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PHARMACOLOGY OF BONE CANCER

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ABSTRACT

Bone cancer is the term for several different cancers that develop in the bones. When cancer cells grow in a bone, it can harm normal bone tissue. The type of cell and tissue where cancer begins determines the type of bone cancer. Cancers that form in the bone itself are called primary bone cancers. Osteosarcoma mainly occurs in young people between the ages of 10 and 30, rare in middle aged people and very less in geriatrics. Causes and symptoms of bone cancer, mechanism and management of bone cancer, cytogenic molecular genetic alterations in bone tumour, genetic of aspects of bone tumour, bones and joint cancer, pathology and genetics, approach to the diagnosis of bone and soft tissue tumours clinical radiologic and classification aspects, epidemiology of primary bone tumours and economical aspects of bone metastasis. Bone tumours are extremely rare, with over 60 different subtypes being recognised. Their scarcity likely contributed to the logistics difficulties in research for improved diagnosis and treatment. Treatment includes surgery chemotherapy, surgery and radiotherapy.

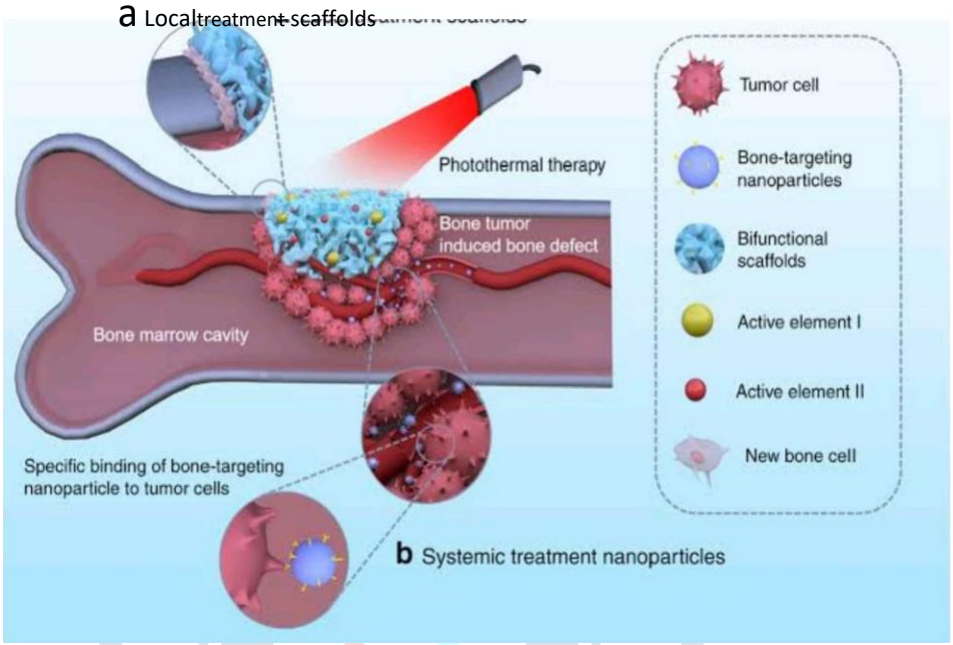
KEYWORDS

Bone Cancer, osteosarcoma, Metastasis, chemotherapy, Radiotherapy.

INTRODUCTION

Bone tumours involve the invasion of tumours into bone tissue and are classified as either primary tumours or metastatic tumours. Osteosarcoma is a well-known primary malignant bone tumour that often occurs in children and adolescents. It has been reported that this disease has become the second leading cause of tumour related death in young teenagers. 1 The majority of patients die from lung metastases. Its annual incidence worldwide is N I -3 cases per million.2 The clinical signs of osteosarcoma are not obvious without spontaneous fracture or severe pain early on. Therefore, this disease is not easily diagnosed, but the tumours grow quickly. As a result, osteosarcoma causes a large bone defect and limitations in motion and can metastasize to the lungs.3 The ethology of osteosarcoma is still not clear.4 To date, the most common clinical treatment methods for bone tumours include chemotherapy, wide surgical resection, and radiotherapy.5 However, osteosarcoma is not sensitive to radiotherapy and is

prone to chemotherapy resistance. Surgical resection often fails to completely remove the tumour, which is the main cause of postoperative recurrence and metastasis. Moreover, osteosarcoma invades large areas of bone, which cannot repair itself, and has serious effects on the quality of life of patients.6 The 5-year survival rate of patients with osteosarcoma is [N] 60%.7 Unfortunately, advances in osteosarcoma treatment have reached a plate over the past 40 years.



TYPES OF BONE CANCER

1. osteosarcoma
2. Ewing sarcoma
3. Chondrosarcoma

- Dedifferentiated chondrosarcoma
- Mesenchymal chondrosarcoma
  - Clear cell chondrosarcoma

Osteosarcoma (also most common primary form of bone cells. It people between the ages

osteosarcomas develop Satellite lesion in middle-aged people,

than females. These bones of the arms, legs,

Bone

OSTEOSARCOMA

called osteogenic sarcoma) is the bone cancer. It starts in an early most often occurs in young

of 10 and 30, but about 1 in 10 in people older than 60. Its rare and is more common in males tumours develop most often in or pelvis.

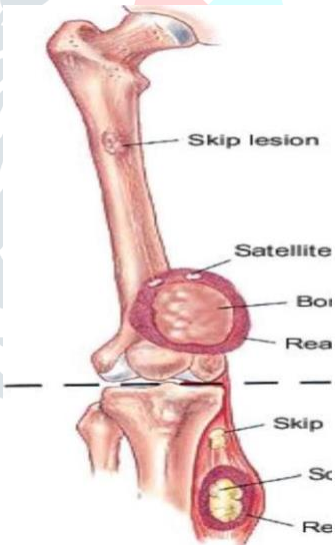
sacraria

Reactive zone

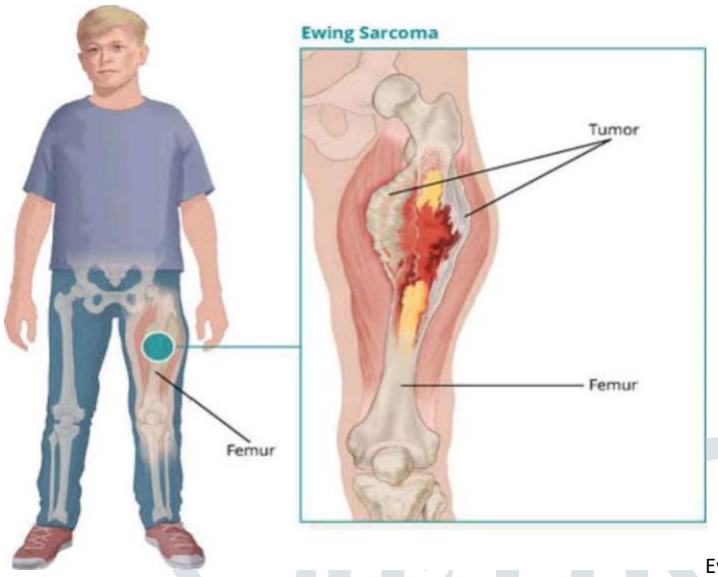
Skip lesion

Soft tissue sarcoma

Ewing sarcoma



Ewing tumours are the second most common type of primary bone cancer in children, teens, and young adults, and the third most common type of bone cancer overall. These tumours are in adults older than 30. They occur most often in white people and are rare among African Americans and Asian Americans. Most Ewing tumours develop in bones, but they can start in other tissues and organs. The most common sites for this cancer are the hip (pelvic) bones, the bones in the chest wall (such as the ribs or shoulder blades), the bones of the spine, and the long bones of the legs This type of cancer is not discussed further on our Bone Cancer pages. For more information on it, see Ewing Family.

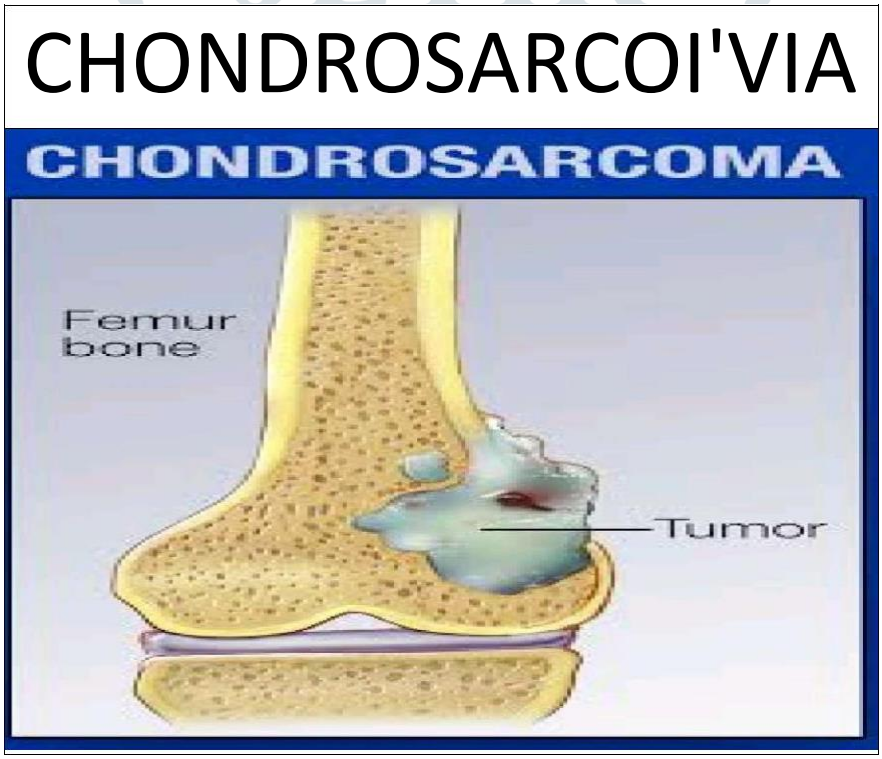


Ewing Sarcoma

CHONDROSARCOMA

Chondrosarcoma starts in early forms of cartilage cells. It's the second most common primary bone cancer. It’s rare in people younger than 20, and the risk of chondrosarcoma goes up as people get older. Chondrosarcomas can start in any place there's cartilage. Most develop in bones like the pelvic (hip) bones, legs, or arms. Some start in the trachea, larynx, chest wall, shoulder blades, ribs, or skull. Benign (noncancerous) tumours such as enchondromas and osteochondromas are more common in the cartilage than are chondrosarcomas. These benign tumours rarely turn into cancer. People who have many of these tumours have a slightly higher chance of developing cancer, but this isn't common.

Chondrosarcomas are given a grade from 1 (l) to 3 (lll), which is a measure of how fast they are likely to grow. The lower the grade, the slower the cancer tends to grow and the less likely it is to spread: Low-grade (grade l) chondrosarcomas, also called atypical cartilaginous tumours, tend to grow the slowest and are very unlikely to spread. Intermediate-grade (grade ll) chondrosarcomas are slightly more likely to spread. High-grade (grade lll) chondrosarcomas are the most likely to spread. Most chondrosarcomas are grade I or grade ll.



CAUSES

- A Tumour is a lump or mass of tissue that forms when cells divide in controllably.

- For most bone tumours, the cause is unknown. A growing tumour is may replace healthy tissue with abnormal tissue. It may weaken bone, causing it to break.

COMMON SYMPTOMS

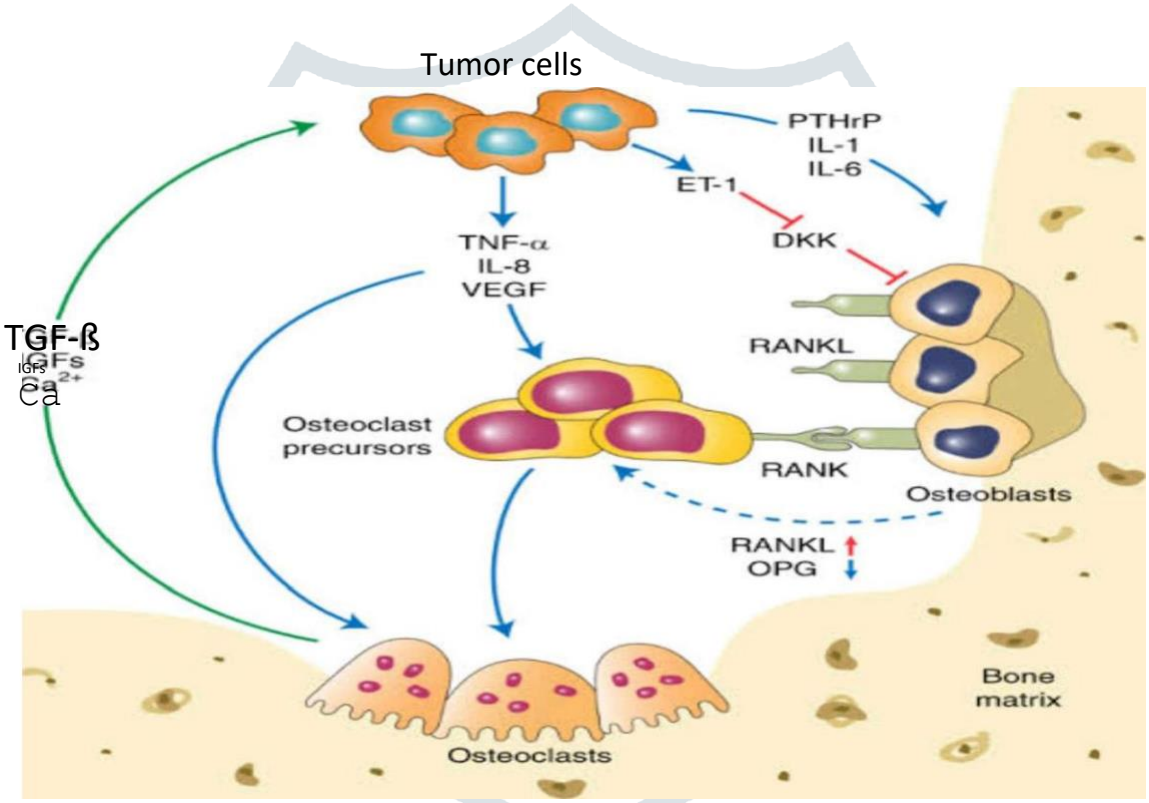
- Pain. You might have pain or tender ness most of the time, even when you are in resting.
- Swelling. You might have some swelling, but it is not always possible to see or fell a lump.
- Problems moving around.
- Feeling tired.
- High temperature.
- A weakened bone.
- Weight loss.

MECHANISM OF BONE CANCER

Bone metastasis are almost always multiple and involve axial skeleton.4 It has been suggested that this distribution might be in relation to the haematopoietically active red bone marrow. 13 There exists a paravertebral network that may play a role in the development of bone metastasis. 14 This theory is supported by the high incidence of bone metastases without corresponding lesions in the lung (suggest an alternative pathway of spread). In addiction, themicro environment must be favorable for tumor cell survival. Once the tumor cell is in circulation, it needs Vascular adhesion and extravasation: the cell interacts with endothelium in order to extravasate and stay in a specifictissue.15 Chemoattractive and adhesion molecules play a fundamental role in this selective retention of cancer cells in bone marrow vasculature. Cancer cells use equivalent molecules to vascular cell adhesion molecules (VCAM) and E-selectin to adhere to endothelium. 16,17 We also know that chemokines, integrins, osteopontin, bone sialoprotein and type I collagen are critical for organ colonization by cancer cells. 1 8,19 Examples of such interactions are: expression of CXCR4 by neuroblastoma tumors that mediates the attachment to stromal-cell derived factor 1 in bone (SDF-I or CXCL12);20 expression of RANK by BC that mediates the attachment to RANKL in bone;21 expression of sialoprotein by non-small cell lung cancer that facilitate binding to collagen type I in bone.22

Micro-environmental support: The seed-and-soil hypothesis tells us that the microenvironment provides a fertile ground (the soil), for the survival and growth of metastatic cancer cells (the seed).23 The bone formation and reabsorption release and activate survival and growth promoting factors that may contribute to bone metastases development.24

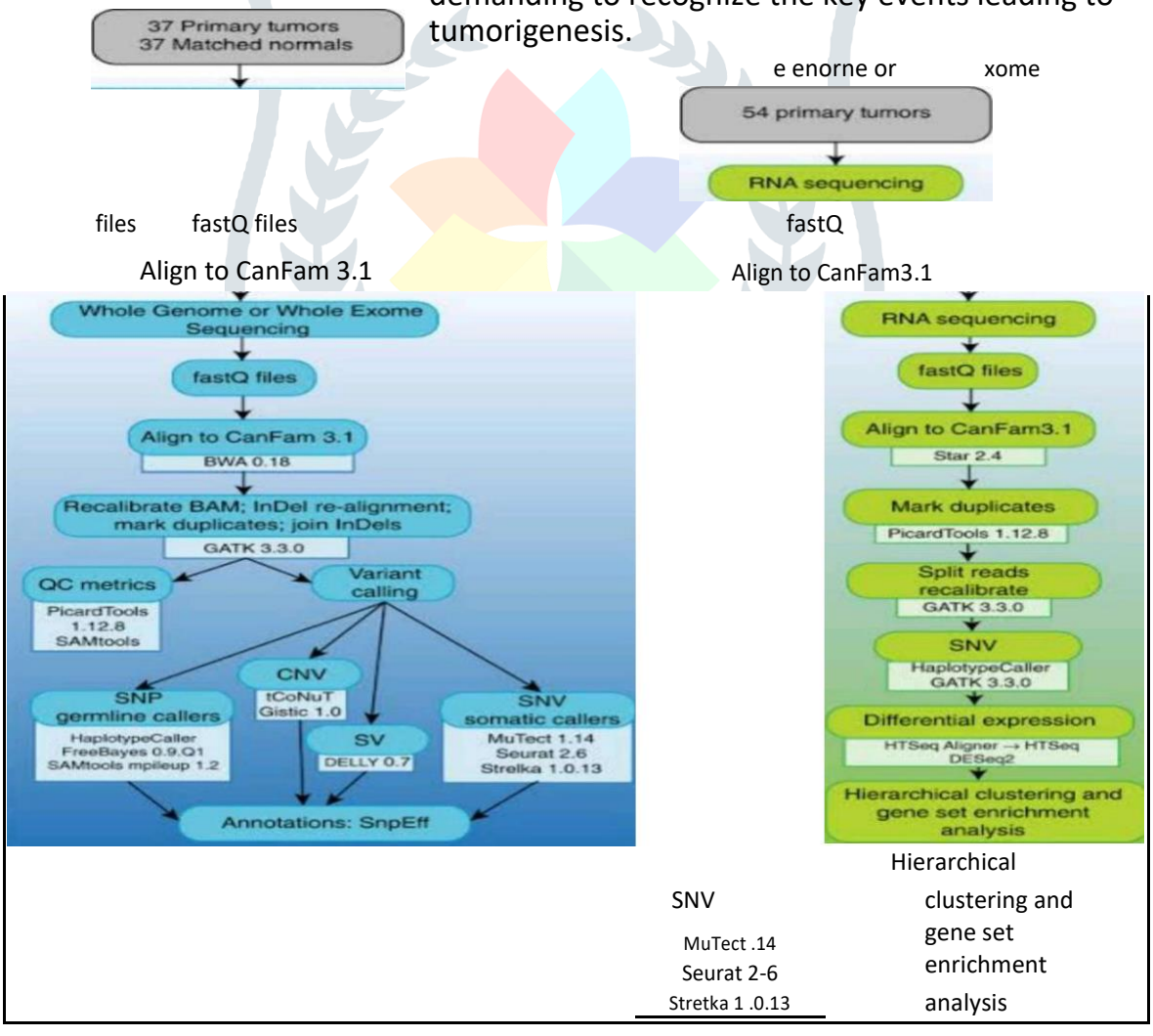
Epithelial - Mesenchymal transition: Normal cell can lose their epithelial features and acquire mesenchymal characteristics. This process is called Epithelial-Mesenchymal Transition, and enables epithelial cells to migrate to a new environment. This occurs mainly during embryogenesis, but in cancer cells this process confers the invasive phenotype.4



CYTOGENETIC AND MOLECULAR GENETIC ALTERATIONS IN BONE TUMOR

Genetic changes are detected in most bone tumors and these rearrangements are recognized as playing a pathogenic role in an increasing number of bone tumors. Cytogenetic and molecular genetic changes have also refined and clarified the classification of bone tumors. Moreover, some of these genetic imbalances have shown to be clinically and prognostically relevant. However, especially in malignant bone

tumors, there is a need for a wider and better knowledge of genetic changes on the whole genome scale, since most of these tumors lack a recurrent and specific genetic rearrangement that could be used as a biomarker in the diagnostic or prognostic sense. Since a remarkable hare of bone tumor patients—particularly with osteosarcoma and Ewing [l] s sarcoma—are children, continuous research is especially significant for this group of pediatric patients. Therefore, screening for genomic rearrangements is a fundamental task in finding novel biomarkers in malignant bone tumors for more accurate diagnosis, prognostication and, most importantly, in identifying targets for novel therapeutic approaches. New molecular genetic techniques with higher resolutions, specificity and accuracy continue to emerge and these new techniques may prove useful both in bone tumor research and clinical diagnostics. Genome-wide analysis of aberrations in gene expression, copy number, miRNA expression and methylation in array-based or other high-throughput applications holds great promise for understanding the underlying events in neoplastic development of bone tumors. However, due to the complexity of these alterations in cancer cells, it is extremely demanding to recognize the key events leading to tumorigenesis.



DNA analysis	RNA analysis

GENITIC OF ASPECTIES OF BONE TUMOR

Over the past few years, the molecular genetic changes underlying cartilaginous and bone tumor development and progression have been increasingly elucidated. However, the development of optimal treatment strategies for some of these entities has been greatly complicated by the large number of subtypes, the heterogeneity in their genetics and biological behavior, and the rarity of these tumors. In addition, inconsistencies have emerged from different studies examining prognostic factors, probably as a result of different study designs and treatment protocols, confounding variables associated with retrospective analyses and the use of diverse molecular methods. In order to resolve these issues, prognostic factors should be validated using uniform and multiple methods in both retrospective investigations and prospective multi-center studies. The advent of the human genome map and molecular techniques, such as microarray-based copy number and gene expression profiling, provide a new approach to classifying tumors and promise to improve our ability to predict both the probability of metastasis and overall clinical course. In addition, an understanding of the molecular biology of these tumors is leading to the identification of targets for novel therapeutic approaches.

BONES AND JOINT CANCER : PATHOLOGY AND GENETICS PATHOLOGY

Pathology Conventional osteosarcomas have different cell shapes that are often spindle shaped and highly anaplastic with considerable pleomorphism including epitheloid, plasmacytoid, fusiform, ovoid, small round cells, clear cells, giant cells (both mono- and multi-nucleated) and spindle cells. Most cases contain a complex mixture of two or more of these cell types. Aspiration cytology alone is not sufficient to give a diagnosis with 100% certainty, even when combined with data from X-rays and histochemical detection of alkaline phosphatase. It can, however, be used to asses the mesenchymal nature and probably malignant nature of the tumour Histologically, osteosarcoma is characterised by the presence of osteoid-extracellular matrix, consisting mainly of collagen I with a dense pink amorphous appearance on haematoxylin/eosin staining (Fig. 1b). The matrix (present/absent and nature) of the tumour determines the histological subtype (Table 2). The histological subtype has been described as a factor predicting survival, with chondroblastic osteosarcoma having a better prognosis fibroblastic better than osteosarcoma.

GENITICS

Bone cancer is rare type of cancer that occurs in the skeletal system.It typicaly occurs due to changes in genes that affect how cells grow. While people typically acquire these genes changes throughout life , inheriting certain genes may increases a persons risk of bone cancer. Certain rare genetic syndromes passed through families increase the risk of bone cancer ,including Li-fraumeni syndrome and hereditary retinoblastoma.

DIAGNOSIS

The diagnosis and treatment of osteosarcoma in general, and the differential diagnosis versus other, benign matrix-producing bone lesions is based on an intense interdisciplinary cooperation, involving orthopaedic surgeons, radiologists, oncologists and pathologists.

Imaging Conventional radiography is used for the initial detection of the primary tumour. The radiographic appearance of conventional osteosarcoma is highly variable, but the locatioofthis tumour at the methaphyseal centre is an important feature for the differential diagnosis. Most times the tumour appears as a mixed lytic/blastic lesion with cortica destruction.

Further imaging to detect extension of the tumour in adjacent joints and its possible relationship with soft tissue components is performed with MRI or dynamic enhanced MRI (DEMRI). In addition, DEMRI is able to monitor the effect of neoadjuvant chemotherapy prior to surgery [35]. Lung metastases or skip-lesions, non-contiguous metastases in the parent bone or across adjacent joints, can best be detected by CT, but identification of metastases can also be performed by isotope bone scanning [32]. Another application of this technology is the determination of multidrug resistance (MDR) of the tumour prior to treatment, since lipophilic radiopharmaceutical agents such as 99mTc-labelled MIBI and tetrofosmin are actively eradicated from tumour cells by the same MDR mechanism as used for cytostatic drugs .

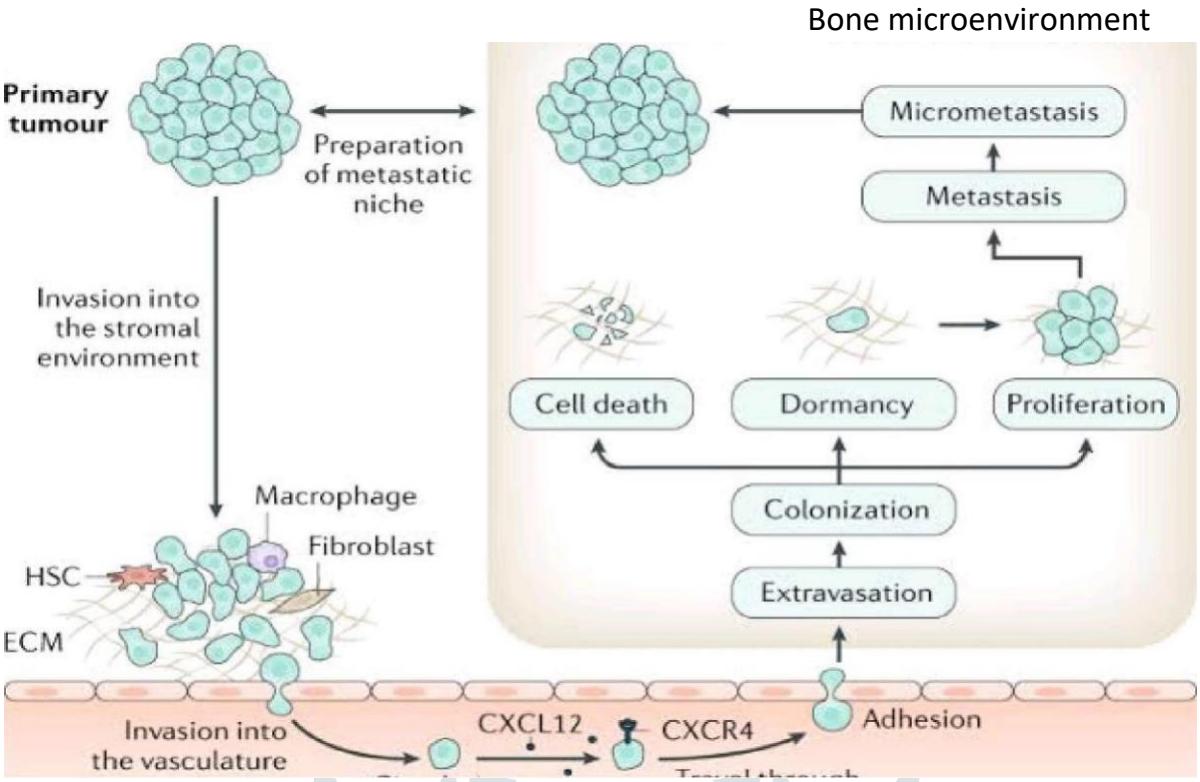
EPIDEMIOLOGY OF PRIMARY BONE TUMOR AND ECONOMICAL ASPECTS OF BONE METASTASIS

Primary bone tumors are relatively uncommon and this has certainly limited the collection of data about their relative frequency and to the insufficient understanding of the risk factors. Although the incidence of benign bone tumors is higher than the incidence of primary malignant tumors, it is likely that benign lesions are underestimated because they often are asymptomatic and not clinically recognized. In addition, primary bone tumors are outnumbered by metastases from carcinomas, melanoma, or hematologic malignancies, such as plasmacytoma.

According to the analysis of the Surveillance, Epidemiology and End Results (SEER) Cancer Statistics Review of the National Cancer Institute, it is estimated that 2,81 0 men and women (1,620 men and 1,190 women) will be diagnosed with and 1,490 men and women will die of cancer of the bones and joints in 2011. Overall, bone sarcomas account for 0.2% of all malignancies diagnosed in the United States, and the age adjusted incidence rate for all bone and joint malignancies is 0.9 per 100,000 persons per year. The overall 5-year relative survival for 2001-2007 was 66.3% and the ageadjusted death rate based on patients who died in 2004-2008 in the US, was 0.4 per 100,000 men and women per year.

In Italy, according to the 2006 report on tumors by the AIR-TUM (Association of Italian Tumor Registries) primary malignant bone tumors represented 0.2% of all malignancies diagnosed in males and females in the period 1998-2002, while mortality represented 0.3% of all cancer deaths in both sexes in the same period. In the area covered by the Italian Network of Cancer Registries, there were on average 1.3 new bone malignant tumors diagnosed per 100,000 males/year and 1 .1 per 100,000 females/year. Overall, in the year 2002, there were 208 deaths in Italy due to bone cancer among males and 145 among females. As expected, bone cancer was relevant among young subjects, since more than 50% of cases were diagnosed before the age of 59 years. The cumulative risk (0-74 years) of developing a bone cancer was 0.9% among males (1 case every 1,099 men) and about 0.7% among females (1 case every 1,370 women) while the cumulative risk of dying from this cancer was 0.5% among males and 0.4%among females, respectively. Incidence rates for primary malignant tumors of bone vary considerably across Italy, with a ratio between areas with higher and lower rates of approximately 3 to 4 times. These differences may be explained, at least in part, by the use of different coding rules for the bone site, which may have determined the inclusion, especially for cancer deaths, of secondary tumors. Considering time trends, bone cancer shows a stable incidence over time, while mortality is decreasing. The most frequently diagnosed histologic subtypes were chondrosarcoma (30% in males and 29% in females), osteosarcoma (16% in males and 17% in females) Ewing's sarcoma (14% in both males and females) and chordoma (8% in males and 5% in females).

The age specific incidence rates of bone sarcomas typically show a bimodal distribution, with a first peak occurring in the second decade, and a second peak occurring in patients older than sixty years of age. This is related to the different age distribution of the main histological subtypes, since Ewing's sarcoma and osteosarcoma are the most frequent histologic subtypes in the first two decades, while chondrosarcoma, malignant fibrous histiocytoma, chordoma and secondary osteosarcoma show an increased incidence after the fourth decade. On the other hand, the majority of benign bone tumors and tumor-like lesions occur in the first two decades of life. In general, there is no significant gender predilection, although some tumors (e.g. Paget's sarcoma, chordoma) show a higher prevalence in males. According to SEER data, in the period 2004-2008, the median age at diagnosis for cancer of the bones and joints was 40 years of age. Approximately 29.0% were diagnosed under age 20; 15.4% between 20 and 34; 10.5% between 35 and 44; 13.0% between 45 and 54; 11.4% between 55 and 64; 8.3% between 65 and 74; 9.1% between 75 and 84; and 3.5% over 85 years of age.



ECONOMICAL ASPECTS OF METASTASIS

Studies on the economic impact of bone metastasis are rare and only report on the costs for the health-care sector. The first study on the subject was done in the Netherlands in 2003. Groot investigated the cost of treatment for SREs in patients with prostate cancer metastatic to the bone. They followed 28 patients with SRE because of prostate cancer metastatic to the bone for a period of 24 months. The overall cost of treatment per patient for this period was € 13,051 of which € 6973 (50%) was spent for the treatment of SREs. The overall cost was calculated on the whole of the medical care including manpower, material, overhead cost (housing, etc.). For the cost directly related to the treatment of SREs, the cost of radiation therapy, hospitalization, and surgical intervention were taken into account. Thus, this is the direct cost for the health-care sector. They did not look for eventual cost of patient care in a nursery, direct costs for the patient, or indirect costs. Indirect costs are estimated to be limited in patients with prostate cancer. In their study on 28 patients, bone metastases developed after the age of 60 with a mean age of 73 years. This is a nonactive population from the viewpoint of employment.

In 2004 a second study was published, this time from the United States on the cost of treating SREs in patients with lung cancer [34]. In a US health insurance claim database 534 patients were identified with lung cancer and skeletal involvement. Cost were estimated on the basis of the claims made and did not include overhead costs. Of these 534 patients 55% developed at least 1 SRE. In the SRE patient group 68% received radiation therapy, 35% suffered a pathologic fracture, and 14% had bone surgery. The mean age at first SRE was 66.4 years, which also indicates that indirect costs due to loss of productivity tend to be limited. The mean survival after first SRE was 4.1 months. The estimated lifetime SRE related cost after 36 months is $ 11,979 of which 61% goes to radiation therapy. Data are difficult to compare due to the difference in costs included, the method of treatment, e.g., single fraction or multiple fraction radiation therapy, the period over which the costs are calculated, the method of calculation, and index changes over the years.

IMAGING TECHNIQUES INTERPRETATION AND STRATEGIES

1. Evaluation of the bone lesion

Radiologist plays an important role in initial diagnosis, work up and staging of bone tumors and subsequently in deciding the management of the tumors. The diagnostic work up of the bone tumors often requires multimodality approach, ranging from radiography, to CT, MRI, bone scintigraphy and PETCT/PETMRI. Every modality contributes differently in the evaluation of bone tumors and in varying combinations customized to the disease process under evaluation will provide a precise road map for the radiographic diagnosis and management of bone tumors. Radiography Radiographs are performed for any clinical symptoms of bone pain or swelling and the x-rays are preferably obtained in two planes AP and Lateral/oblique. Conventional radiography is the initial imaging modality and is the most optimal way to evaluate the primary bone tumors. Its relatively inexpensive and unique advantage of 2D image allows characterization of the lesion based on the features seen on radiographs. The

information of site of lesion in bone, along with imaging characteristics of tumor including margin and edges of the lesion, matrix mineralization, cortical involvement and periosteal reaction all can be seen on plain radiography.3 Radiographs are thus the mainstay for initial diagnosis in most cases and cornerstone for differential diagnosis.

A deficit of conventional radiography is with lesions which are located in complex anatomical locations, like in spine, iliac bones and in posterior elements of vertebrae where overlapping of structures on 2D planes limits the evaluation. The evaluations of soft tissue along with precise extent of medullary involvement are other limitations.

CT scan Multidetector CT allows precise anatomical delineation and evaluation of the lesions in complex anatomical location, where radiographs are not sufficient due to limited contrast resolution. Visualization of minor bony changes, small calcifications, tumor mineralization, cortical changes and periosteal reactions are best seen on CT scans.5 Isotropic imaging with latest 16 slices and above CT scanners provides excellent 3D evaluation of lesion and bone and also provides images in all planes, which can be used for accurate measurements required for the surgery. Along with tumor evaluation, staging of tumor through abdominal or chest CT remains the fundamental protocol.

The lack of characterization of soft tissue along with lack of precise extent of medullary involvement are major limitations for precise delineation of the lesion extent.

Nuclear scan A bone scan has excellent sensitivity for assessing bony changes and is irreplaceable as screening tool for the primary lesion and distant bony metastasis. Therefore, the conditions, which may not be evident on other images, can be detected with nuclear imaging. Its a best tool to assess the cause of pain, by doing screening test for the entire skeleton, when the cause of the pain cannot be localized, Protocols may vary, but standardized technique is to acquire images 2-6 h after intravenous administration of 740-925 MBq of Tc-99m-labeled diphosphanates. The images are acquired once the tracer is washed out of the soft tissue and persisting in bone thus improved visualization of the bones. Images are acquired of the whole body in both anterior and posterior projections and additional images are taken if required.

MRI MRI is considered the best tool for local staging of bone tumors. The inherit capability of soft tissue characterization and visualization of bone marrow by MRI remains the mainstay for evaluation of suspected or diagnosed bone tumor. Tumor contents and hence characterization of bone tumors on basis of tissue composition can be done on MRI along with precise depiction of bone marrow and soft tissue involvement.

If the patient continues to have symptoms and radiographs do not show any abnormality, additional imaging is recommended. Lytic bone lesions can be seen on plain radiographs only when there is more then 30-50% loss of mineralization.8 Therefore MRI is the preferred modality in these cases to assess bone marrow. MRI should be interpreted only with concurrent radiographs.

Newer state of the art imaging techniques compiled under functional MRI includes dynamic contrast enhanced imaging (Perfusion MRI), Diffusion Weighted Imaging

(DWI) and MR Spectroscopy. Functional Magnetic resonance imaging has added advantages over structural MRI, in tissue characterisation and in staging of bone tumours. Standard MRI helps to evaluate the structural changes in bones and extent of the disease, and the morphology of the tumor is better assessed by DWI and perfusion MRI which also helps in differentiating benign from malignant etiology. The evaluation of tissue cellularity and presence of viable tissue or necrosis which are criteria to assess follow up post chemotherapy can not be determined by standard MRI, where perfusion MRI and DWI plays an important role.

Perfusion imaging representing dynamic contrast imaging is the acquisition of data post contrast enhancement, acquiring multiple sets of data through the specified diseased segment. The enhancement pattern is then plotted against time curve and early enhancement is evaluated representing the vascularisation and perfusion and hence viability of tissue within the tumour. Dynamic MRI, therefore helps to guide biopsy site by delineating the viable tumour location and monitoring the changes post chemotherapy by differentiating fibrous tissue/scarring/necrosis from viable tissue.

DWI adds on functional information over the structural evaluation by providing qualitative assessment of the tissue cellularity. Tumours differ in the cellular structure with malignant tumours being more cellular displaying restricted diffusion. Diffusion weighted images show restricted diffusion and reversal of signal on ADC (apparent diffusion coefficient) of the tissue which are highly cellular and resultant has less Brownian movement, the principle behind DWI.

Monitoring the treatment response Treatment response is monitored by multimodality approach, primarily by X-Rays and MRI. Standard MRI protocols provide a composite outlook of the tumor response to treatment. However in the cases where there is no obvious decrease or increase in the size of lesion the viability of the tissue will help to evaluate the treatment response. This information to some extent can be interpreted from standard MRI, and the functional MRI is used as an adjunctive imaging modality complementing morphological imaging.

In bone tumours, the dynamic contrast scans showing early and rapidly progressive enhancement indicates residual or recurrent tumour, whereas absence of early enhancement indicates a good response. Similarly DWI with ADC calculation helps to

differentiate viable from non-viable component of the tissue, demonstrating restricted diffusion in residual tumour.

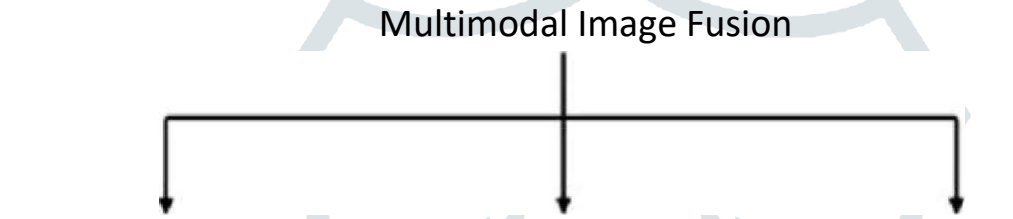
PET CT/PET MRI FDG PET scans provides a noninvasive method to assess the aggressiveness of tumor. Its a one-stop solution for staging the tumor and to rule out distant bony and soft tissue (liver or lung or lymph nodal) metastasis. It's again a useful technique to assess the skip lesions in equivocal conditions.

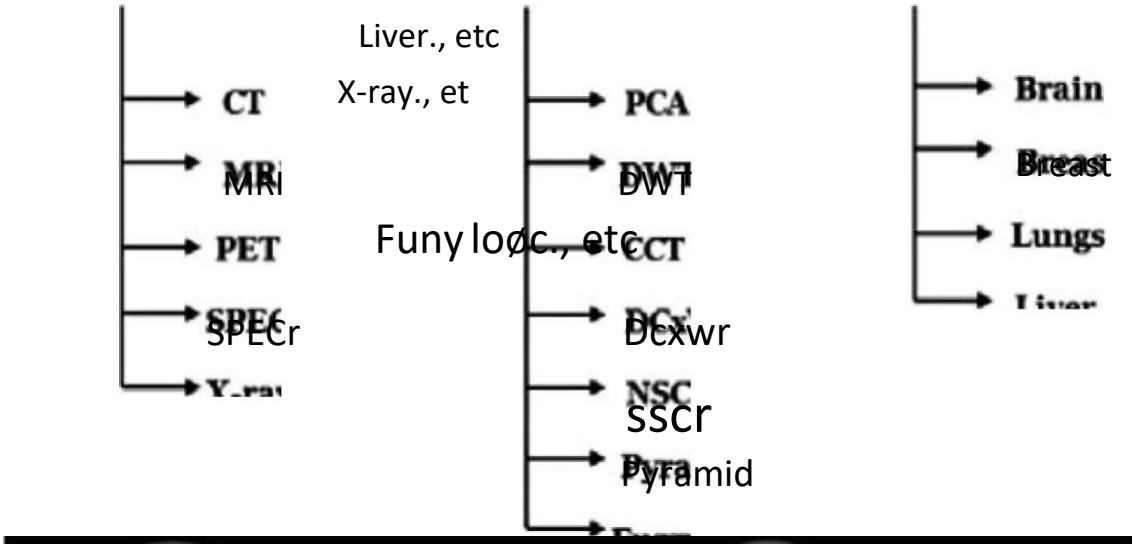
Bone lesions frequently seen in F18FDG PET/CT are FDG avid. FDG uptake in a bone lesion does not decide the morphologic features of lesion and hence does not characterize the bone tumor. FDG avidity and morphology of the tumor are

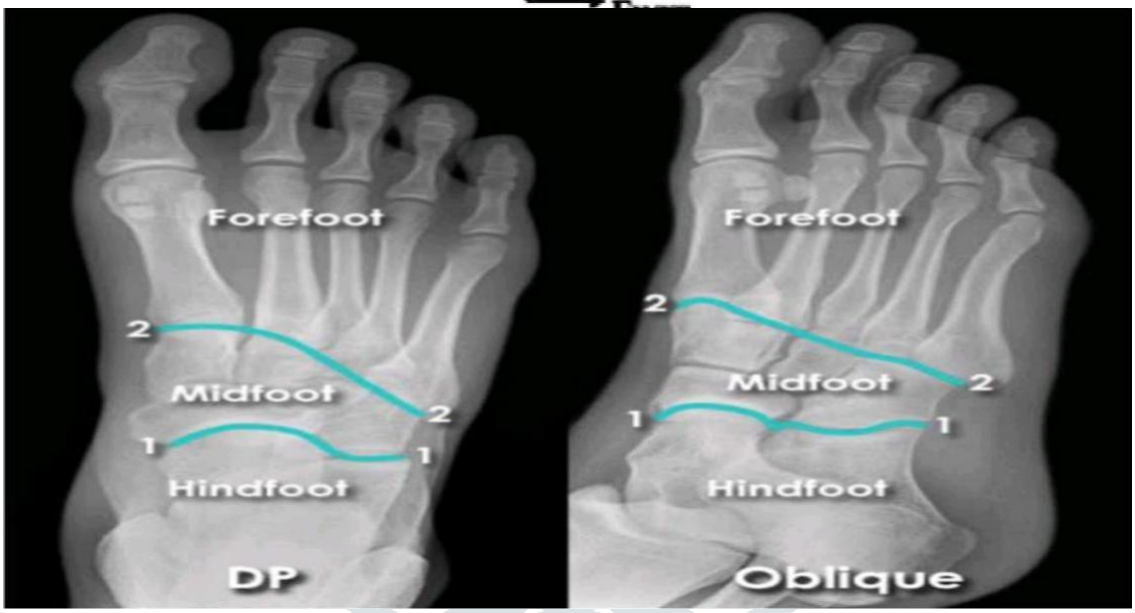
independent factors and together are important in staging the tumor and determining the treatment response. Morphological features are seen best on radiographs or CT done as preliminary part of FDscan. Once a primary diagnosis of the bone tumor has been made, like that of Ewing [l] s or Osteosarcoma, PET scan of the whole body is done for staging and also for evaluation of therapeutic response.

FDG avidity of the lesion decides the aggressiveness of the lesion with malignant lesion being more avid then the benign bone lesions of same histological types.

FDG PET/MRI is another emerging imaging modality, which results in reduced radiation with increased anatomical resolution. PET/MRI has been proven superior to PET/CT in evaluation of brain, soft tissue component of the lesions and also in bone marrow evaluation.







TREATMENT

The treatment options for your bone cancer are based on the type of cancer you have, the stage of the cancer, your overall health and your preferences. Different bone cancers respond to different treatments, and your doctors can help guide you in what is best for your cancer. For example, some bone cancers are treated with just surgery; some with surgery and chemotherapy; and some with surgery, chemotherapy and radiation therapy.

SURGERY

The goal of surgery is to remove the entire cancerous tumor. In most cases, this involves special techniques to remove the tumor in one single piece, along with a small portion

of healthy tissue that surrounds it. The surgeon replaces the lost bone with some bone from another area of your body, with material from a bone bank or with a replacement made of metal and hard plastic.

Bone cancers that are very large or located in a complicated point on the bone may require surgery to remove all or part of a limb (amputation). As other treatments have been developed, amputation is becoming less common. If amputation is needed, you'll likely be fitted with an artificial limb and go through training to learn to do everyday tasks using your new limb.

CHEMOTHERAPY

Chemotherapy uses strong anti-cancer drugs, usually delivered through a vein (intravenously), to kill cancer cells. However, this type of treatment works better for some forms of bone cancer than for others. For example, chemotherapy is generally not very effective for chondrosarcoma, but its an important part of treatment for osteosarcoma and Ewing sarcoma.

RADIATION THERAPY

Radiation therapy uses high-powered beams of energy, such as X-rays, to kill cancer cells. During radiation therapy, you lie on a table while a special machine moves around you and aims the energy beams at precise points on your body. Radiation therapy is often used before an operation because it can shrink the tumor and make it easier to remove. This, in turn,can help reduce the likelihood that amputation will be necessary.

Radiation therapy may also be used in people with bone cancer that can't be removed with surgery. After surgery, radiation therapy may be used to kill any cancer cells that may be left behind. For people with advanced bone cancer, radiation therapy may help control signs and symptoms, such as pain.

CONCLUSION

Finally,the bone cancer involves the invasions of tumors into bone tissue.osteosarcoma is awell known primary malignant bone tumor the often occurs in children and adolescents.it starts in early form of bone cells.it most often occurs in young people between the ages of 10 and 30. It is rare middle aged people and very less in geriatrics is classified into osteosarcoma, Ewing bone cancer. Sarcoma and chondrosarcoma the most bone tumors,the cause is unknown.the growing tumour is may replace healthy tissue with abnormal tissue and the symptoms of bone cancer is pain, swelling and lump formation problems moving around feeling tired around high temperature, weight loss.mechanism of bone cancer by metastasis, micro environmental support and mesenchymal transitions and cytogenic and molecular genetic alterations in bone tumour also happens . And osteosarcoma cells have different cell shapes that are often spindle shaped and highly anaplastic with considerable pleomorphism.the diagnosis and treatment of osteosarcoma is by involving orthopedic surgeons radiologist, oncologist and pathologists and imaging conventional radiotherapy is used for the initial detection primary tumor. Epidemiology of primary bone tumor and economical aspects of bone metastasis and imaging techniques interpretation and strategies treatment and surgery for bone cancer.

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