Original Article

Diagnosis and staging of osteosarcoma

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Abstract

Osteosarcoma is a primary malignant tumour of the skeleton characterised by the direct formation of immature bone or osteoid tissue by the tumour cells. The classic osteosarcoma is a rare (0.2% of all malignant tumours). highly malignant tumour, with an estimated incidence of 3 cases/million population/year. Osteosarcoma arises predominantly in the long bones and rarely in the soft tissues. The age at presentation ranges from 10 to 25 years of age. Plain radiographs, computed tomography, magnetic resonance imaging, angiography and dynamic bone scintigraphy are used for diagnosis, evaluation of the extent of tumour involvement and decision of the type of operation and, if necessary, the type of reconstruction. The biopsy confirms the diagnosis and reveals the grade of the tumor. Enneking system for staging malignant musculoskeletal tumors and American Joint Committee on Cancer (AJCC) staging systems are most commonly used for extremity sarcomas. Today, for localised osteosarcoma at onset (80% of cases) treated in specialized bone tumour centres with pre- and postoperative chemotherapy associated with surgery, the percentage of patients cured varies between 60% and 70%. Surgery is conservative (limb salvage) in more than 90% of patients. Prognosis is more severe (cure rate about 30%) for tumours located in the axial skeleton and in patients with metastasis at onset.

Keywords: Osteosarcoma, imaging, biopsy, Enneking staging.

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INTRODUCTION

The term "osteosarcoma" as opposed to "osteogenic sarcoma" is preferred by the World Health Organization (WHO). The eponym was introduced by Boyer in 1805 [1]. In 1879, Gross published a paper entitled "Sarcoma of the Long Bone Based upon a Study of One Hundred and Sixty-five Cases" [2]. Osteosarcoma is defined as the primary malignant mesenchymal bone tumor where the malignant tumor cells directly form the osteoid or bone or both.[3-1] Demonstration of osteoid directly formed by the malignant cells in histopathology is essential for making the diagnosis of osteosarcoma.[4,5] The risk of developing postradiation osteosarcoma correlates with radiation dose and use of electrophilic chemotherapeutic agents.[15,16,17] An etiological relationship has not been proven in prosthesis and metal hardware associated osteosarcomas.[18]

Epidemiology

Classic osteosarcoma represents approximately 15% of all biopsy-analysed primary bone tumours. Among primary malignant bone tumours, it ranks second in frequency after multiple myelomas. The incidence of classic osteosarcoma is 3 cases/million population/year. It represents 0.2% of all malignant tumours[19].

Etiology

Etiology of osteosarcoma is unknown. A viral origin was suggested by the evidence that bone sarcomas can be induced in selected animals by viruses or cell-free extracts of human osteosarcomas[20]. The only environmental agent known to cause osteosarcoma in human is ionising radiation[20]. Radiation is implicated in approximately 2% of osteosarcomas. An increased incidence of radio-induced osteosarcoma is likely to be seen with a longer survival after primary irradiation. Several families have been described with multiple members who developed osteosarcoma, suggesting genetic predisposition to this tumour[21] So far, the

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strongest genetic predisposition is found in patients with hereditary retinoblastoma. In patients with retinoblastoma, osteosarcoma occurs 500 times more frequently than in the general population[22]. Screening large series of children with osteosarcoma revealed that approximately 3% to 4% carried a constitutional germline mutation in p53[23]. The majority of cases with germline p53 mutations represent patients with a family history suggestive of Li-Fraumeni syndrome.

Signs and Symptoms

Most patients who present with osteogenic sarcoma of the extremities complain of pain prior to soft tissue swelling. This is true of any primary bone tumour, because stretching of the periosteum usually causes pain before the tumour is discernible. Pain could also result from weakening of the bone with development of minute stress fractures. Development of sudden and severe pain heralds gross pathologic fracture, which is an uncommon finding in adult patients. Up to 15% of paediatric patients present a pathological fracture. The second most common complaint is swelling, which is related to the soft tissue mass. Although about 90% of osteosarcoma show soft tissue extension, a few patients complain of swelling. Systemic symptoms as weight loss, pallor, fever, anorexia are very uncommon.

Classification

Osteosarcomas are classified as primary and secondary. Primary are further sub-typed as intramedullry/central and surface osteosarcomas as per World Health Organization classification[4] [Box 1].

Primary osteosarcomas
Conventional-intramedullary/central high grade (most common) further sub-typed as:
Osteoblastic (50%)
Chondroblastic (25%)
Fibroblastic (25%)
Small cell
Telangiectatic
Low grade central
Surface osteosarcomas:
Parosteal
Periosteal
High grade surface
Secondary osteosracomas can occur in Paget's disease and after radiation exposure.[1,2]
Unusual forms of osteosarcoma given below are viewed as subtypes of conventional osteosarcoma because their biological behavior is similar.[2]
Osteoblastic osteosarcoma-sclerosing type
Osteosarcoma resembling osteoblastoma
Chondromyxoid fibroma-like osteosarcoma
Chondroblastoma-like osteosarcoma
Clear-cell osteosarcoma
Malignant fibrous histiocytoma-like osteosarcoma
Giant cell rich osteosarcoma
Epithelioid osteosarcoma

Box 1: Classification of osteosarcoma

Diagnostic methods

Plain X-ray

The characteristic radiological features are sun-burst appearance, periosteal lifting with formation of Codman's triangle [Figure 1], new bone formation in the soft tissues along with permeative pattern of destruction of bone and other features for specific types of osteosarcoma[4,10,24,25] X-ray chest can detect metastasis in form of cannon ball appearance or nodules in the lungs [Figure 3],

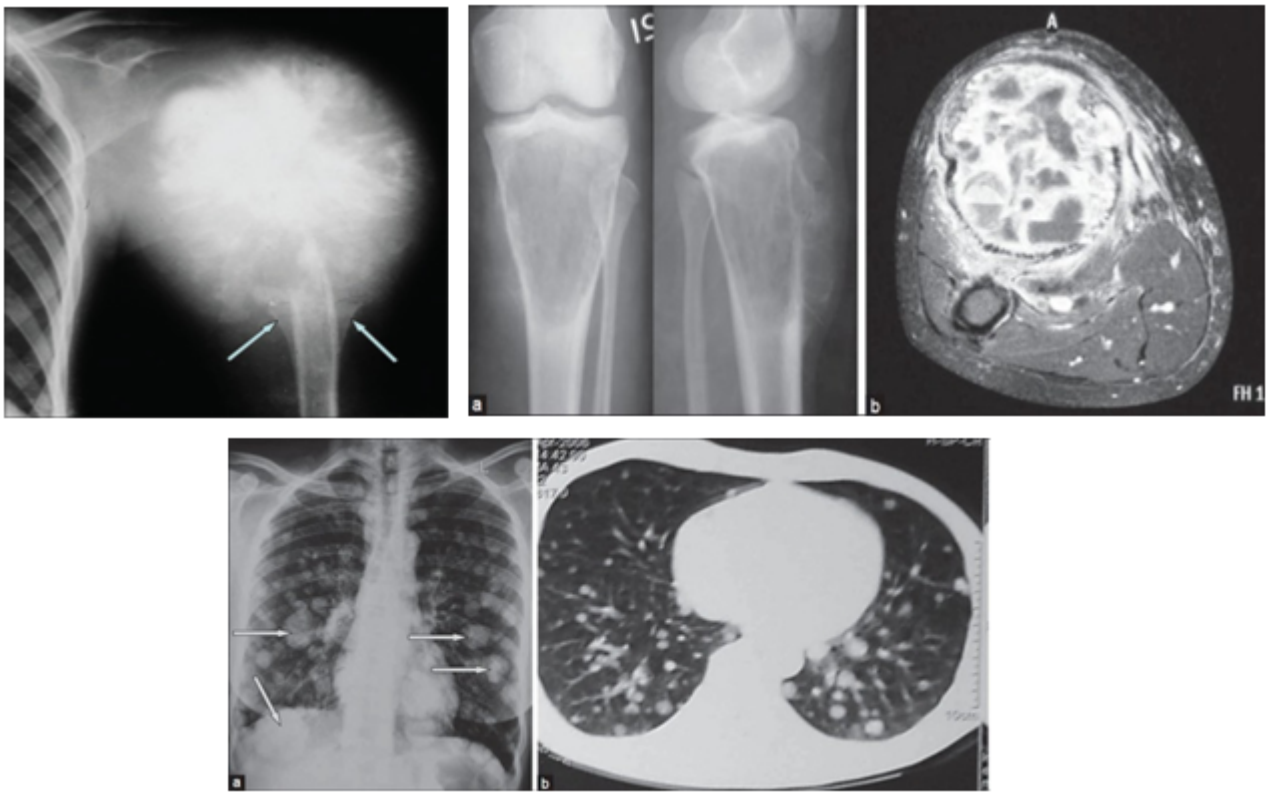


Figure 1: X-ray of humerus anteroposterior view showing osteosarcoma of the proximal humerus- typical sun burst or sun ray appearance, new bone formation in soft tissues, and Codman's triangles (arrows)

Figure 2: Telangiectatic type of osteosarcoma of the proximal tibia: (a) X-ray anteroposterior and lateral views showing lysis and expansion (b) MRI showing fluid levels

Figure 3: Plain X-ray chest of a patient of osteosarcoma showing multiple metastatic lung nodules (b) CT scan (axial section) demonstrating multiple metastases in both lungs.

Computerized tomography scan

CT scan delineates the bony anatomy/architecture like cortical integrity more clearly and picks up pathological fracture and is helpful in assessing ossification and calcification (chondroid component) more accurately.[26,27]

Magnetic resonance imaging

MRI is the most accurate tool for determining the limits of tumor within and outside the bone.[9,28,29,30]

MRI accurately and precisely delineates (1) extent of the tumor into the soft tissues and the medullary canal, (2) involvement of joint, (3) crossing of the lesion through and/or around the growth plate, (4) any skip lesion in the same bone and across the joint in other bone, (5) proximity and/or encasement of the neurovascular bundle by the tumor.

Radionuclide bone scan

Tc99 methylenediphosphonate (Tc99 MDP) bone scan is the most commonly used investigation for detecting osseous metastasis.

Positron emission tomography

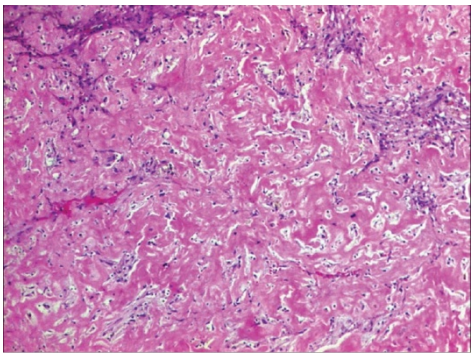
Positron Emission Tomography (PET), which picks up metabolic activity is evolving with tremendous potential in oncology.[31]

Biochemical markers

The role of biochemical markers like serum alkaline phosphatase (ALP) and lactate dehydrogenases (LDH) for diagnosis, prognosis and response to treatment. The response of therapy can be monitored with the levels of these enzymes. High levels after treatment may persist with residual disease or recurrence and in the presence of metastasis.[10]

Biopsy

Biopsy should be performed after complete history, clinical examination and imaging. It confirms the diagnosis, reveals specific type and furnishes the grade of the tumor. It is performed by either an open (incisional) or a closed method. Closed biopsy is performed as fine needle aspiration cytology (FNAC) and core needle biopsy.[9]



Classic osteosarcoma in which there is abundant production of osteoid and bone matrix into which the malignant cells are incorporated.

Staging

The common staging systems for malignant bone tumors are: Enneking system for staging malignant musculoskeletal tumors and the American Joint Committee on Cancer (AJCC) System for staging bone sarcomas.[8]

Table 1: Enneking system for staging malignant musculoskeletal tumors

Stage	Grade	Site	Metastasis
IA	Low	Intracompartmental	None
IB	Low	Extracompartmental	None
IA	High	Intracompartmental	None
IIB	High	Extracompartmental	None
III	Any	Any	Regional or distant metastasis

Table 2: American joint committee on cancer system for staging bone sarcomas

Stage	Grade	Size	Metastasis
I-A	Low	<8 cm	None
I-B	Low	>8 cm	None
II-A	High	<8 cm	None
II-B	High	>8 cm	None
III	Any	Any	Skip metastasis
IV-A	Any	Any	Pulmonary metastasis
IV-B	Any	Any	Nonpulomnary metastasis

CONCLUSION

The plain radiograph provides the best clue to the diagnosis and MRI the local extent. Thorax CT scan and Tc99 bone scan are used for the detection of lung and bony metastasis respectively. The biopsy confirms the diagnosis and reveals the grade of the lesion. The basic principles of biopsy should be followed precisely and meticulously. After clinical, radiological and the histopathological examinations the tumor can be staged adequately.

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