The Many Faces of Chondrosarcoma of Bone

Own Cases and Review of the Literature with an Emphasis on Radiology, Pathology and Treatment

Mnoho podob chondrosarkomu. Vlastní případy a přehled literatury s důrazem na radiologii, patologii a léčbu

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SUMMARY

Chondrosarcoma is the third most frequent primary malignant tumor of bone, constituting up to 16% of the malignant osseous neoplasms. Up to date several genetic alterations and markers were described concerning the pathogenesis and the progression of the chondrosarcoma, which represents actually a heterogeneous group of different types including conventional intramedullary, clear cell, myxoid, mesenchymal, and dedifferentiated chondrosarcoma.

The pathologic appearance varies, however, in general they grow with a lobulated pattern. Histologically the hyaline cartilage demonstrates high water content and typically enchondral ossification is apparent. Imaging reflect this while radiographic findings suggest the diagnosis when the typical "ring-and-arc" chondroid matrix mineralization, endosteal scalloping and soft-tissue extension were apparent.

The CT is used for detecting the mineralization of the matrix, especially when it is subtle or when the lesion is located in complex areas. MRT is the method of choice to detect the high water content of these lesions with a high signal intensity with T2-weighting and its bone marrow extend.

Surgical resection is the primary and preferred treatment modality for most individuals with localized disease. In selected cases of the Grad I conventional chondrosarcoma curettage should be discussed. Systemic chemotherapy may be considered in variant forms such as mesenchymal or dedifferentiated chondrosarcomas.

In knowledge of the "many faces" of the primary chondrosarcoma individualized patient assessment and optimal clinical management is possible.

Key words: chondrosarcoma, CT, MRT, PET, treatment.

INTRODUCTION

Chondrosarcoma is, after multiple myeloma and osteogenic sarcoma, the third most common primary malignant tumor of bone (1). Tumors that arise de novo are called primary chondrosarcomas, secondary chondrosarcomas arise from a preexisting benign cartilaginous lesion such as enchondroma or osteochondroma (16, 19).

Up to date several genetic alterations and markers were described regarding the pathogenesis and progression of the chondrosarcoma, including the PTHR1 mutation, the hedgehog signaling pathway, p53, insulin-like growth factor, cyclin-dependent kinase 4 and others (4, 18)

Chondrosarcomas are a heterogeneous group of tumors. More than 90% are designated conventional chondrosarcomas. Approximately 90% of these are low-grade to intermediate-grade tumors (grade 1 or 2), which habour an indolent clinical behaviour and low metastatic potential; only 5–10% are grade 3 lesions, which have high metastatic potential (8, 11). Its variants are rare and several types are described, including conventional intramedullary, clear cell, juxtacortical, myxoid, mesenchymal, extraskeletal, and dedifferentiated chondrosarcoma (16, 29). Depending on their location, they are categorized as central, peripheral, or juxtacortical (periosteal) tumors.

Radiographic findings strongly suggest the diagnosis of chondrosarcoma by demonstrating a lesion with typical chondroid matrix mineralization (ring-and-arc pattern) and aggressive growth features (21). In addition to the conventional radiography, bone scintigraphy, computed tomography (CT), and magnetic resonance tomography (MR) are employed for the diagnosis and staging of the tumor (21, 29).

Surgical resection is the preferred treatment modality for most individuals with localized disease. In selected cases of the Grad I conventional chondrosarcoma curettage is discussed. And, systemic chemotherapy may be considered in some forms such as mesenchymal or dedifferentiated chondrosarcomas

In this article the various types of the chondrosarcoma are discussed and illustrated.

Conventional intramedullary chondrosarcoma is the most common type of primary chondrosarcoma. They appear at any age, the average being 46 years (1). Clinical symptoms are nonspecific: pain, a palpable soft-tissue mass and pathologic fractures are common (23, 25).

The tumor can involve any bone. In the axial skeleton it mostly could be found in order to appearance in the ribs, spine, scapula and sternum. It rarely affects locations like the craniofacial region, neck (arising from the hyoid as well as laryngeal and tracheal cartilage), forearm, clavicle, sesamoids, and the short tubular bones of the hands and feet. However, the most common skeletal locations are the long bones, especially the femur and the proximal humerus, involving the metaphysic in 50% of cases, followed by the diaphysis in 36%). Tumors in the epiphysis are again unusual (14, 23, 25).

A three-grade system is commonly used: Grade 1 lesions (low grade) have chondrocytes with small dense nuclei, that vara somewhat in size and and show a moderate degree of polymorphy. The stroma is predominantly chondroid. Myxoid areas are usually sparse or absent. Grade 2 chondrosarcomas (intermediate grade) have less chondroid matrix and greater irregularity in the distribution of the tumorous chondrocytes, which may often be found packed closely together in groups. The chondrocyte nuclei are enlarged, bi- and multinucleated chondrocytes occur. Necrotic areas may be present, the stroma is frequently myxoid. Grade 3 chondrosarcomas (high grade, Fig. 1a) exhibit greater cellularity and nuc-

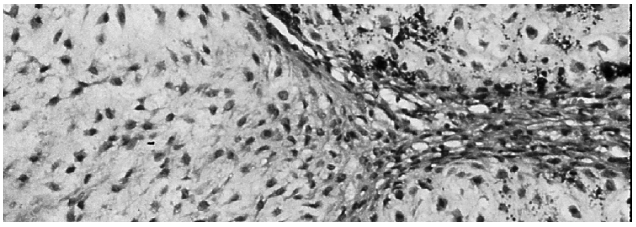
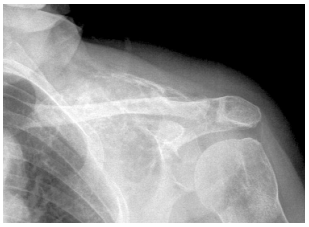


Fig. 1a. Conventional intramedullary chondrosarcoma of the scapula in a 65-y-old man. The typical popcorn-like calcifications within the large tumor-mass are best seen in the CT-scan.

lear pleomorphism than grade 2 tumors. The nuclei vary in size, and often include giant nuclei with a very dense chromatin content. Chondroid matrix is sparse or absent, and the small amount of intercellular material present is often myxoid. Foci of necrosis are almost invariably seen and are more frequently extensive (1, 9, 14).

Radiographs typically reveal a mixed lytic and sclerotic appearance. The lesions are mostly greater than 4 cm in size, many of them are greater than 10 cm (23). The tumor, typically growing with a lobular architecture, frequently causes endosteal scalloping with or without cortical penetration. Areas with mineralization of the matrix (calcification) appear granular and have a "ring-and-arc" pattern. This characteristic usually allows confident radiologic diagnosis of a cartilaginous lesion. Nonmineralized regions (higher-grade chondrosarcomas have larger areas that are not calcified) appear translucent, reflecting the high water content of hyaline cartilage. Aggressive "moth-eaten" and/or permeative bone lysis may be seen with higher-grade chondrosarcomas; more frequently they are associated with mesenchymal, myxoid, and dedifferentiated cell types (21, 28). Because of the relatively slow growth of the chondrosarcoma, the cortex responds by remodeling, thickening, and periosteal reaction (reaction is uncommonly associated with enchondroma).

The CT allows detection and characterization of matrix mineralization (Fig. 1b-c), however, neither the extent nor the presence can help to differentiate long bone enchondroma from chondrosarcoma. To distinguish conventional chondrosarcoma from enchondroma, following criteria are helpful: entrapment/destruction of the trabecular bone is the hallmark of a chondrosarcoma. And, scalloping greater than two-thirds the normal thickness of the long bone cortex is strong evidence of chondrosarcoma. Cortical response, including cortical thickening and periosteal reaction, is equally well demonstrated with CT and radiography (21, 23); identification of soft-tissue extension on CT scans is more frequent than on radiographs and it occurs in about 60% of long bone chondrosarcomas.



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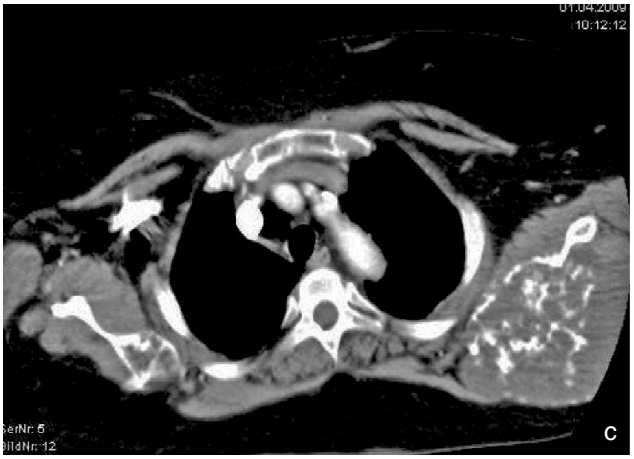

Fig. 1b-c. The most striking feature of the chondrosarcoma grade 3 is the polymorphy of the tumor cells. Note the nodule, which is fairly sharply delineated by a narrow connective tissue septum (HE, 40x).

MR imaging provides the best method for detecting the extent of marrow involvement (26). On T1-weighted MR images, marrow replacement appears as low to intermediate signal intensity. The typical lobulated architecture is seen best at the lesion margin. The nonmineralized components have high signal intensity on T2-weighted images, reflecting the high water content of the tumor-cartilage. Areas of matrix mineralization have low signal intensity with all MR sequences. This

feature often creates marked heterogeneity on T2-weighted MR images. However, areas of low signal intensity on T2-weighted MR images are nonspecific and have numerous other potential causes, e.g. fibrous tissue with high collagen content. Peritumoral edema, which is best seen in the T2-weighted images, also suggest chondrosarcoma over enchondroma. And soft-tissue extension with mass formation essentially excludes the diagnosis of enchondroma (15).

In bone scintigraphy the majority of long bone chondrosarcomas reveal marked increased radionuclide uptake compared with that in the anterior iliac crest. This is in contrast to long bone enchondromas (increased activity up to 20% of cases).

Basically, there are two categories for surgical treatment: (Intralesional) Curettage, adjunct chemical or thermal ablation, and cementation or bone grafting of the defect versus wide excision with structural graft or reconstruction (10).

Acceptable oncologic and functional results have been observed in patients with grade 1 chondrosarcoma treated with curettage and cryosurgery alone (14). However, local recurrence is not unusual if there is inadequate resection (9, 26). Wide excision is performend in higher grade chondrosarcomas, in some cases also in the grade 1 chondrosarcoma. Large lesions and chondrosarcomas in anatomic locations that do not allow adequate margins or complete excision (such as the spine, craniofacial region, ribs, pelvis) have an obvious increased risk of local recurrence and metastatic disease (24, 26). The overall 5-year survival rates for chondrosarcoma are 90% in grade 1, up to 80% in grade 2, and 40% in grade 3 tumors, whereas the 10-year survival rates are 85% (grade 1), up to 60% (grade 2), and up to 30% (grade 3) (24, 26).

Clear cell chondrosarcomais a rare bone neoplasm that constitutes approximately 1%–2% of all chondrosarcomas and 0.2% of all primary bone tumors (9, 11, 26). Patients are most commonly affected between the 3rd and 5th decade, with men being affected twice as often as women (28). Symptoms include localized pain, decreased range of motion of the adjacent joint and pathologic fractures.

It affects the long tubular bones in 90% of cases, with a particular predilection for the proximal femur (60%) and proximal humerus (20%). There is also a marked predilection for epiphyseal involvement, although metaphyseal extension is common (Fig. 2a). Flat bones are affected in up to 10% of cases (1, 11, 28)

Histologically, lesions show unambiguous cartilage structures that make one think of a benign chondroblastoma. The most striking feature is, that tumor reveal numerous cells with vacuolated cytoplasm containing large amounts of glycogen (clear cell chondrocytes) that often lie between heavily calcified trabeculae (Fig. 2b). In contrast to conventional chondrosarcoma, they frequently contain large areas of hemorrhage and cyst formation (1).

Radiographs reveal a predominantly lytic lesion and matrix mineralization is apparent in about 25% – 30%

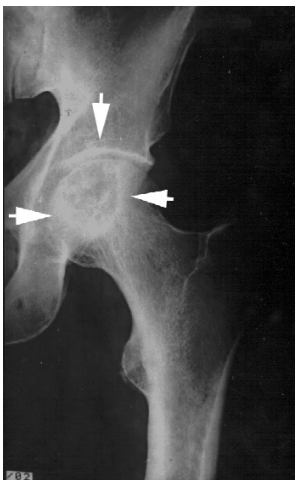

Fig. 2a. The tumor cells of the clear-cell chondrosarcoma are large and have a voluminous, very pale cytoplasma. They are sharply delineated by a prominent cell border. Nuclei are roundish or oval and hyperchromatic, but fairly isomorphic. Multinucleated chondroblasts are rare and there a are no mitosis (HE, 40x).

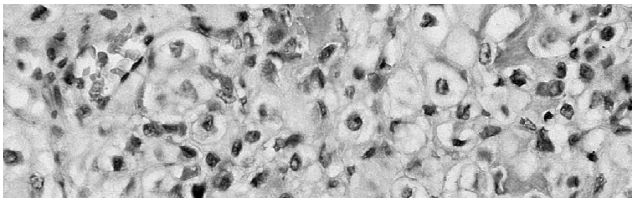

Fig. 2b. Clear-cell chondrosarcoma in a 47-y-old women with hip pain. The osteolytic lesion in head of the proximal femur with its typical origin in the epiphysis.

of cases (17, 21). A peripheral sclerosis, simulating a benign lesion, is detected in 20% of the cases, and in 30% of cases mild expansile remodeling of bone is seen.

CT demonstrates matrix mineralization, cortical destruction, and/or soft-tissue extension. MR imaging typically shows homogeneous intermediate signal intensity with T1-weighted sequences and heterogeneous high signal intensity with T2-weighted sequences (17, 24). Because of the epiphyseal location, clear cell chondrosarcoma can be difficult to distinguish from chondroblastoma, however, patients with clear cell chondrosarcoma are usually older than those with chondroblastoma, and imaging features that suggest clear cell chondrosarcoma include a large lesion, lack of surrounding edema, high signal intensity on T2-weighted MR images and more calcifications (chondroblastomas: extensive surrounding bone marrow edema and soft-tissue edema, areas of low signal intensities in T2-weighted images (17).

Although it is a low-grade tumor, lesions are often inadequately treated with curettage, which leads to recurrence, whereas adequate aggressive initial surgical resection with joint arthroplasty is usually curative (18). Overall recurrence rate is 16%, and approximately 15% of patients die of the disease. Metastases to the lung, brain, and bones have been reported (26, 29).

Juxtacortical chondrosarcomaare also rare lesions, accounting for 2% of all chondrosarcomas (4, 14). These tumors, which arises on the surface of the bone, have also been referred as periosteal and parosteal chondrosarcoma. They most frequently affect adults in the 3rd

to 4th decade of life. Clinical signs are a palpable and painless, slowly growing tumor. Lesions are most frequently seen on the surface of long bones, particularly the posterior distal femoral metaphysis or diaphysis.

At gross pathologic examination, juxtacortical chondrosarcoma arises on the surface of bone (Fig. 3a) and is

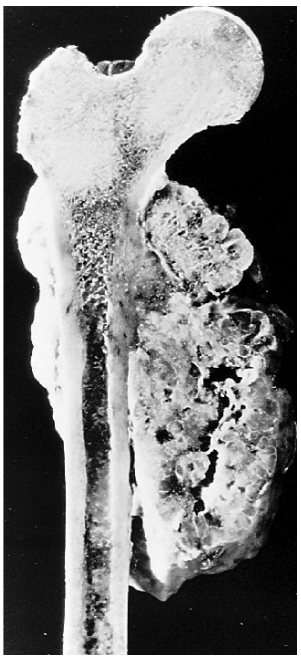

Fig. 3a. Juxtacortical chondrosarcoma of the proximal femur arises on the surface of bone (masceration specimen). From: Adler C.P. Knochenkrankheiten, Springer 2005

covered by a fibrous pseudocapsule that is continuous with the underlying periosteum. Histologically, the cartilaginous part of the tumor shows the characteristic picture of a moderately highly differentiated chondrosarcoma and shows a similar appearance as intraosseous chondrosarcomas (Fig. 3b).

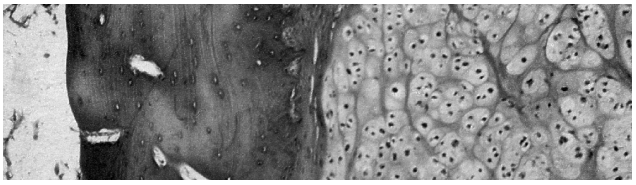

Fig. 3b. The typical histological appearance of the juxtacortical chondrosarcoma shows lobulated cartilaginous tissue in which chondrocytes are irregularly distributed. Most of them have a single nucleus an lie within large cell nests. The nuclei are often only sketchily polymorphic, sometimes roundish (HE, 40x).

Radiographs demonstrate a lobulated mass on the surface of bone. Typical chondroid matrix mineralization is usually present. The underlying cortex is frequently thickened with associated saucerization and Codman triangles (7). Matrix mineralization is better seen on CT scans (Fig. 3 c/d). In the MR the lesion shows a low heterogeneous signal intensity with T1-weighted sequences and heterogeneous high signal intensity with T2-weighted sequences. Use of contrast material with CT or MR imaging often reveals peripheral and septal enhancement. The medullary canal is typically not involved. Differential diagnosis include juxtacortical chondroma, parosteal osteosarcoma, and periosteal osteosarcoma (7). Lesion size is often the best differentiating feature, with juxtacortical chondromas being invariably smaller (2–3 cm in size) than juxtacortical chondrosarcoma (3–14 cm, 5 cm average). Differentiating between juxtacortical chondrosarcoma and periosteal osteosarcoma: the latter is characterized by the presence of periosteal reaction perpendicular to the cortex on radiographs, young patient age (10–25 years), diaphyseal location, and a osteoblastic component (1, 11). Parosteal osteosarcoma may be radiologically similar to juxtacortical chondrosarcoma but it usually has a stalk of attachment to the cortex and extensive osteoid.

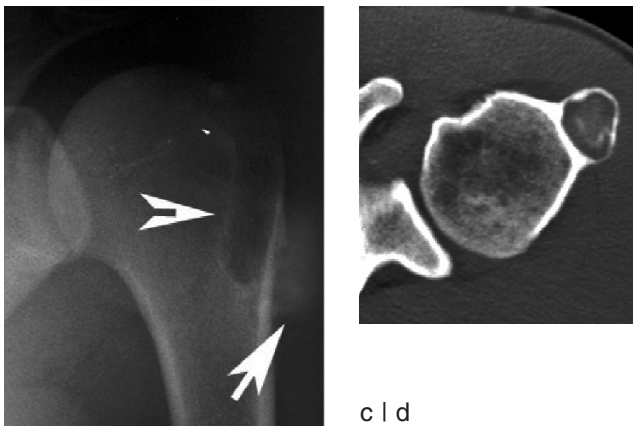

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Fig. 3c-d. Juxtacortical chondrosarcoma: Anteroposterior shoulder radiographs show tumor mass on the surface of bone (a). Typical calcifications in the juxtacortical lesion are visible in the CT-scan of the proximal humerus (b)

Treatment of juxtacortical chondrosarcoma is wide surgical resection. Local recurrence and metastatic disease have been reported, but the prevalence is low, even with higher-grade lesions (24, 26).

Myxoid chondrosarcomarepresents about 2% of all chondrosarcomas of bone. Affected individuals are typically male adults with a mean age 50 years, and half of the reported cases have occurred in the femur (1, 9).

Histologically, the tumor was revealed to have a nodular arrangement with rather well-defined tumor lobules. Individual tumor cells varied slightly in size and shape (usually round to oval) and were separated by abundant myxoid stroma (Fig. 4a) (1).

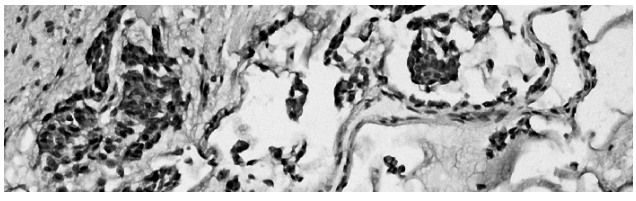

Fig. 4a. The microscopic appearance of the myxoid chondrosarcoma shows individual tumor cells, focally binucleated, that resemble chondroblasts within abundant myxoid stroma. No hyaline cartilage formation is seen. Areas of increased cellularity, marked nuclear pleomorphism, and mitotic activity were apparent (HE, 40x).

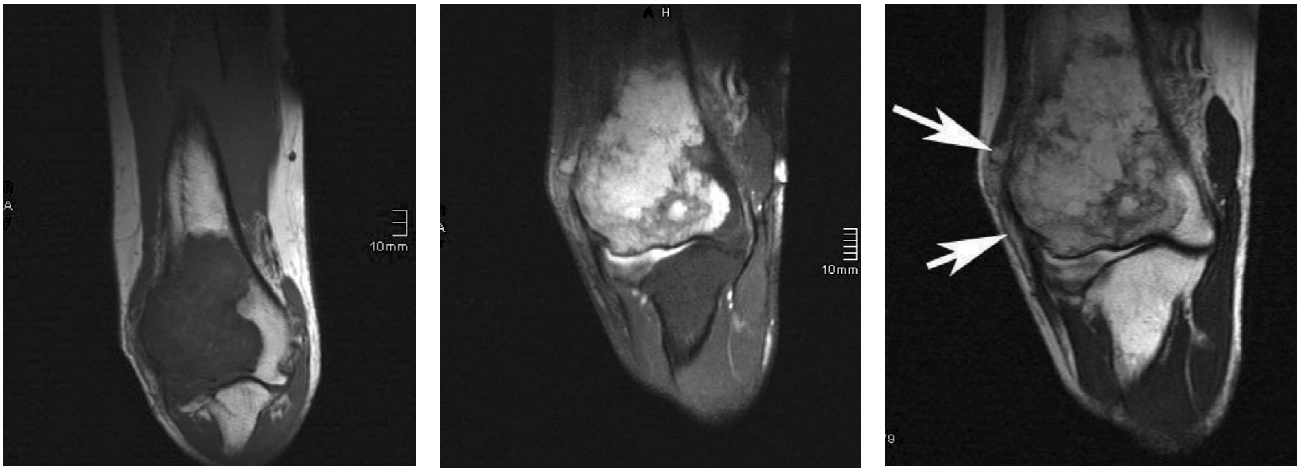

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Fig. 4b–d. Myxoid chondrosarcoma: the outer border of the lesion is well demonstrated in T1 weighted image (b). The very high-signal in the T2 weighted image (c) correlates to the typically high water content of this lesion (d).

Radiographics shows a permeative pattern of osseous destruction and an associated soft-tissue mass. Matrix mineralization is frequently apparent on CT scans but not extensive. Both CT and MR imaging demonstrate the markedly high water content with very high signal intensity in fat-suppressed T2-weighted sequences (Fig. 4b–d). They frequently contains hemorrhage, which appears as areas of high signal intensity in all MR sequences, particularly in the large associated soft-tissue components. Enhancement after intravenous administration of contrast material is often only mild and septal to peripheral in pattern (21, 28).

The lesion has a more aggressive clinical course than conventional intramedullary chondrosarcoma. Initial wide local resection is considered the treatment of choice. Patients commonly developing distant metastases and local recurrence (26).

The most frequent metastatic sites are the lungs and regional lymph nodes. Metastases may even occur after a long delay. Patients with intraosseous lesions have a 5-year survival rate of 60%.

Mesenchymal chondrosarcoma accounts for up to 12% of all chondrosarcomas of bone (9, 22). It is an aggressive high-grade tumor with a strong tendency to metastasize. Clinical symptoms are nonspecific: pain, swelling, and a palpable soft-tissue mass. Men and women are equally affected, most frequently in the 2nd to 4th decade of life. Commonly lesions affects the axial skeleton, the ribs, jaws and long bones, mostly in a diaphysis. Although most cases arise in previously normal bone, it may occur as a secondary lesion associated with pre-existing fibrous dysplasia (23).

Histologically, one can recognize the very clear lobular and nodular formation. The nodules of varying size are fairly sharply separated by narrow connective tissue septa which contain blood vessels. The characteristic histologic feature are large components composed of small, uniform, round to spindle-shaped cells, resemble those of Ewing sarcoma, and focal admixed areas of malignant cartilaginous tissue (Fig. 5a) (1).

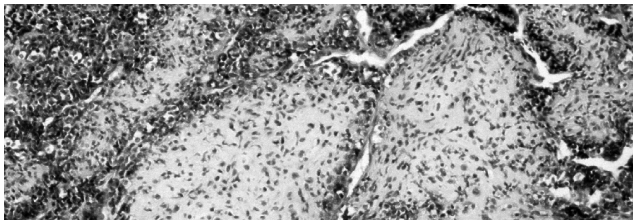

Fig. 5a. The characteristic histologic feature of the mesenchymal chondrosarcoma are large components composed of small, uniform, round to spindle-shaped cells, resemble those of Ewing sarcoma, and focal admixed areas of malignant cartilaginous tissue (HE, 40x).

Radiographs show aggressive bone destruction with a moth-eaten to permeative pattern and ill-defined multilayer periosteal reaction. The tumor is often very large, with extensive extraosseous components. Areas of characteristic "ring-and-arc" chondroid calcifications are seen in up to 70% of cases, although they are often not extensive (3, 22).

CT shows aggressive bone destruction with a large associated soft-tissue mass and chondroid mineralization. MR images show low to intermediate signal intensity with T1-weighted sequences and intermediate signal intensity with T2-weighted sequences (Fig. 5 b–c). The pattern of enhancement varies from homogeneous to heterogeneous but is often diffuse and lacks the typical cartilaginous septal and peripheral enhancement.

Tumor require a wide local excision when possible. Local recurrence is common, as are metastases (lung, regional lymph nodes, and bone). Patients with intraosseous lesions have a 5-year survival rate of 42% and a 10-year survival rate of 28% (22).

Dedifferentiated chondrosarcoma represents approximately 10% of all chondrosarcomas and about 1%–2% of all primary bone tumors. Patients are usually between 50 and 70 years old, men and women are affected equally. Clinical presentation is pain in the most cases,

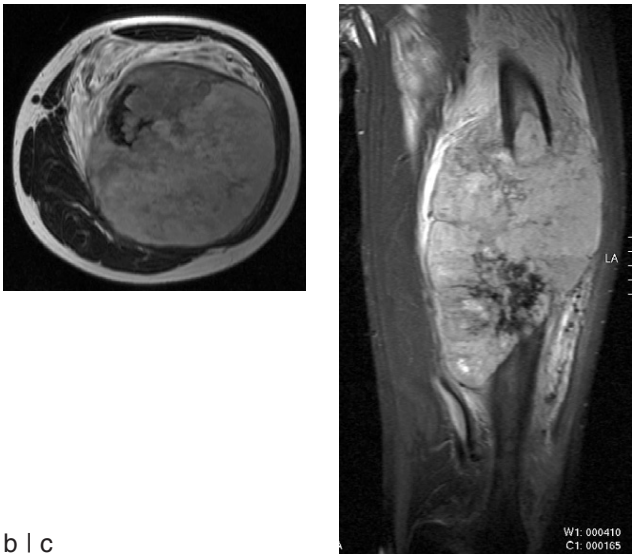

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Fig. 5b–c. Mesenchymal Chondrosarcoma show aggressive bone destruction, with a moth-eaten to permeative pattern and ill-defined multilayer periosteal reaction. The tumor is large with extensive extraosseous components (b): T1 weighted transversal MRI; (c): T2 weighted coronal MRI-scan).

followed by pathologic fracture (31%) and soft-tissue mass (29%) (14, 26). The majority of lesions occur centrally in the medullary bone. Locations mostly including the femur, pelvis and the humerus.

Histologically the tumor shows distinct foci that have dedifferentiated into a more aggressive noncartilaginous component, which is most frequently malignant fibrous histiocytoma, osteosarcoma, or fibrosarcoma (Fig. 6a) (1). The most striking feature is the large number of cells: on the one hand distended chondrocytes of various size, which posseses polymorphic nuclei; on the other hand the highly sarcomatous connective tissue with small densely loaded hyperchromatic nuclei which are markedly polymorphic. The abrupt transition from neoplastic cartilage to spindle-cell sarcomatous tissue is very characteristic (1).

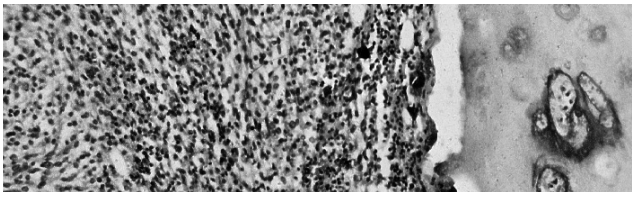

Fig. 6a. The most striking feature in the dedifferentiated chondrosarcoma is the large number of cells. One can seen on the one hand tumorous cartilaginous tissue with distended chondrocytes of various sizes, which posses polymorphic nuclei. On the other hand, there is highly cellular sarcomatous connective tissue (HE, 40x).

Imaging findings vary, depending on the proportion of conventional chondrosarcoma that has transformed to a noncartilaginous high-grade malignancy (21). As the high-grade noncartilaginous focus increases in size, there is a progression of aggressive bone lysis, a decrease in matrix mineralization, and soft-tissue expansion is invariably seen (Fig. 6b–d). CT and MR may therefore demonstrate two distinct areas: the low-grade conventional chondrosarcomatous elements with previously described pattern on imaging, and the noncartilaginous component with variable signal intensity on T2-weighted MR images, lower in signal intensity than the conventional chondrosarcomatous component). Images obtained with i.v. contrast material demonstrate mild septal and peripheral enhancement in the lower-grade (chondrosarcomatous) component as opposed to prominent diffuse enhancement in the high-grade noncartilaginous areas (21, 28).

The tumor is a highly lethal malignancy, despite adequate aggressive initial wide surgical resection or even amputation. Metastases occur early, are frequent, and commonly involve the lungs, lymph nodes, and viscera (14). Most patients die within 2 years.

Further imaging modalities

Bone scintigraphy displays the activity of bone metabolism and has a well established place in the diagnosis of bone malignancies. Radiotracer uptake in chondrosarcoma was described to be variable, but often intense uptake was found (20). Tracer distribution can range from homogeneous to inhomogeneous and irregular uptake, sometimes with less uptake in the center of the lesion than around its periphery ("doughnut" sign). However, a typical pattern of distribution demonstrates areas of focal increased uptake throughout the tumour

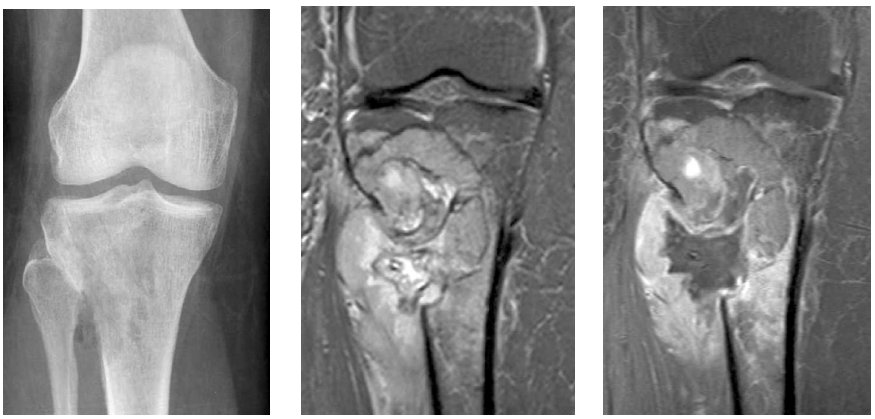

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Fig. 6b-d. Dedifferentiated chondrosarcoma: Anteroposterior knee radiographs demonstrates a lytic lesion with a permeative pattern and extraosseous tumor mass (b). The T2 weighted fat-suppressed MRI reveals not the high-water content of other cartilage tumors (c). The T1 weighted MRI after i.v.-contrast-medium shows a remarkable enhancement of gadolinium within the viable tumor (d).

(20). Nevertheless, a strong correlation between intensity or pattern of uptake and histological grades was not found (28). Bone scintigraphy can be used to exclude further skeletal lesions (Fig. 7a–b).

Positron emission tomography (PET) with fluorine-18 fluorodeoxyglucose (FDG) is able to detect FDG uptake in cells with high metabolic activity and can be used for the detection and characterisation of malignant lesions (Fig. 8). The uptake intensity of PET tracers can be determined reliably by the use of standardised uptake values (SUV).

Several publications reported increased uptake of this radiotracer in chondrosarcomas, showing a good correlation of SUV and tumour grade (5, 12). Significant differences in the uptake levels between low- (grade I) and high grade (grade II und III) chondrosarcomas were reported. Furthermore, pretherapeutic tumour SUV is a useful parameter for predicting patient outcome in terms of local relapse or metastatic disease (5).

Although available studies do not distinguish between the different subtypes of chondrosarcoma, nevertheless generally higher SUV than in other subtypes was reported in the extraosseous myxoid subtype (5).

Beside the application of FDG PET in the primary diagnosis of chondrosarcoma, it can be a useful tool for the diagnosis of metastatic disease and tumor recurrence in follow-up (12), especially in cases of limitations of CT and MRI due to metallic prosthesis after tumour operation. For biopsy planning, FDG PET can be used to localize the tumor site within the highest metabolic activity for selective sampling in cases of heterogeneous cartilage lesions (12).

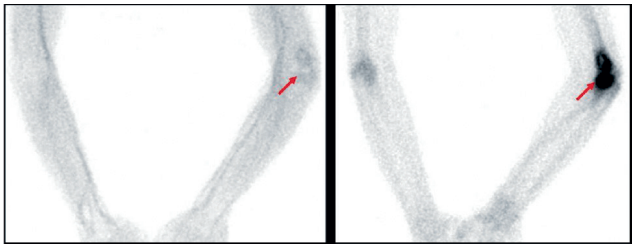

Fig. 7a-b. Bone scintigraphy of a patient with grade I chondrosarcoma of the left elbow. a. Early (blood pool) scan, showing just slightly enhanced extravasal tracer accumulation in the area of the left elbow (arrow). b. In the late (mineralization) scan, intense, predominantly homogeneous tracer uptake can be seen at the tumour site.

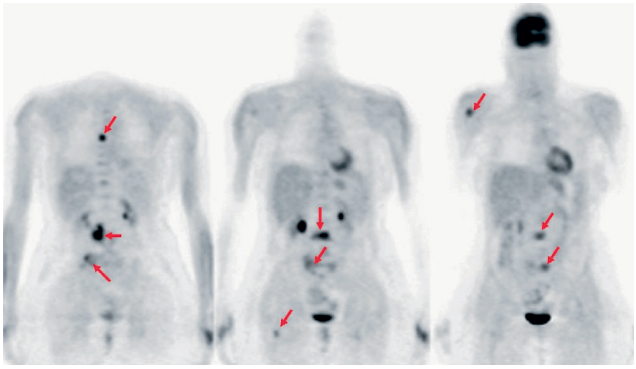

Fig. 8. FDG PET scan of a patient with metastasic high grade chondrosarcoma in coronar slices. Multiple bones metastases with intense tracer uptake (arrows). Physiologic tracer uptake can be seen in brain, heart muscle, kidneys and urine bladder.

In general, surgical resection is the primary and preferred treatment modality for individuals with localized disease. Radiation therapy is only appropriate for palliation of disease-related symptoms. The treatment of advanced, metastatic disease is particularly challenging given the recognition that conventional chemotherapy has proven to be largely ineffective. Systemic chemotherapy may be considered in different forms such as mesenchymal or dedifferentiated chondrosarcomas (24).

CONCLUSIONS

Chondrosarcoma is the third most common primary malignant tumor of the bone, representing up to 16%. Although the pathologic appearance varies within the different types, they grow with lobular type architecture and demonstrate enchondral ossification.

The radiographic appearances reflect the pathologic features: typically a ring-and-arc matrix mineralization, endosteal scalloping and soft-tissue extension could be detected (tab. 1). CT detects the matrix mineralization and depth of endostal scalloping. MR imaging shows the high water content seen in conventional, juxtacortical, and myxoid chondrosarcomas as high signal intensity with T2-weighted sequences. High-grade chondrosarcomas (mesenchymal and dedifferentiated lesions) furthermore contain areas of matrix mineralization that suggest a chondroid neoplasm but also show aggressive patterns of bone destruction and large associated soft-tissue masses.

Radiotracer uptake in chondrosarcoma is variable. A typical pattern of distribution demonstrates areas of focal increased uptake throughout the tumour. Beside in the primary diagnosis of chondrosarcoma, PET can be a useful tool for the diagnosis of metastatic disease and tumor recurrence, especially in cases of limitations of the use of CT and MRI due to metallic prosthesis after tumor operation.

Surgical resection is the primary and preferred treatment modality for the most individuals with localized disease. In selected cases (grade I tumors) the intralesional curettage should be considered.

On a molecular level, several oncogenic pathways have been associated with tumor initiation and/or progression, but not all pathways identified in such studies are likely to lead to effective targeted therapies (4). However, systemic chemotherapy may still be an option in the mesenchymal or dedifferentiated chondrosarcoma (4, 18)

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Table 1. Clinical characteristics of the subtypes of chondrosarcoma (CS) of bone (2, 4, 13, 18, 22, 27)

	Conventional CS	**Clear Cell CS**	**Juxtacortical CS**	**Skelettal Myxoid CS**	**Mesenchymal CS**	**Dedifferentiated CS**
% of all CS	75	2	< 2%	10	2	10
Precursor lesion	Enchondroma	None	Osteochondroma?	None	Fibrous Dysplasia?	Conventional CS
Occurrence with syndrome	Enchondromatosis	none	Osteochondromatosis?	none	none	rarely in En-/Osteochondro-matosis
Age	any age, average 46 years	any age, mostly between 3rd and 5th decade	peak incidence in the third to fourth decade	mean age 50 years	any age, mostly in the 2nd to 4th decade of life	peak incidence between 5th and 7th decade
Main location	pelvis, prox. Humerus and femur, ribs	long tubular bones with predilection for the proximal femur and humerus	short tubular bones and proximal Humerus	long bones, especially the femur	axial skeleton, the ribs, jaws and long bones, mostly in a diaphysis	femur, pelvis and humerus
Histological grading	Grad I-III	low-grade	Grade I-III	low-grade	high-grade	high-grade
Sensitivity to chemotherapie	none	low	none	low	possible role of Chemotherapy	possible role of Chemotherapy
Sensitivity to radiotherapie	low	low	low	low		
Surgery	High-grade: Wide resection, if necessary followed by a site-appropriate reconstruction (custom or modular endoprosthetics, allograft bone, or autologous bone e.g.) Low-grade: There is a trend away from wide resection in selected Grade 1 tumors: surgery is an intralesional procedure (curettage with a high-speed burr to the surrounding bone) with or without treatment of the defect cavity with a local adjuvant therapy (phenol, freezing the bone). The defect can be reconstructed with allograft or autologous bone grafting or polymethylmethacrylate (bone cement) with or without internal fixation of the bone.					
Survival	Grade I: 83% Grade II: 64% Grade III: 29%	roughly 25% of patients experience local recurrences of their tumors or suffer metastasis, but tumor-related death is uncommon, particularly when the lesion has been completely resected en bloc	Overall 5-year metastasis-free survival: 83%. 5-year metastasis-free survival for grade 2 tumors: 50%, grade 1 tumors 94%	5-year survival rate: 90%	5-year survival rate: 54.6% 10-year survival rate: 27.3%	5-year-survival rate: 10.5%

Table 2. Typical radiological criteria of chondrosarcoma (1, 21, 28)

Conventional Chondrosarcoma	– mixed lytic and sclerotic appearance – geographic and multilobulated bone lysis – endosteal scalloping (> 2/3 of the cortex) – cortical remodeling, cortical thickening, and periosteal reaction
Juxtacortical Chondrosarcoma	– lytic lesion, matrix mineralization (30% of the cases) – 95% epiphyseal location – peripheral sclerosis (20% of the cases) – mild expansile bone-remodeling (30% of cases) – T1: intermediate signal intensity – T2: heterogeneous high signal intensity
Clear Cell Chondrosarcoma	– lobulated mass on the surface of bone – chondroid matrix mineralization – T1: heterogeneous signal intensity – T2: heterogeneous high signal intensity
Myxoid Chondrosarcoma	– permeative pattern of osseous destruction – associated soft-tissue mass – matrix mineralization (not extensive) – T2: high signal intensity – hemorrhage: areas of high signal intensity with all MR sequences
Mesenchymal Chondrosarcoma	– aggressive bone destruction: moth-eaten to permeative pattern – ill-defined periosteal reaction, often extraosseous components – areas of ring-and-arc chondroid calcifications (70% of case) – T1: intermediate signal intensity – T2: intermediate signal intensity
Dedifferentiated Chondrosarcoma	– aggressive bone lysis – invariable matrix mineralization and soft-tissue expansion – noncartilaginous component with variable signal intensity on T2 weighted MR – mild septal and peripheral enhancement in the lower-grade chondrosarcomatous component; prominent diffuse enhancement in the high-grade noncartilaginous areas

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