

Characterizing Malignant Bone Tumors on Magnetic Resonance Imaging and Review of Literature

Dr. Pratiksha Yadav^{1*}, Dr. Dhaval Thakkar², Dr. Mansi Jantre³

Department of Radio-diagnosis, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pune, India

Abstract: Purpose of this study is to evaluate the role of magnetic resonance imaging (MRI) in the more specific diagnosis of the bone tumors and characteristic MRI features of the primary malignancies of bones. Primary bone malignancies are uncommon and constitute approx. 0.2 % of all the malignancies. Bone tumors are present with non-specific complaints of pain, swelling and sometimes restricted mobility. Imaging has a very important role in the evaluation of the bone tumors for the location, extent, periosteal reaction, cortical erosion and matrix characteristic. Primary investigation is radiograph however MRI is the best modality to evaluate the osseous as well as extra-osseous component, marrow involvement, exact extent and neurovascular involvement. It is very helpful in staging of the tumor.

Keywords: Bone tumour, sarcoma, multiple myeloma, plasmacytoma,

I. Purpose

To determine Sensitivity and specificity of MRI to detect the bone marrow involvement, neurovascular bundle involvement, extent of the tumor, cortical erosions, soft tissue and joint involvement. All the lesions were evaluate for the MRI characteristics of bone involvement, periosteal reaction, soft tissue component, marrow involvement, cortical erosion, secondary fracture, neurovascular bundle involvement, transition zone, hemorrhage, necrosis. Diagnosis depends upon location of the tumor, age of the patient, aggressiveness and matrix character.

II. Materials and methods

This was a study of 21 patients which was having known malignant bone tumors proven by biopsy after investigations. All patients were referred from orthopedic department who are known or suspicious bone tumors. All the cases were first evaluated with plain film examination. The plain film included at least 2 projections (Anteroposterior and lateral). Followed which Magnetic Resonance Imaging (MRI) was performed on a 1.5 Tesla AVANTO System. Initially a large field of view T1W TSE and STIR TSE sequence was obtained of the area of interest in coronal plane using body coil to ensure that the extent of tumor and skip lesions were identified. This was followed by T1 and T2 weighted TSE sequences in axial plane supplemented by sagittal and coronal planes using surface coil. Second plane of imaging included a STIR sequence. Post contrast fat saturated T1 weighted images were obtained after giving 10ml of IV Gadolinium in all cases. CT scan was also done whenever needed. Biopsy was advised in all the cases and then surgery and the treatment were planned.

III. Conclusion

MRI is an excellent imaging modality for the evaluation of the musculoskeletal tumors. MRI high tissue contrast and multiplanner imaging capability helps in the delineation of the tumor, it's extent in the bone marrow and soft tissue, involvement of the neurovascular bundle, joint involvement and it's staging.

Whereas the radiograph is the primary investigation for the bone tumors to see the location, extent, cortical erosion, periosteal reaction and matrix mineralization, MRI is the best imaging modality to evaluate the marrow involvement and soft tissue component. It is useful to detect the skip lesions and relation to neurovascular bundle to estimate the resectability. In 21 patients 5 patients have osteosarcoma, 4 patients have chondrosarcoma, 3 patients detected ewings sarcoma, 1 patient had plasmacytoma, 4 patients detected multiple myeloma, 1 patient has liposarcoma, 1 patient has angiomyosarcoma and 7 patients detected bone metastasis.

IV. Introduction

Primary bone neoplasms of bones are relatively uncommon accounts only 0.2% of all the neoplasm according to world health organization (WHO) [1]. Diagnostic imaging has an important role in initial detection, characterization, pre-operative assessment and long-term follow-up of malignant bone tumors. Evaluation of bone tumors involves a multimodality approach.

Bone tumors are currently classified according to the line of differentiation of neoplastic cells and their resemblance to normal counterparts. Primary benign and malignant bone tumors have been grouped into fifteen different categories which include cartilage, osteogenic, fibrogenic, fibrohistiocytic, hematopoietic, giant cell,

notochordal, smooth muscle, vascular, lipogenic, and neural tumors, Ewing sarcoma/primitive neuroectodermal tumor, miscellaneous tumors and lesions, and joint lesions [1].

Cancer registry data with histologic stratification indicate that osteosarcoma is the most common primary malignant tumor (approx. 35%), followed by chondrosarcoma (25%) and Ewing's sarcoma (16%) [WHO classification of bone tumors]. Chordomas and malignant fibrous histiocytoma are much less frequent constituting approx. 8% and 5% respectively.

Clinical features of bone tumors are non-specific and generally pain, swelling and discomfort. Limited mobility, fracture may occur. Pain is the most common symptom in nearly all the malignant bone tumors. Initially pain is neuralgia-like pain. In case of involvement of neurovascular bundle there is radiating pain. Swelling is second common feature, swelling is only observed when there is extra-osseous component of tumor or the bone is expanded due to tumor. Skin changes may occur, tight shiny skin prominent veins ulcers may also occur. When tumors occur near the joint there is limitation of movement, sometimes-reactive synovitis pathologic fracture, general features like fever weight loss may occur. Pattern of periosteal reaction depends on its growth, when tumor is benign and slow growing periosteum has enough time to build thick layer of bone. Perpendicular periosteal formation is strongly suggestive of malignancy. Codman's triangle is indicative of elevated periosteum broken by tumor growth. Cortical erosions and soft tissue component usually indicate more aggressive tumors.

The most common primary malignant bone tumors are osteosarcoma (35%), chondrosarcoma (25%) and Ewing's sarcoma (16%). Staging of the lesion is essential for management. The surgical staging system of musculoskeletal neoplasms was initially proposed by Enneking, et al. in 1980[2]. As outlined by Enneking, et al., the purpose of a staging system for musculoskeletal neoplasms was to stratify the stages and provide guidelines for further treatment.^[1]

The later developed American Joint Commission on Cancer (AJCC)– International Union against Cancer (UICC) system is now widely used for the staging of bone tumors [3].

MRI is the preferred modality for identifying the local extent as well as for staging of these tumors. Radiographs provide information regarding lesion location and adjacent periosteal reaction. However, the excellent contrast resolution and multiplanar imaging of MRI enables us to evaluate both intracompartmental and extracompartmental extent of bone. This particularly holds true with regards to invasion of muscle, neurovascular structures and adjacent fat planes and degree of marrow involvement. MRI has also been shown to be superior in assessing intraarticular extension and the presence of intratumoral necrosis and hemorrhage. MRI is the best technique to detect skip lesions, which may often be missed by other imaging means [4]. According to Type of matrix-osteolytic, osteoblastic, and osteolytic with matrix mineralization bone tumors are categorized into osteoid, chondroid, fibrous, cystic (aneurysmal bone cyst), lipoid, vascular (hemangioma), small cell (ewings), plasma cells (plasmacytoma/multiple myeloma) and histiocytes (eosinophilic granuloma).

Lodwick classification –Three main type of bone destruction pattern visible on radiographs

Type I A-Geographic with well-defined borders with sclerotic rim- non-ossifying fibroma

TYPE IB-well defined and sharp borders but without sclerotic rim –aneurysmal bone cyst

Type 1c-geographic but blurred border –giant cell tumor

Type ii-geographic with moth eaten or permeated pattern, patchy lysis-osteosarcoma

Type iii-small, patchy lytic bone destruction with moth eaten or permeated pattern-ewings sarcoma

Periosteal reaction pattern –lamellated, amorphous or sunburst appearance.solid –dense in benign.

Location –epiphysis –metaphysis-diaphysis, centric, eccentric, juxtacortical, age, periosteal reaction, cortical destruction, matrix,

MRI is very useful to determine the intraosseous and extraosseous extent of the tumor. Age specific incidences of the bone sarcomas are bimodal with first peak occurs in the second decade and second peak occurs in patients more than sixty years of age. It is different with soft tissue sarcomas, which show gradual, increase in incidence with age.

V. Osteosarcoma

Osteosarcomas are bone forming malignant tumors, which accounts for approximately 35% of all primary bone tumors (1). They are the second most frequent primary bone tumor after multiple myeloma (5). Osteosarcomas are derived from undifferentiated connective tissue and forms neoplastic osteoid. They are divided into different subtypes depending upon their location and histological composition. They are grossly divided into three subtypes according to their location intramedullary, juxtacortical or extraskeletal. The current World Health Organization classification of osteosarcoma of bone includes eight categories: conventional, telangiectatic, small cell, low-grade central, secondary, parosteal, periosteal, and high-grade surface (6).

It is the most common primary malignant bone neoplasm in young males and females with a peak incidence between 10 to 25 years of age. The long bones of the extremities are the target sites for osteosarcoma.

The knee and shoulder are the most commonly affected joints. Other bones that may be involved are the calvaria, sacrum, pelvis, mandible, maxilla, scapula, clavicle, ribs, hand, calcaneus, and spine.

Radiograph is the primary investigation, which detects the tumor location, size, periosteal reaction and matrix pattern (Figure 1 a& b). Computed tomography (CT) show the features similar to that of plain film radiography but is more sensitive in detecting areas of tumor bone formation, cortical erosions and showing periosteal reactions. In addition, CT is of value in defining the anatomy and osseous changes in those bones, which is difficult to evaluate on plain radiographs. Magnetic resonance (MR) imaging is the modality of choice following routine radiography in the evaluation of osteosarcoma. Osteosarcomas are of low to intermediate signal intensity on T1-weighted pulse sequences (Figure 2 c) and hyperintense on T2 sequences (Figure 2 a& b). It shows heterogeneous post contrast enhancement (Figure 2 d). MR imaging have a better soft tissue, which allows for better evaluation of tumor involvement within the overlying soft tissues, especially the neurovascular bundles. MR imaging can more accurately detect joint involvement. Furthermore, imaging with a large field of view makes detection of skip metastases easier.



Figure 1: Osteosarcoma: Radiograph AP and Lateral view of left knee of 22 years old female showing a mass seen involving the postero-lateral aspect of distal femur, it shows osteoid matrix and elevated periosteum. This mass is displacing the muscles .

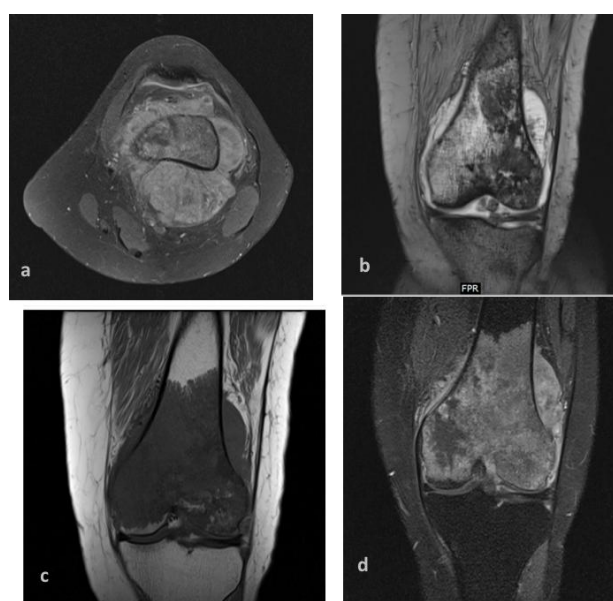


Figure 2: Osteosarcoma: MRI of knee of the same patient showing a mass involving distal femur, it is hyperintense on STIR (a& b) and hypointense on T1WI (c). It shows heterogenous post contrast enhancement (d). Soft tissue component seen around the mass.

Chondrosarcoma: Primary chondrosarcoma is the third most frequent malignant bone tumor after myeloma and osteosarcoma [7]. It is most commonly seen between 30 to 70 yrs. of age, it has male predominance male: female ratio is 1.5: 1. Usually they are present with pain and tenderness with or without mass. Characteristic feature of chondrosarcoma is to produce coalescent cartilage lobules of varying sizes with cystic or necrotic center [8]. Commonest sites are the pelvic bones, femur, humerus and ribs. Chondrosarcoma can occur in preexisting enchondroma or osteochondroma. Central chondrosarcoma predominantly occurs in long bones and peripheral tumors in pelvis and vertebrae [9]. Chondrosarcoma is graded from 1 (low grade) to 3 (high grade). Low-grade chondrosarcoma is close in appearance with enchondroma and osteochondroma, which has occasional binucleated cells. High-grade chondrosarcomas have increased cellularity, atypia and mitosis [10]. Radiograph is very important to locate the tumor and assessment of the tumor matrix, which may be punctate, flocculent, or ring like (Figure 3a). It can be small, disseminated or subtle. Most commonly it is well-defined lytic lesion on radiograph with endosteal scalloping, cortical thinning or thickening and periosteal reaction. Soft tissue involvement can also be seen. Bony destruction and cortical erosions are more clearly seen on CT scan (Figure 3 b). MRI is the best modality to evaluate the chondrosarcoma extent, bone marrow involvement, and extraosseous component. Typically on MRI it shows a lobulated mass with low signal on T1WI (Figure 3 c) and high signal intensity on T2WI (Figure 3 d). It shows multiple septations (Fig 3 d), which enhance after gadolinium injection. High-grade tumors do not have septations and show more diffuse and heterogeneous enhancement. Differential diagnosis includes osteosarcoma or benign cartilaginous lesions. Treatment of chondrosarcoma is radical surgery. Survival rate of patient depends upon location, size and stage of the tumor. Chondrosarcoma of the extremities have better survival rate [10].



Figure 3: Chondrosarcoma: Radiograph of left shoulder of a 60 years old female shows a lobulated expansile osteolytic intramedullary lesion seen in proximal humerus, multiple septations also seen. Axial CT scan in soft tissue window showed intramedullary mass with cortical erosions at places (b). Coronal MRI showed mass is hypointense on T1WI (c) and hyperintense on T2WI (d). Hypointense fibrous septation seen on T2WI. Soft tissue component seen on medial and lateral aspect.

Ewing’s sarcoma:

Ewing’s sarcoma is an aggressive, highly malignant primary bone tumor that is derived from red bone marrow and was first described by James Ewing in the year 1921 [11]. Ewing’s sarcoma is the second most frequent primary bone tumor after osteosarcoma [12]. It occurs almost exclusively in young children and adolescent and is the second most common malignant bone tumor in children and young adults (13). The overall prognosis is poor. Ewing’s sarcoma (ES), peripheral primitive neuroectodermal tumors (PNET), and Askin tumors (AT) are commonly referred to as Ewing’s tumors (ETs) [14]. ES is a round-cell sarcoma, showing varying degrees of neuroectodermal differentiation. In contrast with osteosarcoma, Ewing’s sarcoma has a variable location. ES has a predilection for the pelvis and lower extremities [15,16,17]. The most frequent location is the pelvis, followed by the femur, tibia and humerus. In long bones, lesions are located in the (meta) diaphysis and the epiphyseal involvement is rare. (18). Location in the midshaft rather than at the end of the long bones is more frequent (15). Unlike osteosarcoma this tumors may exhibit systemic symptoms, mimicking

osteomyelitis (15). The radiographic hallmark is an osteolytic lesion with an onion-skin periosteal reaction. The radiographic appearance may be extremely variable and in 25 percent of cases the lesion can be sclerotic. A soft-tissue component is common (15). Typical ewings sarcoma show permeative lesions CT scan is useful to evaluate joint extension, periosteal reaction and matrix of the lesion. MRI is preferred owing to its high contrast resolution and the ability to define the margins of the soft-tissue components. Transverse TSE T2-weighted images best display the interface between tumor and adjacent soft tissues and the anatomical relationship with the neurovascular structures, allowing differentiation between intracompartmental and extracompartmental disease. Contrast between tumor and normal tissue, especially fat-containing tissue, is greatly enhanced by combining TSE with fat-selective presaturation. T1-weighted images after administration of contrast material can be successfully combined with fat-selective presaturation to enhance contrast resolution. It is mixed signal intensity on T1WI (Fig 4 a) and hyperintense on T2WI (fig 4 b&c), it shows significant post contrast enhancement (Fig 4 d).

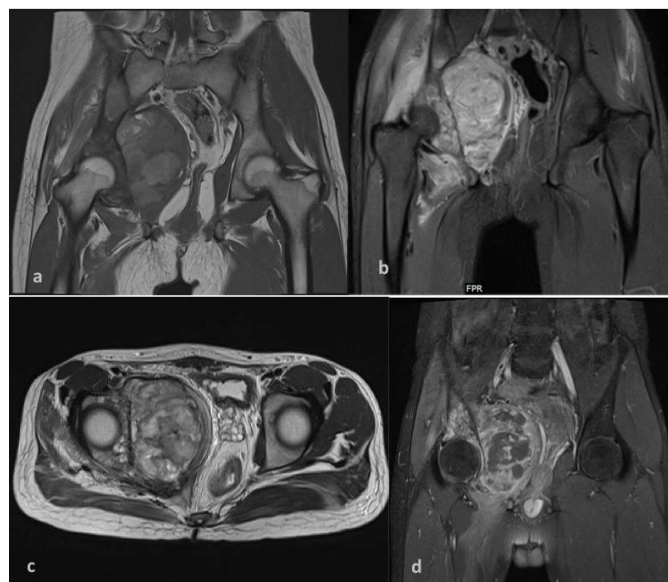


Figure 4: Ewing's Sarcoma: A well defined mass seen involving the right pelvic bone of 17 years old male, it shows mixed signal intensity on T1WI (a), hyperintense on STIR (b) & T2WI (c). It showed heterogeneous post contrast enhancement (d). Mass is displacing the soft tissue of pelvis to contralateral side.

Plasmacytoma/Multiple myeloma: Multiple myeloma is the most frequent primary bone malignancy. It is a neoplastic proliferation of plasma cells and is a form of plasma cell dyscrasias that may manifest as multiple myeloma, primary amyloidosis, or monoclonal gammopathy of unknown significance. Plasmacytoma may be primary or secondary to disseminated multiple myeloma and may arise from osseous (medullary) or nonosseous (extramedullary) sites. Primary extramedullary plasmacytoma can be solitary or multiple. There are three distinct groups of plasmacytoma defined by the International Myeloma Working Group: solitary plasmacytoma of bone (SPB), extramedullary plasmacytoma (EP) and multiple plasmacytomas that are either primary or recurrent [19]. The International Myeloma Working Group (IMWG) has published criteria for the diagnosis of plasmacytomas [19]. They recognize three distinct entities: SBP, EP and multiple solitary plasmacytomas (+/- recurrent). The proposed criteria for SPB is the presence of a single bone lesion, normal bone marrow (less than 5% plasma cells), small or no paraprotein, no related organ involvement/damage and a normal skeletal survey (other than the single bone lesion).

Plasmacytomas are a rare form of cancer. SPB is the most common form of the disease and accounts for 3-5% of all plasma cell malignancies. The median age at diagnosis for all plasmacytomas is 55. Both SPB and EP are more prevalent in males; with a 2:1 male to female ratio for SBP and a 3:1 ratio for EP [20]. The common presentation of SBP is in the axial skeleton, whereas the extramedullary plasmacytoma (EMP) is usually seen in the head and neck.

Primary plasmacytoma, whether osseous or nonosseous, is distinguished from multiple myeloma by the absence of hypercalcemia, renal insufficiency and anemia, normal skeletal survey, absence of bone marrow plasmacytosis, and serum or urinary paraprotein level of less than 2 g/dL [21,22,23]. Plasmacytomas are typically seen as well-defined, "punched-out" lytic lesions (Fig 5 and b) with associated extra-pleural soft-tissue masses, similar in appearance to most metastatic lesions on radiography. In advanced plasmacytoma, there is often marked erosion, expansion, and destruction of bone cortex, sometimes with thick ridging around the periphery,

creating a “soap bubble” appearance. MRI shows Low or intermediate signal on T1-weighted imaging (fig 5a) and hyperintense on T2-weighted imaging(Fig 5 b), and significant enhancement with gadolinium. Whole-body MRI may be an effective technique to detect multiple lesions. Marrow involvement on MRI plays an important role in assessment myeloma bone disease. They include normal appearance of bone marrow despite minor microscopic plasma cell infiltration, focal involvement, homogeneous diffuse infiltration, combined diffuse and focal infiltration.

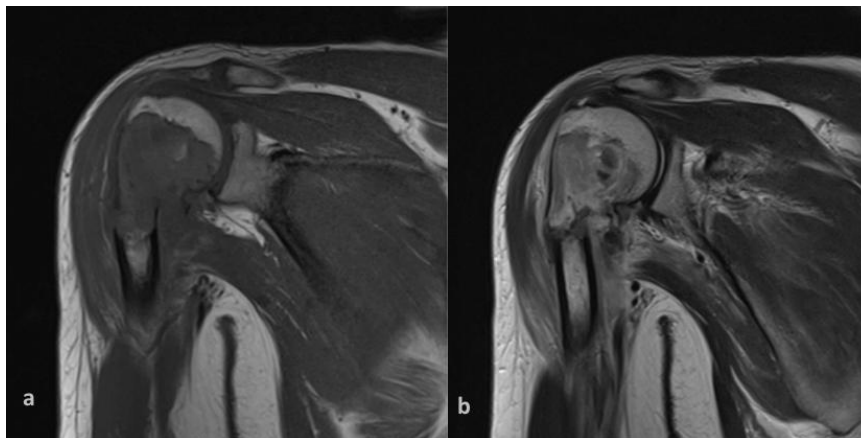


Figure 5: Plasmacytoma: A well defined intramedullary mass involving the metadiaphysis of right humerus of 63 years old male which is hypointense on T1WI & show mixed signal intensity on T2WI. There is secondary (pathological fracture) seen in proximal shaft of humerus.

Soft tissue sarcomas

Sarcomas are rare neoplasms of mesenchymal origin. The three most common soft-tissue sarcomas are malignant fibrous histiocytoma (MFH), liposarcoma, and leiomyosarcoma. The common subtypes in the extremities are MFH and liposarcoma, Leiomyosarcoma are the common in the retroperitoneum and the abdominal cavity. Risk factors for soft-tissue sarcomas include previous radiation therapy, exposure to chemicals (e.g. vinyl chloride, arsenic), immunodeficiency, prior injury (scars, burns), neurofibromatosis, Paget’s disease and genetic syndromes (hereditary retinoblastoma, Li–Fraumeni syndrome). Although CT is preferred for detecting calcifications and assessing bone involvement, MRI is the investigation of choice in the evaluation of soft-tissue lesions owing to its superior contrast resolution. Aggressive features of a soft-tissue neoplasm include size greater than 5 cm, deep location, and absence of central enhancement, which is suggestive of necrosis[24]. A pseudocapsule or capsule is commonly seen around a sarcoma in the soft tissues, producing well-defined margins on MRI.

Malignant fibrous histiocytoma is a tumor that develops from primitive mesenchymal cells and has markers of histiocytoid differentiation. It is the most common malignant neoplasm of soft tissues, which account for 25-40% of all adult soft tissue sarcoma (25) it is seen more often in men, with a peak incidence between 50 and 70 years of age. On MRI, malignant fibrous histiocytoma have low signal intensity with T1 weighting and heterogeneous high signal intensity with T2 weighting [26,27]. On CT its density is the same as that of muscle. Areas of lower attenuation correspond to necrosis. MRI is better than CT in determining the extent of tumor, but CT is considered superior in detecting bone involvement and calcifications within the tumor. Calcifications are seen in up to 20% of malignant fibrous histiocytomas [28].

Liposarcoma is a malignant soft tissue neoplasm that contains cells with lipoblastic or lipocytic differentiation. LPS accounts for 20–25% of adult soft-tissue sarcomas, and the peak age of onset is in the fifth to seventh decades [29,30,31]. It is the second most common malignant soft tissue tumor after malignant fibrous histiocytoma. Liposarcomas are most common in the extremities, especially the thigh, and in the retroperitoneum [32].

The CT or MRI appearance depends based on amount and distribution of fat in tumour: portions of the tumor that contain fat demonstrate a low attenuation coefficient on CT scans and high signal intensity on T1-weighted MR images (Fig 6 a)[29,30]. These tumours are typically relatively well circumscribed, located within or adjacent to muscle, they may exert mass effect on adjacent structures due to their large size at presentation (Fig 6). It shows peripheral post contrast enhancement (Fig 6 b). It shows mixed signal intensity on T2WI (Fig 6 c). Synovial sarcoma is a malignant soft tissue tumor, which develops from undifferentiated mesenchymal cells; less than 10% of synovial cell sarcomas are within a joint. Usually they are adherent to a joint capsule, bursa, fascia, or tendon sheath. They are most common in the lower extremity.

Synovial sarcoma has low to intermediate signal intensity on T1-weighted MR images and heterogeneous high signal intensity on T2-weighted images [33]. This tumor is often multilocular.

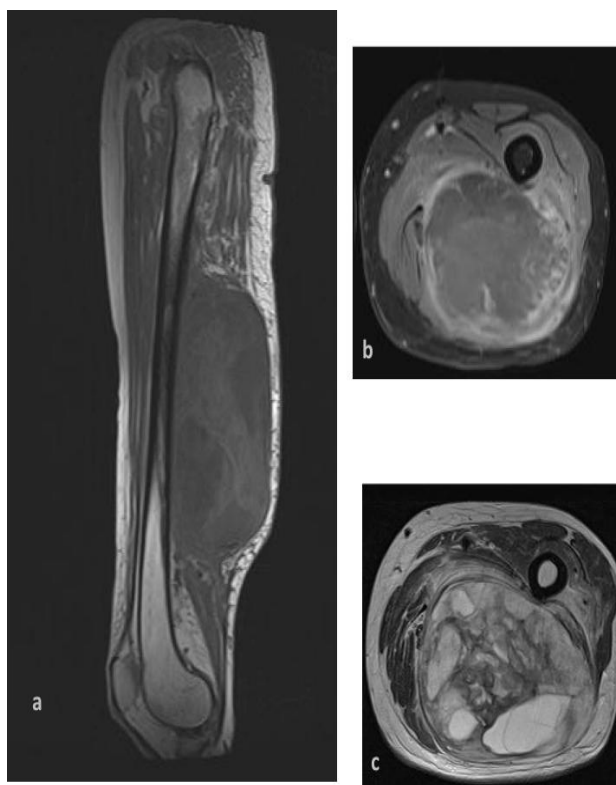


Figure 6:Liposarcoma: A well defined mass seen involving the posterior aspect of mid shaft of the femur of 32 years old male,it shows mixed signal intensity on T1WI(a) and predominantly hyperintense on T2WI(c).It shows peripheral post contrast enhancement (b).

Bone metastasis

Bone metastases are common and often multiple. To differentiate them from other primary bone tumors is essential. Tumors with a high rate of metastasis to bone include tumors of the breast (72%), prostate (84%), thyroid (50%), lung (31%), kidney (37%), and pancreas (33%). These account for more than 80% of primary tumors in patients presenting with metastases [34,35]. CT scan has had a limited impact upon the clinical detection of skeletal metastases although it is more sensitive than conventional radiography for the detection of destructive bone lesions. Magnetic resonance imaging (MRI) is highly sensitive to detect the presence of skeletal metastases compared to other imaging modalities. MRI is the only imaging technique that allows direct visualization of bone marrow with high spatial resolution. The bone marrow contains a high percent- age of fat; hence T1-weighted magnetic resonance images generally reveal metastases as focal areas of low signal intensity and hyperintensity on T2WI & STIR (Figure7). The lesions can be distinguished from focal deposits of red marrow on T1-weighted images because the latter are more focal and may have centrally located fat, giving the appearance of a “bull’s eye”[36].

On fat-suppressed T1-weighted images, metastases demonstrate mixed to high signal intensity [36]. On T2-weighted images, metastatic lesions usually are much brighter than normal marrow due to their high water-content. A variety of different MRI pulse sequences can be utilized. Fat and water distribution in bone marrow, indirect visualization of normal bone trabeculae, indirect evaluation of bone edema and cell density and the study of vascularization are useful in characterization of lesions on MRI.It is noted that magnetic resonance imaging can detect metastases that are not apparent on radioisotope bone scans.

Steinborn et al reported sensitivities of 91.4% for MRI and 84.8% for bone scintigraphy[37].Flickinger and Sanal reported sensitivities of 100% for MRI and 62% for scintiscanning and specificities of 62% for MRI and 100% for scintiscanning[38].Thus in comparison to conventional bone scan, whole body MRI utilizing whole body fast short tau inversion recovery (STIR) sequences has significantly better sensitivity and specificity[39,40].

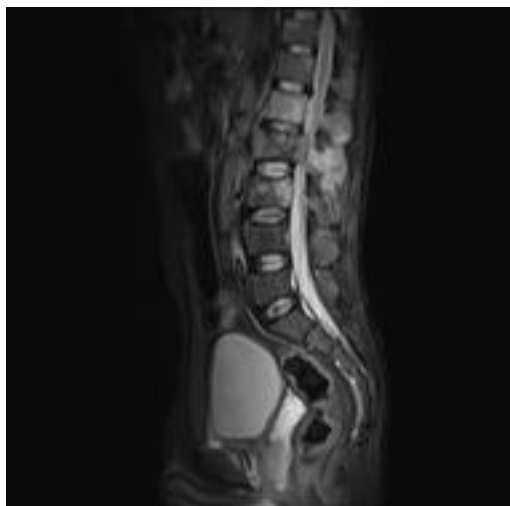


Figure 7: Metastasis : Sagittal STIR MR images of a patient with ewings sarcoma with spinal metastasis . Hyperintense signal intensity seen involving the L1,L2 & L3 vertebral bodies and their posterior elements.

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