

**bone neoplasIAs**

**MANUAL OF BONE NEOPLASMS**



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# BONE NEOPLASIAS

## INTRODUCTION

Like other systems in the body, musculoskeletal system may also develop tumors, either as a primary from this system itself or as a secondary from a distant primary location.

The latter appears to be more common.

Some of the tumors are benign and others are malignant.

The accurate diagnosis of a neoplasm is necessary before planning the treatment strategy.

Diagnosis is best established by history, a proper physical examination and investigations like histological examination, biochemical assays, X-ray, CT scan, MRI, bone scans, arteriography, ultrasound, biopsy (both frozen section and permanent paraffin section).

Primary bone tumors may be benign or malignant.

Here is a quick review of the differences between benign and malignant tumors.

Since the cells of the skeletal system are derived from the mesoderm, primary malignant bone tumors are called sarcomas.

Tumors spreading secondarily to the bone are generally primary carcinomas of breast, kidney, thyroid and lung.

These tumors are called metastatic carcinomas because the tissue of origin is ectoderm.

Tumor cells may produce either tumor bone or osteoid (e.g. osteogenic sarcoma) or may cause reactive bone formation.

Periosteal response may also be seen (e.g. Codman’s triangle or onion peel appearance, etc.).

Treatment of benign tumors is usually by excision and if the defect is large, it is packed with bone grafts.

Malignant tumors require a multi-pronged approach in the form of surgery, radiation, chemo therapy, immunotherapy, etc.

With a combination of the above modalities of treatment, the recurrence rate has dropped considerably.

Knowledge of the origin, biologic behavior and treatment of bone tumors is quite incomplete now and much of the information is conflicting and controversial.

## General Principles of Tumors

A proper understanding of the general principles of tumors enables one to make a correct diagnosis, choose the correct line of treatment, which helps to minimize the recurrence rate and improve the survival rate.

The following are the parameters of general principles of tumors.

History

Salient features are:

x Pain, mass, disability is the usual presenting symptoms.

x Anorexia, weight loss and fever are more pronounced in malignant tumors.

x Onset—it is acute in malignant tumors and insidious in benign tumors.

x Age—certain tumors have predilection for certain age groups, e.g. Ewing’s sarcoma has a predilection for children.

TABLE 43.1: Differences between benign and malignant tumors

Benign tumors Malignant tumors

**Clinical Examination**

General examination for evidence of anemia, cachexia, lymphadenopathy.

Local examination to know the extent, plane of the tumor, presence of pathological fractures, etc.

Joint examination to know the involvement of the joint, mechanical effects, etc.

Neurological examination to assess the damage to the peripheral nerves due to the spread of tumor.

Assessment of the status of arterial and/or venous circulation.

**Investigations**

Routine Laboratory Investigation

Hb percentage is decreased, total WBC count and differential count is increased or decreased, ESR is increased, urinalysis.

Serum calcium and phosphorous is increased, serum alkaline phosphatase is increased in tumors like osteogenic sarcoma, serum acid phosphatase is increased in metastatic tumors, etc.

**Special Investigations**

Radiological examination of the part is done in two planes anteroposterior and lateral.

Chest radiographs for evidence of secondaries.

CT scan detects pulmonary metastasis at the earliest.

It picks up the metastasis of the size of 2 mm compared to X-ray, which does so at 2 cm size.

It also helps in cross-sectional study of the tumor.

Arteriography:

This helps to determine the spread of the tumor to the vessel.

#### Ultrasonography:

This helps in some situations, though it has a very limited role.

#### MRI:

This is the most accurate method of assessing the bone and soft tissue involvement.

It also helps in assessing the medullary spread of the tumor.

Bone scans help to detect the extent of spread of bone tumor to other areas of skeletal system and to detect occult bone metastasis.

Biopsy:

This is an ultimate diagnostic technique in diagnosing bone tumors.

Usually, closed biopsies are preferred in malignant tumors.

Needle biopsy has an accuracy rate of over 90 percent in malignant tumors.

If incisional biopsy is chosen, the incision should be placed longitudinally and should not

exceed more than 2 cm.

Types

Types of biopsy

Remember

Tumor biopsy rules

All the above investigations help to stage the bone tumor.

Staging helps in detecting the type of surgical procedures needed for local control of the tumor.

### Enneking’s Staging

Enneking’s staging is based on three criteria, histological grading, anatomical site, presence or absence of regional or distant metastasis.

IA Low-grade: Intracompartmental (lesion confined to single anatomical plane).

IB Low-grade: Extracompartmental (beyond a single compartment).

IIA High-grade: Intracompartmental.

IIB High-grade: Extracompartmental.

III Lesion high- or low-grade: Intra- or extracompartmental with distant or regional metastasis.

The high- or low-grade is a histological grading done based on changes within the cells like pleomorphism, anaplasia, multicellularity, etc. due to malignancy.

0 = benign; 1 = low-grade malignancy; 2 = high-grade malignancy.

### Surgical Techniques

#### Curettage

Many benign bone tumors and locally malignant tumors are treated this way, but it leaves microscopic remnants.

It gives good results if combined with cryosurgery, bone cement, or allograft.

If the lesion is diaphyseal, bone grafting is rarely necessary but if it is epiphyseal or metaphyseal, allografting is necessary.

Since curettage alone is associated with a high rate of recurrence, its role is limited.

#### Resection or Excision

Tumor removing procedures not involving amputation are called as local (limb sparing) excision or resection. It may be any one of the following.

##### Debulking or intralesional excision:

Here excision is done within the lesion.

##### Marginal margins:

Here excision is done through the pseudo capsule, which is a thin rim of fibrous tissue formed

by the surrounding tissues due to the compression, by the tumor mass.

##### Wide margin:

Here the excision is carried out through the surrounding normal tissues.

It is not useful in high-grade tumors because here the spread is along the fascial planes and this method still leaves some metastasis.

Radical resection:

Here all normal tissues of one or more compartments involved are removed from the origin to the insertion.

##### Radical amputation:

Here amputation is done at a high level.

##### Extracorporeal irradiated and reimplantation (ECIR) with composite arthroplasty:

Here autogenous bone graft is either autoclaved or irradiated and re-implanted back combined

with conventional arthroplasty which is fast emerging as an alternative to limb salvage surgery.

##### Choice of the Surgical Procedures

Surgery is usually advocated for local control of the tumor.

Enneking’s staging of the tumor decides the choice of Surgery.

### Adjunctive Therapy

#### Radiotherapy

It should not be used for benign tumors (exception, pigmented villonodular synovitis) for the fear of inducing malignant changes within the cells.

Its role is mainly palliative in non-respectable malignant tumors; but sometimes, it has a definitive role in shrinking the size of the tumor making the surgery less traumatic, and it is also known to make the cells non-viable and thereby minimize the chances of metastasis elsewhere, when these cells get into the circulation during the surgical procedure.

#### Chemotherapy

This is the treatment of choice for micro-metastasis with almost 100 percent cure rate.

If it is given early, it prevents the formation of metastasis.

If given late, it shrinks the size of the tumor and thereby facilitates excision.

It is highly effective against small tumors when given in combinations.

Dosage, sequence, schedule and proper monitoring are matter of extreme importance.

Frequently, a combination of treatment modalities like radiotherapy, chemotherapy, etc. is used along with surgery.

In these cases, less radical surgery is used to achieve local control.

Limb sparing procedures are preferred over amputations.

#### Newer Modalities of Treatment

##### Hyperthermia:

This is usually tried in combinations with radiotherapy or chemotherapy.

Therapeutic embolization:

Embolizing agents like gelfoam, PVA particles, pure alcohol, etc when introduced through a selective catheter placed in an arterial or venous vessel helps achieve thrombus formation and occlusion leading to ischemia and necrosis in the center of bone tumor.

Immunotherapy:

Bacille-Calmette-Guérin (BCG) vaccines are found to be of use in control of certain tumors.

The above three treatment modalities are at an experimental stage and are outside the scope of discussion here.

## Classification of Bone Tumors

Various classifications have been proposed for bone tumors like Dahlin’s classification, Mercer’s classification, Turek’s classification, etc.

The ABC classification of Bristol Bone Tumor Registry proposed by Charles Price is by far the easiest to understand and remember.

## Bone Tumors of Cartilaginous

### Origin

#### OSTEOCHONDROMA (Exostosis)

This is the most common benign bone tumor.

It is an offshoot from the spongy bone tissue covered with a cartilaginous cap (size of the cap may vary from 1–40 cm).

Age: It is common during the growth period.

Sex: It has a male preponderance.

Area:

Location favors the sites of tendinous attachments, which are usually around the metaphysis of long bones in the region of knee, ankle, hip, shoulder and elbow.

#### Theory of Histogenesis

x Though the exact cause is not known various theories have been postulated suggesting the possible mechanism of origin of this tumor.

The cambium layer of the periosteum retains throughout life its ability to

form cartilage and bone.

It may be due to perverted activity of the periosteum that it reverts to its role as the

“perichondrium”.

x At points of tendinous insertion, there is focal

accumulation of embryonic connective tissue.

### Clinical Features

#### Symptoms

Usually, it is symptom less, but the patient may complain of pain, swelling, etc. once complications like bursitis, malignant change, fracture, etc. have developed

#### Signs

A firm nontender swelling fixed to the bone around the joints are the most common clinical finding A bursa if inflamed will give rise to tenderness and local warmth.

Joint movements may be decreased because of the tumor causing a mechanical block rather than the extension of the tumor into the joint.

#### Radiographs

This consists of an outgrowth of bone at the metaphysis.

This attachment is sessile or pedunculated.

The tumor is composed of cortical and medullary portions, which are continuous with the main bone.

The cartilage and capsules are not seen unless it calcifies.

#### Treatment

Usually, it requires no treatment, but complete surgical excision is indicated in the following situations:

Joint interference:

If the tumor is large and obstructing the joint movements, it needs excision of the tumor along with

its periosteal cover to prevent recurrence of the tumor.

Painful bursitis:

A bursa usually develops because of the constant friction between the tumor and the surrounding

soft tissues.

If inflammation develops within this bursa, it gives rise to pain necessitating its excision.

Fracture of the bony stalk may occur due to trauma.

Malignant change (1–2%):

Local irradiation may convert this benign tumor into malignant.

It grows rapidly and has to be excised.

Pressure on the neighboring vessels and nerves may give rise to neurovascular complications.

#### CHONDROMA

(Enchondroma, Hondromyxoma)

This is a benign cartilaginous tumor centrally located when it occurs in phalanges and humerus.

It causes destruction of the cancellous bone and has a potential for undergoing malignant change, especially when it is situated in the long bones.

x Age: 10–50 years.

x Site: Metaphysis is usually involved.

It is common in the phalanges of hand (little finger common) and feet.

Innominate and large long bones may also be involved.

#### Clinical Features

Symptoms are practically none.

There may be slight pain and the phalanx may be enlarged.

The course of the tumor is very slow.

#### Radiographs

The tumor appears cystic (loculated or non-loculated), cortex is thin and expanded, it may be perforated; and at the center, fibrous septa may be seen interspersing the central cavity.

Stippling or calcification may be present.

There is no reactive bone formation.

There could be pathological fracture.

#### Treatment

Curettage is done and the wall is cauterized if the tumor is small.

The surgery done in cases of large tumors is excision and removal of the capsule to prevent recurrence.

Radical resection is done for tumors of long bones and pelvis.

Recurrence is common with chondromas of the long bones.

#### Prognosis

The incidence of malignant change is 25 percent, especially in the pelvis.

Multiple enchondroma AKA (Ollier’s disease)

#### CHONDROBLASTOMA

This is a highly cellular, vascular, and cartilaginous benign bone tumor of the cancellous bone. Here the cancellous bone is destroyed and multiple calcium deposits are usually found within the tumor.

Age: 10–20 years.

Sex: Male preponderance.

Sites: Epiphyseal ends of long bones are commonly affected.

#### Symptoms:

The patient may present with pain, swelling, joint effusion, etc.

#### Radiographs

Radiographic features of the tumor are areas of rarefaction at epiphysis, eccentric position of the tumor, thin cortex and mottled areas of calcification.

#### Treatment

This consists of curettage and bone grafting if the lesion is small, excision in bigger tumors.

If it is accidentally irradiated, it may turn malignant.

Recurrence rate after excision is 25 percent.

#### CHONDROSARCOMA

This is second in frequency to osteosarcoma.

It arises from the cartilage cells.

It is a malignant but slow growing tumor.

It has a long history and a better prognosis.

Unlike osteogenic sarcoma, there is no neoplastic osteoid formation and alkaline phosphatase is usually not raised.

It ranges from being locally aggressive to high-grade malignancy.

### Classification

Primary/secondary: Secondary tumors develop when benign cartilaginous tumors are irradiated.

Peripheral/central/juxtacortical:

Depending on the situation of the tumor within the bone.

Low-medium- and high-grade malignancy depending on the cellularity.

Antecedent Lesions

Location:

It is common at the sites of proximal femur, humerus, ribs, scapula, innominate bones, rare in hands and feet except in calcaneus, occur in pelvis or upper femora.

Sex: Males are more commonly affected than females.

Age: Twenty to sixty years, rare below 20 years, peak in the sixth decade.

#### Clinical Features

The duration of symptoms are usually less than 2 years in 75 percent of the cases and less than 5 years in the remaining 25 percent.

Pain is usually not a prominent feature unlike osteogenic sarcoma.

The central tumor remains entirely asymptomatic until it has eroded and penetrated the cortex or caused a pathological fracture.

A palpable firm mass attached to the bone is the common physical sign.

The tumor may assume large proportion.

#### Radiographs

Central tumors Central lytic lesion with calcification gives a fluffy, cotton wool, popcorn or breadcrumb appearance.

Metaphysis or diaphysis of the long tubular bone is usually affected.

Very rarely epiphysis may be involved.

Greater degree of calcification is observed in slow growing tumors.

It invades the soft tissue, there is little or no periosteal reaction seen.

Peripheral tumors:

These are very large tumors and the central part is heavily calcified.

Juxtacortical tumors are seen adjacent to the cortex.

#### Diagnosis

Biopsy is the only criterion to establish a diagnosis with certainty.

This tumor is notorious for soft tissue seeding during biopsy.

Hence, the biopsy scar should be small and within the area of resection.

#### Treatment

Surgery is the treatment of choice.

Low- and medium- grade lesions: Require wide excision, e.g.

Forequarter amputation (Thikor-Lindberg) for the shoulder girdle; hindquarter amputation for the pelvic girdle.

High-grade lesions: Require radical marginal excision, role of systemic chemotherapy in chondrosarcoma is controversial.

Palliative radiotherapy is indicated when the tumor cannot be resected because of its enormous size or if the tumor is present in inaccessible region.

#### Prognostic Factors

The following factors indicate poor prognosis:

Location: Axial skeleton and proximal portions of the long bones.

Age: More aggressive in childhood and young adults.

Cytological features: Suggesting high-grade malignancy are:

x Increased water and calcium (85%).

x DNA more than 5.5 μg/mg.

x Excess protein more than 350 μg/mg.

x Increased Ch-4-SO4 decreased Ch-6-SO4 (ratio > 1).

x Decreased keratin sulfate.

x Galactosamine/xylose ratio more than 10.

x Hexosamine concentration less than 75 μg/mg.

Size:

Larger the tumor, greater is the chance of malignancy.

Secondary chondrosarcomas are more malignant.

Survival time after treatment is 10 years.

The comparative statistics are as follows after treatment:

x Low-grade tumors have 70 percent survival rate.

x Medium-grade tumors have 50 percent survival rate.

x High-grade tumors have 30 percent survival rate.

Quick Facts in Chondrosarcoma

#### CHONDROMYXOID FIBROMA

This is the least common benign cartilaginous bone tumor.

Age: Young adults in the 2nd and 3rd decade is commonly affected.

Sex: Equal incidence.

Location: Metaphyseal ends of the long bones are commonly involved.

#### Clinical Features

Usually, the patient does not give a history of pain but complains of increasing swelling.

A tender tumor mass may be palpable.

Symptoms are more severe if the tumor develops in patients less than 10 years of age.

Usually, it does not show sarcomatous change or metastasis.

#### Radiographs

Radiographic features show eccentrically located tumor in the metaphysis.

Cortex is expanded, thin and interrupted.

Medullary margins are scalloped and sclerosed; the base of the tumor shows triangular periosteal bone formation.

#### Treatment

The treatment of choice is local excision and bone grafting for small tumors, wide enbloc excision for large tumors.

## OSSEOUS ORIGIN BONE TUMORS

#### OSTEOMA

Osteoma is a benign bone tumor, occurs in membranous bones of skull and face.

Usually, there are very few complaints, the history is long and the finding is a diffuse

bony hard tumor.

It rarely requires treatment.

#### OSTEOID OSTEOMA

This is a benign osteoblastic tumor with a well-demarcated nidus of less than one cm surrounded by a distinct reactive bone.

This tumor presents very interesting clinical features.

It is a tumor of young adults, benign in nature and occurs in enchondral bones.

Age: It is common in young adults between 10 and 25 years of age.

Sex: Male preponderance (M : F = 2 : 1).

Sites: Long bones usually tibia and femur are more commonly affected.

#### Clinical Features

The patient complains of vague and intermittent pain, which is more at night.

The pain dramatically decreases after giving aspirin so much so that this is called the therapeutic test.

The patient also complains of limp due to pain.

There is a mild swelling, the local area may be tender, temperature is not

raised, and the skin is not stretched, shiny or warm.

When the lesion occurs in the spine, the patient presents with acute low backache.

#### Radiographs

It usually shows small-rarefied lesion <2 cm in diameter found in either the cortex, subcortical or sub periosteal regions.

A thick sclerotic bone surrounds it.

A small dense center of ossification seen in the center as the nidus.

Five percent of the cases of sciatica are due to osteoid osteoma.

CT scan and MRI also help in diagnosing this tumor.

Sex: Male preponderance.

When found in females, it starts at an early age.

Incidence: It is 1/75,000 population.

Site: Ninety percent of the tumor occurs in the metaphysial region of the ends of long bones.

It has a predilection around the knee and upper humerus.

It may affect the jaws in the aged.

#### Location

x Fifty-two percent of the cases occur in the femur (9% in

greater trochanter).

x Twenty percent of cases are seen in the tibia (90% in

upper medial aspect).

x Nine percent are seen in the humerus.

It is common in the upper end but rare below the deltoid tubercle.

#### Exciting Factors

The predisposing factors of this tumor are:

Virus

x DNA virus—Polyoma and SV 40 virus.

x RNA virus—Harvey and Moloney mouse sarcoma virus.

These are known to produce tumors in experimental

animals but not known in humans.

Radiation:

If a dose of more than 2000 rads is given to osteoprogenitor cells situated in areas of active growth at the metaphysis, malignancy sets in.

Chemicals:

20-methylcholanthrene, beryllium compounds are known to induce malignancy changes.

#### Treatment

Conservative line of treatment consists of rest to the part and analgesics.

If the tumor is too troublesome, complete excision of the cortex, containing the nidus is sufficient.

Do You Know What is New in the Management of Osteoid Osteoma?

#### OSTEOGENIC SARCOMA

Osteogenic sarcoma is a highly malignant bone tumor.

Here tumor cells invariably form a neoplastic osteoid, bone, or both.

It arises from a common multifactorial mesenchymal tissue; and hence, the tumor could be either fibroblastic, osteoblastic or chondroblastic.

This is the most frequent primary bone tumor next only to multiple myeloma.

Age: It is common in the second decade, rare below 10 years of age, 75 percent of the cases are seen below the age of 25 years.

#### Pathology

The tumor could be either osteoblastic, chondroblastic or fibroblastic.

Consequently, the tumor may be osteo sclerotic or osteolytic. Most common tumor is both a combination of osteosclerotic and osteolytic variety

### Gross:

The tumor is more commonly situated in metaphysis of a large long bone.

It is a large tumor with areas of destruction gives an appearance of leg of mutton.

The consistency ranges from stony hard to soft.

The color of the tumor could be white if the tumor is fibroblastic, yellowish white if osteoblastic; bluish white; if the tumor is cartilaginous.

At the areas of rapid growth, there are necrotic foci, cavitation and hemorrhage.

Sunray appearance is seen in the subperiosteal space due to bone deposition along

the vessels.

Codman’s triangle is a reactive bone formation parallel to the bone and is triangular.

### Histology

Small spindle cells with hyper chromatic nuclei are seen.

The shape may be round, cuboidal or columnar.

Cells are pleomorphic in nature.

Large spindle-shaped cells are rare.

Giant cells are often present.

Matrix may be myxomatous, cartilaginous or osseous.

Areas of hemorrhage may be present.

Normally, when the bone forms an osteoid tissue, it is preceded by the stage of chondrification. Neoplastic or tumor osteoid formed from the primitive malignant cells skip the stage of chondrification and form the ossified tissue directly without any intervening stage of chondrification.

#### Classification

Primary and secondary.

### Dahlin’s (prognostic) classification:

x Osteoblastic: Poor five-year survival rate.

x Chondroblastic: Five-year survival rate is three times

more than that of osteoblastic variety.

x Fibroblastic: Five-year survival rate is two times more of

osteoblastic variety.

### Geschickter and Copeland classification:

x Sclerosing type.

x Osteolytic type.

x Mixed type of both osteoblastic and osteolytic varieties.

x Telangiectatic type.

#### Secondary Osteosarcoma

This is less malignant than the primary, develops in bones affected with Paget’s disease, diaphyseal aclasia, enchondromas, irradiation, etc.

It is more common in older age groups and is treated on the same lines as the primary.

Lichtenstein’s Criteria to Identify Osteogenic Sarcoma

Include the Presence of the Following:

* Sarcomatous stroma
* Spindle cells
* Direct formation of neoplastic osteoid and bones.

Clinical Features

The patient usually presents with pain as the first symptom.

It precedes the tumor, is seen first at night and is intermittent in nature.

History of trauma is a common feature.

The patient complains of tired feeling and limp.

General condition is good until the late stages.

Pyrexia is seen with increased WBCs. the patient is usually anemic than cachetic.

Skin over the tumor is stretched, shiny and mobile.

Local temperature is increased, consistency of the tumor is variable, dilated veins are present (and is evident at an early stage).

### Investigations

#### Laboratory Tests

This shows low Hb percent, raised ESR, lymphocytosis, etc.

#### Plain X-ray

This shows sclerosis or destruction of the bone at the metaphysis.

Other radiological features are Sunrays appearance is seen in the subperiosteal space.

Osteogenic sarcoma showing widespread destruction of the metaphysis, extension into the soft tissue and epiphysis.

The growth plate limits spread to the joint due to bone deposition along the vessels.

Codman’s triangle is a reactive bone formation parallel to the bone and is

triangular.

Plain X-ray of the chest helps to know the chest metastasis.

#### CT Scan and MRI

These reveal more information and helps to study the extent of spread of the tumor within the bone and outside.

#### Frozen Biopsy

This helps to identify the histopathological changes in the tumor.

#### Bone Scan

Bone isotope studies help to detect the metastasis in different bones.

#### Treatment

General Principles

x Early radical amputation is done to remove the primary tumor.

x An attempt is made to prevent metastasis or control it if it has already formed by preoperative irradiation, chemotherapy or both.

x Resection of large pulmonary metastasis is carried out.

#### Surgery

Early and radical ablation is the surgical procedure of choice.

Having first established the diagnosis by biopsy, the level of amputation is determined after carrying out the various investigations mentioned above.

Surgery is done at the earliest possible time.

#### Newer Techniques

x Limb salvage with tumor endopros thesis:

This is showing a better final clinical outcome in recent times.

x In juxta-articular osteogenic sarcoma, intraepiphyseal excision and biological reconstruction to give excellent functional results.

#### Megavoltage Radiotherapy

Megavoltage irradiation is given preoperatively before amputation to decrease the viability of the cells that may be disseminated into blood stream by surgical trauma.

It is a useful adjunct in the treatment of resectable tumors.

Its efficacy is doubtful in the non-resectable tumors, e.g. vertebra.

Irradiation destroys tumor cells with minimal effect on the uninvolved parts.

Preliminaries before Irradiation

#### Chemotherapy (CT)

Role of chemotherapy is as follows:

x After ablation of the primary tumor, it produces a disease-free state for many months.

x If given before the metastasis is apparent, it improves the 5-year survival rate by 60 percent.

x Chemotherapy approach assumes that at least 80 percent of the patients have microscopic foci in the lungs at the time of initial diagnosis.

x Chemotherapy started early after the diagnosis destroys the microscopic foci at a stage when they are most susceptible to the action of chemotherapy drugs.

x It prevents metastasis in 60 percent of the cases.

The remaining 40 percent become disease free due to aggressive attack on the metastasis.

After metastasis has occurred, chemotherapy decreases the tumor size and enables easy surgical removal.

x When the patient refuses amputation, but accepts local resection and implant, chemotherapy decreases the size of the tumor.

Earlier osteogenic sarcoma was refractory to chemotherapy.

Nevertheless, it has now been found that high doses of Methotrexate, Citrovorum factor rescue (CFR) and Adriamycin are effective.

By using the above drugs in short cyclical courses, toxic effects can be held to a minimum. Addition of an alkylating agent, like cyclophosphamide, has increased the interval between the administrations of individual drugs.

This has markedly reduced the toxicity of the drugs.

In summary, after having established the diagnosis of osteogenic sarcoma with certainty, the patient is initially put on chemotherapy.

The role of chemotherapy has already been discussed.

Local irradiation of the tumor is done next.

Early radical surgical ablation is then carried out at the appropriate time.

#### Treatment of Pulmonary Metastasis

Pulmonary micro-emboli are best managed by chemotherapy.

Large lesions require removal by wide resection or lobectomy after giving chemotherapy.

Another experimental approach to manage the lethal metastasis is the immunological approach. The immunological status is increased by giving specific antibiotics, BCG vaccine, and allergenic sarcoma tumor cell vaccine for two years, interferon therapy, etc.

#### Prognosis

Prognosis of osteogenic sarcoma has dramatically improved by the combined approach of ablation, mega voltage irradiation and chemotherapy.

In untreated cases, survival time after pulmonary metastasis has developed (around 2.9%).

With the combined approach of chemotherapy, radiotherapy and pulmonary resection, the five-year survival rate has increased by 60 percent.

Osteogenic sarcoma is curable and warrants intensive treatment with chemotherapy and surgical resection.

## RESORPTIVE BONE TUMORS

These are not true tumors but tumor-like conditions (hamartoma).

These are benign and may cause pathological fractures.

#### ANEURYSMAL BONE CYST

Aneurysmal bone cyst is a benign lesion eccentrically situated in the metaphyseal ends of the long bones.

It grows outwards and is located subperiosteally.

Age: 10–30 years.

Sex: Males are more commonly affected than females.

### Pathology

It is a thin shell of bone enclosing cystic blood-filled spaces.

Partially organized clots remain in the center of the tumor.

Microscopy shows blood-filled spaces.

Giant cells are seen.

#### Clinical Features

The patient usually gives history of mild trauma.

Pain and swelling are the main complaints. Joint movements may be decreased.

#### Radiographs

Radiographic features of the tumor consist of radio lucent area situated at the metaphysis.

It extends outwards eccentrically, periosteal new bone formation is seen, and pathological fractures may be present.

#### Treatment

Surgery is the treatment of choice.

Curettage and bone grafting are the procedure commonly followed.

### UNICAMERAL BONE CYST

Jaffe and Lichtenstein first described unicameral bone cyst in the year 1942.

It is an uncommon, non-neoplastic lesion commonly seen in the first two decades of life.

It is situated in the metaphysis of the long bones and its proximity towards the

epiphysis may affect the growth plate.

Pathological fracture is a common entity.

The cyst will not disappear on its own and remains so unless obliterated by surgery.

Age: Fifty percent lesions are seen in less than 10 years of age, forty percent between 10 and 20 years.

Sex: The male to female ratio is 2:1.

Location: Upper end of humerus in 55 percent, upper end of femur in 26 percent.

#### Pathology

Gross: It is a fusiform swelling, occupying the metaphyseal

region of the bone. The underlying bone is thin with areas

of hemorrhage present.

Microscopy: The cells are flat and vascular tissue is present.

It has characteristic giant cells.

#### Types of Cyst

There are two types of bone cysts:

Active cyst is so called if the cyst is situated close to the epiphyseal plate.

Latent cyst is so called if the cyst moves away from the growth plate.

#### Clinical Features

The tumor is asymptomatic until fracture occurs through the cyst wall, which causes pain and draws the attention of the patient towards the problem. In most cases, the cyst is juxtaepiphyseal. Due to its proximity to the growth plate, the cysts may cause shortening, lengthening, coxa vara or coxa valga deformities.

The tumor weakens the bone and the patient is susceptible to pathological fractures.

Spontaneous obliteration of the cyst is seen in 15 percent of the cases and in 30 percent of the cases, cyst is displaced down the shaft due to continuous bone growth.

#### Radiographs

Radiographic examination of the tumor shows lytic lesion in the juxtaepiphyseal portion of the metaphysis, the lesion is expansive, the regional cortex is attenuated and pathological fractures may be seen.

#### Treatment

Surgical excision is the treatment of choice.

The following are some of the surgical procedures.

#### Types of Surgery

##### Curettage and bone grafting:

This procedure is associated with high rate of recurrence.

##### Subtotal resection and bone grafting here:

1cm of the normal bone above and below the lesion is excised.

Total resection and bone grafting are the other method of treatment.

##### Intracystic injection of corticosteroids:

Steroids injected into the cysts are known to cause obliteration of the cyst 40–80mg of prednisolone for smaller cysts recommended, larger cysts may require 200 mg of prednisolone.

#### Complications

Since the tumor is situated in the juxtaepiphyseal region, complications like shortening, coxa vara, coxa valga and bone overgrowth may develop.

##### GIANT CELL TUMOR (GCT)

(Syn: Osteoclastoma)

### Benign Giant Cell Tumor

Benign giant cell tumor (GCT) is an osteolytic tumor arising from the epiphysis and is common in young adults.

Though it is benign, it is locally malignant.

The presence of tumor giant cells is the hallmark of this tumor.

Sex: The male : female ratio is 1.5 : 1.

Age: It is common between 15 and 35 years (80% occur in more

than 20 years of age and the average age group is 35 years).

Areas affected are asymmetric portions of the epiphysis of long bones.

About 75 percent of GCT occurs in lower end of femur, upper end of tibia, fibula and the distal end of radius.

#### Pathology

#### Gross

The tumor consists of ragged, friable, bleeding tissue filled with old or fresh blood clots with various sized cysts and cavities.

Color varies from red to brown.

Epiphyseal end of the bone is distorted.

Tumor extension into the joint cavity is usually not seen and there is no evidence of periosteal reaction.

#### Microscopy

The tumor is encompassed by a fibrous capsule at the periphery.

Presence of abundant tumor giant cells is quite characteristic.

These cells are characterized by their larger size, multiple nuclei more than 150 in number which are distributed throughout the cell.

Appearance of spindle cells indicates malignant potential.

Histological Grading (Jaffe’s Criterion)

### Clinical Features

The course of the tumor is chronic.

Unlike osteogenic sarcoma, pain is not the presenting feature but trauma is, the patient complains of swelling which is situated on one side of the bone.

Skin over the tumor is stretched, but there are no dilated veins.

Tenderness is mode rate or absent, eggshell crackling sensation may be present or absent. Limitation of joint movements is not seen until the late stages.

There is no increase in joint fluid and the joint is rarely invaded.

Pathological fracture is a late feature.

Radiographs

x An osteolytic area is seen near the epiphysis.

x The cortex is expanded and thin.

x There is no periosteal new bone formation.

x Thin septa of bone traverse the interior and produce a soap-bubble appearance.

x The cortex may be disrupted in late stages.

x Joint extension is rare.

### Campanacci’s radiographic grading:

Grade 1: Cystic lesion.

Grade 2: Cortex is thin but not perforated.

Grade 3: Cortex is perforated with extension into soft tissues.

MRI reveals more accurate information and shows the intramedullary spread and soft tissue involvement.

#### MALIGNANT GIANT CELL TUMOR

### Primary

This develops as a frank sarcomatous lesion.

The swelling is quite gross and show other features of malignancy.

The X-rays show gross destruction of the epiphyseal region of the affected bone.

#### Secondary

This develops at the site of previously treated GCT.

Enneking’s Staging of Benign GCT

#### Treatment of GCT

#### Principles of tumor treatment:

x The tumor is invasive and aggressive.

x It commonly recurs, may become malignant after unsuccessful removal.

x Recurrence is treated with enbloc excision.

x Enbloc excision is also indicated if the tumor has eroded the cortex and extended into the soft tissues.

#### Surgical Methods

Approach that is more aggressive is adopted for lesions that are more aggressive and the surgical methods described are:

Curettage and bone grafting:

It is a simple technique but is associated with high recurrence rate (about 30%).

En bloc excision:

This is the initial procedure of choice and here 2 cm of normal tissue is also excised.

Defects are filled with cancellous bone grafts, freeze-dried allograft or

prosthesis.

This technique has low recurrence rate.

Curettage and acrylic bone cementation:

This has a low rate of recurrence and the heat of polymerization destroys residual stromal and giant cells (0.5 cm).

Curettage and cryosurgery:

This destroys the residual tumor at its margin of curettage by repetitive freezing and thawing

by liquid nitrogen.

Malignancy change rate decreases from 15–1.9 percent.

Excision and reconstruction:

This procedure can be followed for GCT affecting the lower end of femur or upper end of tibia.

After enbloc excision, one of the following methods can do reconstruction.

x Turn-o-plasty technique:

Here after excision of the tumor in the lower end of femur, the required length of the proximal tibia is chosen, split into two halves and one-half of it is turned upside down and fixed with the left-over stump of the femur.

If the lesion is in the tibia, the procedure is done by taking half of the femur.

x Arthrodesis is done by using the fibula from both the

sides to bridge the excised gap.

x Arthroplasty:

After tumor excision, arthroplasty is done either by using an autograft, allograft or prosthesis.

Irradiation therapy induces malignant change if it is given to the benign lesion.

Megavoltage therapy is permissible only for inaccessible lesions located in the spine, sacrum,

pelvis, etc.

The recommended dosage is 1,500–5,000 rads for 5–6 weeks.

### Other Methods

Marginal resection with curettage:

This is done using power burrs with copious irrigation of 5 percent phenol and 70

percent alcohol.

Resection of distal radius and using ipsilateral proximal fibula to reconstruct the wrist joint.

Amputation is done for widespread aggressive tumor as a last resort.

##### Treatment Facts of GCT

Site Surgical option

#### TUMORS OF NONOSSEOUS ORIGIN

## Ewing’s Sarcoma

Ewing’s sarcoma was first described by Ewing in the year 1928.

This is a rare primary malignant bone tumor (10–14% of all malignant bone tumors) affecting children.

It is a lethal tumor with a poor 5-year survival rate.

Age: Persons commonly affected are 4–25 years of age group (about 80%).

Sex: More common in males.

Site: Long bones affected are femur, tibia, fibula and humerus in that order.

About 20 percent of tumors are seen in flat bones.

Location: Diaphysis of the long bones is commonly affected.

#### Pathology

Gross:

It is a grayish white tumor encapsulated by fibrous tissue.

It may contain hemorrhagic foci and areas of cystic formation.

From the medulla, it reaches to the surface through the haversian canals.

Histology

The tumor is very cellular.

The cells may be small, round or polyhedral in shape and may be arranged as cords or sheets.

Intercellular substance is minimal.

Necrosis is common.

Cells are arranged round the vessels justifying the term perithelioma.

Many tumors show Rosette formation with central fibril.

Pseudorosettes are more common (no central fibril).

Giant cells are not found and there is no new bone formation.

Differential diagnosis is between reticulum cell sarcoma and Ewing’s sarcoma:

x Ewing’s stains for glycogen positivity by PAS.

x In reticulum cell sarcoma silver stain is positive.

#### Clinical Features

The patient presents with pain, which is intermittent in nature.

The pain is worse at night.

The tumor is diaphyseal and fixed to the bone, skin is red, dilated veins may be

present.

Sometimes the tumor may present with constitutional symptoms like fever, sweating, chills,

leukocytosis, and anemia.

This may create confusion as it mimics acute osteomyelitis.

##### Course

x Exacerbation and remission is characteristic.

x Blood and lymphatic spread is common.

James Ewing (1866–1943), Oncologist, USA.

It was first described by Ewing in the year 1928.

x Metastasis to other bones like skull, vertebrae, ribs, lungs, etc. may occur.

#### Investigations

Radiographic Features

x The lesion could be lytic, sclerotic or mixed.

x Diaphyseal lesion with irregular destruction (moth-eaten appearance or cracked ice appearance).

x Periosteal reaction is deposited in layers giving an onion peel appearance.

x Permeative margin.

Biopsy

Biopsy is necessary for diagnosis.

Other Tests

x Urine for vanillylmandelic acid (VMA).

x Tissue for glycogen stain.

x Immunohistochemical markers.

x Electron microscopy study.

### Recommended Treatment

This tumor is highly radiosensitive, disappears with radiation

only to recur (melts like snow). Hence, a combination of

local radiotherapy with systemic chemotherapy brings

down the recurrence rate dramatically. Nevertheless, even

this treatment has a recurrence rate of 20–30 percent and

because of the possibility of radiation-induced sarcomas;

surgical resection for the control of the primary lesion is

being used. The surgery planned is conservative in nature

and aims at limb preservation.

#### Effective Chemotherapy

Effective chemotherapy is given using newer chemo therapeutic drugs like Ifosfamide, cisplatinum, epipodophyllin toxin for a short period.

#### Radiation

Radiation is the mainstay of local treatment, especially in axial skeleton.

Dose required is high 4,000 rads for the entire limb and 1000 rads as boost to the tumor.

#### Surgery

Conservative surgery like debulking of the tumor or limb preservation surgery has a role.

Unfavorable prognostic features are:

x Male patients.

x Humerus if involved.

x Pelvic bones if involved.

x Distant metastasis.

Primary irradiation followed by amputation has a two-year survival rate of 15 percent.

A combination of chemotherapy, radiotherapy with surgery improves the survival rate to 50–75 percent for 3–5 years.

#### MULTIPLE MYELOMA

(PLASMACYTOMA)

This is the most common bone tumor in adults.

It accounts for 50 percent of all bone tumors.

Here plasma cells replace the bone.

It affects elderly persons between 40 and 60 years of age.

Sex: Males and females are equally affected.

#### Pathology

Gross:

The tumor is dark red in color, soft in consistency and lies within the medulla.

The cortex is thin and broken.

Microscopy:

It consists of round cells with eccentrically placed nucleus with nucleolus.

The chromatin is sparse and is arranged in “spokes of wheel fashion”.

Perinuclear halo typical of plasma cells is not seen in multiple myeloma.

#### Associated pathology

x Interstitial fibrosis in the kidney.

x Nodules in the lungs.

x Amyloidosis may occur (in 10–15%).

### Clinical Features

Tumor runs a chronic course.

It is silent at first; later on, the patient complains of vague pain, which is mild and intermittent in the beginning.

It also affects lumbar spine, sacral region, chest and ribs.

Severe attacks of sharp pain, superimposed at intervals may develop.

Often, the patient may complain of a diffuse, persistent, backache.

### Findings

In the early stages, there are hardly any clinical findings.

Later on, the patient may complain of soft tissue swelling in about 10 percent of cases.

Signs of pathological fracture are present in about 20 percent of cases.

The sternum and ribs may be tender and there may be signs of vertebral collapse.

#### Course:

The tumor is chronic, later the marrow replacement causes anemia, thrombocytopenia and hemorrhages.

Renal failure due to tubular block by protein casts may also be seen (myeloma kidney).

#### Investigations

Laboratory Findings

x Bence Jones protein is found in only 30 percent of the

cases.

On boiling, a white precipitate appears at 50°C, dissolves at boiling point after acidifying the urine; on cooling, the precipitate reappears.

x Serum globulin is increased.

x Hypercalcemia.

x ESR is increased (sludged blood).

x Low alkaline phosphatase is seen despite extensive bone destruction or it may be normal.

x Marrow biopsy reveals anemia, is refractory to iron, B12, folic acid, etc.

#### Radiographs

The affected bones show diffuse osteoporosis or lytic lesions.

Biconcave vertebral bodies and collapse of vertebra.

Punched-out lesions in skull and pelvis are the characteristic findings in the X-rays.

Typical Lesions

x Osteolytic lesion penetrates the cortex, but there is no periosteal reaction.

x Rarefaction of vertebrae may be extensive (disappearing vertebrae), vertebral pedicle involvement is more common, when involved it is called as the “pedicle sign” (common in secondaries).

MRI

MRI helps in more accurate assessment of the extent and spread of the tumor.

##### Treatment

When the tumor is widespread, it is usually fatal and then treatment is only palliative.

The tumor is radio sensitive.

Chemotherapy

Agents like steroids, cyclophosphamide, urethane and melphalan (SCUM) are found to be effective.

What is New?

Surgery

x Laminectomy is done when there is evidence of compression of spinal nerves.

x Intramedullary fixation is done for pathological fractures of long bones.

#### Prognosis

x The disease is widespread and fatal.

x Death occurs within three years in majority of cases and in all by five years.

#### Complications

x Pathological fracture of the ribs.

x Spinal cord or nerve root compression.

x Anemia, leukopenia, thrombocytopenia.

x Renal failure.

x Severe infection.

x Amyloidosis.

#### METASTATIC TUMORS OF BONE

### Definition

These are cancerous tumors originating in other organs and involving the skeletal structures of the body.

Bones may be involved by:

x Direct invasion.

x Blood-borne metastasis (most common route).

x Very-rarely through the lymphatic.

Blood-borne metastases to the bone greatly outnumber the primary bone tumors.

Incidence is 27–70 percent.

Tendency Percentagewise

Sites: The secondary bone tumors commonly involve vertebrae, ribs, pelvis, sternum, skull and proximal ends of femur and humerus.

It is unusual for metastatic neoplasm is to involve bones distal to the elbows or knees.

### Occurs in Three Clinical Settings

x Pain in the spine or extremity without a known history of primary tumor (rare).

x Pathological fracture with or without known primary.

x The third and most common is a patient with a known primary tumor with a painful lesion in the spine or extremities.

##### Clinical Features

The patient is usually an adult, in the middle or late life, and may present with pain, pathological fracture or anemia.

The patient complains of headache if the skull is involved.

Spine involvement causes girdle pains, spastic paralysis.

Pathological fractures are frequent in femur.

Collapse of vertebrae may be present.

#### Laboratory Diagnosis

x Blood picture may be normal or bizarre showing features of anemia, thrombocytopenia or thrombocytosis, leukocytosis or leukopenia, eosinophilia, etc.

x Sometimes, anemia is associated with leuko-erythroblastic reaction.

x Sometimes, a syndrome of hemolytic anemia, thrombocytopenia, and fibrinogenopenia can be seen with cancer of stomach and pancreas.

x Alkaline phosphatase is increased normally, but acid phosphatase increases in cancer of prostate.

#### Other Investigations

Radiographs

Radiographs fail to detect secondary in the bone in 20–25 percent of the cases.

Two types are recognized:

x Osteolytic variety is frequent.

x Osteoblastic variety shows increased density (cancer prostate).

Periosteal reaction and mottled or marble appearance are the other radiographic features.

#### Bone Scan

This is the most sensitive method of investigation.

MRI, PET scan helps to assess the extent and spread of the metastasis.

#### Biopsy

Fine needle biopsy is accurate in over 90 percent of the cases.

#### Treatment

The following are the various modalities of treatment.

Radiotherapy is by 60Co 3000–4000 rads for 3–4 weeks.

Surgery:

If the patient has developed pathological fracture, internal fixation with acrylic cement is done. Decompressive laminectomy is done for secondary in the spine.

Endocrine surgery for cancer breast, cancer prostate.

### Hormone therapy

x For prostatic cancer, estrogen.

x For breast cancer, diethylstilbestrol.

x For thyroid cancer, T3 and 131I.

Radioisotope therapy is by using

x Radioactive phosphorus.

x Radioactive 131I.

Chemotherapy is by using drugs like alkylating agents, antimetabolites.

Treatment of hypercalcemia is by using cortisone, mithramycin.

Amputation is indicated for intractable pain and as a last resort.

Prophylactic nailing is considered for those cases with more than 50 percent destruction of the cortex.

What is New?

Radiofrequency ablation (RFA)

#### INCLUSION TUMORS

##### SYNOVIOMA (Synovial Sarcoma)

Definition

Synovioma is a slowly growing malignant tumor occurring in juxtaposition to and attached to the synovial tissue but almost invariably lies outside the joint.

#### Pathology

It is difficult to find the synovial attachment of the tumor.

The tumor may be circumscribed, rounded, lobulated, and may be surrounded by a pseudocapsule. The tumor lies closely to the tendons, bursa and joint capsules.

### Microscopy

Three basic patterns indicate synovial origin:

1. formation of tissue spaces,
2. formation of cell tufts, and
3. the presence of epithelial cell tufts.

Evidence of malignancy is seen in fibro sarcomatous stroma.

#### Clinical Features

This is a tumor of young adults, rare in people more than 40 years of age, common in the lower extremity, around the knee.

Soft tissue outside the joint is involved, painful swelling, slowly increasing in size, firm or soft and tender.

Restriction of joint movements may be seen.

Course:

The course is very slow, metastasis is eventually into the lungs.

#### Radiographs

Soft tissue shadows are seen.

Stippling is observed if the tumor contains small areas of calcification.

#### Treatment

Synovioma is a slow growing tumor.

It metastasizes late.

Surgery is the treatment of choice and includes local excision.

Radical amputation is preferred if the tumor has a widespread involvement.