13	8
51	38	M	116	2	NA	L	7	17	4	5	14	2349/13	14
52	17	M	41704	1	1	L	7	11	2	6	15	2472/13	15
53	*30*	*F*	*414*	*2*	*NA*	*R*	7	*1*	2	*2*	*2*	*2637/13*	*2*
54	*50*	*M*	*387*	*1*	1	*R*	7	*3*	2	6	15	*2875/13*	15
55	18	M	441	1	1	L	5	8	4	8	12	2962/13	12
56	6	F	395	4	NA	L	2	1	2	4	6	3008/13	6
57	17	M	471	3	1	R	7	17	2	6	15	3018/13	15
58	19	M	43543	1	2	L	7	17	4	8	12	3031/13	12
59	16	M	53114	1	1	R	5	8	2	4	6	3231/13	6

S.NO	AGE	SEX	IP/OP NO	COMPLAINTS	NO OF SWELLINGS	LATERALITY	SITE	BONE	MACROSCOPY	RADIOLOGICAL FINDINGS	CLINICO - RADIOLOGICAL DIAGNOSIS	HPE NO	HISTOPATH DIAGNOSIS
60	65	M	18251	1	1	L	7	17	4	8	12	3286/13	12
61	17	M	24755	1	1	L	5	13	4	8	12	3544/13	12
62	35	F	4467	6	NA	NA	5	15	2	3	17	4061/13	16
63	17	M	678	1	1	L	3	9	1	3	5	4552/13	7
64	37	M	744	1	1	L	4	19	2	2	7	4673/13	7
65	19	M	43762	1	1	L	7	1	3	2	11	5048/13	11
66	21	F	821	3	1	L	6	9	4	2	5	5068/13	5
67	26	M	86934	2	NA	L	1	1	2	1	1	5249/13	1
68	60	M	805	3	1	L	6	6	2	3	9	5408/13	16
69	60	F	87193	4	NA	L	2	2	2	3	10	007/14	10B
70	15	M	62	1	1	R	7	11	4	8	12	152/14	12
71	45	M	845	1	1	R	5	8	2	3	16	186/14	9
72	28	M	21	1	1	L	4	20	2	2	7	471/14	7
73	25	M	55	1	2	R	7	6	4	8	12	808/14	12
74	23	F	4873	1	1	R	7	3	4	8	12	829/14	12
75	18	F	3205	2	NA	L	6	17	2	2	13	1668/14	13
76	50	F	2441	4	NA	L	2	2	2	3	10	1726/14	10B
77	20	F	3391	4	NA	R	7	3	2	6	15	1732/14	15
78	14	M	3587	3	1	L	5	8	2	4	6	1830/14	15
79	11	M	3948	1	1	R	7	6	4	8	12	1837/14	12
80	24	F	2909	1	1	L	4	3	3	2	7	1978/14	7
81	5	M	3596	1	1	L	5	13	4	8	12	1986/14	12
82	6	M	3558	2	NA	L	2	18	4	1	14	1995/14	14
83	15	M	28932	1	1	L	7	3	4	8	12	2226/14	12
84	12	M	2546	1	1	R	5	13	4	8	12	2272/14	12
85	20	M	4223	1	1	R	4	17	3	2	7	2283/14	7
86	19	F	12981	1	1	L	3	17	2	2	7	2506/14	7
87	31	F	41187	3	1	R	5	13	4	7	3	2903/14	3
88	33	F	8984	1	1	L	4	17	2	2	7	3080/14	7
89	50	F	7562	4	NA	L	6	6	2	6	10	3144/14	10A
90	20	M	9410	3	1	L	7	6	2	6	15	3177/14	15

ANNEXURE VI B – MASTER CHART FOR FNAC CASES

S.NO	AGE IN YRS	SEX	IP/OP NO.	COMPLAINTS	LATERALITY	SITE	BONE	CLINICO - RADIOLOGICAL DIAGNOSIS	HPE NO	HISTOPATH DIAGNOSIS	FNAC NO	FNAC DIAGNOSIS
1	7	F	9241	3	R	7	17	15	669/12	15	Cy 155/12	20
2	13	F	673974	3	R	7	17	15	4202/12	15	Cy 952/12	19
3	55	F	53	5	NA	5	12	4	480/13	4	Cy 154/13	20
4	32	F	71008	1	R	5	16	10	495/13	10A	Cy 230/13	10A
5	15	M	119	3	R	7	3	15	1221/13	15	Cy 417/13	15
6	37	M	242	1	L	6	17	7	1925/13	7	Cy 756/13	7
7	18	M	32195	1	R	3	17	7	1875/12	7	Cy 985/12	7
8	32	M	326	1	R	6	6	8	2206/13	8	Cy1065/13	19
9	60	M	805	3	L	6	6	3	5408/13	16	Cy 1104/13	16
10	17	M	41704	1	L	7	11	15	2472/13	15	Cy1159/13	15
11	6	F	395	4	L	2	1	6	3008/13	6	Cy1284/13	20
12	17	M	471	3	R	7	17	15	3018/13	15	Cy 1461/13	15
13	17	M	678	1	L	3	9	7	4552/13	7	Cy 2043/13	7
14	37	M	744	1	L	4	19	7	4673/13	7	Cy 2299/13	7
15	28	M	21	1	L	4	20	7	471/14	7	Cy 2537/13	7

ANNEXURE - VII

LIST OF ABBREVIATIONS

ABC	-	Aneurysmal Bone Cyst
CT	-	Computed Tomography
CVS	-	Cardiovascular System
CMF	-	Chondromyxoid Fibroma
CNS	-	Central Nervous System
FNAC	-	Fine Needle Aspiration Cytology
GCT	-	Giant Cell Tumour
H&E	-	Haematoxylin and Eosin
IHC	-	Immunohistochemistry
LCH	-	Langerhans Cell Histiocytosis
MFH	-	Malignant Fibrous Histiocytoma
NOF	-	Non Ossifying Fibroma
MRI	-	Magnetic Resonance Imaging
NHL	-	Non – Hodgkin Lymphoma
PNET	-	Primitive Neuroectodermal Tumour
RS	-	Respiratory System
WHO	-	World Health Organisation

ANNEXURE - VIII

INSTITUTION ETHICAL COMMITTEE APPROVAL

Ref. No. 20735/E4/2/2013 **Govt. Rajaji Hospital,**
Madurai.20. Dated: 20.12.2013

Institutional Review Board / Independent Ethics Committee.
Dr. N. Mohan, M.S., F.I.C.S., F.A.I.S.,
Dean, Madurai Medical College &
Govt Rajaji Hospital, Madurai 625020. **Convenor**

Sub: Establishment-Govt. Rajaji Hospital, Madurai-20-
Ethics committee-Meeting Minutes- for November 2013
Approved list -regarding.

The Ethics Committee meeting of the Govt. Rajaji Hospital, Madurai was held on 18.11.2013, Monday at 10.00 am to 12.00.noon at the Anaethesia Seminar Hall, Govt. Rajaji Hospital, Madurai. The following members of the committee have attended the meeting.

1.Dr. V. Nagarajan, M.D., D.M (Neuro) Ph: 0452-2629629 Cell.No 9843052029	Professor of Neurology (Retired) D.No.72, Vakkil New Street, Simmakkal, Madurai -1	Chairman
2. Dr.Mohan Prasad , M.S M.Ch Cell.No.9843050822 (Oncology)	Professor & H.O.D of Surgical Oncology(Retired) D.No.72, West Avani Moola Street, Madurai -1	Member Secretary
3. Dr. I. Jeyaraj, M.S., (Anatomy) Cell.No 9566211947	Director & Professor Institute of Anatomy /V.P Madurai Medical College	Member
4. Dr. Parameswari M.D (Pharmacology) Cell.No.9994026056	Director of Pharmacology Madurai Medical College	Member
5. Dr.S. Vadivel Murugan, MD., (Gen.Medicine) Cell.No 9566543048	Professor of Medicine Madurai Medical College	Member
6. Dr.S. Meenakshi Sundaram, MS (Gen.Surgery) Cell.No 9842138031	Professor & H.O.D of Surgery i/c Madurai Medical College	Member
7. Mrs. Mercy Immaculate Rubalatha, M.A., Med., Cell. No. 9367792650	50/5, Corporation Officer's quarters, Gandhi Museum Road, Thamukam, Madurai-20	Member
8. Thiru..Pala. .Ramasamy , BA.,B.L., Cell.No 9842165127	Advocate, D.No.72.Palam Station Road, Sellur, Madurai -2	Member
9. Thiru. P.K.M. Chelliah ,B.A Cell.No 9894349599	Businessman, 21 Jawahar Street, Gandhi Nagar, Madurai-20	Member

The following Project was approved by the committee

..2..

Name of P.G.	Course	Name of the Project	Remarks
Dr. G. Shubha	PG in M.D., Pathology, Madurai Medical College, Madurai-20.	Clinical, radiological and histopathological correlation in diagnosis of bone tumours with FNAC correlation and immunohistochemical marker study in selected cases.	Approved

Please note that the investigator should adhere the following: She/He should get a detailed informed consent from the patients/participants and maintain it Confidentially.

1. She/He should carry out the work without detrimental to regular activities as well as without extra expenditure to the institution or to Government.
2. She/He should inform the institution Ethical Committee, in case of any change of study procedure, site and investigation or guide.
3. She/He should not deviate the area of the work for which applied for Ethical clearance. She/He should inform the IEC immediately, in case of any adverse events or Serious adverse reactions.
4. She/He should abide to the rules and regulations of the institution.
5. She/He should complete the work within the specific period and if any Extension of time is required He/She should apply for permission again and do the work.
6. She/He should submit the summary of the work to the Ethical Committee on Completion of the work.
7. She/He should not claim any funds from the institution while doing the work or on completion.
8. She/He should understand that the members of IEC have the right to monitor the work with prior intimation.

Member Secretary **Chairman**
Ethical Committee

DEAN/Convenor
Govt. Rajaji Hospital,
Madurai- 20.

20/12/13

To
The above Applicants
-thro. Head of the Department concerned

ANNEXURE – IX

ANTI – PLAGIARISM CERTIFICATE

A STUDY OF AGREEMENT BETWEEN CLINICORADIOLOGICAL AND HISTOPATHOLOGICAL DIAGNOSIS OF BONE TUMOURS AND TUMOUR – LIKE LESIONS WITH FNAC STUDY IN SELECTED CASES

DISSERTATION SUBMITTED FOR

M.D.,BRANCH – III

PATHOLOGY

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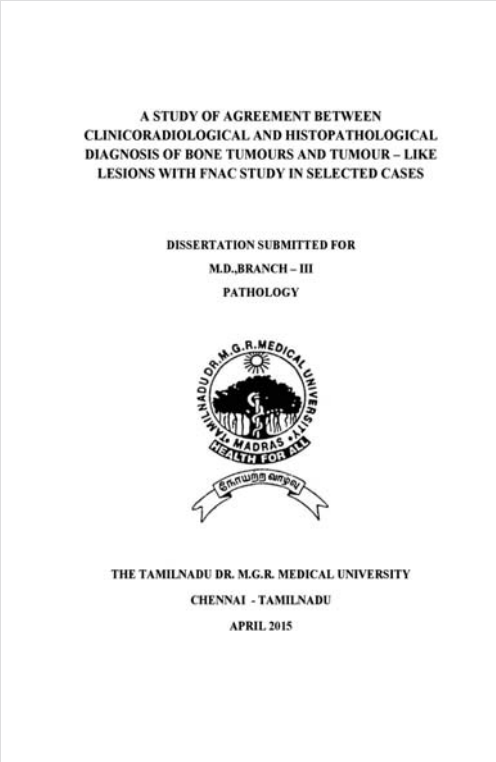

A STUDY OF AGREEMENT BETWEEN
CLINICORADIOLOGICAL AND HISTOPATHOLOGICAL
DIAGNOSIS OF BONE TUMOURS AND TUMOUR – LIKE
LESIONS WITH FNAC STUDY IN SELECTED CASES

DISSERTATION SUBMITTED FOR
M.D.,BRANCH – III
PATHOLOGY

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI - TAMILNADU
APRIL 2015