Osteosarcoma

- Osteosarcoma is the most common primary malignant tumour of bone and accounts for approximately 20% of bone cancer.

The age distribution of osteosarcoma is bimodal, with 75% occurring before 20 years of age.

A smaller peak occurs in older adults, in whom it frequently associated with predisposing conditions such as Paget's disease, bone infarcts, and prior radiation. {secondary osteosarcoma}

- Men are slightly more affected (1.6 : 1)

- any bone can be involved, but tumors usually arise in metaphyseal region of long bones.

almost 50% are near

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Knee in the distal femur (m/c) or proximal tibia.

Radiologically, enlarging tumor forms a destructive, mixed lytic and blastic mass with infiltrative margins.

- The tumour frequently breaks through cortex and lifts periosteum, inducing reactive periosteal bone formation. The triangular shadow between cortex and raised periosteal ends, known radiographically as

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Codman triangle.

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Indicates aggressive tumor.

PATHOGENESIS

peak incidence of osteosarcoma is during adolescent growth spurt.

The tumor occurs most frequently in the growth plate of rapidly growing bone, where increased proliferation may predispose to mutations that drive oncogenes.

approx 70% of osteosarcoma have acquired genetic abnormalities including chromosomal abberations.

PRIMARY OSTEOSARCOMA

They are usually associated with mutations in well known tumour supressor gene & oncogenes, including :

RB MUTATIONS - present in upto 70% of sporadic osteosarcoma, germline RB mutations confer 1000 fold risk.

TP 53 - is mutated in germline of individuals with Li-Fraumeni syndrome, who have greatly increased incidence.

CDKN2A (INK 4a) - encodes p16 & p14, and is inactivated in many osteosarcoma

MDM2 & CDK4 - Inhibits p53 and RB function respectively are overexpressed in many low grade osteosarcoma, often through chromosomal amplification region
→ 12q 13 - q 15.

SECONDARY OSTEOSARCOMA

Osteosarcoma in older persons almost always occur in association with pre-existing disorders like:

- paget's disease.
- Radiation Exposure : therapeutic radiation for lymphoma like.
- chemotherapy.
- pre-existing benign bone lesions like osteomy elitis.

MORPHOLOGY

Osteo Sarcoma are BULKY, GRITTY, GREY-WHITE TUMOORS. that contains : hemorrhage and cystic degeneration.

- Tumor frequently destroys surrounding cortices to produce soft tissue masses, spread extensively in medullary canal and replace hematopoietic marrow.

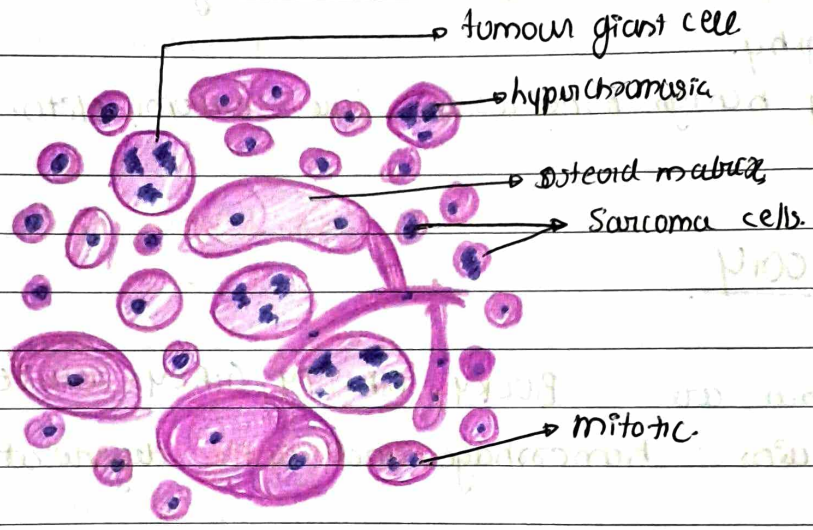
- Osteosarcoma demonstrate pleomorphism, large hyperchromatic nuclei, bizzare tumor giant cell abundant mitoses including abnormal forms (tripolar etc)

- Extensive necrosis, intravascular invasion - common.

DIAGNOSIS → presence of malignant tumor cells producing unmineralized osteoid or mineralized bone, which is typically fine & lacelike, but can also form broad sheets of primitive trabeculae.

Histological Subtypes:

- osteoblastic
- chondroblastic
- fibroblastic
- telangiectatic
- small cell
- Giant cell.



CLINICAL FEATURES

- Based on their known natural history, all osteosarcoma patients are assumed to have occult metastases at the time of diagnosis.
- as a result, treatment generally includes →
  Neoadjuvant chemotherapy
  Surgery, post op adjuvant chemotherapy.
- Chemotherapy has greatly improved osteosarcoma prognosis, with 5 year survival reaching 70% in individuals without overt metastases at initial diagnosis.
- Osteosarcoma metastasizes hematogenously to
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  Lung, bones, brain & other sites.
- the outcome for those with clinically evident metastases recurrent disease or secondary osteosarcoma remains guarded with 5 year survival rate less than 20%