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# Osteosarcoma: Review and Diversity of Cases

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## ABSTRACT

Osteosarcoma is the most common primary malignant tumour of bone in adolescents and young adults. It accounts for approximately 15% of all primary bone tumors confirmed at biopsy. There are numerous types of primary osteosarcoma, including are intramedullary osteosarcoma, juxtacortical (surface) osteosarcoma, and extra skeletal osteosarcoma. Osteosarcoma may also occur as a secondary lesion in association with underlying benign conditions. The identification of neoplastic osteoid matrix formation and aggressive characteristics are necessary for histological diagnosis of osteosarcoma. In all bone tumors, differential diagnosis is best assessed with radiographs, whereas staging is performed with computed tomography or magnetic resonance imaging. Beside literature review, we are going to discuss 26 cases of primary osteosarcomas of bone (majority are of conventional type) and 03 cases of extra- skeletal osteosarcomas.

**Key words:** Osteosarcoma, H.G. (high grade) intramedullary osteosarcoma, gnathic osteosarcoma.

## INTRODUCTION

Osteosarcoma (osteogenic sarcoma) is the second most common (primary) malignant bone tumor while foremost frequent is the multiple myeloma. It is the most common primary malignant bone tumor to affect children and adolescents. Osteosarcoma accounts for approximately 15% of all primary bone tumors confirmed at biopsy[1, 2, 3].

Various types of osteosarcoma have been described, including intramedullary (high-grade, telangiectatic, low-grade, small cell, osteosarcomatosis, and gnathic tumors), juxtacortical (intracortical, parosteal, periosteal, and high-grade surface tumors), and extra skeletal. Osteosarcoma can also develop secondary to malignant transformation within a preexisting benign bone lesion, such as Paget`s disease, osteonecrosis, fibrous dysplasia, or chronic infection, or can arise in previously irradiated areas. These different types of osteosarcoma often have distinctive radiologic appearances that constitute the imaging spectrum for this malignant tumor. Understanding and recognition of the variable appearances of the different varieties of osteosarcoma allow improved patient assessment and are vital for optimal clinical management including diagnosis, biopsy, staging, treatment, and follow-up.

## MATERIAL AND METHODS

We had received bone biopsies and later amputated limbs or radical /modified radical surgery specimens in the Histopathology department of Shaikh Zayed Hospital and private clinical laboratory. Representative sections were taken. The bone is decalcified after being treated with a 10% solution of nitric acid or formic acid (depending upon the size) and later subjected to routine paraffin processing (by using automated tissue processor). Tissue sections were being cut from these paraffin blocks underwent time tested Hematoxilin and Eosin stain (by using automated stainer) and examined under the light microscope.

## RESULTS

Twenty six cases of primary osteosarcomas of bone, majority of which were of conventional

type including 02 cases of Gnathic, 01 case 0f HG intra-medullary osteosarcoma with extensive chondroid differentiation, 01 case of parosteal, 01 case of periosteal and 01 case of fibroblastic type of intramedullary osteosarcoma. In addition 03cases of extra- skeletal primary osteosarcomas were also diagnosed.

## REVIEW OF LITERATURE AND DISCUSSION

In this article, we will review the literature and discuss the different types/cases of osteosarcoma.

### Primary intramedullary osteosarcoma

The majority of osteosarcomas arise in the medullary canal. The tumor originates within the medullary canal and often involves the entire width of the bone. These lesions have been categorized into numerous types, largely on the basis of histological appearance.

### High-grade intramedullary osteosarcoma

The high-grade intramedullary variant of osteosarcoma (conventional osteosarcoma) accounts for approximately 75% of all lesions[1-4]. These lesions are seen in patients in the 2nd and 3rd decades of life, with 75% of cases encountered in patients 15-25 years of age[1-4]. Occurrence in patients younger than 6 years of age or older than 60 years of age is unusual and typically affects whites and males, with a male-to-female ratio of 1.5-2:1[1-5]. While in black females is nearly five times less than that for white males[1-5]. Usually sporadic but isolated cases of familial form are also reported[6] The clinical manifestations are usually nonspecific, with pain and swelling being the most frequent symptoms associated with a history of trauma, which brings the lesion to clinical attention. Pathologic fracture is reported in approximately 15%-20% of cases, either at presentation or during therapy[1-4].

This neoplasm most frequently affects long bones (70%-80% of cases), particularly about the knee (50%-55%)[1-5] with involvement of femur is in 40%-45% of cases, the tibia in 16%-20%, and the humerus in 10%-15%[1-5]. Involvement of the pelvis, fibula, facial bones, and spine is unusual, and the skull, clavicle, ribs, scapula, forearm, and small bones of the feet and hand are rarely affected. Mostly (90%-95%) H.G.I. osteosarcoma arise in the metaphysis[1-5] 2%-11% of cases in the diaphysis, with longer duration of symptoms prior to diagnosis[7,8]. Although Osteosarcoma with metaphyseal involvement often extends into the epiphysis (75%-88% of cases with open epiphysis), initial manifestation within the epiphysis is very rare (<1%)[1, 2]. In this malignant mesenchymal neoplasm, the tumor cells directly produces osteoid or immature bone. Many lesions also contain other elements, like fibrous or chondroid components, but only a minority of the intraosseous tumor is producing osteoid, it is designated as an osteosarcoma. Grossly, osteosarcoma is usually a large (5-10-cm) intraosseous tumor with frequent soft-tissue extension. The osteoid and the chondroid elements may reveal mineralization with foci of hemorrhage. Osteosarcoma has been divided into osteoblastic, chondroblastic, and fibroblastic varieties, depending on the predominant cell type present. Although many lesions have a mixed histological appearance, the predominant pattern is osteoblastic in 50%-80% of osteosarcomas, fibroblastic-fibrohistocytic in 7%-25%, and chondroblastic in 5%-25%[1-4]. Histologically reactive new bone from many reparative processes including fracture can resemble osteosarcoma, and correlation of histological findings with radiologic results is essential to ensure correct diagnosis. Osteosarcoma is graded from I to IV according to the degree of anaplasia, although the prognostic significance of this parameter is controversial.

As in all cases of a bone lesion, the primary evaluation of an osteosarcoma begins with radiographic assessment. HG.I. osteosarcomas are aggressive lesions with rapid doubling times (20-30 days) and therefore are often large (typically >6 cm) at the time of diagnosis. At radiographic examination, the vast majority (approximately 90%) of osteosarcomas demonstrate a variable amount of fluffy, cloudlike opacities within the lesion, characteristic of osteoid matrix production[1-4] most lesions are completely reveal mixed pattern of sclerosis and lucent areas . Occasionally, the lesion may be completely blastic or lytic (these.

osteosarcoma tends to invade the cortex without expanding the boney contours, aggressive pathologic behavior. This reflecting neoplastic behavior is associated with aggressive periosteal reaction (Codman triangle, laminated, hair-on-end, or sunburst patterns) and soft-tissue masses in 80%-90% of cases[1-4].

Most osteosarcomas have typical radiographic appearance at poses little the diagnostic dilemma. Additional imaging techniques such as CT, MR imaging, and bone scintigraphy are typically not needed to diagnose an osteosarcoma. However, unusual radiographic appearances can lead to delay in diagnosis and confusion with benign diseases[9]. This situation is particularly likely when the osteosarcoma involves anatomically complex areas such as the pelvis and in the case of small lesions (often <5 cm and adjacent to the endosteum). In these cases, cross-sectional imaging may not only help confirm the presence of the lesion but also help identify mineralized matrix that is not appreciable at radiography. More important, these imaging modalities are vital in the preoperative assessment and staging of osteosarcoma[10].

At bone scintigraphy, marked uptake of radiotracer is seen on blood flow, blood pool, and delayed images. Presently, however, the chief role of scintigraphy is in evaluating for distant metastases. Both osseous and extraosseous metastatic disease may be detected.

The aggressive characteristics of high-grade intramedullary osteosarcoma, both intraosseous and soft-tissue components, are also well seen at CT (9). Non-mineralized portions of tumor are usually of soft-tissue attenuation and replace the normal low attenuation of fatty marrow. Chondroblastic components may be of low attenuation on CT scans, reflecting higher water content. Areas of central hemorrhage or necrosis, which also have low attenuation, are frequent. Osteoid matrix production is easily appreciated in both intraosseous and soft-tissue tumor components as areas of very high attenuation. The chief advantage of CT is its ability to demonstrate small areas of mineralized matrix that might not be detected with MR imaging in predominantly lytic lesions.

MR imaging has become the cross-sectional imaging modality of choice for preoperative evaluation and staging of osteosarcoma because of its superior contrast resolution and multiplanar capabilities[10]. Tumor is seen primarily as areas of intermediate signal intensity on T1-weighted images and as areas of high signal intensity replacing the normal marrow on T2-weighted images. Areas of low signal intensity on both T1- and T2-weighted MR images are frequent and represent mineralized matrix. Foci of central hemorrhage (which have high signal intensity with all MR pulse sequences) and necrosis (which has low signal intensity on T1-weighted images and high signal intensity on T2-weighted MR images) are common in both the intraosseous and soft-tissue tumor components. As with other musculoskeletal neoplasms, accurate assessment of the intra- and extraosseous extent of osteosarcoma is critical in directing limb-salvage procedures. Multiplanar imaging allows assessment of the following vital information: (*a*) anatomic landmarks for the extent of marrow and soft-tissue involvement and its relationship to surrounding structures, (*b*) invasion of the epiphysis, (*c*) involvement of the joint or neurovascular structures and (*d*) identification of areas of viable tumor and mineralized matrix to improve biopsy accuracy[10]. The true margins of a lesion, whether intra- or extraosseous, may be obscured by perilesional edema on MR images obtained with water-sensitive pulse sequences (inversion recovery and T2 weighting with fat suppression).

The physis has long been considered by radiologists as a barrier to tumor growth. However, pathologic evaluation has shown that approximately 75% 88% of metaphyseal osteosarcomas extend through the open physis into the epiphysis[11, 2]. Epiphyseal extension may be identified at radiography in as few as 17% of osteosarcomas, although this pattern of spread is easily recognized on coronal or sagittal MR images in 80% of metaphyseal osteosarcomas[11, 12]. Joint involvement (most frequently in the knee) can be seen in 19%-24% of osteosarcomas, although the synovium is rarely violated[10]. On MR images, joint involvement is suggested when the hyaline cartilage is penetrated or more commonly when tumor extends through the capsule, such as into the supra-patellar bursa anteriorly or posteriorly to encompass the cruciate ligaments[10]. Fat-suppressed T1-weighted

gadolinium-enhanced images are helpful for delineating extension of tumor into the joint, but enhancing synovium may mimic tumor spread. Although invasion of the joint is unlikely in the absence of an effusion, the presence of an effusion does not allow an accurate prediction of intra-articular invasion.

Treatment of high-grade intramedullary osteosarcoma consists of chemotherapy, followed by wide surgical resection and limb salvage (amputation if salvage is not possible). Clinical outcome of osteosarcoma has dramatically improved over the past 25 years. Currently, the 5-year survival rate is 60%-80%[13-15]. Tumor size (>10 cm) and advanced stage at presentation are important factors that significantly worsen patient outcome. Evidence of pathologic fracture increases the likelihood of local recurrence. Perhaps the most important determinant of long-term survival of patients with osteosarcoma is tumor response to chemotherapy. Patients with greater than 90% tumor necrosis after therapy have a statistically significant higher likelihood of long-term survival[13-15]. Ongoing research is being conducted to quantitate the degree of tumor necrosis radiologically by using various modalities including Doppler sonography, bone scintigraphy, and MR imaging (dynamic subtraction studies) before therapy[15].

Metastatic disease most commonly affects the lungs, bones, and regional and distant lymph nodes. Ossification of pulmonary and lymph node metastases may be apparent on radiographs, CT scans, MR images, and bone scans. Pulmonary metastases may be associated with spontaneous pneumothorax, and, when few in number, are often treated aggressively with local resection.

Skip metastases, which are foci of tumor within the marrow of the affected bone that are distinctly separate from the primary lesion, occur in 1%-25% of high-grade intramedullary osteosarcomas[16, 17]. In our experience, the lower percentage is much more reflective of the true prevalence of this phenomenon. The identification of skip metastases is important not only for defining the extent of disease but also prognostically since the decrement in 5-year survival for patients with skip metastases is similar to that for patients with distant metastatic disease. Skip metastases are best identified with MR imaging, and a study of the entire length of an affected bone should be performed at the time of primary evaluation.

**Telangiectatic osteosarcoma**

Telangiectatic osteosarcoma is a less common lesion representing 4.5%-11% of all osteosarcomas[1-4, 18,-21]. Telangiectatic osteosarcoma was first described by Paget (22) was the first to describe this sarcoma in 1854 as a medullary cancer of bone with extensive development of vessels and blood-filled cysts. In 1903, Gaylord[23] used the term *malignant bone aneurysm* to describe a hemorrhagic, poorly ossified telangiectatic osteosarcoma. In 1922, Ewing[24] was the first to classify telangiectatic osteosarcoma as a distinct histologic variant, characterized by a malignant osteoid-forming sarcoma of bone with large blood-filled vascular channels.

Huvos et al.[18] had reported 124 cases of telangiectatic osteosarcoma including 60% male and 40% female, with an age range of 3-67 years and a mean age of 20 years. The most frequently affected sites were around the knee, representing 62% of cases (48% in the distal femur, 14% in the proximal tibia), with the proximal humerus being the third most frequent site (16% of cases) [18]. Similar to conventional osteosarcoma, telangiectatic osteosarcoma uncommonly occurs in the pelvis, scapula, ribs, and skull, and 90% of the lesions are metaphyseal. Telangiectatic osteosarcoma can also be a secondary lesion (arising in association with fibrous dysplasia or Paget disease or following radiation therapy). Two cases of extraskeletal telangiectatic osteosarcoma have also been reported[3, 18].

Telangiectatic osteosarcoma must, by definition, have hemorrhagic, cystic, or necrotic spaces (both grossly and microscopically apparent) that occupy more than 90% of the lesion before therapy[1-4, 18,19]. At histologic analysis, the cystic cavities are composed of cavernous vessels and blood-filled spaces lined with osteoclastic giant cells. Viable malignant spindle cells with osteoid formation are seen in the periphery of the lesion and in the septations surrounding these cavities. In larger lesions, areas of bone expansion, cortical destruction, and soft-tissue extension are common.

'Telangiectatic osteosarcoma mostly reveals geographic bone destruction with a wide zone of transition. In our experience, more aggressive osseous involvement with a predominant permeative or moth-eaten pattern is rare; many have reported that this appearance is the most frequent manifestation[20, 21]. Marked aneurysmal expansion of bone is not infrequent (19% of cases), and metaphyseal lesions often extend into the epiphysis (87%)[20]. Aggressive periosteal reaction, cortical destruction, associated soft-tissue mass, and pathologic fracture are common features.

The cystic consistency of telangiectatic osteosarcoma is reflected by its radiographic appearance. Bone scintigraphy often demonstrates peripherally increased radionuclide uptake with central photopenia (donut sign). The CT attenuation of the central portion of the lesion is often lower than that of muscle. This central region also shows very high signal intensity on T2-weighted MR images. At MR imaging, hemorrhage is frequently observed as areas of high signal intensity, regardless of MR pulse sequence. Fluid-fluid levels may be seen on CT or MR images, but they are best demonstrated by MR imaging in approximately 90% of cases[20].

Aneurysmal bone cyst most often confused with, and should be distinguished from telangiectatic osteosarcoma, which in our opinion, is that this sarcoma has a rim of viable tumor cells about the cystic spaces that manifests as solid tissue along the lesion periphery and septations. This viable tissue shows enhancement (often nodular) on CT or MR images after intravenous administration of contrast material. Subtle osteoid formation is also frequently seen in the viable peripheral tumor (intraosseous or soft-tissue component). CT is the best modality for detecting osteoid, which appears as nodular calcific foci. In recent review of 31 telangiectatic osteosarcomas, these foci were seen on CT scans in 81% of cases, compared with 61% in which they were seen on radiographs[20]. In our opinion, these features are not seen in aneurysmal bone cyst, which allows distinction from telangiectatic osteosarcoma in most cases.

Treatment is similar to that of conventional osteosarcoma and consists of chemotherapy followed by wide surgical resection and limb salvage or amputation. Results of biopsy of these lesions can be misleading if specimens of only hemorrhagic tissue are obtained. Imaging can be helpful in directing the biopsy sampling to the peripheral regions of viable tumor. Prognosis was previously thought to be much worse than that of conventional osteosarcoma[19]. However, newer studies suggest that the 5-year survival rate (68%) is similar to that of conventional osteosarcoma[18, 22].

**Low-grade intraosseous osteosarcoma**

Low-grade intraosseous osteosarcoma (well-differentiated or sclerosing osteosarcoma) is a variant of conventional osteosarcoma and represents 4%-5% of all lesions[1-4,25-27] and most frequently in patients in the 3rd decade of life (1 decade older than conventional osteosarcoma), but patients have a wide age range, and unlike H.g.I. osteosarcoma, men and women are affected equally[25-27]. Patients usually present with nonspecific symptoms after a protracted clinical course but they may be asymptomatic with the lesion, being discovered incidentally. The sites of L.G.I. osteosarcoma are similar to those of conventional osteosarcoma: The femur and tibia (about the knee) are most frequently affected, and the lesion most commonly involves the metaphysis, often extending into the epiphysis[27].

Unlike conventional osteosarcoma, L.G.I. osteosarcomas frequently have radiologic and pathologic characteristics that of a benign process, including fibrous dysplasia, non-ossifying fibroma, chondrosarcoma, and chondromyxoid fibroma[23, 27]. On radiologic examination, the lesions may reveal well-defined margins, a sclerotic rim, prominent internal trabeculation, and diffuse sclerosis, may cause expansile remodeling of bone[26]. However, radiologic evidence of a more aggressive process, such as associated bone lysis, focally indistinct margins, cortical destruction, soft-tissue mass, and, uncommonly, periosteal reaction is seen even if it is subtle[26].

These lesions usually behave as a locally aggressive tumor, with multiple recurrences developing after intralesional resection. Time to recur is variable and can be delayed up to 20 years after surgery[25, 27]. The lesions initially treated by wide excision with limb salvage, the long-term prognosis are excellent. Kurt et al[27] found

transformation of the initial lesion into a higher-grade osteosarcoma in 15% of incompletely resected lesions, with an increased prevalence of metastatic disease and a poor prognosis. Rarely, these lesions behave aggressively with significant metastatic potential.

**Small cell osteosarcoma**

Small cell osteosarcoma is a kind of conventional osteosarcoma composed of small round blue cells, first described by Sim and coworkers in 1979[28] and is estimated to represent between 1% and 4% of osteosarcomas[1-4,29,30]. Males and females suffer equally, and the age of patients and tumor locations are similar to those for conventional osteosarcoma and the distal femur being the most common site. The lesions are metaphyseal with frequent extension into the epiphysis, but 15% of cases involve the diaphysis[28-30], is involved in the pathologically similar to that of Ewing sarcoma: as these osteosarcoma lesions are composed of small round blue cells. The small cell osteosarcoma is devoid of monotoms population of cells seen in Ewing sarcoma and produces (fine and reticular) osteoid[28,30]. Ewing sarcoma mostly fails to produce any osteoid, although at times reactive bone formation may be seen and histologic differentiation can be difficult. In this setting, molecular and immunohistochemical markers are very helpful in distinguishing between the two tumors.

On radiologic examination, small cell osteosarcoma reveals a predominantly permeative, lytic medullary lesion with cortical breach as marked periosteal reaction, and an associated soft-tissue mass[28, 30]. Osteoid matrix, although subtle, is usually apparent in the medullary or soft-tissue component and is best detected with CT[29,30]. Occasionally, lesions are entirely lytic without evidence of osteoid matrix to suggest the diagnosis of osteosarcoma. The prognosis for this lesion is extremely poor, regardless of treatment.

**Osteosarcomatosis**

Osteosarcomatosis (also known as multifocal osteosarcoma or multiple sclerotic osteosarcomas) is a condition in which there are multiple intraosseous foci of osteosarcoma at the time of presentation. It was previously considered as osteosarcomatosis to represent multicentric primary neoplasia[31]. Recently, all cases of osteosarcomatosis are said to be rapidly progressive metastatic disease[32,33]. This latter concept is controversial, we strongly recognize this based on the identification of a radio graphically dominant (large) lesion in most patients with otherwise symmetric disease and the presence of pulmonary metastases on chest CT scans in the majority of these patients.

Osteosarcomatosis is rare, are seen and occur approximately 3%-4% of osteosarcoma cases[1-4,31-34]. However, multifocal skeletal involvement by osteosarcoma has been found at autopsy in as many as 48% of patients[32,33]. Although osteosarcomatosis has been believed to be more common in skeletally immature patients, Hopper et al.[33] reported a series of 29 cases in which there were relatively equal numbers of skeletally immature and mature patients. Younger, skeletally immature patients tend to have rapidly appearing, usually symmetric, sclerotic lesions, as compared to older patients who typically have fewer, asymmetric sclerotic lesions. In 97% of those cases Hopper et al.[33] had reported, a radiologically dominant skeletal tumor.

Radiologically the dominant lesion reveals ill-defined margins, aggressive periosteal reaction, cortical disruption, and adjacent soft-tissue mass effect[31-34]. These usually contain cloudlike osteoid but purely lytic dominant lesions may be seen. The secondary foci are often smaller, more sclerotic, and better defined and lack periosteal reaction or cortical destruction as compared to the dominant lesion.

The presence of multifocal skeletal osteosarcoma substantially alters both treatment and anticipated prognosis. Parham et al.[34] noted that despite intensive chemotherapy all 09 patients died, with a mean survival of 12 months (range, 6-37 months).

**Gnathic osteosarcoma**

Osteosarcomatous lesions of the mandible and maxilla constitute 6%-9% of all osteosarcomas[1-4, 35-38]. Gnathic osteosarcoma is often affecting older patients (average age, 34-36 years) [36-38].The alveolar ridge, maxillary antrum, and body of the mandible are usually involved. Microscopically, the lesions are often predominantly chondroblastic[35].

Gnathic osteosarcoma radiologically simulate

that of conventional osteosarcoma, with evidence of osteoid matrix (60%-80% of cases), aggressive periosteal reaction in mandibular lesions, and soft-tissue extension (100%)[36,37]. In maxillary lesions the sinuses become opaque. CT detects areas of mineralized osteoid in this complex anatomic location. The intramedullary and extraosseous components are best on MR imaging.

Gnathic osteosarcomas are difficult to treat. Radical and local surgical resection, radiation therapy, and chemotherapy are mode of treatment. Local recurrence is common (50%-80% of cases), particularly in cases of maxillary lesions, and is often uncontrollable, typically leading to patient death[36, 39]. Distant metastases are less frequent than in other osteosarcomas, and the 5-year survival rate is approximately 40%[35, 37].

**Juxtacortical osteosarcoma**

Surface lesions (synonym; Surface Osteosarcoma) account for 4%-10% of all osteosarcomas[1-4,39]. However, we prefer to distinguish intracortical, parosteal, periosteal, and high-grade surface lesions because of differences in radiologic and pathologic appearances as well as in treatment and prognosis.

**Intracortical osteosarcoma**

Intracortical osteosarcoma is the rarest form of osteosarcoma, and the term applies to those cases in which the lesion arises within the cortex. Firstly , Jaffee[40] had described and reported two cases in 1960, and up to 1991, only nine cases had been published[40-44]. Histologically it appears as a sclerosing variant of osteosarcoma that may contain small foci of chondrosarcoma or fibro sarcoma[41-43].

On the basis of such a small number of cases, it is difficult to make generalizations. The typical lesion reveals geographic bone lysis (with small areas of mineralized osteoid), is intracortical; occurs in the femur or tibia; and measures less than 4 cm in diameter[41,44]. The tumor margin may be remarkably well defined with thickening of the surrounding cortex, and medullary invasion is only rarely reported[41, 44].

Although natural history is lacking, Mirra and coworkers[41] reported that in a review of seven patients, five were disease-free after 3-19 years of follow-up. One patient died of metastatic disease and another had inoperable metastases. This high rate of metastasis (29%) may be sufficient to justify adjuvant chemotherapy.

**Parosteal osteosarcoma**

Parosteal osteosarcoma accounts for 65% of all juxtacortical osteosarcomas and is thought to originate from the outer layer of periosteum[39,45-49]. Patients in the 3rd and 4th decades of life are usually affected and show a slight female predilection. Clinical symptoms frequently include a palpable mass. It affect the metaphyseal region of long bones (80%-90% of cases), most frequently the posterior distal femur (50%-65%)[45,48]. Other commonly involved regions are the proximal humerus, tibia, and fibula.

These are frequently low-grade lesions, as suggested by Geschickter and Copeland in the original description in 1951[46], who used the term *parosteal osteoma*. However, these large, lobulated parosteal lesions and contain higher-grade regions in 22%-64% of cases and may demonstrate invasion (retrograde growth) into the medullary canal (8%-59%)[45,48]. Fibrous stroma and extensive osteoid are the predominant histologic characteristics and smaller foci of cartilage are also frequent.

Radiologically this lesion appears as a large, lobulated (cauliflower-like), ossifying (denser centrally), Juxtacortical mass. Initially, only a narrow zone (stalk) of attachment to the cortex may be apparent, creating a partial radiolucent cleavage plane between the lobulated ossific mass and the remaining bone[47]. Later continued tumor growth often obliterates the cleavage plane. Cortical thickening without aggressive periosteal reaction may be seen. CT and MR imaging can demonstrate both the soft-tissue extent and evidence of medullary involvement. The ossified regions show high attenuation on CT scans and low signal intensity on all MR images, regardless of pulse sequence. In addition, Jelinek and coworkers[47] have recently shown that nonmineralized soft-tissue components larger than 1 $cm^3$ identified at CT or MR imaging correspond to high-grade foci. Parosteal osteosarcomas may be confused both pathologically and radiologically with myositis ossificans[50]. However, in contrast to parosteal

osteosarcoma, myositis ossificans is usually not attached to the cortex and is denser at the periphery.

Prognosis is excellent for patients with parosteal osteosarcoma, with 5- and 10-year survival rates of 80%-90%[45,48]. The therapy is altered if high grade foci are seen and should be sampled in biopsy prior to major surgery and also required neoadjuvant chemotherapy. Lesions of higher grade have been called dedifferentiated parosteal osteosarcoma, although this term is reserved for those lesions that contain a second tumor cell line (often fibrosarcoma or malignant fibrous histiocytoma)[49]. The presence of intramedullary back growth thought to imply a worse prognosis. More recent studies suggest that this finding does not change the overall excellent prognosis[47,49]. It remains important to identify medullary extension to ensure adequate resection during limb-salvage surgery.

**Periosteal osteosarcoma**

Unni etal originally had described periosteal osteosarcoma in 1976 which accounts for 25% of all juxtacortical osteosarcomas[39,51]. The age group affected is similar to that for conventional osteosarcoma (patients in the 2nd and 3rd decades of life). Contrary to conventional osteosarcoma, these lesions show a strong propensity to arise in the diaphysis or metadiaphysis of bone. The most commonly affected sites are the femur and tibia (85%-95% of cases), followed by the ulna and humerus (5%-10%)[51-53].

These lesions are of intermediate-grade that arise from the deep layer of periosteum and cause cortical scalloping typically without intramedullary invasion[51]. Microscopically it reveals a highly chondroblastic lesion with smaller areas of osteoid formation.

Radiologically it is characteristic and distinctive from that of parosteal lesions. The surface of the thickened diaphyseal cortex is scalloped, with perpendicular periosteal reaction extending into a broad-based soft-tissue mass[52, 53]. The upper and lower margins of the lesion reveal Solid (cortical thickening) or aggressive (Codman triangle) periosteal reaction. CT and MR imaging show similar findings, with the highly chondroblastic areas corresponding to relatively low-attenuation regions on CT scans, low-signal-intensity areas on T1-weighted images, and very high-signal-intensity areas on T2-weighted MR images[52, 53]. It was recently demonstrated that these lesions usually involve approximately 50% of the osseous circumference and that the perpendicular periosteal reaction is seen as rays of low signal intensity with all MR pulse sequences[53]. Marrow invasion is rare and, when seen, is directly continuous with the surface mass. Marrow invasion should be distinguished from reactive marrow changes, which appear as foci of marrow replacement (low signal intensity on T1-weighted MR images and high signal intensity on T2-weighted or inversion recovery images) adjacent to but noncontiguous with the surface mass, as described in more than 50% of cases by Murphy et al.[53].

Prognosis for patients with periosteal osteosarcoma is improved compared with that for patients with conventional osteosarcoma, but it is not as good as that for patients with parosteal lesions. Metastatic disease leads to patient death in 8%-16% of cases[51]. Surgical treatment is usually wide local excision with an associated limb-salvage procedure.

**High-grade surface osteosarcoma**

High-grade surface osteosarcoma is rare and accounts for 10% of all juxtacortical osteosarcomas[39] with a high predilection to involve the diaphysis of bone and most commonly affect the femur, humerus, and fibula. Pathologically and prognostically, these lesions are identical to conventional intramedullary osteosarcomas[39]. Radiologically, these lesions are similar in appearance to periosteal osteosarcoma[39] and often involve the entire circumference of bone and frequently invade the medullary canal.

**Secondary osteosarcoma**

Most of time osteosarcomas occur as primary neoplasms. These osseous and soft-tissue osteosarcomas can be secondary lesions (5%-7% of all osteosarcomas) resulting from malignant transformation within a benign process[1]. The vast majority of these secondary osteosarcomas arise in Paget disease (67%-90% of cases) or previous

osseous or extraskeletal irradiation (6%-22%)[1-3]. The frequency of malignant transformation to osteosarcoma in Paget disease varies widely, from 0.2% in patients with limited involvement to as much as 7.5% in those with extensive skeletal manifestations[58,59]. The radiation-induced osteosarcoma show a wide range of prevalence, from 0.02% to 4%, that is related to exposure dose (usually >1,000 cGy)[60,61]. Conditions that less commonly lead to osteosarcoma include osteonecrosis, fibrous dysplasia, metallic implants, osteogenesis imperfecta, chronic osteomyelitis, and retinoblastoma (particularly the familial bilateral type associated with a deficient oncogene suppressor on chromosome 13)[1].

Patients are usually middle-aged or in late adulthood, accounting for a small second peak of prevalence in this older age group. Evidence of the long-standing underlying condition is usually radiologically obvious, as is the more aggressive bone destruction in the area of malignant transformation. Large, associated soft-tissue masses are also seen typical of secondary osteosarcoma.

Pathologically, the lesions are usually composed of high-grade anaplastic cells and produce little or no mineralized matrix, and this aggressive behavior results in a bad prognosis. Even after employing extensive treatment, regimens the 5-10-year survival rate is often extremely poor and less than 5%[1-3].

**Extraskeletal osteosarcoma**

Extraskeletal or soft-tissue osteosarcoma is rare, occurring approximately as 1.2% of all soft-tissue sarcomas and 4% of all osteosarcomas[1-3,54-56]. The peak occurs in patients in the 6th decade of life and males are slightly more frequently affected. Symptoms often include a slowly growing painful mass, with a history of trauma (12% of cases)[56]. Common sites of involvement are the deep soft tissues of the thigh (47% of cases), upper extremity (20%), and retroperitoneum (17%)[54-56].

These are usually large (average, 9 cm in diameter) with variable amounts of neoplastic osteoid and bone[55]. Other components, include cartilage, fibrosarcoma, malignant fibrous histiocytoma, and malignant peripheral nerve sheath tumor, are also frequently seen[54].

Radiologically large soft-tissue masses with focal to massive areas of mineralization and a lack of osseous involvement are seen[57]. Nonmineralized areas have muscle attenuation values on CT scans, nonspecific intermediate signal intensity on T1-weighted images, and high signal intensity on T2-weighted MR images and show contrast enhancement[57]. A pseudo capsule may also be apparent. Scintigraphy often reveals increased radionuclide uptake in both primary and metastatic foci.

Treatment includes amputation or wide surgical resection with neoadjuvant chemotherapy or radiation therapy. Tumor size is the most important prognostic factor, patients with lesions larger than 5 cm having a worse outcome. Even with aggressive therapy, overall prognosis is poor; with death of patient occur in at least 60% of cases[54-56]. Frequent metastases are identified; involving the lung, regional lymph nodes, and bone.

## CONCLUSIONS

Osteosarcoma is the most common primary malignant bone tumor in children and second to multiple myeloma in adults. The radiologic features vary widely. We have reviewed the radiologic and pathologic features of the various types of primary osteosarcoma, including intramedullary (high-grade, telangiectatic, low-grade, small cell, osteosarcomatosis, and gnathic), juxtacortical (intracortical, parosteal, periosteal, and high-grade surface), extraskeletal, and secondary lesions. The radiographic appearances of these lesions are often characteristic and suggestive of the specific diagnosis. Perhaps more important, additional imaging modalities, including bone scintigraphy, CT, and MR imaging, provide vital information for preoperative staging in planning surgical management. Radiologic examination also allows evaluation of tumor response to chemotherapy, identification of metastatic disease, and postoperative evaluation of recurrent neoplasm, all of which have important prognostic implications. Recognition of these imaging features is an important guide to our clinical colleagues, throughout the often difficult and complex treatment of patients with osteosarcoma and results in improved clinical outcome.

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